Abstract N°: 21

Early Achievement of 3- and 6-Month Treat-To-Target Goals After 4 Weeks of Abrocitinib Monotherapy in Patients With Moderate-to-Severe Atopic Dermatitis: A Post Hoc Analysis

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Introduction & Objectives: Based on an international treat-to-target proposal for adults with moderate-to-severe atopic dermatitis (AD; De Bruin-Weller M et al. Acta Dermatol Venereol. 2021;101[2]:1068), treatment target goals at 3 months should be a ≥1-point improvement in patient global assessment (PtGA) and improvements in at least 1 of the following disease domains: ≥50% improvement in Eczema Area and Severity Index (EASI-50), ≥50% improvement in SCORing Atopic Dermatitis (SCORAD-50), a ≥3-point improvement in Peak Pruritus Numerical Rating Scale (PP-NRS), a ≥4-point improvement in Dermatology Life Quality Index (DLQI), or a ≥4-point improvement in Patient-Oriented Eczema Measure (POEM). At 6 months, the proposed treat-to-target goals are a PtGA score of ≤2 and at least 1 of the following: EASI-75 (or EASI ≤7), SCORAD-75 (or SCORAD ≤24), PP-NRS ≤4, DLQI ≤5, or POEM ≤7. Treatment continuation should be considered if respective PtGA target goal plus at least 1 disease domain target goal is attained. Clinical trial data indicate that treatment with abrocitinib, an oral, once-daily, Janus kinase (JAK) 1-selective inhibitor, is associated with a rapid improvement in multiple clinical domains. A strong early response may be a predictor of a later response, as well as of adherence to treatment. The objective of this post hoc analysis was to estimate the proportions of patients with moderate-to-severe AD who attained 3-month and 6-month treat-to-target goals after only 4 weeks of abrocitinib monotherapy.

Materials & Methods: Data were pooled from the JADE pivotal phase 3 clinical trials JADE MONO-1 (NCT03349060) and JADE MONO-2 (NCT03575871), in which patients with moderate-to-severe AD aged ≥12 years were treated with abrocitinib (200 mg or 100 mg) or placebo. Proportions of patients attaining the 3- and 6-month treat-to-target goals at week 4 were assessed. Only patients with available PtGA, EASI, PP-NRS, and DLQI data at week 4 were included in this analysis. Data are presented as observed and using descriptive statistics.

Results: The data pool included 487 patients (200 mg, n=196; 100 mg, n=191; placebo, n=100). At week 4, more patients (109 [56%]) treated with abrocitinib 200 mg attained the 3-month treat-to-target goals for simultaneous improvements in PtGA, EASI, PP-NRS, and DLQI, compared with 54 (28%) and 8 (8%) patients who received abrocitinib 100 mg and placebo, respectively (Figure). The corresponding values for 6-month treat-to-target goals were 57 (29%), 20 (10%), and 1 (1%; Figure). Proportions of patients attaining the 3-month targets with abrocitinib 200 mg, abrocitinib 100 mg, and placebo were 77%, 56%, and 27%; these proportions were 64%, 32%, and 19% for the 6-month targets (Figure).

Conclusion: As early as week 4, a substantial proportion of patients treated with abrocitinib 200 mg or 100 mg monotherapy attained proposed 3-month and 6-month improvement goals in skin lesions, pruritus, and dermatology-related quality of life. These data suggest that abrocitinib treatment provides a rapid relief of signs
and symptoms across several clinical domains. Moreover, currently proposed 3-month and 6-month treatment goals for patients with moderate-to-severe AD could be achieved far earlier with oral JAK inhibitors, thus enabling early benefit-risk assessment.

**Figure.** Proportions of Patients Attaining Respective PtGA Target Goals and the 3- and 6-Month Disease Domain Target Goals at Week 4

PtGA Improvement of ≥1-point and 3-Month Disease Domain Goals at Week 4

PtGA Absolute Score ≤2 and 6-Month Disease Domain Goals at Week 4

DLQI, Dermatology Life Quality Index; DLQI4; ≥4-point improvement from baseline in DLQI; DLQI ≤5; DLQI score ≤5 (baseline >5); EASI, Eczema Area and Severity Index; EASI-50, ≥50% improvement from baseline in EASI; EASI-75, ≥75% improvement from baseline in EASI; PP-NRS, Peak Pruritus Numerical Rating Scale; PP-NRS3, ≥3-point improvement from baseline in PP-NRS, PP-NRS ≤4, PP-NRS score ≤4 (baseline >4); PtGA, patient global assessment; QD, once-daily.

Month 3 target met refers to PtGA improvement of ≥1-point and achievement of EASI-50 or PP-NRS3 or DLQI4.

Month 6 target refers to PtGA score ≤2 and achievement of EASI-75 or PP-NRS ≤4 or DLQI ≤5.
Safety of tacrolimus 0.03% and 0.1% ointments in young children with atopic dermatitis: a 36-month follow-up study

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Introduction & Objectives: In the treatment of pediatric atopic dermatitis (AD) tacrolimus ointment is used off-line in small children. However, safety data are limited on its use in under 2 years of aged children and regarding long-term therapy. In this single-centre prospective clinical study we aimed to compare safety profiles of topical tacrolimus (0.03% and 0.1% ointments) and topical corticosteroids (mild and moderate potency) in small children with AD.

Materials & Methods: We carried out a prospective, randomized but not placebo-controlled, 36-month follow-up study with 152 small children aged 1–3 years at baseline with moderate-to-severe AD. The children were followed with frequent doctor’s appointments, and information concerning cutaneous and other infections, AD severity, comprehensive growth parameters, serologic responses to routine vaccinations and other safety-relevant laboratory tests were collected.

Results: We observed no significant differences between topical tacrolimus and corticosteroids treatment groups regarding cutaneous infections (p = 0.198), other infections (p = 0.20), growth parameters (e.g., height, p = 0.60 and body weight, p = 0.81), Eczema Area and Severity Index (EASI) (p = 0.19), serologic responses to routine vaccinations (p = 0.62), morning levels of serum cortisone (p = 0.228) or the total serum levels of inflammatory cytokines (interleukins 4, 10, 12, 31 and interferon-gamma). Therapeutic response was significant (EASI decrease) in both treatment groups (p < 0.001). In patients treated with topical tacrolimus, nine patients (11.68%) had measurable whole blood tacrolimus concentrations at the 1-week visit, which normalized in control samples. During the follow-up, there were no malignancies or severe infections observed, and blood eosinophil counts were comparable in both groups.

Conclusion: Topical tacrolimus ointment (0.03% and 0.1%) and topical corticosteroids (mild and moderate potency) showed good safety profiles and similar therapeutic efficacy regarding the use in small children with moderate-to-severe AD.
Abstract N°: 50

**Downstream effects of IL-13Rα1 blockade on Th2-driven inflammation and Th1 immune axis activation in atopic dermatitis**

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**Introduction & Objectives:**

Atopic dermatitis (AD) is an inflammatory skin disease characterized by dysregulated Th2-driven inflammation. Interleukins (IL)-4 and IL-13 are key cytokines mediating Th2-driven inflammation in AD that signal through the Type 1 receptor (composed of IL-4Ra and the common gamma chain) and Type 2 receptor (composed of IL-4Ra and IL-13Ra1). The most effective way to inhibit Th2-driven inflammation remains unknown.

**Materials & Methods:**

In this study, we treated peripheral blood mononuclear cells (PBMCs) isolated from 10 AD patients with either an anti-IL-4Ra antibody (R&D systems, MAB230) to block both Type 1 and 2 receptors or eblasakimab, a monoclonal antibody that binds IL-13Ra1, to block only the Type 2 receptor. We then investigated the downstream effects of blocking these receptors on cytokines involved in Th2-driven inflammation and other immune axes utilizing the Meso Scale Discovery panel from PBMC media.

**Results:**

We find that treatment with IL-13Ra1 blockade with eblasakimab as compared to IL-4Ra blockade resulted in lower levels of key cytokines implicated in Th2-driven inflammation, including thymus and activation-regulated chemokine (TARC; p=0.0001), IL-13 (p<0.0001), IL-4 (p<0.0001), and monocyte chemotactic protein-4 (MCP-4; p<0.0001). Furthermore, our data demonstrate that IL-13Ra1 blockade prevents subsequent expression changes of Th1 cytokines as observed with anti-IL-4Ra therapy. Specifically, treatment with eblasakimab as compared to anti-IL-4Ra therapy suppressed a paradoxical increase of Th1 cytokines, including tumor necrosis factor alpha (TNF-a; p=0.0319), IL-2 (p<0.0001), granulocyte-macrophage colony-stimulating factor (GM-CSF; p=0.0011), IL-12p70 (p<0.0001), and interferon gamma-induced protein-10 (IP-10; p=0.0017).

**Conclusion:**

These results suggest that targeting different subunits of the same molecular pathway can lead to different downstream effects and subsequent expression of Th1- and Th2-associated cytokines. Eblasakimab may offer a differentiated therapeutic approach to treat moderate-to-severe AD with the potential to spare the Type 1 receptor and the effects seen with targeting IL-4Ra.
Which factors are associated with persistence of depressive and anxiety symptoms in patients affected by atopic dermatitis despite 2-year treatment with dupilumab?

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Introduction & Objectives: Atopic Dermatitis (AD) is a prevalent inflammatory skin disease whose course is often complicated by the presence of concomitant anxiety and depressive disorders. Dupilumab demonstrated to be largely effective in AD. Purposes of the present research are: (1) to verify the effectiveness of 2-year dupilumab treatment on depressive and anxiety symptoms of patients affected by AD and (2) to identify predictors of persistence of psychiatric symptoms despite maintenance treatment with dupilumab.

Materials & Methods: 331 patients with severe AD were assessed at baseline and at different times until 2 years by a large set of rating scales including: Eczema Area and Severity Index (EASI), Hospital Anxiety and Depression Scale (HADS) and Dermatology Life Quality Index (DLQI). Paired sample t-tests were performed to verify the effectiveness of dupilumab on severity of AD and mental health items. Two binary logistic regression models were then performed to identify the predictors of persistence of clinically significant depression and anxiety defined by a score ≥ 8 on each sub-scale of HADS.

Results: After 2 years of treatment with dupilumab patients benefited of a significant improvement both of dermatological disease and comorbid depression/anxiety (p<0.01 for all scales). 17.5% and 13% of patients reported respectively residual depressive and anxiety symptoms after 2-year treatment with dupilumab. Baseline predictors of the persistence of clinically significant depressive symptoms after 2-year treatment with dupilumab resulted to be: a higher body mass index (BMI) (p=0.012), less quality of life (p=0.15) and more severe depressive symptoms (p<0.01), while for anxiety the only predictor resulted to be female gender (p=0.03).

Conclusion: In a multidisciplinary approach, dermatologists should more closely monitor patients at baseline who are at greater risk of maintaining residual psychiatric symptoms despite therapy, such as those with more severe depressive symptoms, obesity, or a poorer quality of life.
Abstract N°: 248

Health literacy and topical corticosteroid adherence in parents of children with atopic dermatitis in France
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Introduction & Objectives:

Therapeutic nonadherence is frequent amongst the parents of children with atopic dermatitis (AD) treated with topical corticosteroids (TCs). Therapeutic nonadherence is a multidimensional phenomenon involving the interaction of numerous factors, particularly health literacy (HL), that refers to the ability to access, understand, communicate, calculate and process specific information on medicinal products.

Materials & Methods:

A cross-sectional study describing parents of AD children was conducted in France between March and April 2022. A dedicated questionnaire was used to identify parents of AD children from a representative sample of French adults, characterized using the quota method: age, sex, location and socio-professional status. In case of a prescription of topical steroid for the treatment of AD for their child, it was proposed to the parents, a description of their attitude regarding this topical therapy.

Results:

Three populations were identified: 1/steroid adherents (SA) who reported following the TCs prescription unquestioningly, 2/steroid sceptics (SS) who reported following the prescription after researching TCs, and 3/steroid phobes (SP) who reported rejecting the TCs prescription due to fear of its effects. 35.5\% (n=5343) of our sample reported living with at least one child under the age of eighteen. Among them 25\% (n=1335) reported having a child affecting by AD and/or eczema (21.8\% of men vs 29.6\% of women).

61.5\% (n=822) of these parents reported a prescription of topical steroid for the management of AD for their child. In total, a population of 822 parents of AD children who have received TCs treatment was identified. The mean age of parents was 37.82 y.o +/-10.01 years with 334 (40.6\%) fathers and 488 (59.4\%) mothers respectively. Within the population, 146 parents (17.8\%) were identified as SP. 676 parents (92.2\%) demonstrated some health literacy: 90 (10.9\%) were identified as steroid sceptics and 586 (71.3\%) as SA. The sociodemographic profile of SS parents was not significantly different from SA parents. Compared to SS parents, SP parents were significantly younger (38.37 vs 34.43, p 0.005) and often live in urban areas (78.1\% vs 54.4\%, p 0.012). Compared to SA parents, SP parents were significantly more often men (54.1\% vs 38.4\%, p 0.02), younger (34.43 vs 38.58, p<0.001), living in urban areas (78.1\% vs 61.3\%, p 0.01) and with a recent history of dermatoses (37.7\% vs 28.8\%, p <0.001).

Conclusion:

To our knowledge, our study is the first to propose the evaluation of the prevalence of health literacy in a large population of parents of AD children. Easy access to information [media, social network] on TCs and their side effects, may contribute to increasing fear and concern, heightening the risk of steroid phobia. Therefore, the role of healthcare professionals such as dermatologist and/or General practitioner appears crucial to provide clear and comprehensible information on the disease and how to use the topical therapies prescribed. Patients must also be encouraged, via their organizations, to ask questions and
request clarifications in order to ensure that they fully understand their treatment plan. Therapeutic education in atopic dermatitis as well as share decision the also has an essential role to play in the respect and knowledge of the treatments.

Health literacy levels should be improved in parents of AD children so that they can better manage their health.
Abstract N°: 324

Neuromodulation beyond itch is blocked by targeting IL-13Ra1 with eblasakimab

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Introduction & Objectives:

Interleukin-4 (IL-4) and IL-13 are cytokines known to drive inflammation and play a role in atopic dermatitis (AD) pathogenesis. Both enhance neuronal itch via the Type 2 receptor. Eblasakimab, a high affinity IgG4 monoclonal antibody, which binds IL-13Ra1 and blocks signaling of IL-4 and IL-13 via the Type 2 receptor, is being developed for the treatment of moderate-to-severe AD. This study evaluated 1) whether IL-4 and IL-13 exert redundant or distinct functions in human sensory neurons, and whether eblasakimab can 2) attenuate cytokine-enhanced neuronal responses to itch and 3) reduce spontaneous neuronal activity.

Materials & Methods:

Human dorsal root ganglia neurons were treated with IL-4, IL-13, or their combination with or without eblasakimab and subsequently either challenged with pruritogens (BAM8-22 [bovine adrenal medulla 8–22 peptide] and PAMP-20 [pro-adrenomedullin peptide 1-20]) or tested for spontaneous neuronal activity. Neuronal responses to pruritogens and spontaneous neuronal activity were measured via live-cell calcium imaging.

Results:

Treatment with IL-4, IL-13, and their combination enhanced neuronal responses to BAM8-22. Only IL-13 treatment increased neuronal responses to PAMP-20 by amplifying activity of the itch-specific receptor MRGPRX2 (Mas-related G-protein coupled receptor X2). This suggests a novel neuroimmune pathway besides the receptor’s mast cell specific function. Eblasakimab significantly reduced cytokine-enhanced itch responses to both pruritogens (p<0.0001, BAM8-22; p<0.05, PAMP-20; Figures 1 and 2). Spontaneous neuronal activity was not impacted by IL-13 treatment (data not shown) but was increased with IL-4 treatment (p<0.05 vs vehicle), which was also effectively reduced by eblasakimab (p<0.05; Figure 3).

Conclusion:

These results reveal that IL-4 and IL-13 exert nonredundant neuronal function in enhancing itch and inducing spontaneous neuronal activity. They also demonstrate the ability of eblasakimab to block these cytokine-mediated effects. Together, these data provide a mechanistic basis for the reduction of itch observed in moderate-to-severe AD patients treated with eblasakimab in a phase 1b clinical trial.

Figure 1. Neuronal Responses to BAM8-22 in the Presence of Cytokines and Eblasakimab
BAM8-22, bovine adrenal medulla 8–22 peptide; ebla, eblasakimab.

***p<0.0001. Error bars indicate standard error of mean.

Figure 2. Neuronal Responses to PAMP-20 in the Presence of Cytokines and Eblasakimab

PAMP-20, pro-adrenomedullin peptide 1-20.

*p<0.05, **p<0.01. Error bars indicate standard error of mean. **

Figure 3. Summary Of Spontaneous Neuronal Activity Induced by IL-4 With and Without Eblasakimab
*p<0.05. Error bars indicate standard error of mean.
Abstract N°: 336

The role of the microbiome in severity, symptoms and etiology of hand eczema: the importance of Staphylococcus aureus colonization and presence of skin flora

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Introduction & Objectives: The role and causality of the microbial ecosystem on the skin in relation to the development of hand eczema (HE) is still unknown. The objective of this study was to investigate the prevalence of different bacterial colonizations in HE patients and their association with the severity, symptoms and etiology of the disease.

Materials & Methods: In a retrospective cohort study of 178 HE patients, bacterial swabs from lesional skin were collected for culturing. Patients were categorized according to bacterial colonization, HE severity, HE symptoms and HE etiology.

Results: The majority of the patients were tested positive for Staphylococcus aureus (S. aureus) (n=138, 77.5%) and/or skin flora (n=140, 78%), while other bacteria species were found only sporadically. S. aureus was a significant risk factor for HE severity (OR 3.71, 95%-CI:1.69-8.14), while skin flora had a protective effect (OR 0.27, 95%-CI:0.08-0.92). S. aureus colonization was also associated with atopic HE etiology (p<0.001) and acute HE symptoms such as blisters, erosions and crusts (p=0.002).

Conclusion: The main colonization of HE patients is with S. aureus and is associated with disease severity, acute HE symptoms and atopic HE etiology. Skin flora may have a protective effect on the severity of HE, which could result in new therapeutic approaches.
Abstract N°: 449

Self-management support for patients with atopic dermatitis: a qualitative interview study.

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Introduction & Objectives:

Self-management support for patients diagnosed with atopic disease can increase self-management skills and alleviate the burden of disease experienced by individuals and their families as well as reduce poor health outcomes, and healthcare utilization. Access to self-management support should ideally be offered to all patients with atopic dermatitis, therefore, the aim of this study was to determine how the patient’s needs for self-management support should be addressed in consultations with patients with atopic dermatitis.

Materials & Methods:

To create in-depth and nuanced knowledge of the patients experiences this study was based on individual interviews with patients diagnosed with atopic dermatitis. Interpretive description methodology was chosen for iterative data collection and analysis. This flexible, inductive approach is suitable when the goal is to seek out the knowledge needed to change clinical practice in a justifiable way.

Patients were recruited from a department of dermatology and a private dermatology clinic. Recruitment was based on information power. We had a broad aim, did not use specific theory, analysed across cases, had a good quality dialogue, and a dense specificity as all participants were experienced with the healthcare system and atopic dermatitis consultations. On this background we estimated that a minimum of 20 participants was needed to redeem the complexity of our study aim.

Results:

Twenty-six participants were interviewed between September 2022 and January 2023. The interviews included five parents to children with atopic dermatitis (three fathers and two mothers), nine young patients (15-24 years-old) and twelve adult patients with atopic dermatitis. The participants were equally gender distributed. Current treatment of patients included divided between topical (9), systemic (10) and biologicals/JAK inhibitors (7). Twenty-three patients were included from the department and three from the private clinic.

Two mutually dependent themes: Recognition and Guiding for agenda setting were found to be supportive for the patients’ self-management. A relationship between patient and healthcare professionals based on personal and disease-related recognition* was fundamental to successful support, preferably with a solid reference (either nurse or doctor) with profound knowledge of atopic dermatitis. But in addition, guidance for agenda setting from healthcare professionals was needed on the wide range of topics that could be covered in the consultation. Among the patients, there was a high agreement about relevant topics that would help them build upon their self-management skills, but they expressed uncertainties about what was possible to bring up in consultations and described how it would be helpful to see the possible topics in a list or in some way visualized in the consultation.

Conclusion:

In this qualitative interview study with patients suffering from atopic dermatitis it is evident, that the prerequisite for self-management support in consultations depends on a healthcare professional with profound knowledge of
atopic dermatitis who clearly recognizes the individual patient and his or her condition.

Recognition serves as a foundation for self-management support and combined with a guiding towards agenda setting there is a higher chance of focusing consultation time on the patients’ needs and thereby contribute to improving self-management.
Abstract N°: 470

Increased risk of venous thromboembolism among adults with atopic dermatitis: A real-world nationwide cohort study

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Introduction & Objectives:

The associations of atopic dermatitis (AD) with multiple cardiovascular comorbidities have been investigated because of its pathomechanisms regarding chronic systemic inflammation and potential vascular effects. Nevertheless, the association between AD and incident venous thromboembolism (VTE) in adulthood is largely unknown. This study aimed to investigate the association of AD with incident VTE. The objective of this study was to examine the risk of incident VTE among patients with AD.

Materials & Methods:

We performed a nationwide cohort study included adults aged ≥ 20 years from the National Health Insurance Research Database between 2001 and 2017 in Taiwan. Adults with AD newly diagnosed between 2003 and 2017 and their age- and sex-matched controls were included. Patients with AD were sub-grouped according to the severity of the disease. A Cox regression model was used to estimate hazard ratios (HRs) for incident VTE associated with AD. Stratified analyses according age, sex, and systemic steroid exposure were also performed.

Results:

We included a total of 284,858 subjects, with 142,429 subjects in each AD and non-AD cohort. During the follow-up, 1,066 patients in the AD cohort and 829 patients in the non-AD cohort developed VTE, with incidence rates of 1.05 and 0.82 per 1,000 person-years, respectively. Adults with AD had a significantly increased risk of incident VTE (HR 1.28; 95% CI 1.17–1.40) compared to adults without AD. Individual outcome analyses revealed that AD was associated with higher risks of both deep vein thrombosis (HR 1.26; 95% CI 1.14–1.40) and pulmonary embolism (HR 1.30; 95% CI 1.08–1.57).

Conclusion:

AD in adulthood is associated with an increased risk of VTE; however, the absolute risk difference of VTE between AD and non-AD adults appears small. Nevertheless, cardiovascular examination and imperative management may be considered for adults with AD presenting symptoms suggestive of VTE. Future research is warranted to elucidate the pathophysiology linking AD and VTE.
Feasibility and effectiveness of spaced dosing of dupilumab in atopic dermatitis patients: a prospective observational study

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Abstract

Introduction & Objectives:

Dupilumab is a fully human monoclonal antibody targeting the interleukin-4 receptor alpha, used to treat moderate to severe Atopic Dermatitis (AD) with high efficacy and safety. The registered dose for adult patients is a loading dose of 600 mg subcutaneously followed by 300 mg every other week (EOW). Recently, the possibility of spacing the administration of this drug with maintenance of response has been discussed, with obvious clinical and pharmaco-economic benefits.

Materials & Methods:

We conducted a prospective observational study at a GA2LEN ADCARE AD referral center to evaluate the feasibility and effectiveness of extending the interval between dupilumab administrations. Patients had moderate-to-severe AD (Eczema Area and Severity Index (EASI) ≥ 16) treated with 300 mg dupilumab EOW after a loading dose of 600 mg. Baseline demographic data on age, gender, body mass index, family history, and allergic comorbidities were collected. Patient-reported measures such as Itch Numeric Rating Scale (NRS), Sleep NRS, Dermatology Life Quality Index, Patient Oriented Eczema Measure, SCORing Atopic Dermatitis; and objective outcomes such as EASI were captured before spacing of dupilumab dosage and at 6-months assessment.

Results:

18 patients (mean age 33.6 years; 50.0% women) treated with dupilumab 300mg EOW were eligible for analysis. The interval of dupilumab dose administration was extended in 94.4% of patients due to excellent response (response ≥ EASI-85) and in 5.6% of patients due to adverse effects. On average, this spacing was performed at 20.7 months of therapy. 88.9% of patients were proposed to space to 3 weeks and 11.1% to 4 weeks. All patients that were re-evaluated 6 months after showed no loss of response, and none returned to the previous interval.

Conclusion:

Experience in extending the interval between administrations of biotechnological therapy has already been successfully done in Rheumatology and Psoriasis. Since AD is a chronic immune-mediated disease, it is important to offer patients optimal therapy with fewer adverse effects. Maintaining patients with well-controlled disease at the usual dose may represent overtreatment and may lead to adverse effects, in addition to consuming avoidable resources for the National Health Service. In our experience, it is possible to extend the interval between dupilumab administrations in a significant proportion of patients, with stability of the dermatosis.

In conclusion, spacing the dosing intervals of dupilumab in AD patients may be a feasible and effective approach for patients with excellent response with no loss of therapeutic response at 6-months evaluation. It is possible to effectively treat patients with minimal required drug exposure and simultaneously optimize financial resources. Our study provides evidence that the extension of the dosing interval is safe and feasible, with potential benefits for patients and healthcare systems.
Abstract N°: 544

Senile atopic dermatitis - epidemiology and features of the clinical picture

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Senile atopic dermatitis - epidemiology and features of the clinical picture

Introduction & Objectives:

Atopic dermatitis is one of the most common dermatoses, it affects up to 20% of children and 10% of adults. In recent years, senile atopic dermatitis has been isolated, which affects people over 60 years of age. The frequency of senile atopic dermatitis is 1-5%, but varies significantly according to the data obtained in various studies older age groups. However, works that relate to the features of epidemiology, clinical manifestations of atopic dermatitis in people over 60 years of age and approaches to treatment are single.

Objectives: To study the epidemiological and clinical features of atopic dermatitis in people over 60 years of age receiving inpatient treatment.

Materials & Methods:

A retrospective analysis of 1584 inpatient medical records of patients with atopic dermatitis who received treatment from January 2020 to January 2023 in the hospital was carried out. Of these, 420 patients were over 60 years old and made up the study group. The gender composition of patients with senile atopic dermatitis, the frequency and structure of concomitant pathology, and the features of the clinical picture of the disease were assessed.

Results:

Senile atopic dermatitis was diagnosed in 420 patients, which accounted for 26% of all patients with atopic dermatitis who received inpatient treatment. Of these, 285 patients were aged 60-74 (old age), which accounted for 67% of all patients with senile atopic dermatitis and 17% of all patients with atopic dermatitis, and in patients aged 70-89 (great old age) in 135 patients, which amounted to 33% and 9%, respectively.

The number of men was somewhat less than that of women. The number of men is 196, which was 47% and 12% respectively. The number of women is 224, which was 53% and 14% respectively. In a significant number of patients (87%), the disease began in childhood and adolescence, and in half of them (41%) it proceeded chronically with relapses throughout life. In 13% of cases, atopic dermatitis was first diagnosed in patients older than 50 years.

Almost all patients were diagnosed with concomitant pathology, among which hypertension dominated (88%), type 2 diabetes mellitus (12%). Due to comorbidity, patients took various groups of drugs: antihypertensive drugs, hypoglycemic drugs.

The clinical picture of the disease was characterized by a persistent course and a widespread skin lesion with pronounced infiltration and lichenification.
Conclusion:

Senile atopic dermatitis in the age structure of morbidity in hospitalized patients accounts for 26% of the total number of patients with atopic dermatitis. In the vast majority of observations, the disease begins in childhood and adolescence. Comorbidity and its therapy can make a significant contribution to the maintenance of inflammation in senile atopic dermatitis, increasing skin xerosis. Further studies of the clinical manifestations of the disease and the development of principles for its treatment in patients of older age groups are required.
Recapture of response with lebrikizumab: an evaluation of patients from ADvocate1 and ADvocate2

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Introduction & Objectives:

Lebrikizumab (LEB) is a monoclonal antibody that binds with high affinity and slow off-rate to interleukin (IL)-13, thereby blocking the downstream effects of IL-13 with high potency. ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) are identically designed phase 3, randomized, double-blinded, placebo-controlled, 52-week trials evaluating LEB for the treatment of moderate-to-severe atopic dermatitis (AD). In both studies, most patients treated with LEB monotherapy every 2 weeks (Q2W) achieved statistically and clinically meaningful improvements in the signs and symptoms of AD during the first 16 weeks of treatment. At 52 weeks of treatment, LEB showed durability of response in the signs and symptoms of AD. The objective of this analysis is to report the efficacy data of patients from ADvocate1 and ADvocate2 who met LEB response criteria at Week 16, were re-randomized to the placebo withdrawal arm during the maintenance period, lost response, and were then readministered their original dose of LEB Q2W.

Materials & Methods:

Patients who met response criteria to LEB monotherapy at the end of the 16-week induction period were re-randomized 2:2:1 to receive LEB Q2W, LEB every 4 weeks (Q4W), or placebo (LEB withdrawal) for an additional 36 weeks. Response at Week 16 was defined as achieving a 75% reduction in EASI from baseline (EASI 75) or an Investigator’s Global Assessment (IGA) of 0 or 1 with a ≥2-point improvement, and without rescue medication use. During the maintenance period, re-randomized patients who did not maintain at least a 50% reduction in the Eczema Area and Severity Index from baseline (EASI 50) at weeks 24, 32, 40 or 48 were assigned to an Escape Arm to be readministered LEB Q2W as open-label treatment. Intermittent use of topical rescue medications for AD was permitted during the maintenance period. All data reported are as observed.

Results:

In ADvocate1 and ADvocate2, 291 patients met the criteria for response at Week 16 and were re-randomized to LEB Q2W (n=113), LEB Q4W (n=118), or placebo (LEB withdrawal; n=60). From the LEB withdrawal arm, 10 patients were moved to the Escape Arm and readministered their original dose after falling below EASI 50 (ADvocate1: 7 patients; ADvocate2: 3 patients). The baseline (Week 0) EASI mean score for these 10 patients was 26.65 and IGA severity was distributed evenly between IGA 3 (n=5) and IGA 4 (n=5).

At the time of readministration of LEB, the mean EASI % change from baseline (CFB) was -24.2 (n=10). After 4 and 8 weeks in the Escape Arm, the mean EASI % CFB was -70.9 (n=10) and -89.1% (n=8), respectively. Topical rescue medication was started by 3 of 10 patients during the maintenance blinded period and before entering the Escape Arm. Approximately two weeks after moving to the Escape Arm, one patient used systemic rescue medication.
(oral prednisolone).

**Conclusion:**

EASI improvements were seen in patients who were withdrawn from lebrikizumab after meeting response criteria at week 16 and then readministered lebrikizumab as open-label treatment. Most of these patients recaptured EASI 75 upon readministration of lebrikizumab. Additional data are needed to confirm this finding due to the limitations of this analysis including a low number of patients, as observed results, differing times of assignment to the escape arm, and an unblinded readministration period.

**Figure: ADVocate1 and ADVocate2 Study Design**

1. ORAL patients received a 500 mg DL at Week 6 and 12-1. Prednisolone was added as rescue, including ECD if during the induction period were not responding. 2. Responders who achieved EASI<75 re-randomized to ORAL received an LQD of LEB 50 mg at weeks 16, 24, 32, 40, and 48, based on the active treatment group assigned at the Induction Period. Only patients who were randomized to ORAL received a placebo injection at Week 16 and Phase 12. 3. Non-responders who were assigned during the Induction Period received a 500 mg DL at Week 6 and 12-1. 4. Patients not responding to LQD of LEB were reassigned to the escape arm to be readministered lebrikizumab 250 mg every 2 weeks.

**Table: Mean EASI Scores in Lebrikizumab Withdrawal Patients Who were Readministered Lebrikizumab During the Maintenance Period**

<table>
<thead>
<tr>
<th>Time Period</th>
<th>At Time of LEB Q2W Readministration</th>
<th>4 Weeks after LEB Q2W Readministration</th>
<th>8 Weeks after LEB Q2W Readministration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of Patients</strong></td>
<td>10</td>
<td>10</td>
<td>8</td>
</tr>
<tr>
<td><strong>EASI Total Score (mean)</strong></td>
<td>20.63</td>
<td>7.49</td>
<td>2.52</td>
</tr>
<tr>
<td><strong>EASI % CFB (mean)</strong></td>
<td>-24.21</td>
<td>-70.94</td>
<td>-89.09</td>
</tr>
</tbody>
</table>

* Patients not maintaining EASI 50 at Weeks 24, 32, 40 or 48 were assigned to the Escape Arm to be readministered lebrikizumab 250 mg every 2 weeks.

**Abbreviations:** CFB=Change from Baseline; EASI=Eczema Area and Severity Index; LEB=lebrikizumab; M-ANAGE.com; PRO Q2W=PROQoL [QoL]; TCF=Total Change from Baseline; TCF-Change from Baseline
Abstract N°: 595

The Association Between Atopic Dermatitis and Inflammatory Bowel Disease in Adults: A Cross-Sectional Study in A Specialized Atopic Dermatitis Clinic

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Introduction & Objective:

Atopic dermatitis (AD) and inflammatory bowel disease (IBD) share genetic susceptibility loci with immune regulation functions. AD was associated with IBD mostly in database studies.

Our objective was to assess whether AD is associated with an increased prevalence of IBD in a tertiary dermatology clinic.

Materials & Methods:

A retrospective cross-sectional analysis using medical records of adults with verified AD followed-up at an AD clinic, compared to age- and sex- matched (1:2) controls from the general dermatology clinic in the same hospital.

Results:

Overall, 9/364 (2.47%) of patients with AD had verified IBD, compared to 7/725 (0.97%) of controls (p=0.0512). In multivariable logistic regression adjusting for age, gender, and smoking, the association became significant (adjusted OR=3.89, 95%CI: 1.28-11.85). Stratified for AD severity, only moderate-to-severe AD was associated with IBD (p=0.035), with an adjusted OR of 4.45 (95%CI:1.43-13.90). Mild AD was not associated with IBD, but the study was not powered for this sub-analysis. In the AD group, older age was associated with IBD (p=0.0172).

Conclusion:

This study, in a robustly verified cohort of patients, supports an association between AD, especially the moderate-to-severe forms, and IBD. A multidisciplinary approach for patients with moderate-to-severe AD should extend to consider IBD.
Abstract N°: 629

Safety, Pharmacokinetics, and Pharmacodynamics of AK120 in subjects with Moderate- to- Severe Atopic Dermatitis: Results from a Randomized, Double-Blind, Placebo-Controlled Phase I Clinical Study

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Introduction & Objectives:
Interleukin-4 (IL-4) and interleukin-13 (IL-13) are two essential cytokines involved in the Th2-mediated inflammatory response of diseases, such as atopic dermatitis (AD). AK120 is a humanized immunoglobulin G subclass 4 (IgG4) monoclonal antibody (mAb) directed against IL-4 receptor alpha (IL-4Rα) subunit shared by the IL-4 and IL-13 receptor complexes. The binding of AK120 to IL-4Rα results in inhibition of the signaling of the IL-4 and IL-13 cytokines. This study was to evaluate the safety, efficacy, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of AK120 following multiple subcutaneous (SC) administration in AD subjects.

Materials & Methods:
Subjects (male and female) with age ≥ 18 years were enrolled. There were 4 sequential dose escalating cohorts with 40 subjects. 8 subjects were enrolled per cohort, randomized in a 4:1 ratio to receive multiple doses of either the active drug AK120 (N=8) or matching placebo (N=2). For Cohort 1 to 3, subjects received a SC injection of 75mg, 150mg or 300 mg AK120 or matching placebo, respectively. The treatment period was 4 weeks in duration; subjects were followed for 8 weeks after the end of the treatment period.

Results:
Safety: A total of 28 (87.5%) subjects received AK120 treatment and 7 (77.8%) subjects received placebo experienced at least one treatment-emergent adverse event (TEAE). All TEAEs were mild and moderate in severity. 12 (37.5%) subjects experienced at least one treatment-related TEAEs in the AK120 treatment group, and 4 (44.4%) subjects in the placebo group. The most common TEAEs occurred in AK120 treatment group were skin infection (12.5%) and injection site pain (12.5%). There was no death, no serious adverse event (SAE) or treatment-related SAE in the study.

Efficacy: The proportion of subjects in AK120 treatment group who achieved EASI50 and EASI75 was higher than the placebo group, with the percentage of 64.5% (20/31) and 35.5% (11/31), respectively; The placebo group was 12.5% (1/8) and 0%. There were 25.8% (8/31) and 32.3% (10/31) subjects achieved IGA score 0 or 1 and reduction of ≥ 2-point, respectively.
**PK:** The average serum concentration at 168 h after first dose of 75 mg QW, 150 mg QW and 300 mg QW AK120 were 3.446 ug/ml, 7.744 ug/ml and 21.196 ug/ml, respectively. As for 300 mg Q2W (with 600 mg loading dose on day 1), the average serum concentration was 26.396 ug/ml at 336 h after first administration. After multiple dose of AK120, the average trough-concentration (C_{trough,md}) were 9.183 ug/ml, 25.486 ug/ml, 44.284 ug/ml and 29.302 ug/ml, respectively, and the drug accumulation ratios (R_{ac}) for C_{trough} were 2.364, 3.465, 2.141 and 1.122. Mild to moderate drug accumulation was observed in 75 mg QW, 150 mg QW and 300 mg QW dose groups but no apparent drug accumulation was observed in 300 mg Q2W (with 600 mg loading dose) group.

**PD:** Decrease of TARC/CCL17 from baseline were shown below. Serum TARC decreased 66% and 79% on average at day 22 and day 29 (300 mg QW group). In AK120 600mg loading Day 1 then 300mg Q2W group, SC serum TARC decreased 79% on average both at day 22 and day 29.

Decrease of serum total Ig-E level from baseline were dose dependent after day 22 among AK120 treatment groups.
Conclusion:

AK120 administered as a multiple dose via SC injection ranged from 75 mg to 600 mg were safe and well tolerated in AD subjects. Mild to moderate drug accumulation was observed in 75 mg QW, 150 mg QW and 300 mg QW dose groups.
Introduction & Objectives:

Atopic dermatitis (AD) is a common eczematous disorder, typically starting in infancy and early childhood that oftentimes can persist into adulthood. Hallmarks of AD are the chronic-recurrent nature of an eczematous skin rash with associated pruritus and a genetic predisposition. Daily use of moisturizers that contain humectants and ceramides has been shown to reduce the rate of AD flares and the need for topical steroid treatment.

The current consensus recommendations aim to attenuate AD in newborns, infants, and children using prescription medication and daily skincare, specifically ceramide-containing skincare.

Materials & Methods:

The consensus recommendations aim to serve pediatric dermatologists, pediatricians, and other healthcare professionals caring for pediatric AD patients and patients at risk for developing AD. The advisors published a consensus paper, an algorithm on ceramide-containing skincare in newborns and infants, and the mitigation of AD.

Systematic literature searches (20 - 22 December 2022) for publications in the English language from 2010 to December 20, 2022, on PubMed and Google Scholar, informed the draft statements. The advisors convened a meeting on February 10, 2023. First, they reviewed and discussed the literature on AD attenuation with prescription and nonprescription treatment and skincare using cleansers and moisturizers for pediatric patients.

Working with fifteen draft statements, the advisors developed five statements applying the selected literature, drawing from their clinical knowledge and experience, and reached a consensus.

Results:

The systematic literature searches yielded N=234 publications (221 Pubmed, 22 Google Scholar). Excluded were n=49 (duplications and poor quality), leaving n=194 comprising n=126 clinical studies (93 clinical evaluations, 26 randomized controlled trials, 7 other) and n=68 reviews (20 systematic reviews, 9 meta-analyses, 24 consensus, guidelines and algorithms, 15 reviews). Guidelines, algorithms, and consensus papers agreed that skincare should be integrated into AD attenuation approaches as a mono or adjunct to prescription treatment. The systematic literature search publications showed a mixed picture of preventing AD with skincare but demonstrated that
skincare has benefits for AD attenuation. Three meta-analyses showed a low-moderate certainty of skincare benefits for AD prevention, 1 was inconclusive for prevention, 3 displayed benefits for AD attenuation, and one did not include skincare. Ten randomized controlled clinical studies showed low (2/4) certainty evidence on skincare for AD prevention, and eight studies demonstrated moderate (3/4) certainty evidence attenuating AD in a high-risk population. The type of moisturizers used in the studies is a significant source of heterogeneity, and the number of studies was too small to stratify them by type.

Conclusion:

Studies that report significant benefits of prophylactic skin-lipids-containing moisturizers tended to have recommended daily or more frequent applications** of moisturizer to the majority of the skin surface. A growing body of evidence recognizes the benefits of ongoing daily use of skincare, such as ceramide-containing skincare as a monotherapy or as an adjunct to prescription medication for attenuating AD for newborns, infants, and children.
The Landscape of Atopic Dermatitis in Egypt: a post-hoc analysis involving 50 dermatologists

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Introduction & Objectives: Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by pruritis, lichenification, and xerosis. Evidence suggests that immune dysregulation and skin barrier dysfunction play a role in the pathophysiology of AD, most significantly through the impairment of the epidermal barrier. Treatment for AD currently includes topical and oral corticosteroids, immunosuppressants, and biologics in severe cases. Evaluating the guidelines, usage, and access to these treatments is paramount as it helps optimize the journey of patients with AD. To understand the prevalence and clinical pathway of AD in Egypt, this study surveyed 100 healthcare professionals (HCPs).

Materials & Methods: 50 dermatologists, 25 pediatricians, and 25 primary care physicians were surveyed. The survey consisted of 47 closed-ended multiple-choice questions. Responders were questioned on topics such as their patient demographics, approach to advanced treatment, familiarity with JAK inhibitors, and expectations for future treatment.

Results: Of the HCPs surveyed, prevalence statistics demonstrated that roughly one-third of adult patients and one-fourth of patients under 18 had severe AD. In examining lesions of AD, most dermatologists conduct in-house dermoscopies (56%), whereas pediatricians tend to refer patients (53%). Roughly 3 in 5 physicians follow treatment guidelines, with higher adherence among dermatologists. Of those adhering, 41% use American Academy of Dermatology guidelines, and an equal 41% use local or national guidelines.

Emollients, topical calcineurin inhibitors, and topical corticosteroids are preferred as early treatments for mild-to-moderate AD. Oral corticosteroids like prednisolone are preferred early treatments for moderate-to-severe AD, generally used as rescue therapy. Overall, topical corticosteroids were shown to be the most common treatment for all severities of AD, being prescribed at some point to 59% of mild-to-moderate patients and 54% of moderate-to-severe patients seen in an average month.

50% of the HCPs indicated intolerance or failure of both oral corticosteroids and systemic immunosuppressants as the criteria to start advanced systemic treatment. Over half of the physicians reported that advanced treatments have been approved in their country. Approval of Dupilumab was indicated by 42% of physicians, and 15% for Baricitinib. Of dermatologists, 4% have a high familiarity with the oral JAK 1 inhibitor drug Abrocitinib, whereas 41% have no familiarity.

The top three unmet needs in treating moderate-to-severe AD reported by all physicians were treatments with a better safety profile, faster onset of action, and better efficacy profile. Ultimately, long-term control of the disease and rapid onset of action are the most sought-after features of new treatments.

Conclusion: The increased interest in AD research has resulted in the development of novel treatment approaches for patients. This survey helped gain a direct insight into the prevalence, diagnosis, and treatment of AD patients in Egypt. There is considerable variability in the treatment approaches to AD among different medical specialities, especially regarding the use of systemic and advanced treatments. Identifying patterns of these prescribers can help influence clinical decisions in AD management, establish challenges and expectations for the future of treatment, and develop superior outcomes for patients suffering from AD.
Abstract N°: 721

Efficacy, Safety, and Tolerability of JNJ-67484703 in Adult Patients With Moderate to Severe Atopic Dermatitis: Design of a Phase 2a Study

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Introduction & Objectives: Atopic dermatitis (AD) is a chronic immune-mediated inflammatory skin disease characterized by relapsing and remitting flares. AD is characterized by eczematous skin lesions, itch, and sleep disturbances, which can significantly impair the quality of life of patients and caregivers. JNJ-67484703 is a humanized immunoglobulin G1 antibody that binds programmed cell death protein 1 (PD-1) and is being developed as a treatment for systemic immune-mediated disorders. The objective of this study is to evaluate the efficacy, safety, and tolerability of JNJ-67484703 in patients with AD.

Materials & Methods: RESTORE-AD (EudraCT 2022-001528-14) is a phase 2a, randomized, double-blind, placebo-controlled proof-of-concept study enrolling adults with moderate to severe AD (participants with Eczema Area Severity Index [EASI] score $\geq$ 16, validated Investigator Global Assessment for Atopic Dermatitis [vIGA-AD™] score of $\geq$ 3, and body surface area [BSA] $\geq$ 10%). The study consists of a 5-week screening period, a 12-week double-blind treatment period, and a 24-week follow-up period. Approximately 51 participants will be randomized in a 2:1 ratio to receive JNJ-67484703 or placebo administered subcutaneously (SC) through Week 12.

Results: The primary endpoint is the proportion of patients achieving $\geq$75% improvement from baseline in EASI score (EASI-75) at Week 12. Secondary endpoints assessed at Week 12 include the proportion of patients achieving $\geq$4-point improvement in eczema-related Itch NRS, vIGA-AD score of 0 or 1, and EASI-90 ($\geq$90% improvement from baseline in EASI score). Additionally, percent change from baseline in EASI score at Week 12, and percent change from baseline in Itch NRS at Weeks 1, 4, 6, and 12 are also assessed. Safety endpoints include the proportions of patients with treatment-emergent adverse events (AEs) and serious AEs assessed throughout the study. Additional assessments include pharmacokinetic, pharmacodynamic, and immunogenicity evaluations.

Conclusion: The RESTORE-AD phase 2 study will evaluate the efficacy, safety, and tolerability of JNJ-67484703 in adults with moderate and severe AD, using multiple clinical outcome measures.
Lebrikizumab in combination with topical corticosteroids provides significant improvement in quality of life in patients with moderate-to-severe atopic dermatitis not adequately controlled or non-eligible for cyclosporine: a placebo-controlled, randomized phase 3 clinical study (ADvantage)

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Introduction & Objectives

Lebrikizumab (LEB) is a novel monoclonal antibody that binds with high affinity and slow off-rate to interleukin (IL)-13, thereby blocking the downstream effects of IL-13 with high potency. LEB has previously demonstrated clinical efficacy and safety in adults and adolescents with moderate-to-severe atopic dermatitis (AD) in 3 randomized, placebo (PBO)-controlled, phase 3 trials.1-3 Cyclosporine A (CsA) is currently approved in the EU for treatment of severe AD, but its efficacy may not be optimal in some patients and its safety limits longer-term use. Here, we report 16-week efficacy and quality of life in patients with moderate-to-severe AD not adequately controlled or non-eligible for CsA who are treated with LEB combined with low- or mid-potency topical corticosteroids (TCS) in the phase 3 ADvantage study (NCT05149313).

Materials & Methods

ADvantage is a 52-week study with a 16-week, randomized, double-blind, PBO-controlled, parallel-group period followed by a 36-week open-label maintenance period. Eligible patients were adults and adolescents (≥12 to <18 years) with an Eczema Area and Severity Index ≥16, Investigator’s Global Assessment ≥3, and ≥10% body surface area of AD involvement who were not adequately controlled or were non-eligible for CsA. Patients were randomized 2:1 to LEB 250 mg with a loading dose of LEB 500 mg at baseline and week 2, or PBO every two weeks (Q2W). All patients were to receive mid-potency TCS from baseline through week 16; dosage could be tapered to low-potency TCS once lesions were controlled and stopped after 7 days. Efficacy was evaluated with SCORing Atopic Dermatitis (SCORAD) change from baseline (CFB) at week 16. Quality of life outcomes included percentage of patients achieving Dermatology Life Quality Index (DLQI) ≤5 and percentage of patients achieving DLQI of 0 or 1 at week 16. High-potency TCS or systemic treatments were considered rescue medication. Missing data due to lack of efficacy or data after rescue medication usage were imputed using non-responder imputation. Other missing data were imputed using multiple imputation.

Results

331 patients were randomized (220 LEB+TCS and 111 PBO+TCS) and 212 and 100, respectively, completed the 16-week period. Treatment groups had similar baseline characteristics. A greater percent CFB in SCORAD was obtained with LEB+TCS than PBO+TCS (-56.6% vs -36.3%, nominal p<0.01) at week 16. Moreover, a higher percentage of patients on LEB+TCS achieved DLQI ≤5 (55.7% LEB+TCS vs 34.7% PBO+TCS, nominal p<0.05) and DLQI 0/1 (30.6% LEB+TCS vs 8.3% PBO+TCS, nominal p<0.001) responses at week 16, compared to PBO+TCS.
Conclusion

In patients who have failed to CsA or for whom CsA is not medically advisable, LEB 250 mg Q2W with concomitant TCS significantly improved SCORAD and quality of life at week 16 in adults and adolescents with moderate-to-severe AD.

References

Abstract N°: 780

Atopic dermatitis in childhood and subsequent pubertal development: A nationwide cohort study

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Introduction & Objectives:
Atopic dermatitis is a chronic inflammatory skin disease that affects up to 20 % of children. It is characterized by an enhanced immune response and impaired skin barrier. Even though the majority of children outgrow their eczema by the age of 10-12 years, they keep the atopic disposition and the dry, atopic skin type that might affect them later in life. We hypothesized that atopic dermatitis in childhood might delay pubertal development through chronic stress, and sleep disturbances, resulting in dysfunction of the hypothalamic-pituitary-adrenal axis that regulates the hypothalamus-pituitary-gonadal axis that controls pubertal development. Normal pubertal development is crucial for later health like obesity, mental health, and breast cancer. We want to investigate whether severe disease or poor disease control results in subsequent pubertal development.

Materials & Methods:
The study is based on the Puberty cohort, a sub-cohort within a large nationwide cohort. In total, 15,538 boys and girls born between 2000-2003 were included. The mothers provided information about doctor-verified atopic dermatitis when the children were 6 months, 18 months, and 7 years old. Additionally, we included diagnosis codes from the National Patient Registry to identify the most severe cases of atopic dermatitis. Information on pubertal development was obtained from the children’s half-yearly self-reported information provided from age 11 years and throughout puberty. We estimated the mean age difference in months at attaining Tanner stage 2-5 on pubic hair, breast development, genital growth, axillary hair, acne, first ejaculation, voice break, and age at menarche, using an interval-censored regression model.

Results:
In total, 3,449 (22.2 %) children had doctor-verified atopic dermatitis. There was no association between atopic dermatitis in young childhood and pubertal development among those with self-reported doctor-verified atopic dermatitis (the combined estimate: Boys: 0.1 months, (95% confidence intervals (CI): -0.7; 0.9) and girls: -0.1 months (95% CI: -0.9; 0.7)). Boys with a diagnosis code (i.e., more severe disease) tended to have later pubertal development than boys without atopic dermatitis (5.6 months (95% CI: -2.8; 14.0)), however the estimate was also compatible with no effect.

Conclusion:
We found indication that the most severe grade of atopic dermatitis was associated with later pubertal development in boys, but the 95% confidence intervals overlapped the null. No associations were observed between atopic dermatitis and pubertal development in girls and for milder atopic dermatitis in boys.
Follow-up survey on 19 women with atopic eruption of pregnancy

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Follow-up survey on 19 women with atopic eruption of pregnancy

Introduction & Objectives

Atopic eruption of pregnancy (AEP) is the most common specific dermatosis of pregnancy. It is characterized by eczematous and/or papular lesions, which occur within the first two trimesters in 75% of cases. It represents the first manifestation of skin changes in atopic women in up to 80% versus an exacerbation of atopic dermatitis (AD) in the rest. Treatment is usually very effective with emollients, topical corticosteroids, and tacrolimus or UV-light therapy. So far, the course of skin changes in AEP patients after delivery has not been studied systematically.

Materials & Methods

Between 05/2011 and 06/2021, 28 pregnant women with AEP were seen at the Department of Dermatology, State Clinic Wiener Neustadt, Austria, of whom 19 could be followed beyond delivery. Two independent specialists at our gynecology-dermatology outpatient clinic made the diagnosis of AEP on clinical and anamnestic grounds. Differential diagnoses were excluded appropriately, including clinical examination, laboratory parameters, microbiology, or skin pathology.

Results

The 19 women were aged between 26-39 years (median, 31 years), 12 (63%) were primigravidae. Five of the 19 patients (26%) had a history of allergic asthma and/or rhinoconjunctivitis. Nine women (47%) had a type I and/or type 4 sensitization. AEP occurred between 9-41 gestation weeks (median, 19 weeks), in 16 patients (84%) before the third trimester. The lesions were mostly located on the trunk and/or extremities in all patients. Morphology was eczematous in 9 (47%), papular in 7 (37%), and mixed in 3 patients (16%). The median IGA score was 2 (range 1-4), the median VAS pruritus score was 7 (range 1-10). In 15 out of 19 patients (79%) atopic lesions occurred for the first time during pregnancy. Four patients had been suffering from AD since childhood or early adulthood. All patients were sufficiently treated with emollients; fifteen (79%) needed additional topical class II-III corticosteroids, two calcineurin inhibitors (11%) and one was treated with UVB light therapy.

The 19 patients gave birth to healthy babies (15 female, 1 twin pregnancy female/male). Six of the 19 babies (32%) had various atopic stigmata and/or mild transient eczema. In telephone interviews with all 19 patients 3-45 months (median 19 months) after delivery, 6/19 (32%) reported ongoing mild to moderate eczema without correlation to prior eczema or asthma. It cleared completely in 3 patients within 3 months, but persisted in the other three, of whom one was started on dupilumab.

Conclusion

This retrospective study provides reassurance for patients with AEP, since only 3/19 women (16%) had ongoing atopic skin changes beyond 3 months after delivery. However, our analysis is limited by its small sample size and its’ retrospective nature. Prospective, multicenter studies with a larger data set are needed to understand the long-term risk of AEP in women.
Efficacy and Safety of MH004 Cream for the Treatment of Mild-to-Moderate Atopic Dermatitis: Results from a Phase 2, Randomized, Double-Blind Study

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1Minghui Pharmaceutical (Hangzhou) Ltd., Hangzhou, China, 2Huashan Hospital, Fudan University, Department of Dermatology, Shanghai, China

Introduction:
Atopic dermatitis (AD) is an inflammatory skin disorder that is mediated by JAK-STAT pathway. Oral JAK inhibitors have safety concerns due to systemic inhibition of the immune system. Poor skin permeation due to hydrophilicity has hampered the development of topical JAK inhibitors. We have designed an ester prodrug (MH004) of tofacitinib, a pan-JAK inhibitor, to enhance the efficiency of its skin penetration. Preclinical data in minipigs suggested highly efficient permeation into multiple skin layers with little systemic exposure. We present here a phase 2, randomized, double-blinded study in mild-to-moderate AD patients in which convincing efficacy and safety was demonstrated.

Objective: To evaluate the efficacy and safety of MH004 Cream in adults and adolescents with AD.

Methods:
A total of 150 patients aged ≥ 12 years with an IGA score of 2 or 3, and 3%-20% affected BSA were enrolled, equally randomized, and treated with MH004 Cream (0.3% BID, 1.0% BID) or vehicle for 4 weeks. The primary endpoint was the mean percentage change from baseline of EASI score at week 4. Secondary endpoints included the proportion of patients achieving an IGA score of 0 to 1 with an improvement of 2 or more points at week 4 vs baseline (IGA-TS) and the proportion of patients who achieved EASI-75 at week 4. Blood samples were collected to assess the Ctrough of MH004 and its active metabolite, tofacitinib, at week 2 and 4. Safety and tolerability were assessed by monitoring the frequency, duration, and severity of adverse events (AEs) throughout the study.

Results:
Between March 24, 2022 and August 27, 2022, 150 patients were randomized (vehicle, n = 52; 0.3%, n = 49; 1.0%, n = 49). The median age was 35 years with 52.7% of male participants. The mean baseline EASI score was 6.9 ± 3.0, with 38.4% and 61.6% of patients presenting with IGA score of 2 and 3, respectively. The mean itch NRS score at baseline was 6.3 ± 2.1. 1.0% MH004 demonstrated a significantly greater mean percentage change from baseline of EASI scores vs vehicle at week 4 (-78.7% vs -46.7%; P = 0.0003). Significantly more patients treated with 1.0% MH004 achieved EASI-75 and IGA-TS responses vs vehicle at week 4 (EASI-75: 79.6% vs 42.0%; P < 0.0001; IGA-TS: 46.9% vs 20.0%; P = 0.0011). Significant reductions in itch NRS scores were observed at week 2 (1.0% MH004 vs vehicle, -48.4% vs -22.0%; P = 0.0005), and were sustained to the end of treatment. In 0.3% MH004 group, a clear trend of mean EASI score change at week 4 was observed, although not statistically significant. The overall rate of treatment-emergent adverse events (TEAEs) was comparable between MH004 Cream and vehicle. Most common treatment-related AEs were dermatitis contact, application site pruritus and application site pain. All TEAEs were grade 1 or 2 in severity and no serious AE was reported. The Ctrough of tofacitinib was approximately equal to 2% of the Cmax in its approved oral tablet dose regimen (5 mg BID). No
specific pattern of changes in hematologic laboratory parameters were reported.

**Conclusion:**

MH004 Cream (1% BID) demonstrated quick onset of action and superior efficacy in the current phase 2 study. The safety profile was comparable to vehicle and the rate of application site reactions was low. These results support the potential of MH004 Cream as an effective and well-tolerated topical treatment for mild-to-moderate AD.
Introduction & Objectives:

Dupilumab is a monoclonal antibody that binds specifically to the shared α-chain subunit of interleukin-4 and interleukin-13 receptors, approved as a treatment for moderate to severe atopic dermatitis (AD). Currently, although its therapeutic efficacy and favorable safety profile have been widely elucidated, data on real-world, long-term experience with the drug are only beginning to emerge.

The aim of this study is to determine the effectiveness of dupilumab for the treatment of the different subtypes of AD in a real-world setting.

Materials & Methods:

We conducted a retrospective enrolling 73 patients followed up for atopic dermatitis in our center (Dermatology Unit, University of Florence), who started the treatment between December 2017 and July 2021. Every patient included in the study had been on dupilumab for at least one year in order to evaluate long-term efficacy. We classified patients into five clinical subtypes: classic, face and neck AD, nummular eczema, hand dermatitis and prurigo nodularis (PN). Eczema Area and Severity Index (EASI), Dermatology Life Quality Index (DLQI) and Pruritus Numerical Rating Scale (pNRS) were used to assess the severity of AD. Other clinical data (sex, age, concomitant treatments, side-effects) were also recorded.

Results:

The study included 73 patients with AD with a mean age of 39.29 (17.05 SD) years. Baseline mean EASI score was 27.89 (6.42 SD). After 16 weeks of treatment, mean EASI score was 6.26 (4.28 SD). Lastly, after one year, mean EASI score was 3.79 (4.06 SD). Stratifying by clinical phenotype, we found a notable improvement after 16 weeks of treatment in every clinical subtype for all the assessed scores mentioned above, lasting up to week 52. The greatest improvement was observed in subjects with classic phenotype, while the clinical phenotype with the worst and slowest response was PN (mean EASI score at baseline of 37.67 (9.29 SD), decreasing to 9.67 (4.04 SD) at week 16 and remaining stable at week 52.

Conclusion:

Results from this retrospective study suggest that PN represents the clinical phenotype with the worst and slowest response to dupilumab.
IL-4 and IL-13 Coordinate Distinct And Overlapping Effects In The Pathobiology Of Atopic Dermatitis

Subhashini Srivatsan*1, Audrey Le Floc’h1, Brianna Buonagurio1, Kirsten Nagashima1, Wei Keat Lim1, Seblewongel Asrat1, Michael Garcia1, Daria Zamolodchikov1, Dharani Ajithdoss1, Dylan Birchard1, Angelos Papathedorou1, Nicole Alessandri-Haber1, Andrew Murphy1, Matthew Sleeman1, Jamie Orengo1

1Regeneron Pharmaceuticals, Inc., Immunology and Inflammation, Tarrytown, United States

Introduction & Objectives:

IL-4 and IL-13 are pleiotropic cytokines involved in the pathobiology of atopic dermatitis (AD). IL-4 signals through both the type I (IL-4Ra and IL-2Rg) and type II receptors (IL-4Ra and IL-13Ra1), while IL-13 signals through the type II receptor only. Dual cytokine blockade with an antibody directed against IL-4Ra, offers clinical benefit in AD. To dissect their individual roles in disease, we evaluated cytokine-dependent effects in primary human immune and skin structural cells. Furthermore, we characterized the effects of IL-4Ra blockade in a relevant mouse model of AD.

Materials & Methods: Primary human structural (dermal fibroblasts, keratinocytes) and immune (mast cells, eosinophils) cells were stimulated with IL-4 or IL-13. Gene expression and cytokine/chemokine release were evaluated by next generation sequencing (NGS) and Luminex, respectively. Skin inflammation (cytokines, Taqman, histology) and itch were assessed with IL-4Ra blockade in a mouse model of AD, using repeated topical application of oxazolone.

Results:

While both human structural and immune cells express the type II receptor, only immune cells express the type I receptor. Consistently, IL-4 and IL-13 exerted largely overlapping effects on gene expression in fibroblasts and keratinocytes. On the other hand, relative to IL-13, IL-4 regulated more genes in mast cells and eosinophils. By alignment with a meta-analysis derived AD (MADAD) disease transcriptome and published reports, we found that several key genes associated with human AD are modulated by both cytokines in structural and immune cells. In addition, there is a noteworthy regulation of AD-associated genes more prominently by IL-4 in immune cells. Overall, these data suggest that, due to their shared and individual effects on relevant cell types, dual blockade of IL-4 and IL-13 may be necessary to inhibit features of disease in AD. Thus, we implemented IL-4Ra blockade in the oxazolone AD-like model and show that itch, epidermal hyperplasia, skin cytokines and immune cell infiltrates are reduced by anti-IL-4Ra treatment.

Conclusion:

The sister cytokines, IL-4 and IL-13 coordinate distinct and overlapping effects in primary human cells relevant to AD as determined by transcriptomic analysis and alignment with disease-associated genes, suggesting that blockade of both IL-4 and IL-13 may normalize disease signatures in AD. In a mouse model of AD, we confirmed that inhibition of both cytokines with anti-IL-4Ra results in reduced itch and skin inflammation.
Abstract N°: 878

Expert Consensus on the Systemic Treatment of Atopic Dermatitis in Special Populations

David Adam¹, ², ³, Melinda Gooderham³, ⁴, Jennifer Beecker³, ⁵, ⁶, ⁷, Chih-Ho Hong³, ⁸, ⁹, Carolyn Jack¹⁰, ¹¹, Vipul Jain³, ¹², Perla Lansang¹, ¹³, ¹⁴, Charles Lynde¹, ³, ¹⁵, Kim A. Papp¹, ³, ¹⁶, Vimal Prajapati³, ¹⁷, ¹⁸, ¹⁹, ²⁰, ²¹, Irina Turchin³, ²², ²³, Jensen Yeung¹, ³, ¹³, ¹⁴

¹University of Toronto, Division of Dermatology, Temerty Faculty of Medicine, Toronto, Canada; ²CCA Medical Research, Ajax, Canada; ³Probity Medical Research, Waterloo, Canada; ⁴SKiN Centre for Dermatology, Peterborough, Canada; ⁵University of Ottawa, Division of Dermatology, Ottawa, Canada; ⁶The Ottawa Hospital, Division of Dermatology, Ottawa, Canada; ⁷Ottawa Hospital Research Institute, Ottawa, Canada; ⁸The University of British Columbia, Department of Dermatology and Skin Science, Vancouver, Canada; ⁹Dr Chih-Ho Hong Medical Inc, Surrey, Canada; ¹⁰McGill University, Division of Dermatology, Montréal, Canada; ¹¹Research Institute of the McGill University Health Centre, Montréal, Canada; ¹²McMaster University, Division of Clinical Immunology and Allergy, Hamilton, Canada; ¹³Sunnybrook Health Sciences Centre, Division of Dermatology, Toronto, Canada; ¹⁴Women’s College Hospital, Division of Dermatology, Toronto, Canada; ¹⁵Lynde Institute for Dermatology, Markham, Canada; ¹⁶K. Papp Clinical Research, Waterloo, Canada; ¹⁷University of Calgary, Division of Dermatology, Department of Medicine, Calgary, Canada; ¹⁸University of Calgary, Section of Community Pediatrics, Department of Pediatrics, Calgary, Canada; ¹⁹University of Calgary, Section of Pediatric Rheumatology, Department of Pediatrics, Calgary, Canada; ²⁰Dermatology Research Institute, Calgary, Canada; ²¹Skin Health & Wellness Centre, Calgary, Canada; ²²Brunswick Dermatology Centre, Fredericton, Canada; ²³Dalhousie University, Department of Medicine, Halifax, Canada

Introduction & Objectives:

With several new systemic therapies for treating patients with moderate-to-severe atopic dermatitis (AD), clinicians need guidance on selecting a systemic agent for specific patient populations. Herein, we summarize the literature and provide pragmatic consensus statements on selecting a systemic agent for six specific scenarios of clinical interest: (1) comorbid asthma, (2) ocular surface disease, (3) history of cancer, (4) past or ongoing infections of interest, (5) pregnancy and lactation, and (6) the elderly.

Materials & Methods:

We convened an expert panel of twelve members consisting of eleven dermatologists and one allergist/immunologist with clinical and clinical research expertise in treating patients with AD. The steering committee identified six clinical scenarios as topics for review based on gaps in the literature regarding the choice of a systemic agent in these scenarios. Literature searches within PubMed in February 2022 examined each clinical scenario with respect to three major categories of systemic treatments: traditional systemics (azathioprine, AZA; cyclosporine A, CsA; methotrexate, MTX; and mycophenolate mofetil, MMF), Janus kinase inhibitors (abrocitinib, ABR; baricitinib, BAR; and upadacitinib, UPA), and biologics (dupilumab, DUP; lebrikizumab, LEB; and tralokinumab, TRA). The steering committee assigned two authors to review the literature for each topic and provide a data summary with drafted statements. The expert panel met virtually to review the data and discuss preliminary consensus statements. We used a modified Delphi process to arrive at the final consensus statements related to the systemic treatment of AD in these specific patient populations.

Results:
The expert panel agreed on 25 statements (Table 1) to guide clinical practice. The statements refer to the systemic treatments for AD listed above but exclude systemic corticosteroids, which may be used as a short-term rescue treatment for AD. Summaries of the data considered from the literature review included: clinical trial data for common treatments in asthma and AD, rates of ocular adverse events (from both real-world studies and at primary and long-term analysis from phase 3 monotherapy and combination therapy clinical trials in AD), cancer rates from pivotal clinical trials in AD, infection rates at primary analysis from pivotal phase 2 and 3 clinical trials in AD, real-world studies in pregnancy and lactation in AD patients, and data in elderly populations including real-world studies and clinical trials of AD.

**Conclusion:**

Certain comorbidities and clinical scenarios guide physicians in choosing a systemic treatment for AD. Herein, we provide a review and practical approach to choosing a systemic therapy that clinicians can consider when treating patients in specific clinical scenarios.

**Table 1. Final Consensus Statements.** Statements achieving 75% or more agreement (i.e., rating 6-10 on an 11-point Likert scale) and included by the steering committee as relevant practical guidance. Systemic treatments below do not include systemic corticosteroids.

<table>
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<td>1. For patients with AD and comorbid asthma, inhibition of IL-4 and IL-13 via blockade of the IL-4 receptor (IL-4R) is effective for both conditions. Medications singly targeting IL-4 or IL-13 have failed in asthma to date. Medications targeting IL-5 have failed in AD to date.</td>
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<td>2. JAKIs are in early phase studies for asthma management.</td>
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<td>3. Apart from prednisone, traditional systemic medications used to treat patients with AD (AZA, CsA, MMF, and MTX) play no role in the treatment of comorbid asthma.</td>
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<td>5. TH2 blockade with IL-4 and/or IL-13 inhibitors in patients with AD increases incidence of OSD; however, this increased incidence is not observed when these drugs are used in other conditions including asthma, chronic rhinosinusitis with nasal polyps (CRSwNP), and eosinophilic esophagitis (EE).</td>
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<td>6. Although OSD may be induced or exacerbated by Th2 blockade with biologics, most cases are mild to moderate and do not warrant drug discontinuation.</td>
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<td>7. There is no evidence that MTX, CsA, MMF, AZA, or JAKIs increase the incidence of OSD.</td>
</tr>
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<td>8. When choosing a systemic treatment option for patients with a history of severe OSD, the treating dermatologist should consider starting with a JAKi or traditional systemic agent. If initiating an IL-4 and/or IL-13 inhibitor, consider an ophthalmology assessment prior to commencement of treatment.</td>
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**Conclusion:**

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**History of Cancer**

9. Risk of cancer recurrence is highly related to baseline age as well as cancer grade and stage. Accordingly, an individualized approach considering risks and benefits of systemic treatments for AD on a per-patient basis is recommended.

10. Despite the novelty of evidence to support direct estimates of risk in patients with AD and a history of cancer, biologics are the preferred option based on the mechanism of action and expert opinion.

11. Prior to initiating advanced systemic therapies, confirmation of AD diagnostic criteria and exclusion of cutaneous T-cell lymphoma (CTCL) misdiagnosis in the case of severe adult, rapidly progressive, and/or erythrodermic disease are important considerations.

**Past/Ongoing Infections of Interest**

12. In patients with AD, the frequency of herpes simplex virus (HSV) may be modified by systemic treatment. Physicians should screen for history of HSV and consider prophylaxis or prompt antiviral treatment for patients with a history of frequent or severe HSV.

13. Patients with AD treated with JAKIs, but not biologics, are at an increased risk of herpes zoster (HZ). Patients should be considered for HZ vaccination as per local guidelines.

14. a. Patients with HBV infection who are surface antigen positive should be evaluated for concomitant therapy for HBV prior to initiating any oral systemic treatment for AD.

b. If there is no benefit to accessing concomitant therapy for HBV, biologic therapies with proven efficacy in AD are the preferred option.

15. a. Patients with latent tuberculosis (TB) should not be treated with JAKI or traditional systemic treatments for AD until latent TB is treated as per local guidelines.

b. In patients with untreated latent TB, biologic therapies with proven efficacy in AD are the preferred option based on their mechanism of action.
Pregnancy & Lactation

16. For pregnant or nursing women who require systemic treatment for AD, CsA has the most evidence supporting its use during pregnancy and lactation.

17. MTX and MMF are contraindicated during pregnancy and lactation.

18. According to prescribing information, JAKIs are contraindicated during pregnancy and lactation.

19. DUP is likely safe during pregnancy and lactation considering the pharmacology and data from a small number of pregnancies. Conclusions cannot be made for other biologics due to lack of data, although most biologics are anticipated to behave similarly in pregnancy and lactation due to their molecular weight.

Elderly

20. Special considerations are warranted prior to making treatment decisions in elderly patients with AD. These include the patient’s cognitive ability, functional independence, ability to self-administer medication, renal function, comorbidities, polypharmacy, and potential for drug interactions.

21. In elderly patients who require systemic treatment for AD, biologic therapy should be prioritized where possible. DUP has the most data supporting its use in elderly patients.

22. MTX may be used as an alternate option to biologics in treating elderly patients with AD. Lower starting doses and close monitoring/follow-up are suggested due to the increased risk of adverse events in the elderly.

23. MMF may be considered based on limited real-world evidence.

24. AZA and CsA are not recommended in elderly patients due to lack of data in AD and higher risk of toxicity.

25. JAKIs are indicated for elderly patients with AD, however elderly patients appear to be at a higher risk of adverse events compared to younger patients.
Molecular classification of hand dermatoses - New clinical data on treatment of occupational dermatological patients

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¹University Hospital Heidelberg, Occupational Dermatology, Heidelberg, Germany, ²University Hospital Freiburg, Dermatology and Venereology, Freiburg im Breisgau, Germany, ³Osnabrück University, iDerm, Osnabrück, Germany, ⁴BG Klinikum Hamburg, iDerm, Hamburg, Germany, ⁵SLK-Kliniken: Klinikum am Gesundbrunnen, Dermatology, Allergology, Phlebology, Heilbronn, Germany, ⁶Universitätsklinikum des Saarlandes, Dermatology, Venereology, Allergology, Homburg/Saar, Germany, ⁷Hautarztpraxis Dr. Leitz und Kollegen, Stuttgart, Germany, ⁸University Hospital Augsburg, Dermatology and Allergology, Augsburg, Germany

Introduction & Objectives:

It has always been challenging to diagnose psoriasis and eczema of the hands. Fortunately, molecular disease classifier (MC) have been introduced in dermatology. This cohort study with occupational dermatology patients was started in 2020 and is the largest collective of patients receiving MC for differentiation of both diseases. The aim is to investigate the influence of MC on disease severity and course, quality of life (QoL), therapies and occupational status.

Materials & Methods:

285 patients were included in the study. The probability of psoriasis vs. eczema was determined based on the expression of the genes NOS2 and CCL27. RNA is extracted from formalin-fixed paraffin embedded tissue and the method is therefore applicable in addition to conventional histopathological analyses. Studies showed a test sensitivity of 92% and specificity of 100%. Patients are then being followed-up over 3 years and data on clinical (e.g. severity, therapies) and patient reported outcomes (e.g. quality of life, sick leave) are collected. To determine the influence of MC it will then be compared to an existing cohort without use of MC.

Results:

As of May 2023, 153 men and 132 women from 62 departments of dermatology and dermatological practices throughout Germany were included. The mean age was 50.5 (±12.3) years. Skin disease had persisted for a mean of 7.2 years with a high range (0.5-48 years). In 90% the hands were affected, mainly the palms (69%), interdigital spaces (40%) and backs (28%).

The MC decided in 2/3 in favor of eczema (n=192), ¼ (n=69) in favor of psoriasis; 6.6% (n=19) remained ambiguous. Clinicians diagnosed eczema in 35% (n=101) and psoriasis in 23% (n=67). In 106 cases (39%), the diagnosis was clinically unclear at study entry. By using MC, 95% of these cases received a diagnosis. Clinical and molecular diagnoses were concordant in only 36% of participants (Cohen’s k = .04 (95%-confidence interval (CI): -0.02-0.1)). A weak statistically correlation can be seen (χ²(4)=11.47, p=.02, Cramers V=.15, n=272).

Histopathological results were available for half of the patients and diagnosed eczema in 49% (n=73), psoriasis in 28% (n=42); 22% (n=34) were unclear. Concordance was slightly higher but at the same time showed a higher dispersion (Cohen’s k = .04 (95%-CI: 0.01-0.24). Correlations were again weak (χ²(4)=10.46, p=.03, Cramers V=.19, n=146).
Conclusion:

The use of molecular diagnostics reduced the number of unclear cases significantly and helped to confirm a diagnosis in occupational dermatology. Weak associations with existing diagnostics such as histopathology speak for the novelty of this approach.
Impact of real-life ozone exposure on skin in vitro and in vivo.

Fabien Girard¹, Caroline Lajoye¹, Christophe Jones¹, Eric Arbey³, Dang Man Pham², Laurence Denat*¹

¹L’Oréal, Research and Innovation, Aulnay-sous-Bois, France, ²L’Oréal, Research and Innovation, Chevilly-Larue, France

Impact of real-life ozone exposure on skin in vitro and in vivo

Introduction & Objectives:
Skin is one of the main organs directly exposed to environmental insults, like pollution and especially ozone. Tropospheric ozone is produced at the ground level by human activities. Its concentration can reach 0.1 ppm during peaks. This gas is extremely reactive and constitutes the strongest oxidizing agent in contact with the skin in daily life. This pollutant directly interacts with epidermal surface layers and especially with unsaturated lipids present in sebum and stratum corneum, generating oxidized molecules that can lead to damaging cascades of biochemical reactions. Ozone exposure has been correlated with disruption of skin integrity and dermatological disorders like atopic dermatitis, but no causal link has been shown yet under real-life ozone exposure. To address this issue, the present study focused on evaluating the in vitro and in vivo impact of real-life concentrations of ozone on skin.

Materials & Methods:
Ozone generator consisted in an ultraviolet lamp generating photolysis of the oxygen molecule from air. Ozone was dispersed in a chamber inside a cell culture incubator or in a cylindrical cup fitted onto the skin of subjects.

In vitro: In vitro reconstructed human full-thickness skin model was exposed to various concentrations of ozone from 0.8 ppm to 0.1 ppm, either with 1, 2 or 3 exposures for 18 hours each. Reconstituted sebum was applied on reconstructed skins at a concentration of 300µg/cm² before the first ozone exposure. Skin samples were analyzed for lipid oxidation, protein carbonylation, gene and protein expression.

In vivo: The upper back skin of 10 subjects was exposed to ozone, using specially designed cylindrical cups. Exposure protocol lasted 2 weeks and included 6 two-hour exposures to 0.3 ppm of ozone. Sebum and tape strip samples were analyzed to determine lipid oxidation, protein carbonylation and protein expression.

Results:
Our results showed that ozone exposure at high concentration (0.8 and 0.4 ppm) induced lipid peroxidation and protein carbonylation. Interestingly, at 0.1 ppm of ozone exposure, corresponding to realistic conditions, the results were similar. In addition, sebum application was exacerbating the impact of ozone on protein carbonylation. To go further with these mechanisms, biochemical markers of oxidation were analyzed. Ozone exposure increased different types of aldehydes and forms of oxidized lipids and amino acids in vitro. These lipid metabolite biomarkers were confirmed to be increased also in vivo. Moreover, after ozone exposure either with or without sebum, inflammation increased with higher levels of interleukins, like IL6 and IL8. Many biomarkers implicated in barrier function were found modulated both at gene and protein level.

Conclusion:
Ozone pollution is a worldwide urban concern that is rapidly worsening and with the escalating global climate
warming, this trend is only set to intensify. Most notably, maximal health threshold recommended by the World Health Organization is widely exceeded in a large part of the world. The current study brings for the first-time new insights on real-life ozone exposure conditions and its impact on skin and particularly the barrier function. This can lead to a range of skin issues and could explain the increased number of patients with atopic dermatitis flare observed after high ozone peak levels.

C1 - Internal use
Abstract N°: 945

Efficacy and safety of delgocitinib cream in adults with moderate to severe chronic hand eczema: results of the Phase 3 DELTA 1 trial

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1Innovaderm Research, Montréal, Canada, 2Dermatology Centre, Salford Royal NHS Foundation Trust and NIHR Biomedical Research Centre, The University of Manchester, Manchester, United Kingdom, 3Dermatology Section, Department of Medicine and Surgery, University of Perugia, Perugia, Italy, 4LEO Pharma A/S, Ballerup, Denmark, 5Department of Dermatology, University Hospital of Centre of Paris, Cochin Hospital, AP-HP, Paris, France, 6Department of Occupational and Environmental Diseases, University Hospital of Centre of Paris, Hotel-Dieu Hospital, AP-HP, Paris, France

Introduction & Objectives: Chronic hand eczema (CHE) is the most frequent inflammatory disorder affecting hands. It is associated with pain, pruritus, and significant occupational, functional, social, and psychological burden. Delgocitinib is a topical pan-JAK inhibitor targeting key mediators involved in the immunopathogenesis of CHE. The objectives of this study were to: (1) study the efficacy of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle; (2) evaluate the safety of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle; and (3) study the effect on health-related quality of life of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle, in the treatment of adults with moderate to severe chronic hand eczema in the Phase 3 DELTA 1 trial.

Materials & Methods: In the Phase 3 DELTA 1 trial (NCT04871711), adults (aged ≥18) with moderate to severe CHE were randomized 2:1 to twice-daily delgocitinib cream 20 mg/g (n=325) or cream vehicle (n=162) for 16 weeks followed by a 36-week extension trial (NCT04949841). The primary endpoint was Investigator’s Global Assessment for CHE (IGA-CHE) treatment success at Week 16 (IGA-CHE TS), defined as IGA-CHE score of 0/1 (clear/almost clear) with ≥2-step improvement. Key secondary endpoints included ≥75%/≥90% improvement in Hand Eczema Severity Index (HECSI-75/90) and ≥4-point improvement in the Dermatology Life Quality Index (DLQI).

Results: At Week 16, a significantly greater proportion of delgocitinib-treated patients, compared to cream vehicle, achieved IGA-CHE TS (19.7% vs. 9.9%; p=0.006), HECSI-75 (49.2% vs. 23.5%; p<0.001), HECSI-90 (29.5% vs. 12.3%; p<0.001), and ≥4-point improvement in DLQI (74.4% vs. 50.0%; p<0.001). There was no difference between delgocitinib and cream vehicle in proportion of patients who presented adverse events (AEs; 45.2% vs. 50.6%) and serious AEs (1.8% vs. 1.9%). Rates of AEs related to IMP or leading to discontinuation of IMP were numerically higher with cream vehicle compared to delgocitinib (delgocitinib 3.7% vs. vehicle 8.0% and 0.6% vs. 3.7%, respectively).

Conclusion: Overall, delgocitinib cream provided greater improvements in both patient- and clinician-reported efficacy outcomes versus cream vehicle and was well-tolerated over 16 weeks.
Lebrikizumab demonstrates efficacy in adult patients with moderate-to-severe atopic dermatitis who received non-live vaccinations

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Introduction & Objectives: Lebrikizumab (LEB) is a monoclonal antibody that binds with high affinity and slow off-rate to interleukin (IL)-13, thereby blocking the downstream effects of IL-13 with high potency. The efficacy of LEB for patients (pts) with moderate-to-severe atopic dermatitis (AD) has been established in previous studies [1,2]. This analysis examined the efficacy of LEB in pts with moderate-to-severe AD who received non-live vaccinations.

Materials & Methods: ADopt-VA was a Phase 3, 16-week (W) randomized, double-blind, placebo (PBO)-controlled study carried out in the United States to assess LEB impact on non-live vaccine immune responses in adult pts with moderate-to-severe AD. Eligible participants were randomly assigned 1:1 to receive either LEB (N=125) or PBO (N=122). LEB was given as a 500 mg loading dose at baseline and W2, followed by 250 mg LEB Q2W. At W12, both vaccines (Tdap and MCV) were administered to all pts. Low- and mid-potency topical corticosteroids (TCS) and topical calcineurin inhibitors (TCI) were permitted. Secondary efficacy endpoints included percentage change from baseline in Eczema Area and Severity Index (EASI), Pruritus Numeric Rating Scale (NRS), and interference of itch on sleep (Sleep-Loss scale), and change from baseline in percentage body surface area (BSA) and Patient-Oriented Eczema Measure (POEM).

Analyses were performed on a modified intent-to-treat population, excluding 7 pts (from two study sites) whose eligibility could not be confirmed. For EASI, Pruritus NRS, and Sleep-Loss scale, pts who discontinued for lack of efficacy or received rescue medication were considered non-responders and analysed with non-responder imputation, and missing data were imputed with multiple imputation. For BSA and POEM, data after discontinuation or rescue were considered missing and all missing data were handled with mixed-model repeated measures.

Results: At W16, pts who received LEB achieved a significantly greater percentage change from baseline in EASI score compared with pts who received PBO (-73% vs -47%, p<0.001; Fig 1A). A significantly greater percentage change from baseline in Pruritus NRS score was reported by pts who received LEB compared with PBO (-57% vs -33%, p<0.001; Fig 1B). A significant difference was also observed at W16 for change from baseline in EASI score for pts who received LEB compared with PBO (-28 vs -19, p<0.001; Fig 1C). Pts treated with LEB reported a significant improvement in sleep-loss due to pruritus (Fig 1D), with a percentage change from baseline in Sleep-Loss scale of -55% compared with -27% for PBO (p<0.05). Pts who received LEB also reported significant improvements in interpretation of disease severity compared with PBO (POEM change from baseline -9.4 vs -6.6, p=0.014; Fig 1E). A significant improvement of LEB vs PBO was seen from W4 for Pruritus NRS, BSA, Sleep-Loss scale and POEM. Use of concomitant TCS/TCI was low (7% for LEB, 14% for PBO).

Conclusion: LEB with and without TCS/TCI demonstrated significant improvement in signs and symptoms of AD compared with PBO in this 16W phase 3 trial, consistent with previous LEB studies in pts with moderate-to-severe
AD. Co-administration of non-live vaccines and LEB had no impact on each other in terms of their respective efficacies (vaccine efficacy not shown [3]).

References:


3. Soung et al. ISID 2023 congress [abstract]; LB1702
Abstract N°: 1020

Reported Pregnancy Outcomes in Women With Severe Atopic Dermatitis Treated With Dupilumab: A Systematic Review

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Introduction & Objectives:

Atopic dermatitis (AD) is the most common dermatosis during pregnancy, accounting for 36% to 49.7% of all pregnancy-related dermatoses.¹ About 46% of females with AD are likely to experience a flare in pregnancy. Dupilumab was the first biologic treatment approved for moderate-to-severe AD. However, there is limited data concerning the safety profile of its use during pregnancy. This systematic review aims to consolidate published cases on pregnancy outcomes in women with moderate to severe AD treated with dupilumab.

Materials & Methods:

Following PRISMA criteria, a MEDLINE and Embase search was conducted on July 8, 2022, using synonyms of the keywords “atopic dermatitis”, “pregnancy” and “dupilumab”. After independently screening 38 articles by two reviewers, seven case reports were included consisting of seven patients using dupilumab during pregnancy; extracted data are presented in Supplemental Table 2. The mean patient age was 32.7 years (range: 28-36). All patients had severe AD at the initiation of treatment.

Results:

Six patients were exposed to dupilumab prior to conception with an average duration of 8.7 months prior to conception while one patient was exposed starting at 24 weeks gestation. The most reported adverse reaction was eye irritation post-dupilumab injection (42.8%). Concomitant therapies were lubricating eye drops (14.2%), immunoglobulin (14.2%) and prednisone (14.2%). All patients responded to dupilumab with improvement in their AD. One case of intrauterine growth restriction (IUGR) and a breech position were reported at 38 weeks. A C-section was performed without complications. All other cases neither had complicated pregnancies nor deliveries. The average gestational age at delivery was 38 weeks and 6 days. The average birth weight for babies delivered was 3.01 kg (range: 2.48-3.49). Cases were followed for an average of 8 weeks (range: 4-16) with no postpartum complications. Data from the European Medicines Agency with 31 pregnancies exposed to dupilumab reported fourteen live births, five elective abortions and six spontaneous abortions. The rate for spontaneous abortions did not exceed that of the general population.

Conclusion:

Overall, it is reassuring that there were few negative pregnancy outcomes in reported cases of women with severe AD treated with dupilumab. In one cohort of 10,688 births from women with AD, an increased association with premature rupture of membranes and staphylococcal neonatal septicemia was observed. This outcome was not observed in this review. We hypothesize that decreasing the inflammatory burden of AD by adequately treating the disease with dupilumab may decrease these complications to a rate comparable to women without AD. Within the same cohort, rates of low birth weight (1.5, 2.5 kg) was reported in 4.7% in women with AD. Although IUGR resulting in a birth weight of 2.48 kg was seen in 1 case (14.2%) in this review, statistical comparison is not possible.
This review, while limited to case studies, highlights that dupilumab may be an option during pregnancy for patients with refractory AD after careful risk-benefit assessment. Larger sample sizes of reported data are needed to establish the safety of dupilumab during pregnancy.
Abstract N°: 1050

Upadacitinib Rapidly Improves Atopic Dermatitis-Related Night-time Itch and Sleep Disturbance: An Integrated Daily Analysis from Two Phase 3 Trials (Measure Up 1 & 2)

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Introduction & Objectives: Atopic dermatitis (AD) is a chronic, inflammatory skin disease that significantly impacts patient’s quality of life. Patients with moderate-to-severe AD report sleep disturbance as among the most burdensome effects of the disease, with itch being a key factor disrupting sleep. Upadacitinib (UPA), a selective oral Janus kinase inhibitor, approved to treat moderate-to-severe AD, has a positive benefit-risk profile demonstrated in several phase 3 studies. Here, the effect of UPA on improving night-time itch and sleep disturbance was evaluated.

Materials & Methods: The current study analyzed integrated data from Measure Up 1 and Measure Up 2, which are replicate phase 3 multicenter, randomized, double-blinded studies comparing the safety and efficacy of upadacitinib 15 mg (UPA 15) and upadacitinib 30 mg (UPA 30) to placebo (PBO) in adolescents and adults with moderate-to-severe AD. Individual items from the Atopic Dermatitis Symptom Scale (ADerm-SS) and Atopic Dermatitis Impact Scale (ADerm-IS) were used to evaluate night-time itch and overall sleep disturbance, respectively. Patients were asked to rate their worst itch during sleep hours (from “no itch” to “worst imaginable itch”) and the overall impact of their disease during sleep hours (from “not at all” to “extremely”), with a recall period of 24 hours on an 11-point numeric rating scale, with higher scores indicating worse outcomes. Daily data from day 2 (representing the first night after treatment) to day 28 were analyzed. Proportions of patients with an improvement (reduction) ≥4 from baseline scores and proportions of patients achieving a score of 0 or 1 on both night-time itch and sleep disturbance were compared between UPA arms and PBO using Cochran-Mantel-Haenszel tests. Missing data at study visits were imputed using non-responder imputation, with no special handling for missing data due to COVID-19 (NRI-NC).

Results: Integrated data from Measure Up 1 and Measure Up 2 included 1683 adolescents and adults randomized to UPA 15 (N=557), UPA 30 (N=567), or PBO (N=559). Greater proportions of patients in the UPA 15 and UPA 30 groups had improvements ≥4 from baseline compared to PBO for night-time itch as early as the first night after treatment (data on day 2) (UPA 15: 11.0%, UPA 30: 14.0% vs. PBO: 3.0%), at the end of the first week (data on day 8) (31.2%, 40.5% vs. 7.2%), and at the end of the first month (data on day 28) (57.6%, 70.6% vs. 13.2%) (Fig 1). A similar finding was observed for improvement in overall impact on sleep at first night (UPA 15: 14.4%, UPA 30: 16.7% vs. PBO: 5.5%), first week (33.8%, 42.6% vs. 8.9%), and first month (60.9%, 68.4% vs. 14.5%) (Fig 2).
Proportions of patients achieving a score of 0 or 1 for night-time itch was similarly greater for patients taking UPA 15 and UPA 30 compared to PBO at first night (UPA 15: 5.6%, UPA 30: 5.8% vs. PBO: 1.9%), first week (15.3%, 22.9% vs. 2.6%), and first month (40.5%, 55.5% vs. 6.0%), as were the proportions of patients achieving a score of 0 or 1 for overall impact on sleep at first night (UPA 15: 7.6%, UPA 30: 9.7% vs. PBO: 4.2%), first week (22.3%, 29.7% vs. 4.6%), and first month (42.7%, 56.8% vs. 8.2%). Comparisons vs. PBO yielded p values <0.05.

**Conclusion:** Treatment with upadacitinib 15 mg and 30 mg in patients with moderate-to-severe AD resulted in rapid improvements in AD-related night-time itch and sleep disturbance as early as the first night after treatment compared to PBO. This effect increased and was maintained through the first month of treatment.
Clinical efficacy of emollients in atopic dermatitis patients: long-lasting efficacy

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Introduction & Objectives:

Atopic dermatitis (AD) is a chronic inflammatory skin disorder that involves alteration of skin physical barrier, microbiome and immune system. It affects children and adults with a substantial impact on quality of life (QoL). Emollients are the baseline therapy for any severity of AD with emollient “plus” being emollients with active ingredients to maintain healthy skin microbiome.

This study assessed the efficacy of an emollient “plus” containing Aqua Posae filiformis, Microresyl, LRP Thermal Spring Water, Shea Butter and Niacinamide to improve AD after 1 month and maintain the improvement for 5 additional months.

Materials & Methods:

Monocentric, open label study conducted with 56 subjects (45% children ≥3 years old (YO); 55% adults) having mild AD under dermatological control. All subjects were treated twice daily for 6 months with the emollient “plus”. The evaluation of the efficacy of the emollient “plus” was based on the SCORing Atopic Dermatitis (SCORAD) reduction after 28 days and the SCORAD maintenance during the following 5 months (assessed at D84 and D168). Additionally, impact of AD on QoL was evaluated through a DLQI and CDLQI questionnaire.

Results:

At D28, the average SCORAD was 40% lower compared to baseline (D0: 15.29; D28 9.11; p<0.001). During the maintenance phase, the average SCORAD at Day 84 and D168 was respectively reduced by 8% and 17% compared to Day 28 (D84: 8.37; D168: 7.52; p<0.05). The continuous use of the emollient “plus” improved 90% of the adults and 84% of the children QoL scores by the end of the study (Adults: D0: 6.6; D168: 0.7; Children: D0: 5.3; D168: 0.8; p<0.001).

Conclusion:

This study highlights the short and long-lasting efficacy of emollient “plus” containing Aqua Posae filiformis, Microresyl, LRP Thermal Spring Water, Shea Butter and Niacinamide for managing mild AD.
Abstract N°: 1166

Real-world data of abrocitinib treatment in patients with atopic dermatitis: results from the BioDay registry

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Introduction & Objectives: Abrocitinib has proven to be an effective treatment for patients with atopic dermatitis (AD) in clinical trials. However, no daily practice studies are available. The aim of this study is to evaluate the effectiveness and safety of abrocitinib in patients with AD, including those with previous inadequate response to dupilumab and/or upadacitinib, in daily practice.

Materials & Methods: This multicentre prospective observational cohort study included clinician- and patient reported data on all AD patients treated with abrocitinib. Results: Ninety patients were included: week 4 (n=80), week 8 (n=69), week 16 (n=47), and week 28 (n=26). At baseline, 45 patients (50.0%) used concomitant systemic immunosuppressive/immunomodulating treatment. Eczema Area and Severity Index (EASI)-50/75/90 was achieved by 68.0%, 46.7%, and 21.3% at week 4, respectively, 82.2%, 48.9%, and 17.8% at week 16, respectively, and 79.2%, 54.2%, and 16.7% at week 28, respectively. After 4, 16 and 28 weeks, 35.9%, 21.7% and 25.0% achieved (almost) clear (≤1) on the Investigator Global Assessment and 62.5%, 61.7% and 66.7% achieved a weekly average Numeric Rating Scale-pruritus ≤4, respectively (Figure 1). At week 28, absolute cut-off score EASI ≤7 was achieved by 70.8%, EASI ≤4 by 54.2%, Patient-Oriented Eczema Measure ≤7 by 43.8%, Dermatology Life Quality Index ≤5 by 62.5%, and Patient Global Assessment of Disease rating of at least ‘good’ (≥3) by 50.0% (Figure 1). Atopic Dermatitis Control Tool <7 was achieved by 56.0% at week 16 (Figure 1). Of the 63 patients who could have reached week 16, 51 patients (81.0%) had failed on previous dupilumab treatment. Reasons for discontinuation of dupilumab were: ineffectiveness (n=20), adverse events (AEs) (n=14), both (n=11), or other reasons (n=6). Twenty-two patients (34.9%) failed on previous upadacitinib treatment due to ineffectiveness (n=16), AEs (n=3), both (n=2), or other reasons (n=1). In the Generalized Estimating Equations analysis, all outcomes until week 16 did not significantly differ when adjusted for an inadequate response (drop-out due to ineffectiveness or ineffectiveness/AEs) to dupilumab and/or upadacitinib. In total, 23 patients (25.6%) dropped out in this study: 10 patients due to ineffectiveness, 8 due to AEs, 2 due to ineffectiveness/AEs, and 3 due to other reasons. Age, sex, drop-out due to ineffectiveness of dupilumab or upadacitinib, and drop-out due to AEs of dupilumab or upadacitinib were no predictors for drop-outs of abrocitinib. Most frequently reported AEs were acneiform eruption (n=23 (0.85/patient year (PY))) and nausea (n=21 (0.78/PY)). Conclusion: Abrocitinib can be an effective treatment for patients with AD in daily practice, including those with previous inadequate response to dupilumab and/or upadacitinib.
Figure 1. Clinician- and patient reported outcomes
Achievement of super-response over time in patients with moderate-to-severe atopic dermatitis treated with abrocitinib versus dupilumab: A post hoc analysis of the head-to-head phase 3 JADE DARE study

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Introduction & Objectives:
In patients with moderate-to-severe atopic dermatitis (AD), attainment of super-response, which may be defined as achieving high-threshold efficacy on at least 3 clinician- or patient-reported efficacy measures, may be an important goal of therapeutic intervention. In JADE DARE trial (NCT04345367), efficacy of abrocitinib on individual outcome measures was superior to that of dupilumab, especially at early visits. However, the dynamics of super-response with these 2 therapies in a head-to-head comparison over the long-term have not been analyzed. In this post hoc analysis of JADE DARE, we assessed the attainment of super-response over time with abrocitinib versus dupilumab.

Materials & Methods:
JADE DARE was a randomized (1:1), double-blind, double-dummy, active-control, phase 3 trial of adult patients with moderate-to-severe AD who received oral abrocitinib 200 mg once daily (QD) or subcutaneous dupilumab 300 every 2 weeks (Q2W) for 26 weeks, on the background of topical therapies. Super-response was defined as attaining ≥90% improvement in Eczema Area and Severity Index (EASI-90), Peak Pruritus Numerical Rating Scale score of 0 or 1 (PP-NRS 0/1; PP-NRS, used with permission from Regeneron Pharmaceuticals, Inc., and Sanofi), and Dermatology Life Quality Index value of 0 or 1 (DLQI 0/1) at any time point. The treatment groups were compared using a Kaplan-Meier time-to-event analysis, with the achievement of super-response as the event. We implemented an accelerated failure time model using a Weibull distribution to examine variables associated with time to become a super-responder. Statistical significance of between-group differences was assessed using the log-rank test.

Results:
JADE DARE enrolled 727 individuals (abrocitinib, n=362; dupilumab, n=365).** Proportions of super-responders were higher in the abrocitinib group versus dupilumab group from week 2 (4% [13/362] vs 0% [0/365]) to week 26 (37% [135/362] vs 21% [76/365]) (Figure). With abrocitinib, the time to achieve super-response was shorter and the probability of obtaining super-response higher than with dupilumab (Figure). The difference between the cumulative incidence curves by treatment was statistically significant (nominal P<0.001); however, the median time to achieve super-response was not evaluable. Controlling for other variables, time to achievement of super-response was significantly shorter in women versus men and in patients who were cyclosporine-naïve versus those
who were not.

**Conclusion:**

From week 2 to week 26, treatment with abrocitinib 200 mg QD was associated with higher proportions of super-responders compared to treatment with dupilumab 300 mg Q2W.
Abstract N°: 1211

Evaluation of cleansing foam based on mild surfactants and humectants for patients with atopic dermatitis

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Introduction & Objectives:

Proper skin cleansing procedures play an important role in the management of atopic dermatitis, especially in infants and young children. The skin must be cleansed thoroughly, but gently, to get rid of crusts and mechanically eliminate microorganism contaminants and allergens.

Here we investigate a safety and efficacy of face, hair and body cleanser, in a form of thick foam based on mild surfactants and humectants (glycerine and betaine). It can be used during showering or can be added to the bath tub.

Materials & Methods:

An in vitro safety of the cleansing foam was evaluated by MTT cytotoxicity test (L929 cells) and ex vivo irritation potential on EpiDerm skin model according to ISO 10993.

In addition to this to check sensitization properties of the cleanser, the flow cytometry of IL-1\textbeta, IL-6, IL-8 was measured in the cell medium collected after 1 hrs of product contact with RHE (EpiDerm).

During Dermatological patch\textsuperscript{*} test, the skin of 20 healthy adult females with history of allergy was exposed to cleanser with Finn Chamber patches. The appearance of skin irritations was assessed by a dermatologist after 48 and 72 hours.

The moisturization and pH level of the skin before and after 1 hrs of cleanser usage was evaluated.

The efficacy of the product was performed in group of 19 children (age 0,5-6 y.o.) with dry, sensitive and atopic skin.

Results:

The tested cleanser did not show skin irritation potential. The tissue viability was 96,2% compared to the control. It has been confirmed no cytotoxic effect towards L-929 cells at the concentration of at least or equal to 0,01%.

Flow cytometry showed no significant changes in concentration of IL-1\textbeta and IL-8 in cell medium, after 1 hrs contact of cleanser with RHE. However the significant increase in IL-6 level could be observed in comparison to negative and positive control (PBS, SDS and mixture of parabens, respectively). While taking into consideration a detergent character of tested cleansing foam, and high viability of the tissue, it does not influence general safety of the product.

The tested cleanser did not affect moisturization level of the skin and slightly decreased its pH.

Also product was very well tolerated in a group of children with dry and atopic skin. Parents assessed that tested foam effectively cleansed the skin, was suitable for everyday use without the risk of drying the hair and scalp,
ensured an adequate level of skin hydration, reduced the feeling of dry skin, soothed existing irritations or skin flacking and relieved itching of the scalp.

Similarly, the patch test results in adults showed that use of foam does not irritate the skin.

**Conclusion:**

The foam was well-tolerated. The safety of the product was confirmed in both in vitro and in vivo tests. It may be considered as an effective formulation for cleansing procedures of patients (including infants and children) with atopic dermatitis.
Initial report from the AD-REAL study on baseline characteristics and Week 12 results in patients with moderate-to-severe atopic dermatitis treated with baricitinib and other oral systemic treatments in real-world clinical practice

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Introduction & Objectives:

Atopic dermatitis (AD) is a common, chronic inflammatory skin disease, with limited evidence on the use of oral systemic therapies in clinical practice. Amongst those therapies, baricitinib (BARI) was the first oral Janus Kinase inhibitor (JAKi) approved in Europe for the first treatment of adults with moderate-to-severe AD. AD-REAL is an international, prospective, observational cohort study. This interim analysis reports on baseline characteristics, disease severity and patient reported outcomes (PROs) over 12±2 weeks for the first 89 adult AD patients enrolled into AD-REAL receiving either BARI or other oral systemic (OOS) therapies, including, abrocitinib, azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate mofetil, and upadacitinib.

Materials & Methods:

Patients ≥18 years with moderate-to-severe AD for ≥6 months who presented within routine medical care and for whom the decision had been made to initiate an oral systemic treatment were enrolled in France, Germany and the UK. Biologics could be used post-baseline. Data were collected at routine clinical visits at baseline, week 4±1 and week 12±2, and included demographics, disease characteristics, clinician-assessed outcomes (Eczema Area and Severity [EASI], validated Investigator Global Assessment for AD [vIGA-AD], Body Surface Area [BSA]) and PROs. In addition, PROs were collected within the first 4 weeks, daily (Itch Numerical Rating Scale [NRS], Skin Pain NRS, Atopic Dermatitis Sleep Scale [ADSS]) or weekly (Patient-Orientated Eczema Measure [POEM], Dermatology Life Quality Index [DLQI]) using electronic patient diaries. Continuous outcomes were reported using mean and standard deviation and categorical variables using frequencies. Data was reported as observed.

Results:

This analysis included a total of 89 patients, 41 (46%) of which were initiated at baseline with BARI and 48 (54%) with OOS. Overall, 40 (98%) and 35 (85%) from the BARI cohort and 47 (98%) and 31 (65%) with OOS respectively, reached Weeks 4 and 12 visits in the data collection schedule. Patients in the BARI and the OOS cohorts had longstanding AD (27.2 and 25.3 years), about half of patients were female (53.7% and 52.1%, respectively), and mean age was 42.8 and 34.3 years, respectively (Table 1). In the BARI cohort, 20% and in the OOS cohort 44%, were systemic naïve. At baseline, patients in the BARI cohort had a mean EASI of 15.7 (vs 21.8 for OOS), a mean affected BSA of 33.0 (vs 50.0 for OOS), and about a quarter of patients had a vIGA-AD score of 4 (24% vs 35% for OOS). Reported baseline itch NRS for patients in the BARI cohort was 5.1 and 6.6 for the OOS cohort (Table 1). After 4 and 12 weeks of treatment, respectively, 55% and 50% of patients in the BARI cohort and 32% and 50% in the OOS cohort achieved EASI75 response (Figure 1A). In both cohorts, itch NRS decreased from baseline until week 4, with mean scores being 3.3, 2.9 and 0.5 for the BARI and 3.7, 2.5 and 0.8 for the OOS cohort,
at week 12 (Figure 1B-D).

**Conclusion:**

This interim analysis of AD-REAL indicates that patients initiated on BARI in clinical practice are frequently systemically experienced and their disease severity improved with BARI treatment across signs and symptoms of AD. Despite limitations, including a small sample size, limited observation period, and missing data, this analysis reflects the fast onset of action of BARI in a real-world setting, as observed in phase 3 clinical trials.

![Figure 1: Effectiveness outcomes over the first 12 weeks in the BARI and other oral systemic treatment cohorts (A) Mean EASI75 response rate at week 4 and week 12, and mean scores for (B) itch NRS, (C) skin pain NRS, and (D) ADSS item 2 over 12 weeks.](image_url)

Other Oral Systemic Cohort, including: abacavir, atorvastatin, corticosteroids, cyclosporine, methotrexate, mycophenolate mofetil, and upadacitinib. (N=49)
Table 1: Baseline Demographics and Disease Characteristics for the BARI and Other Oral Systemic Treatment Cohorts, including, azathioprine, corticosteroids, cyclosporine, methotrexate, mycophenolate mofetil, and upadacitinib

<table>
<thead>
<tr>
<th></th>
<th>BARI Cohort N=41</th>
<th>Other oral systemic Cohort, N=38</th>
<th>Overall N=89</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>42.8 (17.0)</td>
<td>34.3 (14.0)</td>
<td>38.2 (16.0)</td>
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<tr>
<td>Female, n (%)</td>
<td>22 (53.7)</td>
<td>25 (65.2)</td>
<td>47 (52.8)</td>
</tr>
<tr>
<td>Duration since AD diagnosis, years</td>
<td>27.2 (17.2)</td>
<td>25.3 (14.4)</td>
<td>26.2 (15.7)</td>
</tr>
<tr>
<td>Systemic Naive, n (%)</td>
<td>8 (19.5)</td>
<td>21 (43.1)</td>
<td>29 (32.6)</td>
</tr>
<tr>
<td>EASI</td>
<td>15.7 (11.0)</td>
<td>21.8 (11.7)</td>
<td>19.0 (11.7)</td>
</tr>
<tr>
<td>BSA</td>
<td>33.0 (22.8)</td>
<td>50.0 (27.1)</td>
<td>42.2 (26.5)</td>
</tr>
<tr>
<td>VIQ-A-D* (n)</td>
<td>23 (56.1)</td>
<td>26 (56.5)</td>
<td>49 (56.3)</td>
</tr>
<tr>
<td>3</td>
<td>10 (24.4)</td>
<td>16 (34.8)</td>
<td>26 (29.9)</td>
</tr>
<tr>
<td>Itch NRS</td>
<td>5.1 (2.2)</td>
<td>6.6 (2.3)</td>
<td>6.0 (2.4)</td>
</tr>
<tr>
<td>Skin Pain NRS</td>
<td>4.1 (2.7)</td>
<td>5.2 (2.9)</td>
<td>4.7 (2.8)</td>
</tr>
<tr>
<td>ADSS item 2</td>
<td>1.9 (1.9)</td>
<td>3.1 (3.6)</td>
<td>2.5 (3.0)</td>
</tr>
<tr>
<td>DLQI</td>
<td>14.7 (6.4)</td>
<td>16.7 (7.1)</td>
<td>15.9 (6.9)</td>
</tr>
<tr>
<td>POEM</td>
<td>11.4 (6.5)</td>
<td>16.7 (9.4)</td>
<td>14.4 (8.6)</td>
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</table>

Data are reported as mean (standard deviation) unless stated otherwise. * Two patients from the other oral systemic cohort had missing VIQ-A-D values (n=40/48).
Abstract N°: 1227

Implementation and evaluation of a patient action plan for adult patients with atopic dermatitis

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Introduction & Objectives:

Management and treatment of atopic dermatitis (AD) are complex and therefore bear the risk of therapeutic failure. Individualized patient action plans for patients have been shown to improve AD management, eczema monitoring and therapy adherence. Purpose: This project aimed at implementing a patient action plan to improve eczema management and evaluating its effects on disease severity and patient-related outcomes. Little is known about the use of patient action plans in the adult setting.

Materials & Methods:

This quality improvement project had a pre- post-test design and evaluated AD severity and patient-related outcomes after implementing a patient action plan. A convenience sample of 20 adult patients with AD were included. Socio-demographic, diagnostic and clinical variables were collected from the electronic health records. Trained staff assessed AD severity (SCORAD) and person-centered dermatology self-care index (PeDeSi-G) pre as well as one month post intervention. Patients completed dermatology life quality index (DLQI) and patient benefit index (PBI). For comparison of SCORAD, DLQI, PeDeSi-G, paired t-test was applied. PBI was presented using descriptive statistics.

Results:

Upon intervention, a significant decrease of disease severity ($p < .0001$), in parallel with a significant increase of DLQI ($p < .001$) and PeDeSi-G ($p < .0001$) was observed. A PBI $\geq 1$ was reached in 95% of participants (mean 2.73; SD 0.9).

Conclusion:

Our findings confirm the importance of providing a patient action plan for adult patients with AD. The patient action plan is an additional tool by which disease severity can be decreased and quality of life and self-management are increased. In the future, the long-term clinical effects of providing a patient action plan to patients with AD should be determined.
Effectiveness and tolerability of an emollient+ formulation in patients with xerosis or atopic dermatitis: results of a real-world observational study conducted in the United Kingdom

Flavia Aslanian1, Christos Kasparis2, Delphine Kerob3, Louisa Gayford4, Julie Whyte5, Somali Burgess6, Hiba Alkaissi4

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Introduction & Objectives:

Emollients are recommended as basic skin care in patients with any severity of atopic dermatitis (AD). Data from a previous randomized double-blind study suggest that an emollient+ plus comprising shea butter, niacinamide, mannose, Vitreoscilla filiformis biomass extract grown in thermal spring water (VFB-TSW) and Ophiopogon japonicum root extract had significantly greater improvements in pruritus versus standard emollient in patients with moderate-to-severe AD on systemic treatment.1 The impact of this emollient+ on symptom management and health-related quality of life (HRQoL) in patients with xerosis or AD was assessed.

Materials & Methods:

The current observational study included patients aged >16 years with mild-to-severe xerosis, a history of skin disease, and prone to AD. Patients with severe/very severe AD receiving oral corticosteroids or other oral immunosuppressants were excluded. The study was conducted by dermatologists in the United Kingdom. Patients were recommended to use the emollient+ once or twice daily. Patients and physicians completed questionnaires to evaluate effectiveness, satisfaction, and tolerability, while patients also assessed their HRQoL. Questionnaires were completed at baseline (Visit 1 [V1]; 0 weeks) and end-of-study (Visit 2 [V2]; typically 8–12 weeks).

Results:

In total, 98 patients were evaluated: mean (standard deviation [SD]) age, 42 (16) years; 58.2% female, with mainly either Fitzpatrick skin type II (34.7%) or IV (25.5%). AD was the most common skin condition (48.5%), followed by severe xerosis other than AD (22.7%), senile xerosis (12.4%), psoriasis (6.2%), and other skin conditions (10.3%). Mean disease duration was 21.4 (standard deviation [SD] 15.1) years for patients with AD, 21.0 (15.1) years for those with psoriasis and 6.1 (6.0) and 8.4 (8.8) years for those with senile or severe xerosis, respectively. Physicians recommended treatment over a mean (SD) of 9.2 (3.0) weeks, and twice-daily application for most patients (74.5%).

Compliance was good, with 84.7% of patients indicating daily application. Tolerability and satisfaction were high, with 83.7% of patients reporting high/excellent tolerability and 94.9% being satisfied/very satisfied with treatment. Symptoms improved following treatment, with a greater proportion of patients having no/mild symptoms at V2 (>75%) versus V1 (Table). More patients had lesion-free skin at V2 (46.9%) versus V1 (24.5%). Dermatology Life Quality Index scores showed improvement in HRQoL, with “no effect at all on patients’ lives” reported for 46.9% of patients at V2 versus 16.5% at V1.

Conclusion:

These real-world data support the clinical effectiveness of an emollient+ in patients with mild-to-severe xerosis including AD.
Reference:

1. Jaenicke T et al. EADV 2022; abstract 3490.

### Table. Clinical skin assessments, symptoms and quality of life endpoints

<table>
<thead>
<tr>
<th>Physician rating of patients’ symptoms</th>
<th>Absent/mild</th>
<th>Moderate</th>
<th>Severe/very severe</th>
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<tbody>
<tr>
<td></td>
<td>V1</td>
<td>V2*</td>
<td>V1</td>
</tr>
<tr>
<td>Skin disease intensity</td>
<td>47 (48.0)</td>
<td>76 (79.2)</td>
<td>49 (50.0)</td>
</tr>
<tr>
<td>Skin dryness</td>
<td>36 (36.7)</td>
<td>86 (89.6)</td>
<td>57 (58.2)</td>
</tr>
<tr>
<td>Pruritus</td>
<td>47 (48.0)</td>
<td>81 (84.4)</td>
<td>41 (41.8)</td>
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<tr>
<td>Intensity of daily discomfort</td>
<td>63 (64.3)</td>
<td>87 (90.6)</td>
<td>30 (30.6)</td>
</tr>
<tr>
<td>Sleep impact</td>
<td>74 (75.5)</td>
<td>90 (93.8)</td>
<td>22 (22.4)</td>
</tr>
<tr>
<td>Inflammatory lesions, (skin surface affected)</td>
<td>24 (24.5)</td>
<td>45 (46.9)</td>
<td>67 (68.4)</td>
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</table>

<table>
<thead>
<tr>
<th>DLQI score</th>
<th>None</th>
<th>&gt;0—&lt;30%</th>
<th>≥30—&lt;75%</th>
<th>≥75%</th>
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<tr>
<td></td>
<td>V1</td>
<td>V2*</td>
<td>V1</td>
<td>V2*</td>
</tr>
<tr>
<td>Inflammatory lesions, (skin surface affected)</td>
<td>24 (24.5)</td>
<td>45 (46.9)</td>
<td>67 (68.4)</td>
<td>50 (52.1)</td>
</tr>
<tr>
<td>Effect of skin condition on patients’ lives</td>
<td>16 (16.5)</td>
<td>46 (46.9)</td>
<td>32 (32.7)</td>
<td>34 (34.7)</td>
</tr>
</tbody>
</table>

Data shown are n (%) of participants.
*Data available from n=96 participants.
DLQI, Dermatology Life Quality Index; V, visit.
Abstract N°: 1267

Diagnostic value of procalcitonin in the clinical course of allergic skin diseases.

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¹Republican specialized scientific and practical medical center of dermatovenereology and cosmetology, dermatology, Tashkent, Uzbekistan

Introduction & Objectives: Procalcitonin is a 14.5 kDa prohormone and is the precursor of calcitonin. Procalcitonin is produced mainly in C-cells of the thyroid gland and neuroendocrine cells of the lungs. The lipopolysaccharide of the bacterial wall has a stimulating effect on the production of procalcitonin. In severe infection, the level of procalcitonin rises quite quickly and persists for a long time, which makes it a specific marker of bacterial infection. Purpose of the study: to study the significance of the procalcitonin test in the clinical course of allergic dermatoses.

Materials & Methods: We examined 57 patients with allergic skin diseases aged from 3 to 74 years. Among them, there were 32 females and 25 males. According to the clinical form, among 57 patients with a diagnosis of atopic dermatitis (AD), there were 40 patients and allergic dermatitis - 17. The control group (III) consisted of 23 healthy individuals of the appropriate age without skin diseases. All patients underwent clinical (determining the severity of the index SCORAD, DISHS), microbiological cultural studies of the severity of colonization, ELISA studies, statistical studies.

Results: The results of the ELISA study of the level of procalcitonin in the examined patients showed an increase in concentration in 34 out of 74 patients with allergic dermatosis compared with healthy individuals, which amounted to 45.9% of cases. Analysis of the quantitative characteristics of the level of procalcitonin averaged 0.13 ± 0.005 ng/ml. Whereas in the group of healthy individuals, this indicator averaged 0.1009 ± 0.0003 ng/ml. In patients with allergic skin diseases, an unreliable increase in the level of procalcitonin in the blood serum was noted, however, they had a direct correlation with opportunistic microorganisms St. aureus r = +0.8, St. saprophyticus – r = +0.5, St. Haemoliticus = r = +0.6 had a direct high correlation (P<0.05), opportunistic flora St. epidermidis had a noticeable correlation - r = +0.4.

Conclusion: An increase in the concentration of procalcitonin, taking into account the skin microbiome and the duration of the disease in patients with allergic dermatoses, indicates the development of a chronic superficial invasive form of a bacterial infection on the skin, which can be a pro-inflammatory mediator in determining the infectious process.
Abstract N°: 1312

Gut microbial dysbiosis is associated with intestinal barrier damage and IgE-mediated food allergy in adult patients with atopic dermatitis.

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1Medical University of Warsaw, Department of Dermatology, Warsaw, Poland, 2Medical University of Warsaw, Department of Immunopathology of Infectious and Parasitic Diseases, Warsaw, Poland, 3Polish Academy Of Sciences, Institute of Biochemistry and Biophysics, Warsaw, Poland, 4Medical University of Warsaw, Department of Clinical Immunology, Warsaw, Poland, 5Medical University of Warsaw, Warsaw, Poland

Introduction & Objectives:

Gut microbial dysbiosis is associated with altered expression of bacterial metabolites and impaired intestinal barrier function. Atopic dermatitis (AD) frequently coexists with elevated IgE and IgE-mediated food allergy related to intestinal barrier damage. The latter could be aggravated by pathogenic microbiome.

To determine the gut microbiota composition and biomarkers of gut barrier damage in adult patients with AD and to correlate these findings to 1) clinical parameters of the study group 2) serum levels of IgE (total and food-specific).

Materials & Methods:

Adult patients with active AD were involved. Disease severity was determined using EASI score. Itch severity was assessed with 12-item pruritus severity score. Gut microbiome was evaluated using 16S rRNA sequencing. The presence of specific IgE (sIgE) against food allergens was detected by immunoblotting. Serum concentrations of short-chain fatty acids (SCFA), total IgE and biomarkers reflecting gut barrier damage were determined using GC-MS method and a combination of ELISA and Luminex assays, respectively.

Results:

Fifty patients were enrolled. Alpha-diversity of the gut microbiota was significantly lower in mild than in moderate-to-severe AD and in patients with low IgE than in patients with elevated IgE. AD severity correlated negatively with mean values of SCFA and positively with indoxyl. The presence of food allergy was associated with higher severity of AD and itch (EASI, 12-item pruritus severity score). In patients with food allergy, mean values of SCFA and IL-22 were lower, and levels of LBP and IL-10 were higher than in patients without food allergy.

Conclusion:

The results suggest that gut microbial dysbiosis is associated with intestinal barrier damage and increased risk of IgE-mediated sensitization which possibly translates to increased AD severity. This could point to a possible role of dietary interventions in alleviating the symptoms of AD.
Efficacy and safety of Jaktinib, a novel JAK inhibitor in the treatment of patients with Moderate to Severe Atopic Dermatitis: a randomized, double-blind, placebo-controlled phase II study

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Introduction & Objectives:

Atopic Dermatitis (AD) is a chronic, relapsing inflammatory skin disease characterized by eczematous lesions associated with intense pruritus. The JAK-signal transducer and activator of transcription (JAK-STAT) signaling pathway has recently been implicated in AD. Jaktinib, a novel JAK inhibitor has shown promising therapeutic activities in several indications. We present here the preliminary data from a randomized, double-blind, placebo-controlled and multicenter phase 2 study, which evaluated the efficacy and safety of Jaktinib in patients with moderate to severe AD (NCT04539639).

Materials & Methods:

This was a two-stage phase 2, double-blind, placebo-controlled trial. In the main stage, 166 adult subjects with moderate to severe AD were randomized in a ratio of 2:2:2:1 to receive 50 mg Bid, 75 mg Bid, 100 mg Bid Jaktinib, or placebo for 12 weeks (wk). In the extended stage (13-24 wk), subjects in the placebo group were randomly assigned to receive Jaktinib 50 mg Bid, 75 mg Bid, or 100 mg Bid treatments at a ratio of 1:1:1, the Jaktinib group subjects maintained the original dose. The primary endpoint was the proportion of subjects achieving EASI-50 response at wk 12. The key secondary endpoints were EASI-75 and IGA response at wk 16. Adverse events were recorded throughout the treatment.

Results:

Patients (N=166) were enrolled from November 26, 2020, to May 19, 2022, wherein 165 were analyzed for efficacy and safety (50 mg Bid Jaktinib group, n=47; 75 mg Bid Jaktinib group, n=47; 100 mg Bid Jaktinib group, n=49; placebo group, n=22). Demographics and baseline characteristics were balanced across the arms. The median (range) baseline EASI score was 22.9 (16.0–65.4), BSA was 36.8% (11.0–100.0%), NRS was 7.0 (4–10) points. IGA score was 3 (moderate), 4 (severe), or 5 (extremely severe) in 95 (57.6%), 64 (38.8%), and 6 (3.6%) patients,
respectively. Most patients (90.4%) completed the 12-week treatment. At wk 12, an EASI-50 response was observed in 80.9% (38/47), 72.3% (34/47), and 65.3% (32/49) in the Jaktinib 50-, 75-, and 100- mg Bid group, respectively, versus 54.5% (12/22) of the placebo group (p=0.016, 0.094, and 0.409). At wk 16, an EASI-75 response was observed in 64.4% (29/45), 65.1% (28/43), and 71.4% (30/42) of the Jaktinib 50-, 75-, 100-mg Bid group, an IGA response was observed in 24.4% (11/45), 41.9% (18/43), and 35.7% (15/42), respectively. During the 12-wk treatment, adverse events were reported in 80.9% (38/47), 76.6% (36/47), and 85.7% (42/49) of patients in the Jaktinib 50-, 75-, and 100- mg Bid group, respectively, versus 50.0% (11/22) of the placebo group. The adverse events were Grade 1 or 2 (based on CTCAE version 5.0) in most cases. No serious adverse event was reported. In the extended stage, the AE profile was similar to the main stage.

**Conclusion:**

Jaktinib showed a high efficacy and good safety profile in adult patients with moderate to severe AD. Jaktinib 75mg twice a day and 100mg twice a day showed a better efficacy.
Abstract N°: 1383

Effectiveness and safety of Upadacitinib in the treatment of patients with moderate-to-severe atopic dermatitis included in the early access program in France

Ziad Reguiai, Marie Jachiet, Anne Benedicte Duval Modeste, Audrey Lamirand, Sébastien Barbarot, Pierre-André Becherel

Courlancy-Bezannes Polyclinic, Department of Dermatology, Reims, France, University of Paris, Faculty of Medicine, AP-HP, Saint-Louis Hospital, Department of Dermatology, Paris, France, University Hospital Rouen, Department of Dermatology, Rouen, France, Abbvie, Department of Medical Affairs, Rungis, France, Nantes University, University Hospital, PhAN Nantes, INRAE, UMR 1280, Department of Dermatology, Nantes, France, Antony Private Hospital, PARIS VI University, Clinical Dermatology and Immunology Unit, Antony, France

Introduction & Objectives

Previous clinical trials demonstrated the efficacy and safety of upadacitinib (UPA) in the treatment of patients with moderate-to-severe atopic dermatitis (AD). Before European market approval and reimbursement, UPA was thus made available in France as part of an early access program (EAP) including nominative then cohort Temporary Authorization for Utilization (nATU and cATU) finally converted in Early Access Authorization (EAA) for the treatment of moderate-to-severe AD. This EAP provided early real-life data on UPA effectiveness and tolerability in this indication.

Materials & Methods

Eligible patients were adults and adolescents ≥12 years with moderate-to-severe AD, who were candidates for systemic therapy, after failure, intolerance, or contraindication to reimbursed available treatments. Data were collected at UPA initiation, month (M) 1, M3, and then every 3 months. Patient and disease characteristics, effectiveness and tolerability of UPA were described.

Results

Between March 17th 2021 and November 22nd 2022, 267 patients, included by 90 dermatologists throughout France, received UPA for AD in the context of a cATU or EAA, including 107 patients since nATU. At UPA initiation, the mean age of patients was 35±14 years (<18 years: 5%), and 60% were male patients. The median duration of AD was 23.2 years (IQR 8.8-33.8) and all patients received at least one prior treatment for AD: dupilumab (93%), ciclosporin (69%), methotrexate (43%) and/or baricitinib (32%). Overall, 96% of patients had moderate-to-severe AD at UPA initiation [based on SCORing Atopic Dermatitis (SCORAD) >25 or Eczema Area and Severity Index (EASI) >7]. UPA was started at the dosage of 15 mg in 85% of patients, and in combination with other topical AD treatments in 27% of patients (topical corticosteroids (TCS) 23%, topical tacrolimus (TT) 8%). Worth noting, the dosage of 15 mg was the only dose allowed for initiation over the cATU interval (between March 17th 2021 and November 24th 2021). Over follow-up, the median duration of UPA treatment was 10.3 months (IQR 5.3-19.2) and it was combined with topical AD treatments in 31% of patients (TCS: 27%, TT: 10%). At least one change in UPA dosage was reported in 29% of patients (increase: 27%, decrease: 5%). An improvement in AD since the last visit (as assessed by physicians) was reported up to M9 in the majority of patients (between UPA initiation and M1: 81%, M1-M3: 78%, M3-M6: 60%, M6-M9: 58%). Median SCORAD was 50 at initiation (range: 20-100) and 18 at M1 (range: 0-85). Median EASI was 18 at initiation (range: 1 - 58) and 10 at M1 (range: 0-45). An improvement in pruritus was also measured as early as M1 (median NRS pruritus: 7 at initiation and 3 at M1). Overall, 25 patients (9%) definitively stopped UPA treatment during follow-up in cATU/EAA, mainly due to treatment failure (11
patients, 44% of the cases). From March 17th 2021 to December 30th 2022, 261 adverse effects (AEs) were reported including 8 serious and 253 non-serious AEs. The most frequent AEs were acne, atopic dermatitis and eczema. No new safety signals were identified during the reporting interval. Safety data and information obtained during the reporting interval continues to support the positive benefit-risk profile of UPA.

**Conclusions**

Data from UPA-treated AD patients in the French early access program confirm UPA effectiveness in a real-life setting, with a quick reduction in disease severity and pruritus. Safety was consistent to that observed in previous clinical trials.
Abstract N°: 1385

Patient-reported outcomes in 8 patients with atopic dermatitis treated with upadacitinib in a Spanish hospital.

Marta Elosua Gonzalez1, Marta Loro1, Ángel Manuel Rosell-Díaz2, Paula Andújar1, María Mercedes Sigüenza-Sanz1, Elena López Negrete1, Lucía Turrión Merino1, Constanza Martinez-Mera1, Fernando Alfageme Roldán1, Rita Cabeza Martínez1, Irene Salgüero1, Ángela María García Miñarro1, Mercedes Hospital1, Gaston Roustan1

1Puerta de Hierro Majadahonda University Hospital, Dermatology, Majadahonda, Spain

Introduction & Objectives: Upadacitinib is a small molecule JAK inhibitor with increased selectivity for JAK1 over JAK2, JAK3, and tyrosine kinase 2. Its use has been recently approved for the treatment of atopic dermatitis (AD) both in Europe and the United States. This study aims to present the clinical evolution and patient-reported outcomes (PROs) of 8 patients with atopic dermatitis treated with upadacitinib in a Spanish hospital, at the 24 and 52-week follow-up.

Materials & Methods: At the beginning of treatment, an evaluation was performed in which demographic, clinical, and patient-reported outcomes of AD were collected. The disease severity was measured by EASI score, and the PROs where Dermatology Life Quality Index (DLQI), Atopic Dermatitis Control Tool (ADCT), Patient-oriented Eczema Measure (POEM), and Numerical Rating Scale Pruritus (NRS Pruritus) scales. The evaluation was repeated at weeks 24 and 52 of treatment.

Results: The mean age of the sample was 31.8 years (15-47), and 5 patients (62.5%) were male. The mean years of disease duration were 14.4 years (10-20). 3 of the patients (37.5%) received 15 mg per day. All had received previous systemic treatment: cyclosporine (87.5%), narrowband UVB phototherapy (62.5%), methotrexate (50%), dupilumab (37.5%), and 1 patient baricitinib and omalizumab. At baseline visit, the mean score of the EASI scale was 30 (SD 7.3) points. The mean score of NRS Pruritus was 7.4 (SD 0.8), the mean score in DLQI was 10.5 points (SD 1.5), in ADCT 12.3 points (SD 2.7), and in the POEM scale was 23.2 (SD 1.5). All patients reached 24 weeks of treatment, although in two cases the corresponding evaluation was not carried out. Evaluating the remaining 6 cases, a mean of 9.6 points (SD 14.4) on the EASI scale was obtained. The mean score for NRS Pruritus was 1.8 (SD 1.7), 1.8 (SD 1.8) on the DLQI scale, 0 on the ADCT scale, and 6.5 points on the POEM scale (SD 9.7). One patient discontinued treatment due to lack of efficacy and 4 patients reached 52 weeks of treatment. At this point, the mean score on the EASI scale was 5.9 (SD 2.9). The mean score for NRS Pruritus was 2.5 (SD 1.6), 1.7 (SD 0.9) on the DLQI scale, 1.7 on the ADCT scale (SD 0.9), and 4.3 on the POEM scale (SD 2.2). Five patients had minor adverse events which did not lead to discontinue the treatment (2 acne, 2 uncomplicated herpes simplex and 1 increase in triglycerides in week 12 which subsequently normalized).

Conclusion: Upadacitinib represents an effective treatment for severe AD. After 24 weeks of follow-up, patients perceived improvements in the severity of their AD as well as in their PROs, which are maintained after 52 weeks of treatment.
Abstract N°: 1494

**Survival, efficacy and safety of tralokinumab after 32 and 52 weeks of treatment for moderate-to-severe atopic dermatitis in adults: a multicentre real-world study**

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**Introduction & Objectives:** Tralokinumab a fully human monoclonal antibody inhibiting signalling of IL-13, is a new treatment for adult patients with moderate-to-severe atopic dermatitis (AD). Trials investigating tralokinumab long-term efficacy and safety are ongoing. We conducted a 16-week real-life case series study in AD adults receiving tralokinumab. No real-world studies both at week 32 and 52 have yet been reported. Herein, we extended the same case series analysis of AD patients beyond 16 weeks, together with data of AD patients referring to 5 dermatological centres, to evaluate tralokinumab drug survival, efficacy and safety up to week 32 and 52.

**Materials & Methods:** This prospective cohort study included all consecutive adult patients with moderate-to-severe AD receiving tralokinumab for at least 4 weeks. The first patient was recorded in April 2022; the last one in March 2023. Drug survival was assessed using Kaplan-Meier survival analysis. Eczema Area and Severity Index (EASI), Itch (Numerical Rating Scale) NRS, sleep NRS, Dermatology Life Quality Index (DLQI), and Adverse events (AEs) were assessed at each visit. Descriptive data were generated using mean and standard deviation (SD) or median as well as absolute numbers and proportions. P values were significant at P < .05.

**Results:** 171 patients (98 F, 57.3%; mean (SD) age 40.6 (17.4) years) were included (Table 1). By the data lock, 96.5% patients were still using tralokinumab, while 6 patients had permanently discontinued it, due to psoriasis, inefficacy, AD remission, and pregnancy. The tralokinumab survival rate at week 52 was 85.9%. There was a continuous improvement in EASI, itch NRS, sleep NRS, and DLQI from week 16 to week 52 of tralokinumab treatment (Figure 1). The mean EASI (24.4 at baseline) decreased to 1.6 at week 32 and to 1.1 at week 52, with a mean percentage decrease of 93.4% and 95.5%, respectively. The mean percentage reduction of itch NRS (mean value 7.7 at baseline, 1.6 at week 32 and 1.3 at week 52) was 79.2% at week 32 and 83.1% at week 52. The mean percentage reductions of sleep NRS (mean value 6.1 at baseline, 0.7 at week 32 and 0.8 at week 52) were 88.5% and 86.8%, respectively. The mean percentage reductions in DLQI score (13.2 at baseline, 2.4 at week 32 and 1.5 at week 52) were 81.8% and 88.6%, respectively. All the mean percentage reductions were statistically significant (p <0.01). 100% (61/61) of patients reached EASI-50, 95.1% (n=58/61) reached EASI-75 and 73.8% (n=45/61) reached EASI-90 at week 32. After 52 weeks, the proportion of patients achieving EASI-50, EASI-75, and EASI-90 was 100% (n=22/22), 95.4% (n=21/22), and 95.4% (n=21/22), respectively. AEs were reported 5.3% patients, including injection-site reaction (5/171), conjunctivitis (3/171), psoriasis (2/171), herpes viral infection (1/171), and erythroderma (1/171).

**Conclusion:** Our results support a good survival of tralokinumab after 32 and 52 weeks. Tralokinumab maintained long-term control of AD signs and symptoms and was well-tolerated. This is a long-term prospective cohort study with limited sample size; additional real-world studies are needed to increase the reliability of our findings.
Table 1. Baseline demographic and clinical characteristics of the study population.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total (%), Total (n)</td>
<td>171 (100)</td>
</tr>
<tr>
<td>Sex (%)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>98 (57.3)</td>
</tr>
<tr>
<td>Male</td>
<td>73 (42.7)</td>
</tr>
<tr>
<td>Age, years, mean (SD)</td>
<td>40.6 (17.4)</td>
</tr>
<tr>
<td>BMI, mean (SD)</td>
<td>23.8 (3.1)</td>
</tr>
<tr>
<td>Age at AD onset (%)</td>
<td></td>
</tr>
<tr>
<td>Early onset (&lt;18 years)</td>
<td>113 (66.1)</td>
</tr>
<tr>
<td>Late onset</td>
<td>58 (33.9)</td>
</tr>
<tr>
<td>AD duration, years, mean (SD)</td>
<td>21.8 (13.4)</td>
</tr>
<tr>
<td>AD Phenotype (%)</td>
<td></td>
</tr>
<tr>
<td>Classical</td>
<td>127 (74.3)</td>
</tr>
<tr>
<td>Prurigo</td>
<td>30 (17.5)</td>
</tr>
<tr>
<td>Generalized Lichenoid</td>
<td>3 (1.7)</td>
</tr>
<tr>
<td>Generalized inflammatory</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>Nummular</td>
<td>9 (5.3)</td>
</tr>
<tr>
<td>Erythroderma</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Immunosuppressive drug history (%)</td>
<td></td>
</tr>
<tr>
<td>no prior immunosuppressive drug</td>
<td>25 (14.6)</td>
</tr>
<tr>
<td>1 prior immunosuppressive drug</td>
<td>91 (53.2)</td>
</tr>
<tr>
<td>≥ 2 prior immunosuppressive drugs</td>
<td>55 (32.2)</td>
</tr>
<tr>
<td>Baseline systemic immunosuppressants</td>
<td>28 (16.4)</td>
</tr>
<tr>
<td>Baseline topical immunosuppressants</td>
<td>153 (89.5)</td>
</tr>
<tr>
<td>Atopic comorbidities (%)</td>
<td></td>
</tr>
<tr>
<td>Allergic rhinitis</td>
<td>65 (38.0)</td>
</tr>
<tr>
<td>Allergic conjunctivitis</td>
<td>50 (29.2)</td>
</tr>
<tr>
<td>Allergic asthma</td>
<td>40 (23.4)</td>
</tr>
<tr>
<td>Food allergy</td>
<td>17 (9.9)</td>
</tr>
<tr>
<td>Other comorbidities (%)</td>
<td></td>
</tr>
<tr>
<td>Diabetes</td>
<td>5 (2.9)</td>
</tr>
<tr>
<td>Alopecia areata</td>
<td>2 (1.2)</td>
</tr>
<tr>
<td>Autoimmune thyroiditis</td>
<td>9 (5.3)</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>3 (1.8)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>26 (15.2)</td>
</tr>
<tr>
<td>Cancer</td>
<td>3 (1.8)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>3 (1.8)</td>
</tr>
</tbody>
</table>

**Abbreviations:** SD: Standard Deviation; BMI: Body Mass Index; AD: Atopic Dermatitis

Figure 1. Median percentage improvement in EASI, itch NRS, sleep loss NRS, and DLQI from baseline through 52 weeks of tralokinumab treatment.
The impact of self-reported itch on the total score of commonly used atopic dermatitis severity scores - data from an observational study of remote AD severity assessment

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Introduction & Objectives:

Itch is one of the most debilitating symptoms of atopic dermatitis (AD), and it has a significant impact on the quality of life (QoL) of individuals with this condition. Several studies have investigated the relationship between itch and various aspects of AD severity, including skin lesion characteristics, disease extent, and QoL, but the perceived impact of itch on the global health of the individual patient may be underestimated by physicians. The aim of this study is to explore the relation between itch and other AD related signs and symptoms.

Materials & Methods:

Data from an observational study evaluating the reliability of remote assessment of AD compared to in-person assessment was analysed post-hoc. The study involved calculation of the Eczema Area and Severity Index (EASI), SCORing Atopic Dermatitis (SCORAD), and Investigator’s Global Assessment (IGA) scores for each participant by two on-site investigators. Following the visit, the participants submitted photos of their lesions, self-reported body surface area (BSA) and symptoms (itch and trouble sleeping, both rated on an 11-point NRS scale), which were used to remotely assess the composite scores. In this post-hoc analysis, the correlation between self-reported itch severity and various components of the AD severity scores was evaluated using the Pearson correlation coefficient.

Results:

A total of 88 participants were analyzed as shown in Table 1. Of these, 67 were female, the mean age was 35 (SD: 15.1) years, the mean age of onset of AD was 6.8 (SD: 10.7) years.

The results revealed a significant correlation between itch and the three composite severity scores, with a moderate correlation observed for SCORAD ($r=0.53$, $p<0.0001$) and IGA ($0.48$, $p<0.0001$) and a modest correlation with the EASI score ($r=0.23$, $p=0.02$), meaning that itch severity is explaining 28, 23, and 5% of the variation in the reported scores, respectively. A strong positive correlation was found between itch and trouble sleeping. The only significant correlation observed among the intensity elements used for SCORAD and itch was with erythema ($r=0.45$, $p<0.0001$). A moderate and significant correlation ($0.40$, $p=0.02$) was found between the age of onset of AD and itch.

Conclusion:

The present study provides important insights into the relationship between itch and various aspects of AD severity scores. The strong correlation between itch intensity and IGA score highlights the importance of considering itch as a key symptom in the assessment of AD severity. The significant correlation between itch and trouble sleeping suggests that itch may be the culprit in sleep interference, and may have a significant impact on
the QoL of individuals with AD. The data indicates that itch is a modestly important element in the SCORAD and IGA assessments, and a minor element of the EASI score. In conclusion, this study provides information that may facilitate further research, and aid in the development of new strategies for the assessment and management of AD-associated itch.
Real-world case series of upadacitinib in adults with severe atopic dermatitis

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¹Ramón y Cajal Hospital, Dermatology, Madrid, Spain

Introduction & Objectives:

Upadacitinib is an oral Janus kinase (JAK) inhibitor approved by the European Medicine Agency for the management of moderate to severe atopic dermatitis (AD) of patients aged ≥ 12 years and candidates to systemic therapy. Its efficacy and security have been demonstrated in clinical trials (Measure Up), however, real clinical practice experience is still lacking in the literature.

Materials & Methods:

We performed a retrospective cohort collecting data from twelve adults with severe atopic dermatitis treated with upadacitinib 30 mg per day in our center. Effectiveness was measured by reduction of two points in the validated Investigator’s Global Assessment for atopic dermatitis (vIGA-AD) and patients reaching Eczema Area and Severity Index (EASI) 75 at week 4, week 12 and week 24. All treatment-emergent adverse events (AE) were collected.

Results:

The mean age of the subjects included in the cohort was 30.92 years. All of them had been treated with corticosteroids and cyclosporine, and 83.3% had received dupilumab without achieving acceptable control, which was the reason for discontinuation in all of them. One of them had been treated with baricitinib with poor symptom control. The rest of the characteristics of the included population are shown in Table 1.

Regarding effectiveness, all patients reported rapid pruritus relief, which in 75% of patients was absolute; in these patients the mean time to control was 3.78 ± 1.86 days. At baseline, the mean ± standard deviation (SD) values for EASI and IGA-AD were 30.24 ± 7.5 and 3.58 ± 0.5 respectively. EASI 75 was reached by 91.7%, 83.3% and 75% of patients at weeks 4, 12 and 24, respectively. Decline of 2 or more points on the IGA-AD scale was reached by 83.3%, 75% and 75% at weeks 4, 12 and 24, respectively. The mean values ± SD of both scales during follow-up can be found in Table 2.

Regarding the collected adverse effects, all patients presented at least one mild AE. Analytically, all patients presented slight elevation of CK at some time during follow-up; other findings were hypercholesterolemia (50%), hypertriglyceridemia (16.7%) and mild elevation of hepatic transaminases (8.3%). Regarding infectious disorders, one of them suffered a multimetameric herpes zoster episode that did not require hospitalization. No severe clinical or analytical AE were recorded. All the reported AE are detailed in Table 3.

Conclusion:

Our efficacy findings are consistent with those reported in previously performed clinical trials, as well as with previous real clinical practice reports. Regarding AE prevention we emphasize the importance of including herpes zoster vaccination in routine clinical practice prior to the initiation of upadacitinib.

The strength of our study lies in it being a real-life experience and in the fact that the included patients suffer AD refractory to multiple therapies. Limitations include the low number of patients included and the relatively short
Table 1. Baseline clinical and demographics features patients with severe atopic dermatitis treated with upadacitinib.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, n</td>
<td>12</td>
</tr>
<tr>
<td>Age, years; mean ± SD</td>
<td>30.92 ± 12.40</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>5 (41.7)</td>
</tr>
<tr>
<td>AD duration, years; mean ± SD</td>
<td>25.33 ± 12.26</td>
</tr>
<tr>
<td>Renal disease, n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Liver disease, n (%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Atopic comorbidities, n (%)</td>
<td></td>
</tr>
<tr>
<td>Rhinitis</td>
<td>6, (50)</td>
</tr>
<tr>
<td>Asthma</td>
<td>7, (50)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>6, (50)</td>
</tr>
<tr>
<td>Food allergy</td>
<td>10, (83.3)</td>
</tr>
<tr>
<td>Any</td>
<td>11, (91.7)</td>
</tr>
<tr>
<td>Contact dermatitis, n (%)</td>
<td>2, (16.7)</td>
</tr>
<tr>
<td>Prior topical medications for AD, n (%)</td>
<td></td>
</tr>
<tr>
<td>Emollients</td>
<td>12, (100)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>12, (100)</td>
</tr>
<tr>
<td>Calcineurin inhibitors</td>
<td>12, (100)</td>
</tr>
<tr>
<td>Prior systemic treatments for AD, n (%)</td>
<td></td>
</tr>
<tr>
<td>Banimotin</td>
<td>1, (8.3)</td>
</tr>
<tr>
<td>Ciclosporin</td>
<td>12, (100)</td>
</tr>
<tr>
<td>Metotrexate</td>
<td>3, (25)</td>
</tr>
<tr>
<td>Corticosteroids</td>
<td>12, (100)</td>
</tr>
<tr>
<td>Number of cycles; mean ± SD</td>
<td>4.92 ± 1.24</td>
</tr>
<tr>
<td>NB-UVB phototherapy</td>
<td>4, (33.3)</td>
</tr>
<tr>
<td>Dupilumab</td>
<td>10, (83.3)</td>
</tr>
<tr>
<td>Reason for dupilumab discontinuation</td>
<td></td>
</tr>
<tr>
<td>Loss of efficacy</td>
<td>10, (100)</td>
</tr>
<tr>
<td>Dupilumab treatment duration before discontinuation, weeks; mean ± SD</td>
<td>48.90 ± 31.82</td>
</tr>
<tr>
<td>Baseline</td>
<td></td>
</tr>
<tr>
<td>EASI, mean ± SD</td>
<td>30.24 ± 7.5</td>
</tr>
<tr>
<td>IGA-AD; mean ± SD</td>
<td>3.59 ± 0.5</td>
</tr>
</tbody>
</table>

| SCORAD, mean ± SD                        | 57.09 ± 6.9     |
| Pruritus NRS; mean ± SD                  | 6.25 ± 2.1      |
| BSA; mean ± SD                           | 41.75 ± 23.1    |

AD, atopic dermatitis; NB-UVB, narrowband ultraviolet B; EASI, Eczema Area and Severity Index; IGA-AD, Investigator’s Global Assessment for atopic dermatitis; SCORAD, SCORing Atopic Dermatitis; NRS, numerical rating scale; BSA, body surface area.
Table 2. Effectiveness data of upadacitinib in patients with severe atopic dermatitis.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Week 4</th>
<th>Week 12</th>
<th>Week 24</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>EASI; mean ± SD</td>
<td>30.24 ± 7.5</td>
<td>3.17 ± 3.6</td>
<td>4.58 ± 3.0</td>
<td>6.87 ± 6.2</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>IGA-AD; mean ± SD</td>
<td>3.58 ± 0.5</td>
<td>0.83 ± 0.9</td>
<td>1.25 ± 0.7</td>
<td>1.56 ± 1.0</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

EASI, Eczema Area and Severity Index; IGA-AD, Investigator’s Global Assessment for atopic dermatitis.

Table 3. Safety data in patients with severe atopic dermatitis treated with upadacitinib.

<table>
<thead>
<tr>
<th>Adverse effect</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acne</td>
<td>7 (58.3)</td>
</tr>
<tr>
<td>Headache</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>Conjunctivitis</td>
<td>3 (25.0)</td>
</tr>
<tr>
<td>Gastrointestinal discomfort</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>Malaise</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Epistaxis</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Severe</strong></td>
<td></td>
</tr>
<tr>
<td>Cardiovascular events</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Thromboembolic events</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Laboratory findings</strong></td>
<td></td>
</tr>
<tr>
<td>Hypercholesterolemia</td>
<td>6 (50)</td>
</tr>
<tr>
<td>Hypertriglyceridemia</td>
<td>2 (16.7)</td>
</tr>
<tr>
<td>Transaminase elevation</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>CK elevation</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Renal function deterioration</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Anemia</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Leukopenia</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Thrombocytosis</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Infectious</strong></td>
<td>12 (100)</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>1 (8.3)</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Upper respiratory tract infections</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>Mucocutaneous candidiasis</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Herpes simplex reactivation</td>
<td>4 (33.3)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0 (0)</td>
</tr>
<tr>
<td><strong>Any AE</strong></td>
<td>12 (100)</td>
</tr>
</tbody>
</table>

AE, adverse effect; CK, creatin kinase.
Abstract N°: 1540

Sustained Dupilumab Efficacy in Adult Patients with Moderate-to-Severe Atopic Dermatitis Transitioning From Weekly to Every Other Week Dosing: Results From a 5-Year Open-Label Extension Trial

Lisa A. Beck, Robert Bissonnette, Mette Deleuran, Takeshi Nakahara, Ryszard Galus, Faisal A. Khokhar, Anna Coleman, Guy Gherardi, Jing Xiao, Robert Dingman, Christine Xu, Elena Avetisova, Ariane Dubost-Brama, Arsalan Shabbir

1University of Rochester Medical Center, Rochester, NY, United States, 2Innovaderm Research, Montreal, QC, Canada, 3Aarhus University Hospital, Aarhus, Denmark, 4Kyushu University, Fukuoka, Japan, 5Medical University of Warsaw, Warsaw, Poland, 6Regeneron Pharmaceuticals Inc., Tarrytown, NY, United States, 7Regeneron Pharmaceuticals Inc., Dublin, Ireland, 8Sanofi, Reading, United Kingdom, 9Sanofi, Bridgewater, NJ, United States, 10Sanofi, Chilly-Mazarin, France

Introduction & Objectives: Atopic dermatitis (AD) is a chronic systemic inflammatory disease requiring long-term management. Systemic immunosuppressive treatments for moderate-to-severe AD are not recommended for continuous use due to safety concerns. We evaluated the long-term maintenance of efficacy in the subgroup of adult patients with moderate-to-severe AD who switched from weekly (qw) to every other week (q2w) 300 mg dupilumab treatment during a 5-year, open-label extension (OLE) study.

Materials & Methods: The LIBERTY AD OLE 5-year study (NCT01949311) enrolled adults with moderate-to-severe AD who had participated in any dupilumab parent study (phase 1 through phase 3). In 2019, patients transitioned from 300 mg dupilumab qw to q2w to align with approved dosage. Concomitant topical treatments were permitted. Data shown are presented as observed for Eczema Area and Severity Index (EASI) and Investigator’s Global Assessment (IGA), or reported for Peak Pruritus Numerical Rating Scale (PP-NRS) for the full population switching from dupilumab 300 mg qw to 300 mg q2w (N = 226).

Results: The cohort of patients that transitioned from 300 mg qw to q2w (N = 226) had an initial exposure duration of at least 3 years to 300 mg qw. Subsequently, 222 (98.2%) patients received the q2w dosing regimen for ≥ 24 weeks, with mean (standard deviation) q2w exposure of 66.4 (21.6) weeks, and median q2w treatment exposure of 66.0 weeks. Patients at the time of transition vs 48 weeks post transition and at the end of study period showed stable median EASI scores (0.3 vs 0.25 and 0.4, respectively) and proportion of patients achieving IGA score of 0/1 (75.2% vs 76.3% and 77.4%, respectively). Median PP-NRS score was consistent in patients between the time of transition vs 48 and 88 weeks post transition (2.0 vs 2.0 and 2.0, respectively). Dupilumab was generally well tolerated, with an acceptable safety profile.

Conclusion: In this long-term OLE, dupilumab showed sustained efficacy following dose regimen transition from 300 mg qw to q2w, with stable signs and symptoms post switch (including skin lesions and pruritus). Safety was consistent with the known dupilumab safety profile previously observed in controlled studies.
Abstract N°: 1559

**Real-world effectiveness and safety of baricitinib and its effect on biomarkers and laboratory data concerning its safety in Japanese adult patients with atopic dermatitis: A single-center retrospective study**

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**Title:** Real-world effectiveness and safety of baricitinib and its effect on biomarkers and laboratory data concerning its safety in Japanese adult patients with atopic dermatitis: A single-center retrospective study

**Introduction & Objectives:** Baricitinib demonstrated efficacy and tolerable safety in clinical trials for atopic dermatitis (AD); however, real-world data are limited. We examined the effectiveness and safety of baricitinib, and laboratory data in AD patients treated with baricitinib in our department.

**Materials & Methods:** All adult AD patients treated with baricitinib in our department between January 2021 and February 2023 were included. Data were collected retrospectively from patients’ charts. This study was approved by the Institute Institutional Review Board of our university.

**Results:** Data on 30 Japanese AD patients (10 females, 20 males) were analysed. The mean age was 31.8 ± 11.4 (standard deviation) years. Regarding systemic therapies within six months before initiating baricitinib, nine patients had received dupilumab, three patients had received cyclosporine, and one patient had received upadacitinib. 28 patients received 4 mg/day of baricitinib, while two received 2 mg/day. Objective severity scores and patient-reported outcomes significantly improved at 1 and 3 months, except for the affected body surface area (BSA) at 1 month. The proportions of patients who achieved eczema area and severity index (EASI)-50% improvement were 30.0% (9/30) at 1 month and 53.3% (16/30) at 3 months; the proportions who achieved EASI-75% improvement were 20.0% (6/30) at 1 month and 23.3% (7/30) at 3 months. There were no significant changes in AD biomarkers. Regarding laboratory findings concerning the safety of baricitinib, no significant changes were observed except for increased serum creatine phosphokinase (CPK) levels at 3 months. 6 patients (20%) discontinued baricitinib within 3 months (2 in 1 month, 4 in 3 months) due to insufficient efficacy; 4 of them switched to upadacitinib and 2 switched to dupilumab. As for adverse effects, acne and/or folliculitis was observed in 7 patients (23.3%), elevated serum CPK levels in 7 patients (23.3%), elevated liver enzymes in 1 patient (3.3%), and elevated total bilirubin in 1 patient (3.3%). No patient discontinued baricitinib due to these adverse effects. One case (3.3%) of herpes zoster was observed after 3 months of administering baricitinib, leading to discontinuation of baricitinib. One case (3.3%) of ocular herpes was observed after 3 months of administering baricitinib, leading to dose reduction.

**Conclusion:** Our study demonstrated favorable laboratory data in AD patients receiving baricitinib in the real-world setting. Its effectiveness and safety profiles were similar to those obtained in clinical trials. Our study indicated that AD biomarkers did not reflect clinical improvement during baricitinib treatment.
Abstract N°: 1586

Long-term effectiveness of dupilumab in adult patients with atopic dermatitis: a retrospective study

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Introduction & Objectives:

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by the presence of eczematous lesions, xerosis and intense pruritus. Dupilumab is indicated in moderate-to-severe AD patients from 12 years and in patients with severe AD from 6 months of age, who are candidates for systemic therapy. The primary objective of this study was to evaluate the real-world persistence of dupilumab in adult patients with moderate-to-severe AD in a multicentre analysis in Comunidad Valenciana (Spain). Secondary objectives of the study were to analyse the effectiveness and safety of dupilumab in the same cohort of patients.

Materials & Methods:

This retrospective cohort study used registries and medical records from 5 different hospitals. Adults with moderate-to-severe AD who initiated dupilumab treatment at any date (first dispensation was considered the index date) were identified and followed-up until December 31, 2021, or discontinuation. Baseline demographic and clinical characteristics studied included: sex, age at diagnosis, current age, time from AD diagnosis, previous treatments, and comorbidities. To analyse the effectiveness of dupilumab we analysed the eczema area and severity index (EASI) and investigator global assessment (IGA) scores at baseline and during the follow-up period in different age ranges (18-35, 35-65 and >65 years).

Results:

The patients included in the study (N = 251) were 59.4% male with 64.4% of patients having at least one atopic comorbidity. Mean time and standard deviations from AD diagnosis was 14.5 ± 14.8 years. Over half (51.4%) of included patients were ≥18 years of age at diagnosis and had been receiving dupilumab for one year or longer at the time of follow-up. Baseline mean EASI and median IGA scores were 27.9 ± 14.8 and 4.0 ± 0.5, respectively. Basal values of these parameters according to age ranges are shown in Table 1. Dupilumab treatment resulted in a fast (16 weeks) and statistically significant improvement (p < 0.0001) in both parameters. After 16 weeks of treatment, we analysed 201 y 210 patients with EASI and IGA data respectively, of these, 70.6% (n=142) and 54.7% (n=115) of patients reached EASI ≤7 and IGA ≤1, respectively. After one year of treatment, we analysed 135 y 136 patients with EASI and IGA data respectively, of these, 76.3% (n=103) of patients reached minimal activity AD (EASI ≤3) and 38.2% (n=52) had complete AD clearance (IGA = 0). Our results showed consistency across all age ranges studied (Figure 1). During the study, 15.1% patients discontinued dupilumab treatment.
Dupilumab persistence at 1-year, 2-year, 3-year, and 4-year was 89%, 78%, 75% and 71%, respectively. The observed safety was consistent with the known safety profile of dupilumab.

**Conclusion:**

Dupilumab is an effective treatment for patients with moderate-to-severe AD in all assessed age groups with a favourable safety profile.

**Table 1.** Baseline EASI and IGA scores according to patient age at follow-up.

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>n (%)</th>
<th>Mean EASI</th>
<th>Mean IGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>18-35</td>
<td>101 (40,2)</td>
<td>28,3</td>
<td>3,6</td>
</tr>
<tr>
<td>36-65</td>
<td>109 (43,4)</td>
<td>27,0</td>
<td>3,5</td>
</tr>
<tr>
<td>&gt;65</td>
<td>41 (16,3)</td>
<td>19,0</td>
<td>3,7</td>
</tr>
<tr>
<td>Total</td>
<td>251 (100)</td>
<td>27,9</td>
<td>3,6</td>
</tr>
</tbody>
</table>

EASI: eczema area and severity index; IGA: investigator global assessment.

**Figure 1.** Number of patients and mean evolution at baseline and during follow-up of (A) EASI and (B) IGA scores according to age group.
Systemic Therapies for Moderate-to-Severe Atopic Dermatitis in France: Results of a National Cross-Sectional Descriptive Study in 2021

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Introduction & Objectives:
Assessing AD severity often differs between physicians, despite international recommendations and is needed for therapeutic management. The main objective of this study was to estimate the percentage of moderate-to-severe AD adult patients in France who were eligible for systemic therapy (ST), who received ST or did not respond to it.

Materials & Methods:
A national cross-sectional observational study was conducted from January 11 to April 15, 2021. Adults with moderate-to-severe AD were included if they had a v-IGA-AD score ≥ 3 and/or pruritus intensity VAS score ≥ 4 and/or a history of current or prior treatment with ST (conventional or biologics except for antihistamines and phototherapy). Patients considered eligible for conventional STs were defined as those failing topical treatments and/or phototherapy despite good compliance and therapeutic education (TE). Data was collected by general practitioners, dermatologists and allergists in electronic case report forms.

Results:
A total of 803 patients were identified in this study composed of 55.5% females aged 42.1±18.0 years (median=38.0 years). Most patients had moderate to severe AD (n=649, 80.8%) and only 33.4% (n=217) received STs. The most commonly prescribed medications were corticosteroids (49.3%), cyclosporine (39.2%), methotrexate (34.1%), azathioprine (6.0%), and mycophenolate (1.8%). More than half of the prescribed treatments were already discontinued due to ineffectiveness. In the case of corticosteroids mostly were due to ineffectiveness or the improvement of the patient’s condition. Only 109 patients (16.8%) received biologics or targeted treatments with the most common drug being dupilumab (93.6%). Oral JAK inhibitors treated 6.4% of patients. Most treatments were still ongoing in 2021. Over half the patients (n=342, 52.7%) were eligible for conventional ST of which 158 (46.0%) had been treated but were poorly controlled and had not receive biologics, and 184 (54.0%) were eligible but were not treated. Regarding TE, only 19.6% of patients benefited from it, mainly through educational medical consultations and/or hospital-based programs.

Conclusion:
Our results suggest that a large portion of patients with moderate-to-severe AD may not be receiving adequate treatment with conventional ST or biologics. Most patients were treated with topical products such as emollients or corticosteroids, while only 1/3 were receiving or had previously received conventional ST and under 1/5 with biologics. Hence, patients were prescribed topical medication despite almost 60% of them being suitable for ST, and 1 in 2 patients deemed eligible for a systemic therapy never received one. AD is not being managed to its full potential given the treatment options available. This study highlights the major challenge of identifying those
patients who have failed topical care and are eligible for systemic treatment.
Abstract N°: 1594

Minimal-to-no itch with baricitinib in patients with moderate-to-severe atopic dermatitis: results from three randomized, phase 3 clinical trials

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Introduction & Objectives: Patients with atopic dermatitis (AD) report symptoms of itch and sleep disturbance, which can have a significant impact on quality of life. Baricitinib, an oral selective JAK1/JAK2 inhibitor, is approved in many countries for moderate-to-severe AD in adults. Here we assessed minimal-to-no itch over 16-weeks treatment with baricitinib monotherapy or in combination with topical corticosteroids (TCS).

Materials & Methods: Minimal-to-no itch was evaluated in patients with moderate-to-severe AD in two baricitinib monotherapy trials (BREEZE-AD1; NCT03334396 and BREEZE-AD2; NCT03334422) and one baricitinib and TCS combination trial (BREEZE-AD7; NCT03733301). Minimal-to-no-itch (score of 0/1) was assessed at Week-2 and Week-16 using the Itch Numeric Rating Scale (NRS): 11-point scale from 0 (“no itch”) to 10 (“worst itch imaginable”). Data from monotherapy trials were integrated and results for BREEZE-AD1/AD2 and BREEZE-AD7 are shown respectively for baricitinib 4-mg (n=248 and n=111), the recommended dose for most patients, versus placebo (n=493 and n=109). Data after discontinuation or rescue were excluded from the analysis. Logistic regression was used to analyze the data with non-responder imputation. Analyses were not adjusted for multiplicity.

Results: In the monotherapy studies, a higher proportion of patients treated with baricitinib 4-mg achieved an Itch NRS score of 0/1 at Week-2 compared to placebo (8.9% versus 1.6%; p<0.0001) and these improvements continued to increase to Week-16 (14.1% versus 3.9%; p<0.0001). In the combination study, a higher proportion of patients treated with baricitinib 4-mg achieved an Itch NRS score of 0/1 compared to placebo at Week-2 (16.2% versus 2.8%; p=0.0064) and maintained these improvements through to Week-16 (22.5% versus 8.3; p=0.0287).

Conclusion: Overall, minimal-to-no itch was observed in patients with moderate-to-severe AD as early as Week-2 and continued through Week-16 of treatment with baricitinib 4-mg. Total or near total itch relief can be achieved with baricitinib monotherapy and combination therapy with TCS compared to placebo.

Previously presented at World Congress of Dermatology - 25th; 3rd-8th July, 2023; Singapore.
Abstract N°: 1615

The Correlation between EASI score and Multiple Allergen Simultaneous Test (MAST) Results in Atopic Dermatitis patients

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Introduction & Objectives:

Eczema area and severity index (EASI) score is a widely used method to evaluate the severity of atopic dermatitis. It is known that serum IgE is associated with severity in atopic patients. Multiple allergen simultaneous test (MAST) is a good method to measure allergen-specific IgE level, and can evaluate the degree of response to allergens. The objective of this research is to investigate the correlation between the EASI score, total IgE and allergen specific IgE in atopic patients.

Materials & Methods:

Patients over 13 years of age with atopic dermatitis who underwent MAST were included retrospectively. MAST consisted of 19 inhalant-allergen and 42 food-allergen panels. For each allergen, all classes of 1 or more were judged as positive.

Results:

131 patients (82 males and 49 females; mean age 32.3 ± 14.1 years) were enrolled. Of these, 57 patients were subjected to EASI scoring. Total IgE was measured from 4.04 up to 5000kU/L. The most common inhalant allergens were D.farinae (67.9%), D.pteronyssinus (67.1%), and Housedust (61.1%), and food allergens were Peach (18.3%), Apple (15.3%), Garlic (12.2%) in order. Total IgE and the number of specific IgE positives were statistically correlated ($p < 0.05$). The EASI score had a statistically positive correlation with both total IgE and the number of specific IgE positivity ($p < 0.05$).

Conclusion:

EASI score, total IgE and number of positive allergen-specific IgE measured by MAST in adolescent and adult atopic patients all have significant positive correlations with each other.
Abstract N°: 1620

Efficacy and safety of delgocitinib cream in adults with moderate to severe chronic hand eczema: results of the Phase 3 DELTA 2 trial

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Introduction & Objectives:

Chronic hand eczema (CHE) is an inflammatory, pruritic, often painful disorder of the hands and wrists that strongly impacts quality of life and occupational capabilities of patients. Delgocitinib is a topical pan-Janus kinase (JAK) inhibitor that was well tolerated and demonstrated significant improvement in primary and all key secondary efficacy endpoints in the DELTA 1 (NCT04871711) pivotal phase 3 trial. The aim of this study was to confirm the efficacy, safety, and effect on health-related quality of life of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle in the treatment of adults with moderate to severe CHE in the Phase 3 DELTA 2 trial (NCT04872101).

Materials & Methods:

DELTA 2 was a randomized, double-blind, vehicle-controlled trial. Adults (aged ≥18 years) with moderate to severe CHE were randomized 2:1 to twice-daily delgocitinib cream 20 mg/g (n=314) or cream vehicle (n=159) for 16 weeks followed by 2-week safety follow up or transfer to a 36-week open-label extension trial (NCT04949841). The primary endpoint was Investigator’s Global Assessment for CHE (IGA-CHE) treatment success at Week 16 (IGA-CHE TS), defined as IGA-CHE score of 0/1 (clear/almost clear, defined as only barely perceptible erythema) with ≥2-step improvement. Key secondary endpoints included ≥75%/≥90% improvement in Hand Eczema Severity Index (HECSI-75/90) and ≥4-point improvement in the Dermatology Life Quality Index (DLQI) from baseline at Week 16.

Results:

At Week 16, a significantly greater proportion of delgocitinib-treated patients, compared to cream vehicle, achieved IGA-CHE TS (29.1% vs. 6.9%; p<0.001), HECSI-75 (49.5% vs. 18.2%; p<0.001), HECSI-90 (31.0% vs. 8.8%; p<0.001), and ≥4-point improvement in DLQI (72.2% vs. 45.8%; p<0.001). There was no difference between delgocitinib and cream vehicle in proportion of patients who reported adverse events (AEs; 45.7% vs. 44.7%) and serious AEs (1.6% vs. 1.9%). Rates of AEs assessed as probably or possibly related to study drug were consistent between delgocitinib (31.29 per 100-patient years of observation [PYO]) and cream vehicle (30.87 per 100 PYO). Rates of AEs leading to discontinuation of study drug were numerically higher with cream vehicle (11.02 per 100 PYO) compared to delgocitinib (1.04 per 100 PYO).

Conclusion:
Overall, delgocitinib cream demonstrated greater improvements in both patient- and clinician-reported efficacy outcomes versus cream vehicle and was well-tolerated over 16 weeks. These results were consistent with those previously reported from the identically designed DELTA 1 study.
Abstract N°: 1621

Minimal systemic exposure of delgocitinib cream in adults with moderate to severe chronic hand eczema in the phase 3 DELTA 2 trial

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Introduction & Objectives:

Delgocitinib is a topical pan-Janus kinase (JAK) inhibitor that was well tolerated and demonstrated significant improvement in primary and all secondary efficacy endpoints in the DELTA 1 (NCT04871711) pivotal phase 3 trial for treatment of chronic hand eczema (CHE). The identical DELTA 2 pivotal phase 3 trial (NCT04872101) was designed to confirm the efficacy, safety, and effect on health-related quality of life of twice-daily applications of delgocitinib cream 20 mg/g compared with cream vehicle in adults with moderate to severe CHE. Here we present additional DELTA 2 analyses examining systemic exposure parameters of delgocitinib cream, which allow comparisons with systemic exposure data of oral delgocitinib from a phase 1 trial (NCT05050279).

Materials & Methods:

DELTA 2 was a randomized, double-blind, vehicle-controlled trial. Adults (aged ≥18 years) with moderate to severe CHE were randomized 2:1 to twice-daily delgocitinib cream 20 mg/g (n=314) or cream vehicle (n=159) for 16 weeks followed by a 2-week safety follow-up or were transferred to a 36-week extension trial (NCT04949841). Blood samples collected 2–6 hours after application of the investigational medicinal product at Weeks 1, 4, and 16 were used to analyse plasma concentrations of delgocitinib using a liquid chromatography/mass spectrometry-based method with a lower limit of quantitation of 5 pg/ml. The inhibitory concentration of 50% (IC\(_{50}\)) of delgocitinib was assessed using an in vitro IL-4 release assay in whole-blood of healthy volunteers (n=4). In the phase 1 trial, single oral doses of delgocitinib (1.5, 3, 6, and 12 mg) were tested in healthy volunteers (n=40). Data are reported as geometric means.

Results:

The DELTA 2 analysis included samples from 313 subjects on active treatment. The plasma concentration of delgocitinib was 0.21, 0.20 and 0.12 ng/ml at Weeks 1, 4 and 16, respectively (Figure 1). IC\(_{50}\) of delgocitinib was 17.2 ng/ml. In the phase 1 study, the lowest tested oral dose of delgocitinib (1.5 mg) was perceived as a sub-therapeutic dose. Peak systemic exposure (C\(_{\text{max}}\)) of the 1.5 mg orally dosed delgocitinib was 7.2 ng/ml, meaning that systemic exposure after topical application in DELTA 2 was ≥30-fold lower (7.2 ng/ml divided by 0.21 ng/ml).

Conclusion:

Twice daily application of delgocitinib cream resulted in minimal systemic exposure, at least 80-fold below the whole-blood IC\(_{50}\) over 16 weeks (17.2 ng/ml divided by 0.21 ng/ml), and at least 30-fold below oral 1.5 mg delgocitinib dose with no overlap in plasma exposure between oral and topical administration. These data further support the favourable safety profile of topical delgocitinib cream and suggest that no systemic pharmacological effect is expected with 20 mg/g dosing in patients with moderate to severe CHE.
Figure 1. Scatter plot* of delgocitinib concentration by visit at Week 1 (n=286), Week 4 (n=275) and Week 16 (n=261).

*One subject was excluded from this analysis due to an outlier value at Week 4.
Assessment of Patient-Reported Outcomes at 48 months of treatment with Dupilumab for severe atopic dermatitis: a real-life monocentric study of 120 patients

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Assessment of Patient-Reported Outcomes at 48 months of treatment with Dupilumab for severe atopic dermatitis: a real-life monocentric study of 120 patients

Introduction & Objectives:

Atopic dermatitis (AD) is a chronic inflammatory-type disease associated with multiple skin manifestations and whose symptoms, such as feeling of dryness, pain, and itching, adversely affect patients’ quality of life. The Eczema Activity and Severity Index (EASI) is used as the primary measure to assess clinical response in AD studies. Patient Reported Outcomes (PROs), such as itch intensity (Pruritus Numerical Rating Scale), sleep (Sleep Numerical Rating Scale), quality of life (Dermatology Life Quality Index), patient’s perception of the disease (such as the Atopic Dermatitis Control Tool and the Patient Oriented Eczema Measure), and anxiety and depression (Hospital Anxiety and Depression Scale) are also used in clinical monitoring. Dupilumab has shown good clinical results in both trials and real-life studies, however, there is little information regarding PROs during treatment in real-life studies to date. The purpose of the study is to evaluate the trend of PROs during treatment with Dupilumab. In this regard, we will report data of 150 patients with severe AD from the population of a tertiary care center up to 48 months of treatment with Dupilumab.

Materials & Methods:

We collect data from 150 patients with severe AD from treated with Dupilumab at standard dose. POEM, ADCT, DLQI and HADS were collected at baseline (T0) and after 12 (T12), 24 (T24), 36 (T36) and 48 (T48) months of therapy. Statistical analyses were performed using SPSS software (IBM, version 29.0). Descriptive statistics are reported as mean ± standard deviation (SD) for quantitative variables and frequencies (%) for categorical variables.

Results:

Statistical analysis will be completed in July 2023 so as to collect as many patients as possible. Based on a preliminary analysis of 70 patients, all scores improve significantly within the first year (T12) of treatment, with maintenance of the outcome over the following 3 years. The following graphs represent the trends of DLQI, POEM, ADCT and HADS scores over the 4 years of treatment.
Figure 1. Trend of DLQI score over the 4 year of treatment with Dupilumab

Figure 2. Trend of POEM score over the 4 year of treatment with Dupilumab

Figure 3. Trend of ADCT score over the 4 year of treatment with Dupilumab
Figure 4. Trend of HADS score over the 4 year of treatment with Dupilumab

**Conclusion:**

Based on a preliminary analysis of 70 patients, Dupilumab has shown good clinical results in improving PROs, thus improving the overall quality of life of our patients.
Development and psychometric validation of a new patient-reported outcome measure to assess the signs and symptoms of chronic hand eczema (CHE): the Hand Eczema Symptom Diary (HESD)

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Introduction & Objectives:

CHE is a heterogeneous inflammatory skin disorder of the hands. The Hand Eczema Symptom Diary (HESD) is a new patient-reported outcome (PRO) measure of worst severity of core signs and symptoms of CHE over the past 24 hours that meets regulatory guidelines for PRO measures. Item scores and the total score (an average of the items) range from 0-10. The HESD was developed based on a literature review and qualitative concept elicitation interviews with CHE patients and clinical experts. The study aim was to perform content validity testing and psychometric evaluation of the HESD.

Materials & Methods:

An overview of the HESD development and validation is provided in Figure 1. Qualitative cognitive interviews with 20 CHE patients were performed to evaluate content validity by assessing understanding and relevance of the items, response options and recall period. Psychometric properties of the HESD (item performance and dimensionality, reliability and validity of scores and estimation of meaningful change thresholds) were assessed initially using data from a phase 2b (NCT03683719) and confirmed using data from the first 280 subjects completing this Week 16 phase 3 trial (NCT04871711; DELTA 1) of twice-daily delgocitinib 20mg vs cream vehicle, pooled across treatment groups.

Results:

Cognitive interview results supported refinement of item wording and removal of items due to conceptual overlap, resulting in an 11-item version of the HESD. All 11 items were well understood and relevant to patients. Assessments of item properties and dimensionality in the phase 2b data and expert clinical input supported removal of 5 items; the 6-item HESD (assessing worst itch, pain, cracking skin, redness, dryness and flaking) was included in the phase 3 trial.

In the phase 3 psychometric analysis, missing data were low for all 6 items. Unidimensionality of the 6-item HESD was supported by strong inter-item correlations among all HESD items (all >0.70) and Rasch analysis. Internal consistency (Cronbach’s alpha= 0.96) and test-retest reliability (intra-class correlations >0.89) results were very strong. Convergent validity was supported by moderate correlations with measures of related concepts (correlation range: 0.53-0.64). Significant differences between severity groups (p<0.001) further supported construct validity. Large within-group effect sizes for mean change scores in improved subjects indicated ability to detect improvement, as did significant differences between change groups (p<0.001). Anchor-based analyses supported 4-point responder definitions for improvements in 7-day average HESD Itch, HESD Pain, and HESD scores.

Conclusion:
The HESD itch score, HESD pain score and 6-item HESD score have strong content validity, reliability, construct validity and are responsive to change. Within-subject improvements of $\geq 4$ points can be regarded as real, important changes on the 7-day average scores for the HESD itch, HESD pain and HESD.
Abstract N°: 1626

Psychometric Validation of the Investigator Global Assessment of Chronic Hand Eczema (IGA-CHE): a new clinician reported outcome measure

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Introduction & Objectives:

CHE is a heterogeneous inflammatory skin disorder of the hands and wrists, characterized by flares and poor prognosis. The Investigator Global Assessment of Chronic Hand Eczema (IGA-CHE) is a new single item ClinRO that allows investigators to assess current global disease severity using a 5-level severity scale (0=clear, 1=almost clear, 2=mild, 3=moderate, 4=severe). Clinical characteristics of erythema, scaling, lichenification/hyperkeratosis, vesiculation, oedema and fissures provide guidelines for the overall severity assessment. The IGA-CHE, developed by clinical experts in accordance with regulatory guidance, was first used in a phase 2b trial (NCT03683719) of delgocitinib cream. It was subsequently modified for the phase 3 DELTA trials to articulate more distinct categories, including definition of ‘almost clear’ as the presence of barely perceptible erythema only. The aim of this study was to evaluate the psychometric properties of the IGA-CHE including responder definition estimation, to support its use as a CHE trial endpoint.

Materials & Methods:

The IGA-CHE was used to derive the primary endpoint in a phase 3 clinical trial (NCT04871711) to evaluate the efficacy of delgocitinib cream 20 mg/g in adults with moderate to severe CHE (n=280). Analyses were conducted to assess test-retest reliability, construct validity (including convergent validity and known groups validity), ability to detect change and anchor-based analyses to support estimation of a responder definition. These psychometric analyses were performed on blinded data from the first 280 completers (2:1 delgocitinib vs. vehicle) in the phase 3 trial, pooled across treatment groups.

Results:

Test-retest reliability results were moderate to strong with kappa coefficients ranging from 0.63-0.76. Correlations with measures of related concepts were all moderate or strong (range: 0.65-0.72) and exceeded hypothesized thresholds, providing strong evidence of convergent validity. Known groups validity was supported by significant differences between severity groups (p<0.001). Larger within-group effect sizes for improved compared to stable patients provided strong evidence of ability to detect improvement. Anchor-based analyses generated within-subject meaningful change estimates ranging from -0.8 and -2.3. Triangulation using a correlation weighted average with Fisher’s z transformation resulted in a value of 1.68. Thus, a conservative approach is to adopt a 2-level responder definition, which is aligned with the trial endpoint (clear or almost clear with a 2-level reduction). However, the findings also support a 1-level change as being clinically meaningful.

Conclusion:

These findings provide evidence that the IGA-CHE has strong reliability, validity, and ability to detect change, supporting its use as an endpoint in CHE clinical trials and in clinical practice. Evidence generated supports 2-level
change in IGA-CHE scores as being clinically meaningful.
Abstract N°: 1670

Study of molecular genetic characteristics of clinical strains of S. aureus, isolated from locus morbi and other biotopes of patients with widespread dermatoses

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Introduction & Objectives:

To date, there are limited data in the literature regarding the authenticity (probable genetic kinship) of S. aureus strains that grow on different areas of the skin of patients with widespread dermatoses. The use of the RAPD-PCR analysis method (Random Amplified Polymorphic DNA) or PCR with universal primers makes it possible to study the polymorphism of the entire genome without prior knowledge of specific DNA sequences, and is based on the use of primers with an arbitrary sequence of nucleotides. Based on the distribution of the reaction products - RAPD spectra, which are DNA fragments of different lengths - it is possible to register differences between the genomes of closely related microorganisms.

The aim of the study: to establish the relationship between the genotypes of S. aureus strains extracted from patients with atopic dermatitis (AD) and psoriasis and the relationship with the severity of the disease.

Materials & Methods:

Determination of genotypic polymorphism among S. aureus strains extracted from affected and intact areas of the skin and nasal passages of patients with widespread dermatosis was carried out using RAPD-PCR.

Results:

A generally high genetic polymorphism of staphylococci was established and no specific (single) genotype or a limited group of dominant genotypes was identified, which would be associated with the occurrence of complications of staphylococcal genesis and the development of severe forms of diseases. However, it was established that with increasing severity of the course of AD, genetic polymorphism decreases and monotypic isolates of the pathogen increases. Between S. aureus strains isolated from different biotopes of the same patients with AD, a high level of genetic relatedness was revealed, which according to the relative similarity of RAPD spectra for strains from the mucous nasal passages and from the locus morbi reached (79.5 ± 1.6) %, and between strains from areas of intact and affected skin increased from (75.1 ± 4.4) % to (98.8 ± 0.8) % in parallel with the increase in the severity of the course of dermatosis from mild to severe forms, respectively (p ≤ 0.05).

Comparative analysis of RAPD spectra showed a significantly lower level of affinity (p ≤ 0.05) between the reference culture S. aureus ATCC 25923 and strains of the same species of staphylococci extracted from patients with AD - (52.0 ± 2.5) %. When studying the RAPD spectra of clinical strains of S. aureus extracted from locus morbi and intact skin of patients with psoriasis, no genotype was identified that would be associated with this dermatosis or its severity. The average indicator of variability was (43.2 ± 3.4) %, which indicates the probability of their different origin, while the degree of affinity with the reference culture S. aureus ATCC 25923 was only 33.6 %.

Conclusion:

Both the generally high genetic polymorphism of S. aureus strains isolated from AD patients and the high level of
affinity of isolates from different biotopes of the same patient substantiate the autogenesis of staphylococcal strains colonizing the locus morbi, and the significant difference between the genotypes of the latter and the reference cultures of *S. aureus* ATCC 25923 determines the expediency of using autostrains of staphylococci in determining indicators of cellular and humoral immunity in patients with allergic dermatoses.
our experience with upadacitinib in a terciary hospital in madrid

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Introduction & Objectives: In Spain, the prevalence of atopic dermatitis (AD) in adults is between 1’9 and 7’2%. The 8-10% of the patients present severe AD, needing immunosuppressive treatment like cyclosporine. Upadacitinib is a new selective reversible inhibitor of the Janus Kinasa (JAK), specific for JAK-1. It is indicated for treatment of severe AD in patients older than 12 years that have fallen to oral cyclosporine, have any contraindications or have presented any adverse effect. The main objective of this study is determinate the efficacy and the safety of upadacitinib in real life in our hospital.

Materials & Methods: An observational retrospective study was performed, including those patients with severe AD who start upadacitinib between July-22 until April-23. Parameters such as gender, age, date of AD diagnosis and previous systemics treatments were registered. To study efficacy, the following disease severe scales were registered at the beginning of the treatment and at the weeks 4, 12, 24 and 28: Eczema Area and Severity Index (EASI), Pruritic Sleep Disorder (Numerical Rating Scale) and Investigators Global Assessment (IGA).

Results: Until April-23, eight patients (75% male and 25% female) were evaluated. The mean age is 23’73 years. One adolescent of 13 years was included. The AD diagnosis was in childhood in the 75% of the patients. All the patients received systemic therapies before upadacitinib (100% with cyclosporine, 37’5% with methotrexate, 37’5% with azathioprine) and one patient was treated with dupilumab, previous failure to mofetil mycophenolate and ustekinumab. Initial doses of 30mg daily were prescribed to all the patients except to the youngest one, who received 15mg daily. In our series the 87’5% of the patients were naives for biologics treatments. All the patients complete 12 weeks of treatment. The data of week 24 and 28 is referred only to 3 and 2 patients respectively. At week 12, the pooled proportion of patients achieving 50% and 75% EASI score improvement was 75% and 50% respectively. The reduction of ≥2 points from baseline on a 0-4 IGA scale at week 12 happened in 62’5% of the patients. The mean of pruritic sleep disorder decreased on 77’29% at week 12. Two flares were noticed at week 12, totally recovered (with corticosteroid therapy) during the next weeks of monitoring. The treatment was discontinued only in one patient due to facial V2-V3 herpes zoster, recovered after valacyclovir treatment. No others serious adverse effects were observed. Two patients reported mild acne/folliculitis and one an upper respiratory tract infection. No laboratory abnormalities were reported.

Conclusion: According to our experience, the reduction in the scales is lightly worse than the evidence in clinical trials, but this fact could be influenced by two flares in our series. The limited number of patients, the time of study inferior to 52 weeks and the observational nature of this work are the main limitations. We hope to complete the study and to share the results in the posteriors communications.
Abstract N°: 1721

Dynamic pollutants’ measurement in Atopic Dermatitis patients

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Introduction & Objectives:

Atopic Dermatitis is a chronic inflammatory disease with multifactorial etiology: its pathogenesis involves genetic and environmental factors, including pollution. This prospective observational study aims to assess the possible association between the clinical expression of Atopic Dermatitis and exposure to pollutants such as Nitrogen Oxides (NO₂) and Benzene-Toluene-Ethylbenzene-Xylene (BTEX), or the possible correlation to the therapeutic response.

Materials & Methods:

Patients are evaluated using clinimetric, subjective and biochemical parameters: EASI (Eczema Area Severity Index), SCORAD (scoring Atopic Dermatitis), pp-NRS (peak pruritus Numerical Rating Scale), Sleep-NRS, blood count, PCR, total IgE. Patients are given a questionnaire that investigates the impact of the disease on the patient’s life, the Dermatology Life Quality Index (DLQI). In addition, the PROs (Patient-Reported Outcomes) are evaluated in order to have an accurate picture of the progress of the pathology. The concentration of pollutants is measured through a passive sampler that the patient wears for seven days in three periods of the year. The analytical methods used in this work’s experimental phase are six, corresponding to two types of pollutants (BTEX, NO₂). Ring samplers are used for passive sampling, supplied by Aquaria Research S.r.l. Each patient received a personal sampler and a sampler to be exposed outside their home, to compare the pollutants to which they are exposed personally with those of the urban environment in which they live.

Results:

Patients assessed to date are 8 (62% M; 37.5% F); average age: 28 years (range 22-53); average disease duration: 23.5 (range 18-45); average EASI: 1.5 (range 0-4); comorbidity: conjunctivitis (50%), rhinitis (25%), allergic asthma (25%), food allergy (12%), iron deficiency anemia (12%); therapy: Dupilumab (87.5%), Upadacitinib (12.5%). Sampling period: February/March. Average concentration of substances: Benzene external sampler: 9,85 μg/m³ (0.83 μg/m³ -18,42 μg/m³); Benzene personal sampler: 25 μg/m³ (2,3 μg/m³-67,93 μg/m³); Toluene external sampler: 5,8 μg/m³ (1,75 μg/m³-16,37 μg/m³); Toluene personal sampler: 22,37 μg/m³ (2,06 μg/m³-139,79 μg/m³); Ethylbenzene external sampler: 0,57 μg/m³ (0,18 μg/m³-0,92 μg/m³); Ethylbenzene personal sampler: 0,51 μg/m³ (0,22 μg/m³-0,83 μg/m³); Xilene external sampler: 0,3 μg/m³ (0,21 μg/m³-0,6 μg/m³); Xilene personal sampler: 0,35 μg/m³ (0,1 μg/m³-1,02 μg/m³).

Conclusion: The preliminary results of this study show a higher exposure to pollutants of the personal sampler than that placed in the outdoor environment, confirming recent studies that evaluate the greater impact of indoor pollution compared to outdoor on the course of the skin disease.
Clinical Management of Moderate to Severe Atopic Dermatitis: Results of a Retrospective, Observational, Two-cohort Study in France

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Introduction & Objectives:
Atopic dermatitis (AD) is a recurrent skin disorder. Its prevalence in France is 4.6%, with moderate to severe cases affecting more than half the adult patients and is a challenge in daily practice. Clinical management includes topical and systemic therapies; however, practice guidelines currently do not exist. The launch of dupilumab as a last-line treatment for moderate to severe cases may have changed the clinical care pathway, however, real-world evidence on this is limited. We aimed to describe the clinical management of AD for patients who initiated dupilumab during its temporary use authorization (TUA) and marketing authorization (MA).

Materials & Methods:
A retrospective observational two-cohort study was conducted using data from the national health insurance database (SNDS) between March 7, 2017 and December 31, 2019. Patients who initiated dupilumab under the TUA from March 7, 2017 to March 8, 2019, were the first cohort (C1) and the second cohort (C2) comprised of patients initiating treatment after the MA period in France from March 9 to December 31, 2019. Analysis of treatment lines was performed using a data visualization method (TAK).

Results:
Overall, 2,643 patients were included (C1: n=1,323, C2: n=1,320). The proportion of patients with a long-term illness status was 43.9% (C1) and 44.1% (C2) and the primary comorbidities were asthma (C1:70%; C2: 63%), allergic rhinitis (C1:67%; C2:64%), and allergic conjunctivitis (C1:46%; C2:41%). After matching, C1 and C2 were comparable for all criteria except for severe asthma or allergic conjunctivitis. Before initiating dupilumab, most patients received 2 to 3 lines of therapy, mostly topical treatments with cyclosporine (C1:30%; C2:39%), methotrexate (MTX) (C1:14%; C2:15%) or cyclosporine and MTX (C1:14%; C2:10%). A significant difference was found for patients that had received at least 1 round of cyclosporine and received at least one round of MTX (C1: 33%; C2: 27%) before dupilumab. The TAK analysis showed that dupilumab was rarely used as a first-line treatment, and that MTX was still widely used to manage AD in France. Clinical management was similar between the two cohorts; however, the use of healthcare services increased after the dupilumab initiation and AD-related costs decreased and were higher in C1 compared to C2 with a mean difference of €1,143 per patient.

Conclusion:
This was the first study to describe the evolution of clinical AD management following the launch of dupilumab in France. Although MTX did not have MA for AD management, we showed that it was prescribed more than dupilumab despite its decreasing prescription rates since the launch of dupilumab. A better follow-up of patients, particularly for monitoring adverse events, may explain the increase of patient seeking care after dupilumab use.
This study provides real-world evidence of dupilumab in the management of severe to moderate AD. Our findings may offer new insights to improve the clinical management of AD in daily practice.
Abstract N°: 1758

Greater Skin Clearance and Itch Improvement in Atopic Dermatitis Are Associated With the Achievement of Stringent Patient-Reported Outcomes: Results From the Cross-Sectional MEASURE-AD Study

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Greater Skin Clearance and Itch Improvement in Atopic Dermatitis Are Associated With the Achievement of Stringent Patient-Reported Outcomes: Results From the Cross-Sectional MEASURE-AD Study

Introduction & Objectives:
Clinical trial outcome measures for evaluating treatment response in atopic dermatitis (AD) commonly include assessments of skin clearance (e.g., Eczema Area and Severity Index [EASI]) and itch severity (e.g., Worst Pruritus Numerical Rating Scale [WP-NRS]). However, interrelationships of EASI and WP-NRS with other measures are currently not well understood in the real-world population. This post hoc analysis of patients with AD evaluated the association of EASI and WP-NRS with patient-reported outcome (PRO) measures assessing disease severity and symptoms, sleep, emotional state, and quality of life (QoL).

Materials & Methods:
MEASURE-AD was a cross-sectional, noninterventional cohort study to evaluate the multidimensional burden associated with AD. Patients aged ≥ 12 years with a physician-confirmed diagnosis of moderate-to-severe AD who were receiving systemic AD therapy or were candidates for systemic AD therapy were enrolled between December 2019 and December 2020 during routine clinic visits. Favorable PRO assessment scores were defined as Patient-Oriented Eczema Measure score of 0–2 (clear or almost clear eczema), Atopic Dermatitis Symptom Scale (ADerm-SS) 7-item total symptom score (TSS-7) of 0–11 (no/minimal AD symptoms), Dermatology Life Quality Index score of 0–1 (no impact on QoL), Atopic Dermatitis Impact Scale (ADerm-IS) Sleep score of 0–3 (no/minimal impact of AD on sleep), ADerm-IS Daily Activities score of 0–2 (no/minimal impact of AD on daily activities), and ADerm-IS Emotional State score of 0–2 (no/minimal impact of AD on emotional state). The proportion of patients with favorable PRO scores were summarized by EASI (score of 0–3, 3.1–7, 7.1–21, and > 21) or WP-NRS (score of 0–1, 2–3, 4–7, and 8–10) categories.

Results:
A total of 1558 patients were included in the analysis. The mean (SD) age was 37.2 (16.9) years, 8.0% of patients were adolescents, and 48.1% were female. At baseline, the mean (SD) EASI score was 15.0 (12.9) and the mean (SD) WP-NRS score was 5.3 (3.1). The proportions of patients reporting favorable PRO scores were incrementally higher at more stringent EASI and WP-NRS categories. Across all PRO measures, rates ranged from 31.0%–69.8% and 41.0%–85.2% among patients with EASI scores of 0–3 and WP-NRS scores of 0–1, respectively (Figure). Conversely, rates across all PRO measures ranged from 0.9%–12.9% and 0.2%–4.7% among patients with EASI scores > 21 and WP-NRS scores of 8–10, respectively. Similar patterns were observed among the subgroup of patients with EASI scores of 0–3, as well as the subgroup with WP-NRS scores of 0–1. The highest rates were observed in patients with both EASI scores of 0–3 and WP-NRS scores of 0–1 and ranged from 51.9%–91.8%
across all PRO measures.

**Conclusion:**

Greater degrees of skin clearance and itch resolution (especially EASI scores of 0–3 and WPNRS scores of 0–1) are associated with more robust outcomes across multiple dimensions of AD, including disease severity, sleep, emotional state, and QoL.

**Figure. Proportion of Patients With Favorable PRO Assessment Scores by EASI and WP-NRS Categories (AO).**

A. **PRO Rates by EASI Categories**

<table>
<thead>
<tr>
<th>Category</th>
<th>EASI 0–3</th>
<th>EASI 3.1–7</th>
<th>EASI 7.1–21</th>
<th>EASI &gt; 21</th>
</tr>
</thead>
<tbody>
<tr>
<td>POEM 0–2</td>
<td>31.0</td>
<td>5.5</td>
<td>2.0</td>
<td>0.9</td>
</tr>
<tr>
<td>ADerm-SS TSS-7 0–11</td>
<td>63.1</td>
<td>22.3</td>
<td>9.7</td>
<td>6.6</td>
</tr>
<tr>
<td>DLQI 0–1</td>
<td>43.8</td>
<td>9.5</td>
<td>3.4</td>
<td>2.0</td>
</tr>
<tr>
<td>ADerm-IS Sleep 0–3</td>
<td>69.8</td>
<td>21.9</td>
<td>12.9</td>
<td>7.7</td>
</tr>
<tr>
<td>ADerm-IS Daily Activities Emotional State 0–2</td>
<td>62.3</td>
<td>24.4</td>
<td>15.5</td>
<td>13.8</td>
</tr>
<tr>
<td>ADerm-IS Emotional State 0–2</td>
<td>63.0</td>
<td>26.6</td>
<td>13.8</td>
<td>7.8</td>
</tr>
</tbody>
</table>

B. **PRO Rates by WP-NRS Categories**

<table>
<thead>
<tr>
<th>Category</th>
<th>WP-NRS 0–1</th>
<th>WP-NRS 2–3</th>
<th>WP-NRS 4–7</th>
<th>WP-NRS 8–10</th>
</tr>
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<tr>
<td>POEM 0–2</td>
<td>41.0</td>
<td>80.1</td>
<td>35.3</td>
<td>13.9</td>
</tr>
<tr>
<td>ADerm-SS TSS-7 0–11</td>
<td>53.5</td>
<td>6.0</td>
<td>53.6</td>
<td>2.7</td>
</tr>
<tr>
<td>DLQI 0–1</td>
<td>53.5</td>
<td>6.0</td>
<td>53.6</td>
<td>2.7</td>
</tr>
<tr>
<td>ADerm-IS Sleep 0–3</td>
<td>85.2</td>
<td>54.7</td>
<td>53.6</td>
<td>27.0</td>
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<tr>
<td>ADerm-IS Daily Activities Emotional State 0–2</td>
<td>73.4</td>
<td>38.7</td>
<td>70.5</td>
<td>14.0</td>
</tr>
<tr>
<td>ADerm-IS Emotional State 0–2</td>
<td>70.5</td>
<td>35.4</td>
<td>70.5</td>
<td>14.0</td>
</tr>
</tbody>
</table>

ADerm-IS, Atopic Dermatitis Impact Scale; ADerm-SS, Atopic Dermatitis Symptom Scale; AO, as observed; DLQI, Dermatology Life Quality Index; EASI, Eczema Activity and Severity Index; POEM, Patient-Oriented Eczema Measure; PRO, patient-reported outcome; TSS-7, 7-Item Total Symptom Score; WP-NRS, Worst Pruritus Numeric Rating Scale.

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Retreatment with upadacitinib: a new therapeutic strategy in atopic dermatitis

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Introduction & Objectives

Upadacitinib (UPA) is a selective oral JAK-1 inhibitor approved for adults and adolescents with moderate-to-severe atopic dermatitis (AD). Although it has demonstrated efficacy and a safety profile in clinical trials, there are still many gaps regarding its use in daily practice.

Materials & Methods

We present three scenarios focusing on UPA retreatment in patients with severe AD.

Results

Case 1 is a 43-year-old woman who had been treated with UPA 30mg during 2.5 years. Due to the sustained complete response, UPA was discontinued. Three months later the patient relapsed, presenting with generalised eczema (Eczema Area Severity Index – EASI – 21, Body Surface Area – BSA – 40%) and severe pruritus (Worst-Itch Numerical Rating Scale – WI-NRS – 9). UPA 30mg was reintroduced reaching complete response in 4 weeks.

Cases 2 and 3 are two men, aged 42 and 22 respectively, who had been treated with UPA 30mg, with a secondary failure after a complete response maintained for 1.5 years in case 2 and for 2 years in case 3. Both patients were subsequently treated with a biologic drug (tralokinumab in case 2 and dupilumab in case 3), with an insufficient response after 6 months. In case 2, UPA 30mg was reintroduced, achieving total control in 4 weeks (baseline EASI, BSA and WI-NRS of 31, 80% and 10, respectively). In case 3, dupilumab was maintained and UPA 30mg was reintroduced in combination, achieving a complete response after 8 weeks (baseline EASI, BSA, WI-NRS of 31, 80% and 10 respectively).

After 6 months (case 1) and 4 months (cases 2 and 3) of follow-up, there have been no flares or adverse effects.

Conclusion

The effect of withdrawal and retreatment with UPA was evaluated during an interim analysis from a phase 2b trial in patients with moderate-to-severe AD. In this study patients were randomized to receive UPA or placebo; after 16 weeks they were rerandomized, and 53 patients who were being treated with UPA began receiving placebo. 81% of the cases that had discontinued UPA required its reintroduction, and most of them achieved an EASI reduction >75% after 8 weeks, recapturing the initial response, as in case 1.

We report three different severe AD patients in which withdrawal and reintroduction of UPA achieved a good disease control. This UPA intermittent regimen and its reintroduction after a secondary failure is scarcely reported in daily practice.

JAK inhibitors are oral molecules, and therefore the probability of promoting immune responses against the drug if
suspended and reintroduced is low. Our observations need to be corroborated, but we consider that they may be relevant when managing a chronic disease that occurs in outbreaks.
Abstract N°: 1829

Impact on severity and quality of life of severe atopic dermatitis after one month of upadacitinib treatment

Matheus Alves Pacheco*, Jane Da Silva, Ana Paula Souza, Athos Martini

Introduction & Objectives:

Severe atopic dermatitis (AD) is considered a complex condition, and more recent treatment options have shown success in controlling the disease. Among them, the Janus kinase (JAK) inhibitors stand out. The aim of this study is to present data from a case series of patients with severe AD after using upadacitinib, a JAK inhibitor.

Materials & Methods:

Quality of life scores were measured, such as the “Patient-Oriented Eczema Measure” (POEM) and “Dermatology Life Quality Index” (DLQI) and AD severity scores, such as the “Severity Scoring of Atopic Dermatitis” (SCORAD) in 4 patients before and 1 month after starting treatment with upadacitinib 15 mg/day. A one-tailed paired Student’s T test was applied to compare the results before and after treatment, with p values <0.05 being considered significant.

Results:

Patient A had the following pretreatment measurements: POEM: 22, DLQI: 21, SCORAD:80; patient B pretreatment: POEM: 24, DLQI: 24, SCORAD: 65.9, patient C pretreatment: POEM: 18, DLQI: 23, SCORAD: 56; and patient D pretreatment: POEM: 14, DLQI: 17, SCORAD: 78.3. After 1 month of upadacitinib use the data were as follows: Patient A post-treatment: POEM: 4, DLQI: 2, SCORAD: 34.4; patient B post-treatment: POEM: 3, DLQI: 0, SCORAD: 18.3; patient C post-treatment: POEM: 8, DLQI: 13, SCORAD: 34.9, and patient D post-treatment: POEM: 7, DLQI: 7, SCORAD: 44.2. After treatment, there was a significant reduction in the SCORAD (p< 0.01), POEM and DLQI (p<0.05) scores. All the pacientes reported a significant reduction in itching in less than 10 days of treatment. One patient had a respiratory infection and mild herpes labialis. Other patients had no complaints of adverse reaction.

Conclusion:

Patients with severe AD had a significant improvement in quality of life scores and reduction in disease severity scores in the first month of upadacitinib use. Side effects, when present, were well tolerated. This therapy seems to be effective in the short term.
Abstract N°: 1853

Patient-reported asthma severity in adults with atopic dermatitis: a population-based cross-sectional survey

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Introduction & Objectives:

Asthma is frequent in adults with atopic dermatitis (AD). A systematic review and meta-analysis reported the prevalence of asthma to be higher in AD patients (25.7%) than in individuals without AD (8.1%), but also concluded that there is little knowledge about asthma severity in AD patients. With the introduction of advanced systemic medication in AD treatment, by inhibiting type 2 inflammation, the potential of reducing both moderate-to-severe AD and asthma symptoms has become a reality. The asthma severity in adults with AD is currently unknown, and there is little insight into a possible linear relationship. Therefore, we performed a nationwide survey to investigate the relationship between the severity of AD and the severity of asthma.

Materials & Methods:

A national questionnaire investigating AD and asthma was constructed and sent through E-boks, a secure public mail, to all adult Danes (³18 years, N=16,718) with a hospital diagnosis of AD (ICD-10 code L20.x) between 2000-2019. The primary outcome was the distribution of asthma severity according to AD severity. AD and asthma severity was measured as the Patient-Oriented SCORing Atopic Dermatitis (PO-SCORAD) and the Global Initiative for Asthma (GINA) based on self-reported medication use, respectively. Adjusted odds ratios (aOR) and 95% confidence intervals (CIs) for age, sex, smoking, and asthma control questionnaire-5 (ACQ-5) score were calculated using logistic regression models.

Results:

A total of 7,049 adults (42.1%) with AD completed the questionnaire. Women accounted for 67.3% (n=4,607) and the mean age was 39.0 (standard deviation [SD] 15.0) years. According to PO-SCORAD, 49.0% had mild AD, 35.0% had moderate, 10.0% had severe, and 6.0% had inactive AD. The lifetime prevalence of physician-diagnosed asthma was 44.3% and 59.1% of these patients reported asthma symptoms within the last 12 months. Report of asthma symptoms within the last 12 months increased with increasing AD severity (inactive 47.6%, mild 54.5%, moderate 61.6%, severe 70.7%). The odds for lifetime asthma increased for mild, moderate, and severe AD when compared to inactive AD (aOR=1.5, 95% CI 1.1-1.9; aOR=2.1, 95% CI 1.6-2.8; aOR=3.0, 95% CI 2.2-4.1). Odds of having asthma symptoms in the last 12 months increased for respectively, moderate and severe AD (aOR=1.7, 95% CI 1.0-2.7; aOR=2.6, 95% CI 1.5-4.2), when compared to inactive AD. Severe AD was associated with increasing asthma severity when compared to inactive AD in crude analysis (OR=2.1, 95% CI 1.1-4.2), but no association with mild or moderate AD was found when compared to inactive AD. In adjusted analyses, there was no significant association between AD severity and asthma severity when compared to inactive AD.

Conclusion:

We found an association between increasing AD severity and respectively, self-reported asthma symptoms in the last 12 months and lifetime physician-diagnosed asthma. No significant association between AD severity and asthma severity was observed in adjusted analyses.
Figure 1 - Distribution of asthma severity according to AD severity defined by PO-SCORAD. Abbreviations: AD = atopic dermatitis, GINA = global Initiative for asthma, PO-SCORAD = patient-oriented scoring atopic dermatitis
Abstract N°: 1867

Prevalence of metabolic syndrome among adults with atopic dermatitis in Lithuania

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Introduction:

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by eczematous lesions, pruritus and
xerosis [1]. The chronic inflammation associated with AD and the resultant oxidative stress may contribute to the
development of the metabolic syndrome. Controversial data exist regarding the association between AD and the
metabolic syndrome [2].

Objectives:

To evaluate the prevalence of the metabolic syndrome and its components in males and females with atopic
dermatitis.

Materials & Methods:

A cross sectional study was performed in the Skin and Venereal Diseases Clinic, Kaunas Clinics, Lithuania, between
2022 and 2023. The sample consisted of 48 patients with AD of Caucasian origin, aged between 18 – 56 years,
inclusive. The diagnosis of AD was confirmed by the Hanifin Raika criteria and evaluated by trained
dermatologists. In this abstract, we analyze the association between AD and metabolic syndrome and its
components for the entire study population, adults (age > 18). The metabolic syndrome diagnosis was made by
the International Diabetes Federation’s (IDF) consensus definition. According to the IDF, a patient must have
central obesity (waist circumference ≥90 cm for men and ≥85 cm for women) plus two of the other four factors:
raised triglycerides (≥1,7 mmol/l or taking medications for hypertriglyceridaemia), reduced high-density
lipoprotein (HDL) (<1,0 mmol/l in men and <1,3 mmol/l in women), raised blood pressure (systolic blood
pressure ≥130 mmHg or diastolic blood pressure ≥85 mmHg, or receiving antihypertensive treatment), and
hyperglycaemia (≥5,6 mmol/l or taking medications for increased glucose) to be defined as having metabolic
syndrome [3].

Results:

The total of 48 subjects with a mean ± SD age of 29.27± 9.9 years were enrolled in the study. 66.7% of patients
were women (n=32). Among all participants, the BMI was 23.9 ± 3.9 kg/m2. The findings revealed that male
patients had a considerably greater prevalence of hypertension than female patients (87.5% vs 34.4%; p = 0.001),
and decreased HDL levels (81.3% vs 40.6%, p = 0.004) respectively. Other metabolic risk factors, such as increased
waist circumference (37.5 % vs 34.4 %; p = 0.831), increased glycemic levels (33.3 % vs 63.6 %; p = 0.335), and
lipid profile including high triglyceride levels (7.1 % vs 21.4 %; p = 0.392), were not significantly different between
the two groups.

Conclusion:
Male patients with atopic dermatitis have a higher prevalence of hypertension and decreased HDL levels than females, according to our findings. This emphasizes the necessity of screening for and controlling hypertension and lipid profiles in male atopic dermatitis patients to lower the risk of cardiovascular consequences. More research is needed to understand the underlying mechanisms that link atopic dermatitis and components of metabolic syndrome in this population.

References:


Abstract N°: 1888

Three-year drug survival of dupilumab, cyclosporine A and methotrexate in a large multicenter cohort of pediatric atopic dermatitis patients

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Introduction & Objectives:

Pediatric patients with moderate-to-severe atopic dermatitis (AD) who are inadequately controlled with topical therapies are eligible for systemic therapy, including the frequently prescribed immunosuppressants cyclosporine A (CsA) and methotrexate (MTX) and biologic dupilumab. However, long-term safety and effectiveness data of these systemic agents in pediatric patients are scarce. Therefore, we aimed to describe the drug survival of dupilumab, CsA and MTX in a long-term daily practice cohort of pediatric AD patients. Secondly, predictors for drug discontinuation for the three systemic agents were identified.

Materials & Methods:

This multicenter retrospective study included AD patients aged ≥2-17 years who were treated with dupilumab, CsA, or MTX at one of four tertiary centers in the Netherlands between 2012 and 2022. Data were extracted from electronic medical records. Drug survival was analyzed using Kaplan-Meier survival analyses. A log-rank test (Mantel-Cox) was used to test for differences in drug survival. A Cox regression model was used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs). Sub-analyses of CsA and MTX assessing drug survival before and after dupilumab approval (2019 for ≥12-17 years; 2020 for ≥6-12 years) were conducted. Predictors for drug discontinuation were analyzed using a univariate Cox regression model.

Results:

Data of approximately 300 pediatric AD patients will be presented. At the moment, preliminary results of 210 treatment episodes in 151 unique patients, comprising 73 dupilumab episodes, 117 CsA episodes, and 22 MTX episodes from one tertiary center are shown. The mean duration of treatment with dupilumab, CsA, and MTX was 2.72 years (95% CI 2.44-2.99), 1.40 years (95% CI 1.15-1.64), and 1.57 years (95% CI 0.96-2.18), respectively (Figure 1). Drug survival of dupilumab was significantly longer compared to CsA (HR 7.12 [95% CI 3.44-14.65], p<0.001) and MTX (HR 6.03 [95% CI 2.56-14.19], p<0.001). For all treatments, ineffectiveness was the most frequent reason for treatment discontinuation, followed by side effects. Sub-analyses showed longer drug survival of CsA before compared to after dupilumab approval (HR 1.90 [95% CI 1.19-3.04]; p=0.007); these differences were not significant for MTX. No significant differences in HRs were found for all analyzed predictors.

Conclusion:

The preliminary results of this daily practice comparative study show superior 3-year overall drug survival of
dupilumab compared to CsA and MTX in pediatric AD patients. These results provide insight in long-term safety of these systemic treatment options and may help clinicians in the decision-making process when choosing treatment options for pediatric AD patients in daily practice.

Figure 1. Overall drug survival for dupilumab, cyclosporine A, and methotrexate. Abbreviations: DUP, dupilumab; CsA, cyclosporine A; MTX, methotrexate.
Abstract N°: 1894

Can professional cleaners and healthcare workers recognize hand eczema? A challenge to self-reported complaints

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Introduction & Objectives:

Cleaners and healthcare workers (HCW) have an increased risk of developing hand eczema (HE) due to exposure to wet work and cleaning products. Timely intervention is known to reduce the risk of a poor prognosis in HE, making early recognition of HE important in high-risk professions. However limited data exist regarding cleaners’ and HCW’ ability to recognize HE.

The aim of the study was to examine cleaners’ and HCW’ ability to recognize HE in clinical photos based on a previous validated photographic guide and to assess the disease severity.

Materials & Methods:

Cleaners and HCW completed a questionnaire consisting of 16 questions followed by a structured interview referring to a validated photographic severity guide for chronic HE (CHE) consisting of clinical photos of HE at various severity levels. To investigate participants’ ability to recognize HE and assess the disease severity, four clinical photos from the guide depicting different levels of severity were presented one at a time. The photos were randomized twice, i.e. first in regard to severity level, secondly in regard to the selection of each picture within the categories of almost clear (mild), moderate, severe and very severe HE.

Results:

Eighty cleaners and 201 HCW (total n=281) took part in the study (participation rate 80.3%). The rates of correctly identified HE in clinical photos (cleaners/HCW) were: 41.2%/57.7 % (P=.013) for mild HE, 81.2%/92.0% (P=.009) for moderate HE, 85.0%/94.5% (P=.009) for severe HE and 82.5%/97.0% (P=.001) for very severe HE. The HCW proficiency in recognizing HE was significantly higher than that of the cleaners.

Conclusion:

The study indicates that a significant proportion of cleaners and HCW fail to recognize mild HE in clinical photos. HCW achieved higher success rates in recognizing HE in all severity categories. Underestimation of symptoms may lead to an underreporting of the true prevalence of HE and lost opportunities for prevention.
Impact of a digital application on the quality of life of patients with atopic dermatitis

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Atopic dermatitis is a chronic skin disease. Educational measures and a continued medical support is often necessary for an optimized disease management. Digital applications potentially increase the patients knowledge and selfcare by providing high quality educational material, but also allow a detailed documentation of the disease course using standardized patient-related outcomes supporting the patient – physician communication.

To investigate the effectiveness of an app based patient educational and clinical assessment tool, 55 adult patients with a disease-related quality of life above 6 were recruited into this study. Those patients were randomly assigned into the app group or the control group (1:1). Patients in the app group were asked to regularly access the educational material and to document the disease activity in the app “Nia” for 12 weeks concomitant to a standard care consisting of the application of class II corticosteroids (2x/week) in combination with emollient therapy. The control group received the standard care for 12 weeks without access to the app. The change in quality of life before and after 12 weeks was the primary endpoint. The disease severity and disease-related symptoms were assessed before and after 6 and 12 weeks of digital intervention.

At baseline, the cohort of 55 adult patients (29.4% male, 70.6% female) with a median age of 30 years (interquartile range 14) and the median age since diagnosis was 28 years. The mean Dermatology life Quality Index (DLQI) significantly decreased from 9.5 ± 3.7 points at baseline to 5.6 ± 4.0 points after 12 weeks in the app group. For the control group the mean DLQI did not significantly change from baseline (11.5 ± 5.2 points) to the observation end after 12 weeks (8.3 ± 5.0). In the app group the mean EASI decreased from baseline at 4.4 ± 2.6 points to 2.9 ± 2.3 points after 6 weeks and 3.2 ± 2.6 points after 12 weeks, but not in the control group the EASI (baseline (3.4 ± 2.5 points) to the observation end after 12 weeks (2.5 ± 0.3)).

Our first results suggest an impact of the use of the digital app Nia on the Quality of Life (DLQI), but also the disease activity (determined by EASI) in adult atopic dermatitis patients. More data are needed to better identify whether certain age groups, the educational background of a given patient or other individual factors predispose for a response for such an application.
Abstract N°: 1965

The use of Verbascum phlomoides oil in dermatological disorders – the in vivo study

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Introduction & Objectives:

Skin is the largest organ in the human body. Being in contact with the environment, it is exposed to numerous external factors which can lead to various damages. Internal factors, such as a lack of essential nutrients, can also lead to changes often manifesting as dry skin.

For centuries, Verbascum species have been used in traditional folk medicine to treat respiratory disorders, hemorrhoids, rheumatic pain, wounds, and fungal infections. Mullein oil (an oil produced by macerating mullein flowers in vegetable oil), can be topically applied in the case of eczema and other skin conditions.

Our study aimed to assess the impact of creams containing 10% (w/w) V. phlomoides flower oil on artificially irritated human skin aiming to assess its potential as an additional treatment for some dermatological disorders.

Materials & Methods:

According to the traditional prescription, fresh flowers of V. phlomoides L. were used to prepare mullein oil extract by maceration in virgin olive oil (DER of obtained oil extract was 1:5). We formulated and tested two creams: placebo cream (PC) with 10% olive oil and active cream (MC) with 10 % mullein oil. The study lasted for 7 days and included 13 healthy volunteers.

In vivo non-invasive measurements of the biophysical skin parameters were measured with Multi Probe Adapter MPA® 9 device on human skin pre-irritated with sodium-lauryl-sulfate (SLS). SLS irritation leads to skin damage, usually characterized by increased skin erythema and transepidermal water loss (TEWL) and/or decreased skin moisture, and is often used in testing the potential of topicals to reduce the damage and improve dry skin. We observed the changes in EC (electrical capacitance), TEWL, and skin pH values before and after SLS irritation and subsequent treatment with tested creams. The study was approved by the local Ethical Committee (approval number 12-2307-2/2 from 10.03.2016.) and all principles of the Declaration of Helsinki were fulfilled.

Results:

The obtained results are presented in Figure 1 (EC), Figure 2 (TEWL), and Figure 3 (pH). There was a significant increase in skin hydration after the application of both cream samples compared to post-irritation EC values. A greater improvement of hydration on artificially irritated skin was observed for MC compared to PC application with an increase in EC and decreased TEWL (compared to values obtained just after irritation). Changes in pH values were not significant.

Conclusion:

Mullein oil could be used for skin complaints. Our results showed that creams with 10 % mullein oil have beneficial effects on skin pre-irritated with SLS which could imply its use on dry and irritated skin. Further investigation should focus on developing potentially effective topical formulations with Verbasci flos that would provide complementary therapy for dermatologic patients.
Figure 1. % changes of EC related to basal values

Figure 2. % changes of TEWL related to basal values

Figure 3. % changes of pH related to basal values
**Introduction & Objectives:** Atopic dermatitis (AD) or atopic eczema (AE) is a chronic inflammatory skin disease and one of the most common skin diseases in Europe. However, the ideal term for AD/AE has long been controversial. As crowdsourced data opens the possibility to access information from a broad population, this study aims to investigate the use of the terms AD and AE in web searches, as well as the public interest in this disease in different European countries.

**Materials & Methods:** Web search data on AD and AE were generated for 21 European countries (Austria, Bosnia, Croatia, Czech, Denmark, France, Germany, Greece, Hungary, Ireland, Italy, Malta, Netherlands, Poland, Portugal, Romania, Serbia, Spain, Sweden, Ukraine, United Kingdom) using Google Ads Keyword Planner between 02/2019 and 01/2023. The top 20 keywords related to AD and AE in each country were qualitatively categorized into 9 categories: causes, comorbidities, demographics, general, localisation, other disease, others, symptoms, and treatment. Subcategories were formed for recurring keywords, e.g., different localisations (face, etc.). The number of searches per 100.000 inhabitants (/100k) and the categories were described descriptively and differences between countries were assessed with Kruskal-Wallis test.

**Results:** A total of 71,620,240 AD-related searches and 33,913,480 AE-related searches were identified across European countries, with median monthly searches for AD and AE differing between European countries (p<0.001). The highest AD- and AE-related median monthly searches/100k were observed in Poland with 1,307.3 [interquartile range: 1036.3; 1,452.1] and in Czechia with 876.4 [707.9; 1,082.7], respectively. The majority of countries searched for AD more frequently than for AE, except for Czechia, Denmark, Netherlands, and Sweden. In all countries and for both search terms, most searches were general, demographics, localisations, and treatment, although the focus varied slightly between countries, particularly for subcategories. For example, only four countries searched for (natural) remedies, while almost all countries specified their searches to children and babies, except for Austria and Germany. The most searched localisation was the head, especially the face, while searches in Bosnia, Czechia, and Romania tended to focus on the hands. Searches for causes and symptoms of AE were conducted in more European countries than causes and symptoms of AD.
Conclusion: The study highlights the predominant use of AD instead of AE when searching for disease-related online information in Europe. Differences in web search content between AD and AE may indicate confusion in the population and the misconception of two different diseases, which should be addressed. Furthermore, the varying topics and number of searches in different European countries may reflect the need for reliable country-specific information on AD/AE and should be considered in future public AD campaigns.
**Abstract N°: 2019**

**Efficacy and safety of Stapokibart (CM310) in adults with moderate-to-severe atopic dermatitis: results of a randomized, double-blind, placebo-controlled phase 3 trial**

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**Introduction & Objectives:**

Stapokibart (CM310) is a humanized IgG4 monoclonal antibody against the interleukin-4 receptor alpha chain (IL-4Rα) and inhibits IL-4 and IL-13 signaling, which are key drivers of atopic dermatitis (AD). Stapokibart had shown high efficacy and good safety in adults with moderate-to-severe AD in a phase 2 trial (NCT04805411). This phase 3 trial aims to further evaluate the efficacy and safety of stapokibart in adults with moderate-to-severe AD (NCT05265923).

**Materials & Methods:**

In this ongoing, randomized, double-blind, placebo-controlled phase 3 trial, eligible patients were randomized 1:1 to receive subcutaneous stapokibart at a dose of 300 mg (loading dose, 600 mg) or placebo every two weeks (q2w) during a 16-week double-blind period. After 16 weeks of treatment, all patients continued to receive stapokibart for an additional 36 weeks (maintenance period). Co-primary endpoints were the proportion of patients achieving at least a 75% improvement of Eczema Area and Severity Index from baseline (EASI-75) and an Investigator’s Global Assessment (IGA) score of 0/1 with a reduction of ≥ 2 points from baseline at week 16. Other efficacy endpoints were also evaluated, including change from baseline in the Peak Pruritus Numerical Rating Scale (PP-NRS) and the Dermatology Life Quality Index (DLQI). Safety was also assessed.

**Results:**

A total of 500 eligible patients from 59 study sites were included in this trial, with 251 in stapokibart group and 249 in placebo group. The demographics and baseline disease characteristics of the patients were well balanced between the two groups. At week 16, EASI-75 was achieved in 66.9% of patients receiving stapokibart and 25.8% of patients receiving placebo (P<0.0001). An IGA score of 0/1 with a reduction of ≥ 2 points was achieved in 44.2% of patients receiving stapokibart and 16.1% of patients receiving placebo (P<0.0001). Stapokibart was also
superior to placebo in controlling pruritus and improving quality of life. The incidence of treatment-emergent adverse events was similar between the two groups.

**Conclusion:**

Stapokibart demonstrated high efficacy and a favourable safety profile in adults with moderate-to-severe AD.
Abstract No: 2284

Treat-to-Target in the Management of Moderate-to-Severe Atopic Dermatitis in Adults: A Canadian Perspective

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Introduction & Objectives:
Atopic dermatitis (AD) is a chronic skin disease that is associated with substantial burden and quality of life impairment. Systemic treatment may be required for moderate-to-severe AD, and although several options are available, there is limited guidance on how best to modify systemic therapies at the individual patient level to optimize long-term outcomes. The objective of this study is to offer guidance on a pragmatic treat-to-target (T2T) strategy that includes treatment outcomes, measures, and timing of assessments to optimize systemic therapy in adults with moderate-to-severe AD.

Materials & Methods:
A group of 12 Canadian dermatologists with expertise in the management of AD was convened. Following the guiding principles for T2T and a review of evidence from existing guidelines and treatment pathways, a set of recommendations was proposed for assessment timepoints and treatment target criteria. The proposed T2T criteria were then evaluated and rated.

Results:
There was unanimous consensus to assess adult AD patients with at least one physician-rated outcome measure (either the Eczema Area and Severity Index [EASI] or Physician Global Assessment [PGA]) and at least one patient-reported outcome (PRO) measure (pruritus numerical rating scale [NRS], Dermatology Life Quality Index [DLQI] or Patient-Oriented Eczema Measure [POEM]). The recommended timing of assessments is 12-16 weeks, 6-8 months, and one year after the initial visit, followed by maintenance visits every 6-12 months. At each assessment point, treatment should continue if at least one of the physician-rated and one of the PROs is met; otherwise, treatment should be modified or optimized following the principles of shared decision-making.

Conclusion:
The proposed T2T algorithm sets clear outcome targets and timing of assessments for optimization of treatment in adults with moderate-to-severe AD requiring systemic therapy. This pragmatic T2T strategy incorporates scales commonly used in Canadian practice and allows for flexibility in the timing of assessments.
Abstract N°: 2314

A retrospective review of dupilumab-associated side effects in a paediatric population with atopic dermatitis.

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Introduction & Objectives:

Dupilumab is an anti-interleukin 4 (IL-4) and 13 (IL-13) monoclonal antibody used in the treatment of atopic dermatitis. It has been approved for the treatment of atopic dermatitis in adults since 2017, in adolescents since 2019, and was recently approved by the U.S. Food and Drug Administration and the European Commission for the treatment of moderate-to-severe atopic dermatitis in children as young as 6 months old. While dupilumab is well tolerated in the majority of patients, there have been several side effects reported. We review the ocular complications as well as other possible adverse events linked to dupilumab in our local paediatric population.

Materials & Methods:

This is a 4-year retrospective review of paediatric patients being treated with dupilumab for atopic dermatitis in our tertiary hospital. Cases were identified from the dermatology department database, as all patients would receive the first dose of subcutaneous dupilumab administered by our dermatology trained nurse.

Results:

A total of 110 paediatric patients were identified, with ages ranging from 3 to 18 years old. At the time of initiating dupilumab, 48 patients were between 6 – 12 years old while 2 patients were less than 6 years old. 31 patients (28%) had ocular side effects after starting dupilumab, with majority (24 patients) developing conjunctivitis and 7 patients reporting dry and/or itchy eyes without redness. 9 patients had pre-existing eye conditions, 5 of which remained stable while 4 had worsened conjunctivitis after starting dupilumab. The onset of ocular side effects was variable, from within a few days after the loading dose (1 patient) to 14 months after initiation. Most patients improved with topical eye drops alone, 3 patients improved after reducing the frequency of dupilumab, but 3 patients stopped dupilumab due to persistent conjunctivitis. Their conjunctivitis resolved completely after discontinuing dupilumab. 1 patient had injection site pain with no swelling or redness, and 1 patient had persistent facial rash. Another patient developed a viral wart after 10 months of treatment, while 1 patient had tinea capitis after 14 months of treatment. 1 patient was noted to develop vitiligo 4 months into treatment with dupilumab.

Conclusion:

Ocular side effects were the most common adverse effect seen in our paediatric patients receiving dupilumab. Majority of patients were continued on dupilumab, with only 3 out of 110 patients stopping treatment due to side effects. We conclude that dupilumab is overall well tolerated in our paediatric population.
Human Umbilical Cord Mesenchymal Stem Cell Treatment Alleviates Symptoms in an Atopic Dermatitis-like Mouse Model

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Introduction & Objectives:

Atopic dermatitis (AD) is a common inflammatory skin disorder characterized by recurrent eczematous lesions and severe itching. Traditional treatments are less effective and might have side effects in chronic and refractory AD. Therefore, safer and more effective treatments need to be developed. Mesenchymal stem cells (MSCs) have vital ability to modulate immune and inflammatory responses. The results of a clinical trial in South Korea showed 50% reduction in EASI, SCORAD and itching. To elucidate underlying mechanisms of how stem cells therapy alleviates AD-like symptoms, this study established a DNCB-induced AD-like mouse model and adopted human umbilical cord MSCs for exploration of curative effects.

Materials & Methods:

Female six-week-old BALB/c mice were divided randomly into four groups of six mice. The backs of mice were shaved two days before sensitization. For sensitization, 1% DNCB was applied on days 0, 3, 6, and 9. Subsequently, the dorsal skin was repeatedly challenged with 0.5% DNCB solution on days 12, 15, 18, 21, 24, and 27. Each mouse in the MSC treatment group received a dose of 2×10⁶ MSCs on days 13, 17, 21, and 25. Dorsal skin sections and blood samples were collected on day 30 and total RNA was isolated with TRIzol reagent. RNA sequencing was conducted by company. The Differentiated genes were selected by the criteria of |fold change|>2 and p value<0.5.

Results:

Both subcutaneous injection or subcutaneous combined with intravenous injection of mesenchymal stem cells could alleviate AD-like symptoms and pathologic changes of the skin, as well as unexpected hair growth promotion. DNCB induced splenomegaly and enlarged lymph nodes, while the absolute or relative weight of the spleen and lymph nodes were significantly decreased after MSC treatment. RNA Seq-based transcriptomics of skin sections and blood and subsequent analysis indicated MSC treatment rebalances skin and blood homeostasis by modulation of inflammatory and immune responses. MSC treatment effectively restored the gene expression levels of IL-1β, IL-1RAP, IL-1R2, Myd88, Nlrp3, and IL-4 and IL-13 receptors in both the skin and blood, and the IL-17 receptor in blood. Similar results were obtained for JAK-Stat pathway. The suppression of Fcer1g in both skin and blood was found rather than reduction of serum IgE by MSC treatment. MSC treatment restored gene expression patterns related to skin barrier such as Flg, Flg2, Cldn3, Cldn23, Tgm3, Klk14, Elovl3, Elovl4, Elovl5, Elovl6, Sgms2 and Cers4. GSEA analysis showed enriched pathways like Staphylococcus aureus infection, bacterial invasion of epithelial cells in the DNCB group. MSC treatment could rebalance AD related gene expression such as CD14, Ifitm1, Tlr1, Tlr2, Tlr6, Tlr13, Lcn2, Hdc, LilrA6, Trem1, and Mmp9 in both skin and blood. And Adam8, CXCR1 and CXCR2 maybe potential markers for future judgements.

Conclusion:

There are unmet needs for moderate to severe atopic dermatitis patients for long-term and safe control. MSCs may offer the advantage to modulate multiple cytokine signaling targets for treatment of AD. Both subcutaneous injection or subcutaneous combined with intravenous injection of mesenchymal stem cells are effective, different...
routes may be alternatives for patients with different conditions in clinical application. Besides, some common biomarkers in skin and blood may help to diagnose disease progression and efficacy.

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Introduction & Objectives:
Emollients are considered as a mainstay regarding the most recent European recommendations (EuroGuiDerm) for management of atopic dermatitis. A novel generation of emollients, “Emollients Plus” are composed not only with occlusive, moisturizing and skin barrier agents but also non-pharmacological ingredients to target mechanisms in AD pathophysiology. Herewith we tested safety and efficacy of medical device Emollient Plus cream in reduction of AD symptoms. Hence, set of in vitro, ex vivo and in vivo studies were performed.

Materials & Methods:
The safety of a product was evaluated in accordance with ISO 10993 by performing in vitro MTT cytotoxicity test whereas irritation potential was tested on EpiDerm skin model. Medium was collected to perform cytometrics analysis for following interleukins: IL-1β, IL-6, IL-8. In vivo study was conducted on a group of 88 volunteers, members of Polish Association for Atopic Diseases. All participants had symptomatic AD lesions. Among volunteers, 67% of patients were considered as paediatric – below age of 18. After 14 days of using the Emollient Plus cream, participants or their caregivers filled the questionnaire and assessed the efficacy of tested product.

Results:
In vitro MTT study confirmed that the medical device Emollient Plus cream did not exhibit cytotoxic properties towards L929 cells at the concentration of at least or equal to 0.01%. Furthermore, the product did not express irritation potential in test performed on EpiDerm (tissue viability 103%) while compared to the control. Flow cytometry did not show any significant changes in the concentration of IL-1β, IL-6, IL-8. All volunteers that took a part in the study filled the questionnaire among which 86% found that their AD lesions were reduced. In case of 87% patients pruritus was decreased whereas 64% of patients found that the sleeping comfort was improved. Erythema was reduced in 82% participants, 63% patients reported reduction in thickened skin, 84% volunteers found reduced severity of exudative lesions. Taking into account both in vitro and in vivo studies, tested product could be considered as non-irritant for the skin.

Conclusion:
In vitro and ex vivo studies confirmed that medical device Emollient Plus cream was well-tolerated for skin. Furthermore, in vivo trial additionally showed its high efficacy expressed as reduction of AD symptoms including erythema, pruritus, skin thickening, wound exudate and flaking along with general improvement of sleep quality.
Abstract N°: 2398

Reduced Filaggrin Expression in Atopic Eczema Causes Dysregulation of Intracellular Signalling Pathways and Reduced Expression of Key Barrier Genes

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¹Blizard Institute, Queen Mary University of London, London, United Kingdom

Introduction & Objectives:

Atopic eczema (AE) is the most common inflammatory dermatosis, affecting up to 20% of children (Odhiambo et al., 2009). Loss of function (LoF) mutations in the Filaggrin (FLG) gene are the most strongly implicated genetic risk factor for AE (Bin & Leung, 2016), but attempts to restore FLG have so far been unsuccessful (Irvine, 2014). FLG is part of a gene complex, called the epidermal differentiation complex (EDC), the genes of which contribute to various aspects of epidermal barrier function. FLG is expressed in the upper epidermis, where it binds keratin (KRT) fibrils to form a structural barrier (Dale et al., 1997). Part of the FLG protein enters the nucleus, which led us to hypothesise that FLG modulates the expression of other key proteins.

Materials & Methods:

The FLG gene was knocked down (KD) in primary keratinocytes using lentiviral shRNA. Western blotting, RNA-seq, qPCR and phosphoproteomic analysis was performed on lysates from these cells. Western blotting and proteomics was performed from lysates extracted from tape strips (TS) taken from AE patients who were clinically phenotyped and genotyped for FLG mutation status. Immunostaining was performed on biopsies taken from other AE patients. A bioinformatic analysis was performed on repository microarray AE datasets. Rat epidermal keratinocytes were cultured in the presence of recombinant BMP (rBMP) 2 or 6 or the BMP receptor antagonist DMH1.

Results:

FLG KD keratinocytes showed a global reduction in KRT and EDC genes (Fig 1). FLG KD was associated with up-regulation of bone morphogenetic protein (BMP) signalling (Fig 2). Analysis of repository datasets from AE patients showed a negative correlation between FLG and BMP6 expression across multiple datasets (Fig 3). Western blots from TS lysates showed a negative correlation between FLG expression and phospho-SMAD (pSMAD)1/5/9, a marker of active BMP signaling (Fig 4). pSMAD1/5/9 expression was greatest in AE patients with 2 LoF FLG mutations relative to wild type patients (Fig 4). pSMAD1/5/9 negatively correlated with corneometry, a clinical measure of barrier function (Fig 4). Skin biopsies from AE patients showed increased BMP2 expression in patients with low FLG expression (Fig 5). Keratinocytes cultured with rBMP2 or rBMP6 expressed more FLG and KRT1, while keratinocytes treated with DMH1 had reduced FLG and KRT1 expression (Fig 6).

Phosphoproteomic analysis showed 237 significantly differentially phosphorylated proteins following FLG KD. Kinase enrichment analysis identified the ERK, p38 and AKT1 signalling pathways as key pathways responsible for these phosphorylation states (Fig 7). We confirmed that downregulation of the AKT and ERK pathways is associated with loss of FLG using western blotting of FLG KD lysates and immunostaining from AE patient biopsies (Fig 7).

Conclusion:

Our data shows that the role of FLG extends beyond that of a structural protein. Loss of FLG in AE patients
dysregulates intracellular signalling pathways, with associated downregulation of epidermal KRT and EDC expression. BMP treatment increased FLG expression in cell culture, suggesting that BMP signalling is a protective response to barrier disruption. The BMP, AKT and ERK signalling pathways are downstream pathways of FLG, which could be novel therapeutic targets to restore barrier function in AE and other atopic diseases.
**Figure 2**

pSMAD1/5/9 A Marker of BMP Signalling is Upregulated Following FLG KD

**Figure 3**

Correlation Analysis with FLG Gene Expression Across Microarray Datasets

<table>
<thead>
<tr>
<th>Dataset</th>
<th>RPTN</th>
<th>LOR</th>
<th>SPRR3</th>
<th>KRT10</th>
<th>KRT1</th>
<th>KRT2</th>
<th>FLG2</th>
<th>S100A14</th>
<th>LCE1B</th>
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</tbody>
</table>

- **Red** indicates significant positive correlation \( p<0.05 \)
- **Green** indicates significant negative correlation \( p<0.05 \)
Figure 4

Western Blots from AE Patients' Tape Strip Lysates

pSMAD1/5/9 Expression is Highest in FLG Compound Heterozygote AE Patients

pSMAD1/5/9 Negatively Correlates with FLG Expression in AE Patients

pSMAD1/5/9 Negatively Correlates with Corneometry in AE Patients

Figure 5

Immunostaining of Biopsies from AE Patients

Wild type  Heterozygote  Compound Het

BMP2

ID1

BMP2

ID1
Keratinocytes Cultured With rBMP2 or rBMP6 Express More FLG and KRT1

FLG

Profilaggrin

Filaggrin monomer

KRT1

Alpha Tub

rBMP6 (ng/ml)

CT 25 125 200

kDa

FLG Densitometry

rBMP6

0.0168

rBMP2

0.9098

KRT1

0.3285

0.9423

Keratinocytes Cultured With the BMP Receptor Antagonist DMH1 Express Less FLG and KRT1

FLG

DMH1 (µM)

CT 10 20

250 kDa

100 kDa

pSMAD 1/5/9

KRT1

Alpha Tubulin

FLG Densitometry

pSMAD1/5/9

0.0060

0.0012

pSMAD1/5/9 Densitometry

DMH1 Concentration (µM)

0.0016

0.0010
Figure 7
Phosphoproteomic Analysis of FLC KD Keratinocytes

Immunostaining of AE Biopsies

Western Blots from FLC KD Lysates

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Abstract N°: 2466

Effect of delgocitinib cream 20 mg/g on Dermatology Life Quality Index in patients with moderate-to-severe chronic hand eczema: pooled data from the DELTA 1 and DELTA 2 phase 3 trials

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1University Medical Center Groningen, University of Groningen, Groningen, Netherlands, 2LEO Pharma A/S, Ballerup, Denmark, 3University Allergy Centre, University Hospital Carl Gustav Carus, Technical University, Dresden, Germany

Introduction & Objectives:

Chronic hand eczema (CHE) is a chronic inflammatory skin disorder characterized by itch and pain that can have a profound negative impact on patients’ physical and psychological health-related quality-of-life (HRQoL). Patients with moderate-to-severe CHE who do not respond adequately to topical therapies have limited treatment options. Delgocitinib is a topical pan-Janus kinase inhibitor that is effective and well tolerated for the treatment of CHE. The effect of delgocitinib cream 20 mg/g on HRQoL as measured by the Dermatology Life Quality Index (DLQI) score was assessed in a pooled analysis of two pivotal phase 3 trials.

Materials & Methods:

DELTA 1 (NCT04871711) and DELTA 2 (NCT04872101) were phase 3 trials of identical design. In both trials, adult patients with moderate-to-severe CHE were randomised (2:1) to double-blind treatment with delgocitinib cream 20 mg/g or cream vehicle twice daily for 16 weeks. Data were pooled from both trials and changes in DLQI scores were assessed from baseline to week 16 in all patients and in a post-hoc analysis of patients achieving clinical responses, defined as Hand Eczema Area and Severity Index (HECSI) 50, -75, and -90, Investigator’s Global Assessment for CHE treatment success (IGA-CHE TS; a score of 0/1 with a ≥2-step improvement from baseline), and ≥4-point improvements in Hand Eczema Symptom Diary (HESD) itch and pain scores.

Results:

Across the two trials, 639 patients were randomised to delgocitinib cream 20 mg/g and 321 to cream vehicle. The majority of patients were white (90%), female (64%), and had a mean duration of CHE of approximately 10 years. Mean ± SD DLQI score at baseline was 12.4 ± 6.1 in the delgocitinib group and 12.4 ± 6.7 in the cream vehicle group. Delgocitinib resulted in a significantly greater improvement (i.e., reduction) in DLQI from baseline compared with cream vehicle at week 16 (least squares mean change [SE] −7.25 ± 0.22 vs. −3.46 ± 0.31; difference [95% CI] −3.79 (−4.55, −3.04), p<0.001) (Figure). Improvements in DLQI at week 16 were clinically meaningful (minimum clinically important difference = 4) and significantly greater (p<0.001) with delgocitinib versus cream vehicle across all ten DLQI items, in particular those concerning skin-related embarrassment or self-consciousness and effects on work, social and leisure, and other daily activities. When analysed by clinical response, greater improvements in DLQI with delgocitinib versus cream vehicle were observed across all clinical responder categories, with these differences statistically significant for all except HECSI-90 and IGA-CHE TS. This is in addition to a higher proportion of patients treated with delgocitinib than cream vehicle achieving a clinical response as assessed across all responder thresholds (all p<0.001).

Conclusion:

Twice-daily application of delgocitinib cream 20 mg/g resulted in a statistically and clinically significant improvement in HRQoL versus cream vehicle as measured by DLQI in patients with moderate-to-severe CHE. In
patients with a clinical response, the HRQoL benefit was greater with delgocitinib than with cream vehicle.

### Figure. Changes from baseline in DLQI at week 16 in all patients and by treatment response as assessed by HECSI, IGA-CHE and HEDE itch and pain scores

<table>
<thead>
<tr>
<th>Timepoint DLQI</th>
<th>All patients</th>
<th>Clinical responders</th>
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</thead>
<tbody>
<tr>
<td>12.64</td>
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<td>12.96</td>
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<td>12.03</td>
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<td>11.02</td>
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<td>10.32</td>
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<td>12.06</td>
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<tr>
<td>12.62</td>
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<tr>
<td>12.04</td>
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<td></td>
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<tr>
<td>12.54</td>
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</table>

#### Minimum/important difference in change in DLQI ≥ 4

<table>
<thead>
<tr>
<th>Delgocitinib cream 20 mg/g</th>
<th>Cream vehicle</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 41</td>
<td>432 (67.0%)</td>
</tr>
<tr>
<td>411 (66.3%)</td>
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<tr>
<td>131 (26.7%)</td>
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<tr>
<td>154 (29.4%)</td>
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<tr>
<td>234 (46.7%)</td>
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<tr>
<td>254 (47.7%)</td>
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</table>

P values in parentheses: the difference between groups. DLQI: Disease-Related Quality of Life Index; HECSI: Health-Related QoL for Eczema Scale; IGA-CHE: Investigator Global Assessment of Eczema; HEDE itch and pain: Human Eczema Damage Evaluation Tool itch and pain score.
Delgocitinib cream 20 mg/g improves health-related quality of life (EQ-5D) in patients with moderate-to-severe chronic hand eczema: pooled results from two randomised, controlled phase 3 trials

Andrea Bauer1, Henrik Thoning2, Nanna Julie Nyholm Jensen2, Marie Louise Schuttelaar3

1University Allergy Centre, University Hospital Carl Gustav Carus, Technical University, Dresden, Germany, 2LEO Pharma A/S, Ballerup, Denmark, 3University Medical Center Groningen, University of Groningen, Groningen, Netherlands

Introduction & Objectives:

Chronic hand eczema (CHE) is a fluctuating disorder characterized by itch and pain that can negatively impact patients’ health-related quality-of-life (HRQoL), physical functioning, and ability to work. To date, there are no treatments specifically approved for moderate-to-severe CHE that provide long-term disease control. Delgocitinib is a first-in-class topical pan-Janus kinase inhibitor that provides early symptom relief and is well tolerated in patients with CHE. The effect of delgocitinib cream 20 mg/g on HRQoL measured using the EuroQol 5-dimension (EQ-5D) questionnaire was assessed in patients with moderate-to-severe CHE enrolled in two pivotal phase 3 trials.

Materials & Methods:

DELTA 1 (NCT04871711) and DELTA 2 (NCT04872101) were identically designed multicentre phase 3 trials in which adult patients with moderate-to-severe CHE were randomised (2:1) to double-blind treatment with delgocitinib cream 20 mg/g or cream vehicle twice daily for 16 weeks. In a pooled analysis of both trials, changes in EQ-5D scores from baseline to week 16 were assessed in all patients and in a post-hoc analysis of patients achieving clinical responses (defined as Hand Eczema Area and Severity Index (HECSI)50, -75, and -90, Investigator’s Global Assessment for CHE treatment success [IGA-CHE TS; clear or almost clear skin with a ≥2-step improvement from baseline] and ≥4-point improvements in Hand Eczema Symptom Diary (HESD) itch and pain scores.

Results:

A total of 639 patients were randomised to delgocitinib cream 20 mg/g and 321 to cream vehicle across both trials. Most patients were white (90%), female (64%), with baseline moderate CHE disease severity (72%). Mean ± SD EQ-5D score at baseline was 0.65 ± 0.23 in the delgocitinib group and 0.64 ± 0.24 in the cream vehicle group. Treatment with delgocitinib resulted in a significantly greater improvement in EQ-5D from baseline compared with cream vehicle at week 16 (least squares mean change [SE] 0.17 ± 0.01 vs. 0.06 ± 0.01; difference [95% CI] 0.11 (0.08, 0.13), p < 0.001) (Figure). Improvements in EQ-5D were significantly greater with delgocitinib versus cream vehicle across all five EQ-5D dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). When analysed by clinical response, there were clinically meaningful changes in EQ-5D (minimally important difference = 0.082) across the different responder thresholds, suggesting a relationship between HRQoL improvement and clinical response. Furthermore, improvements in EQ-5D were consistently higher with delgocitinib compared with cream vehicle within each clinical responder group, all of which were statistically significant except for the IGA-CHE TS category. This is in addition to significantly more patients treated with delgocitinib achieving a clinical response across different clinical responder thresholds.

Conclusion:
In patients with moderate-to-severe CHE with a substantial HRQoL impairment, 16 weeks of twice-daily treatment with delgocitinib cream 20 mg/g resulted in a statistically significantly greater improvements than cream vehicle in not just clinical outcomes, but also HRQoL as measured by the EQ-5D score. Among patients achieving a clinical response across various responder thresholds, treatment with delgocitinib resulted in an even greater HRQoL benefit than cream vehicle. This HRQoL improvement was considered clinically meaningful.
Abstract N°: 2506

Long-term clinical effectiveness and reasons for discontinuation of dupilumab treatment in patients with atopic dermatitis; 5-year results from the BioDay registry


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Introduction & Objectives: Dupilumab, the first approved biological for the treatment of atopic dermatitis (AD), is frequently prescribed in clinical practice and a substantial number of AD patients experience great benefit from this treatment. So far, limited daily practice data are available on the long-term effectiveness and safety of dupilumab. Therefore, the aim of this study was to evaluate long-term clinical effectiveness and reasons for discontinuation of dupilumab treatment in AD patients in daily practice.

Materials & Methods: This prospective multicenter study consecutively included all AD patients from the BioDay registry treated with dupilumab, including children and adolescents. Effectiveness was evaluated by the Eczema Area and Severity Index (EASI), Investigator Global Assessment (IGA) and Numeric Rating Scale (NRS)-weekly average pruritus, stratified by children (<18 years), adults (<65 years) and elderly (≥65 years). In addition, time to response, (partial) responders, EASI subscores, second treatment episodes, thymus and activation-related chemokine (TARC) and eosinophil levels were assessed. For patients who discontinued dupilumab, the reason for discontinuation was evaluated.

Results: A total of 1286 patients were included with dupilumab treatment up to 5 years (n=130 children/adolescents; n=1025 adults; n=131 elderly). The median age was 38.0 years (interquartile range (IQR) 26.0-54.0) and 56.6% of the patients was male. Most patients achieved controlled AD with EASI ≤7, NRS-pruritus ≤4 and IGA of (almost) clear ranging between 78.6-92.3%, 72.2-88.2% and 44.5-63.6% respectively, while up to 69.4% of the patients prolonged dupilumab interval to 300mg every 3-4 weeks. Dupilumab showed similar effectiveness for all four anatomical body regions. A significant difference in effect over time between children, adults and elderly was found for EASI and IGA (p=0.046 and p=0.010, respectively) (Figure 1A/B), however differences were rather small. No significant difference between age groups was found for NRS-pruritus (p=0.055, Figure 1C). Median TARC levels significantly decreased from 1751pg/ml (95% confidence interval (CI) 1614-1900) to 390pg/ml (95% CI 368-413) after 6 months of treatment and remained low. Median eosinophil levels temporarily increased up to 16 weeks of treatment and then significantly decreased over time (p=0.0002). In total, 305 patients (23.7%) discontinued dupilumab treatment after a median of 54.0 weeks (IQR 28.0-109.0) with adverse events (AEs) (n=98, 7.6%) and ineffectiveness (n=85, 6.6%) as most frequently reported reasons. Forty-
one (3.2%) patients restarted dupilumab treatment after a median stop period of 36.0 weeks (IQR 16.5-56.5) of which most patients recaptured response.

**Conclusion:** During 5 years of follow-up, dupilumab maintained its effectiveness while two-thirds of the patients tapered to an interval of every 3-4 weeks. Approximately 25% discontinued treatment mainly due to AEs and/or ineffectiveness.

**Figure 1.** Primary continuous outcomes (mean, 95% CI) of 1286 AD patients during 5 years of dupilumab treatment, stratified by the total cohort and age groups. **A;** EASI score over time. **B;** IGA score over time. **C;** NRS pruritus over time.

EASI: Eczema Area and Severity Index; IGA: Investigator Global Assessment; NRS: Numeric Rating Scale; CI, confidence intervals; BL, baseline; W, week; y, year; m, month. P-values based on overall likelihood ratio tests for time.
Abstract N°: 2514

Patients´ preferences for systemic treatment of atopic dermatitis: safety and efficacy count the most

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Introduction & Objectives: The advent of biologicals and janus kinase inhibitors has revolutionized treatment of atopic dermatitis. When choosing an agent, patients’ needs and preferences have essential impact on treatment decisions. Therefore, we investigated the preferences of patients with atopic dermatitis for process and outcome attributes associated with systemic treatments and assessed influencing factors.

Materials & Methods: An online discrete choice experiment was conducted in patients with atopic dermatitis from Dermatology departments and self-aid groups throughout Germany to analyze patient preferences for systemic treatments based on outcome attributes (probability of (almost) clear skin at week 16, probability of significant itch improvement at week 16, time to onset of itch relief and type of side effects) and process attributes (application method and frequency of laboratory tests).

Results: The study cohort (n=182, 75.3% female) considered type of side effects (Relative Importance Score (RIS)=31.4) and probability of (almost) clear skin at week 16 (RIS=24.2) most important, followed by probability of significant itch improvement at week 16 (RIS=16.0). Application method (RIS=14.4), time to onset of itch relief (RIS=7.4), and frequency of laboratory tests (RIS=6.8) were less relevant. Treatment preferences were influenced by age, psychiatric comorbidity, current therapy and disease severity.

Conclusion: Overall, participants attached great importance to the type of side effects and symptom control (skin clearance and itch). However, preferences were also significantly influenced by individual characteristics, underscoring the importance of personal counseling. Conjoined with medical considerations, patients’ needs and preferences have to be addressed and considered during shared decision-making for systemic treatment of atopic dermatitis.
Abstract N°: 2531

Rocatinlimab improves SCORAD and DLQI in adults with moderate-to-severe atopic dermatitis and these effects were maintained in the 20-week off-treatment period in a double-blind randomized Phase 2b study

Emma Guttman-Yassky*, Ehsanollah Esfandiari, Camilla Chong, Hirotaka Mano, Kenji Kabashima

Introduction & Objectives: Rocatinlimab, an anti-OX40 monoclonal antibody, was evaluated for moderate-to-severe atopic dermatitis (msAD) in a multicenter, randomized, double-blind, placebo-controlled, Phase 2b trial (NCT03703102). Primary endpoint achievement (Eczema Area and Severity Index [EASI]) has previously been presented. Other important msAD efficacy assessment tools include SCORing of Atopic Dermatitis (SCORAD; combines disease extent, severity, and subjective symptoms) and Dermatology Life Quality Index (DLQI). Here, we evaluate rocatinlimab efficacy in adults with msAD using SCORAD and DLQI.

Materials & Methods: Randomized patients (n=274; 1:1:1:1:1) received 36 weeks subcutaneous rocatinlimab (150/600 mg every 4 weeks or 300/600 mg every 2 weeks [Q2W]; rocatinlimab-rocatinlimab), or placebo (followed by rocatinlimab 600 mg Q2W from Week 18; placebo-rocatinlimab), with off-treatment follow-up (Weeks 36–56). SCORAD and DLQI analyses at Weeks 16, 24, 36, and 56 were predefined endpoints.

Results: The full analysis set included 267 patients. Mean baseline scores ranged from 66.4–69.8 for SCORAD and 11.9–13.8 for DLQI among cohorts. At Week 16, percent change from baseline in SCORAD was significantly improved in all rocatinlimab cohorts vs. placebo (−41.04 to −55.83% vs. −19.99%, all p<0.001), as was DLQI (−38.28 to −50.42% vs. −5.28%; all p<0.02). SCORAD and DLQI improvements from baseline continued to Week 36 (−60.42 to −72.32% and −46.51 to −67.81%, respectively for all rocatinlimab-rocatinlimab cohorts) and were maintained during the 20-week off-treatment period until Week 56 (−59.76 to −69.23%; −47.76 to −60.76%, respectively). For the placebo-rocatinlimab cohort, after switching to active treatment from Week 18, SCORAD and DLQI were comparable to rocatinlimab-rocatinlimab cohorts by Week 36 (−57.47% and −51.41%, respectively) and were maintained during the off-treatment period (−67.42% and −58.43%, respectively).

Conclusion: Consistent with significant EASI improvement, rocatinlimab demonstrated significant SCORAD and DLQI improvements, which were maintained for 20 weeks off-treatment, suggesting rocatinlimab may have potential for disease-modification in adults with msAD.
Abstract N°: 2535

Rocatinlimab improves lichenification compared with placebo in adults with moderate-to-severe atopic dermatitis in a Phase 2b trial

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Introduction & Objectives: Lichenification is a common occurrence for patients with moderate-to-severe atopic dermatitis (msAD) and is often difficult to treat. Furthermore, lichenification can negatively impact patient quality of life, especially when it affects skin in the head and neck (H&N) region. Rocatinlimab (roca) is a monoclonal antibody that inhibits OX40 signalling and reduces the number of OX40+ pathogenic T cells responsible for driving the systemic and local AD inflammatory responses. Roca was evaluated for the treatment of msAD in a multicenter, randomized, double-blind, placebo-controlled Phase 2b trial (NCT03703102). Phase 2b data demonstrating achievement of the primary endpoint (Eczema Area and Severity Index [EASI]) has previously been presented. In this post hoc analysis we assess the lichenification component of EASI across different body regions in adults with msAD.

Materials & Methods: Randomized patients (1:1:1:1:1) received subcutaneous roca every 4 weeks (150 or 600 mg) or every 2 weeks (Q2W; 300 or 600 mg), or placebo for 18 weeks, followed by 18 weeks of roca treatment (placebo group switched to 600 mg Q2W), with a subsequent 20-week off-treatment follow-up period (Weeks 36–56). EASI lichenification score changes from baseline were assessed at Weeks 16, 24, 36, and 56 using mixed models for repeated measures for each roca treatment group and placebo. EASI lichenification scores were assessed separately for the following body regions: H&N, trunk, upper limbs, and lower limbs.

Results: Overall, 267 patients were randomized (roca: n=210; placebo: n=57). At Week 16, treatment with roca resulted in improvements in EASI lichenification scores across all body regions when compared with placebo (Figure 1). Lichenification improvements vs placebo were statistically significant for all roca treatment groups in the H&N region at Week 16. Improvements in EASI lichenification scores across all body regions continued up to Week 36 and were maintained during the off-treatment period, up to Week 56, in all roca treatment groups. In patients who were switched from placebo to roca treatment at Week 18, EASI lichenification scores improved from baseline across all body regions up to Week 36, and the improvements were maintained up to Week 56.

Conclusion: Roca improved EASI lichenification scores consistently in the H&N region and across all body regions vs placebo at Week 16; responses with roca continued through Week 36 and were maintained up to Week 56. Together with previous data demonstrating that EASI score improvements from baseline were maintained up to Week 56 (despite being off treatment for 20 weeks), these data suggest that roca may have potential for disease modification across all body regions in adults with msAD.
Figure 1. LS mean percentage change from baseline in EASI lichenification scores for H&N (A), trunk (B), upper limbs (C), and lower limbs (D) up to Week 56.

A

B

C

D

* Indicates p-values <0.05.

Data represents LS mean percentage change from baseline; p-values represent MMRM for percentage change from baseline vs. placebo at Week 16.

EASI, Eczema Area and Severity Index; H&N, head and neck; LS, least-squares; MMRM, mixed models for repeated measures; Q2W, every 2 weeks; Q4W, every 4 weeks; Raco, rocaltimod; W, Week.
A 28-week evaluation of daily practice experience of tralokinumab in adult patients with moderate-to-severe atopic dermatitis: results from the BioDay registry

Coco Dekkers1, Marijke Kamsteeg-Lemstra2, Wietske A. Christoffers3, Inge Haeck4, Wouter Touwslager5, Klaziena Politiek6, Anneke Lynden - van Nes7, P.P.M. Van Lumig8, Bert Oosting9, Marie-Louise Anna Schuttelaar10, Marlies De Graaf1, Marjolein De Bruin-weller1

1UMC Utrecht, Dermatology, Utrecht, Netherlands, 2Radboud University Medical Center, Nijmegen, Netherlands, 3Isala Zwolle, Zwolle, Netherlands, 4Reinier de Graaf Gasthuis, Delft, Netherlands, 5Catharina Ziekenhuis, Eindhoven, Netherlands, 6Medical Center Leeuwarden, Leeuwarden, Netherlands, 7Meander Medical Center, Amersfoort, Netherlands, 8Maastricht University Medical Center, Maastricht, Netherlands, 9Spaarne Gasthuis Haarlem, Haarlem, Netherlands, 10University Medical Center Groningen, Groningen, Netherlands

Introduction & Objectives:
Tralokinumab – a biological that specifically targets interleukin-13 – is one of the newer advanced systemic treatments for adult patients with moderate-to-severe atopic dermatitis (AD). Although safety and efficacy have been shown in phase-III clinical trials, there are limited daily practice data available. Therefore, the aim of this study is to evaluate 28-week efficacy and safety of tralokinumab in adult patients with AD in daily practice.

Materials & Methods:
In this study we prospectively included all adult patients with AD who started treatment with tralokinumab and participated in the BioDay registry.** Data were collected before start of treatment (baseline), after 4 weeks, after 16 weeks and after 28 weeks of treatment.** Clinical efficacy was evaluated by clinical outcome measures, such as the Eczema Area and Severity Index (EASI) as well as patient reported outcome measures, such as the numerical rating scale (NRS) for itch. In addition, adverse events were evaluated.

Results:
Data of the first 28 weeks of treatment with tralokinumab of approximately 80 AD patients will be presented. At the moment, preliminary results of 72 patients who have been treated with tralokinumab for 16 weeks are described. These patients were divided into two groups based on previous use of dupilumab, resulting in a group of 41 dupilumab naïve patients (dup-N) and 31 patients who previously failed on dupilumab due to ineffectiveness and/or side-effects (dup-F). As 21 patients (67.7%) started treatment with tralokinumab during the wash-out period of dupilumab, the mean EASI at baseline was significantly lower in dup-F compared to dup-N (8.7 vs. 13.5, p=0.021). During treatment, mean EASI (SD) decreased in both groups from 13.5 (9.4) at baseline to 5.7 (5.8) at week 16 in dup-N and from 8.7 (7.9) at baseline to 4.3 (5.3) at week 16 in dup-F (Figure 1a). Mean NRS itch (SD) decreased from 6.7 (2.1) and 5.4 (3.2) at baseline to 4.3 (2.8) and 4.4 (2.0) at week 16 in dup-N and dup-F, respectively (Figure 1b). Adverse events were reported by 26 patients (63.4%) and 9 patients (29.0%) in dup-N and dup-F, respectively. The most reported adverse events were conjunctivitis (25.7%) and hair loss (11.6%). A total of 20 patients (27.7%) discontinued treatment before or at 16 weeks of treatment, mostly due to side-effects (N=7; 35%) or ineffectiveness (N=6; 28.6%). The percentage of patients who discontinued treatment was slightly higher in dup-N than dup-F group (28.6% vs. 23.3%).

Conclusion:
These preliminary results show that tralokinumab is effective in patients with moderate-to-severe AD, in both biological naïve patients and patients who previously failed on dupilumab treatment. Our future analyses will show whether outcomes will further improve during the 28-week follow-up period.

**Figure 1** a) Mean EASI (SD) during treatment with tralokinumab in Dup-N and Dup-F at baseline, after 4 weeks and 16 weeks of treatment. b) Mean NRS Itch (SD) during treatment with tralokinumab in Dup-N and Dup-F at baseline, after 4 weeks and 16 weeks of treatment. Abbreviations: EASI, Eczema Area and Severity Index; SD, Standard Deviation; NRS, Numerical Rating Scale; Dup-N; dupilumab-naïve; Dup-F; dupilumab failure.**
Abstract N°: 2537

Rocatinlimab improves SCORAD compared with placebo in adults with moderate-to-severe atopic dermatitis regardless of baseline demographics in a Phase 2b trial

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1Icahn School of Medicine at Mount Sinai, New York, NY, USA, 2Kyowa Kirin, Marlow, UK, 3Kyowa Kirin, Tokyo, Japan, 4Department of Dermatology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

Introduction & Objectives: Rocatinlimab (roca) is a monoclonal antibody that inhibits OX40 signalling and reduces the number of OX40+ pathogenic T cells responsible for driving systemic and local atopic dermatitis (AD) inflammatory responses. The efficacy and safety of roca in moderate-to-severe AD (msAD) was evaluated in a multicenter, randomized, double-blind, placebo-controlled Phase 2b trial (NCT03703102). SCORing of Atopic Dermatitis (SCORAD) is considered a stringent clinical tool and a validated outcome measure that is used to assess the extent and severity of AD in clinical trials. In this post hoc analysis, we assess changes in SCORAD by baseline characteristic subgroups in adults with msAD.

Materials & Methods: Randomized patients (1:1:1:1:1) received subcutaneous roca every 4 weeks (150 or 600 mg) or every 2 weeks (Q2W; 300 or 600 mg), or placebo for 18 weeks, followed by 18 weeks of roca treatment (placebo switched to 600 mg Q2W) with a subsequent 20-week off-treatment follow-up period (Weeks 36–56). SCORAD changes from baseline were assessed at Weeks 16, 24, 36, and 56 using analysis of covariance. AD severity at baseline was defined by the Eczema Area and Severity Index (EASI) and Investigator’s Global Assessment (IGA) scores: moderate AD was defined by an EASI score of ≥16–<21 and an IGA score of 3; severe AD was defined by an EASI score ≥21 and an IGA score of 4. Baseline characteristics subgroups included: EASI score of 16–<21 and ≥21; IGA score of 3 and 4; body mass index (BMI) of <25 and ≥25 kg/m²; age <40 and ≥40 years; and AD duration of <10 and ≥10 years.

Results: Overall, 267 patients were randomized (roca: n=210; placebo: n=57). For the full analysis set at Week 16, the SCORAD percentage changes from baseline for all roca treatment groups were statistically significant vs. placebo (p<0.001 for all roca groups; Figure 1). Furthermore, all baseline characteristic subgroup categories showed a similar pattern of reduction in SCORAD scores for all roca treatment groups vs. placebo at Week 16 regardless of AD severity (by EASI and IGA), duration of AD diagnosis, BMI, and age at baseline. Most subgroup categories achieved a statistically significant improvement compared with placebo, despite the smaller sizes of subgroup categories (Figure 1). SCORAD scores, consistent with EASI score (primary endpoint) and other endpoints, continued to improve in all subgroups across all roca treatment groups through Week 36, and improvements were maintained in the off-treatment period up to Week 56.

Conclusion: After 16 weeks of treatment, roca improved SCORAD scores vs. placebo in adults with msAD, regardless of their baseline characteristics for AD severity, duration of disease, BMI, and age. Together with previous data demonstrating that treatment effects were maintained up to Week 56 (despite being off treatment for 20 weeks), these data suggest roca may have potential for disease modification in adults with msAD regardless of baseline characteristics.
**Figure 1.** LS mean percentage change in SCORAD from baseline to Week 16 for the FAS and by baseline characteristic subgroups.

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Data represents LS mean percentage change from baseline to Week 16 and 95% CI; p-values represent ANCOVA for percentage change from baseline vs. placebo.

AD, atopic dermatitis; ANCOVA, analysis of covariance; BMI, body mass index; CI, confidence interval; EASI, Eczema Area and Severity Index; FAS, full analysis set; IGA, Investigator’s Global Assessment; LS, least squares; n, number of patients; n/a, not applicable; G2W, every 2 weeks; G4W, every 4 weeks; RosA, rosuvastatin; SCORAD, SCORing of Atopic Dermatitis.
Abstract N°: 2551

**A Maximum-Use Trial of Ruxolitinib Cream in Children Aged ≥2 Years to <12 Years With Atopic Dermatitis: 8-Week Analysis**

Seth Forman*, Salma Elfaki, Steve Sitar, Shaoceng Wei, Xiaohua Gong, Brett Angle, Howard Kallender, Mark Lee

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**Introduction & Objectives:**

Atopic dermatitis (AD) is an inflammatory skin condition affecting ≤23% of children globally, with moderate-severe disease in nearly one-third. Most approved treatments (topical corticosteroids/topical calcineurin inhibitors) have safety, tolerability, and efficacy concerns limiting long-term use. Ruxolitinib cream, a topical formulation of the selective Janus kinase (JAK) 1/JAK2 inhibitor ruxolitinib, was well tolerated in patients (pts) ≥2 years old (yo) with AD in a previous phase 1 study, with efficacy consistent with that from phase 2/3 studies in adolescents/adults. In a previous maximum-use study in adolescents/adults with AD, ruxolitinib cream was generally well tolerated. This open-label study (NCT05034822) evaluated safety, pharmacokinetics (PK), efficacy, and pt-reported outcomes (PRO) in pts 2 to <12 yo using ruxolitinib cream under maximum-use conditions.

**Materials & Methods:**

Pts 2 to <12 yo with an AD diagnosis for ≥3 months (mo), Investigator’s Global Assessment (IGA) 3 (moderate) or 4 (severe), ≥35% affected body surface area (BSA), and (for 6 to <12 yo) mean itch Numerical Rating Scale (NRS) score ≥4 were eligible. Pts applied 1.5% ruxolitinib cream twice a day to baseline lesions for 4 wks, then only to active lesions for 4 wks, followed by a 44-wk long-term safety (LTS) period continuing this regimen. Safety, PK, efficacy, and PROs to Wk 8 are reported.

**Results:**

Overall, 29 pts (median [range] age, 5 [2–11] yo; 55.2% female; 48.3% White; 37.9% Black) were enrolled and applied ruxolitinib cream at least once. Median (range) baseline affected BSA was 48.0% (35%–92%); 82.8% of pts had previous facial and/or neck involvement. Median (range) duration of AD was 52.7 (10.1–141.2) mo. Most pts (82.8%) used topical treatments in the previous 12 mo; 62.1% discontinued due to lack of efficacy. Most (25/29) pts completed the entire first 8-wk period (4 pts withdrawn by parent/guardian). TEAEs were reported in 20.7% of pts through Wk 8; none were serious or led to treatment interruption or discontinuation; 1 pt had 2 treatment-related application site reactions. No TEAEs suggestive of systemic JAK inhibition were reported. Mean (SD) steady-state plasma concentration (Css) of ruxolitinib through Wk 4 was 98.2 (148) nM, well below the half-maximal concentration of JAK-mediated myelosuppression established for adults (281 nM). At Wk 8, 82.6% achieved ≥75% improvement in Eczema Area and Severity Index; 43.5% of pts achieved IGA treatment success (IGA: 0 [clear] or 1 [almost clear]); 100% of evaluable pts aged 6 to <12 yo achieved a ≥4-point improvement in itch NRS score. Mean daily itch NRS score decreased early and was sustained during the 8-wk period. Scores from the Patient Oriented Eczema Measure, Children’s Dermatology Life Quality Index, and Infants’ Dermatitis Quality of Life (QoL) Index indicated improvement in disease severity and QoL, respectively, at Wk 8 compared with baseline.
Conclusion:

Over 8 wks under maximum-use conditions, ruxolitinib cream was well tolerated in pediatric pts with moderate-severe AD aged 2 to <12 yo. Mean Css of ruxolitinib after application of ruxolitinib cream was well below the value associated with myelosuppression, suggesting physiologically meaningful systemic JAK inhibition is highly unlikely. In this more severe population, ruxolitinib cream had anti-inflammatory and prompt anti-pruritic effects, consistent with data from previous adolescent/adult studies and the phase 1 pediatric study.
Prevalence of the subjective features of the dry eye syndrome in children with atopic dermatitis and ichthyosis.

Vsevolod Bobryshev¹, Vladimir Brzhevsky², Denis Zaslavsky², Alexey Taganov³, Daria Kozlova²

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Introduction & Objectives: Dry eye syndrome is a multifactorial disease of the ocular surface characterized by impaired tear film homeostasis due to dysfunction of the meibomian glands. The condition is often recorded in patients with atopic dermatitis and ichthyosis as a comorbidity.

Materials & Methods: For the period from 2020 to 2022, 40 patients with atopic dermatitis, 10 patients with ichthyosis and 15 healthy volunteers aged 4 to 17 years were included in the study. All patients underwent an anamnesis data collection, an objective examination by a dermatovenereologist, then an assessment of the degree of subjective manifestations of dry eye syndrome using the Ocular Surface Disease Index (OSDI) index by an ophthalmologist.

Results: It was found that in patients with atopic dermatitis, OSDI values averaged 18.55±2.12, in most cases they corresponded to the norm (n=12; 30%) or a mild degree (n=16; 40%) of subjective manifestations of the dry eye syndrome. In 8 (20%) children, OSDI values were in the range of moderate subjective disorders. In 4 (10%) children, the values of the indicator exceeded 33 points and corresponded to the subjective signs of severe dry eye syndrome. In patients with ichthyosis, mean OSDI values were 20.90±4.50. At the same time, 2 (20%) children had normal values of the ocular surface damage index, in 4 (40%) its values corresponded to a mild degree of xerosis, in 3 (30%) - moderate, and in 1 (10%) - severe. The mean OSDI in the control group was 2.37±0.74. In the vast majority of healthy children (n=14; 90%), the ocular surface damage index fluctuated within normal values (0–12). Only in one child of the control group (n=1; 6.7%) OSDI values exceeded 12 points and corresponded to subjective manifestations of mild DES. There were no statistically significant differences between the groups of children with atopic dermatitis and ichthyosis according to the OSDI questionnaire (p=0.63), however, between the control group and groups of patients with atopic dermatitis, as well as with ichthyosis, the differences were statistically significant (p<0.05 and p<0.05, respectively).

Conclusion: Thus, in children suffering from atopic dermatitis and ichthyosis, there was a greater prevalence and severity of subjective disorders characteristic of the dry eye syndrome, compared with their healthy peers. At the same time, in 28 children (70%) with atopic dermatitis and in 8 children (80%) with ichthyosis, OSDI values corresponded to the dry eye syndrome.
The raising of Lazarus - re-engagement of adults with atopic dermatitis following the advent of novel effective therapies

Cathal O’connor¹, Emma Porter¹, Michelle Murphy¹

¹South Infirmary Victoria University Hospital, Cork, Ireland

Introduction & Objectives:

Atopic dermatitis (AD) has a devastating impact on quality of life, and persistent AD affects at least 7% of adults. Until recently, options for severe AD beyond topical therapies were limited to phototherapy and conventional immunosuppressive systemic drugs. With the advent of highly effective targeted treatments such as dupilumab and janus kinase inhibitors (JAKi), patients with AD who had lost follow up with dermatology are now returning en masse for consideration of biologic treatment or JAKi.

The aim of this study was to qualitatively analyse the recapture of adults with severe AD who had previously been lost to follow up from dermatology because of disillusionment with suboptimal therapies and care.

Materials & Methods:

Semi-structured interviews were performed with twelve adults with severe AD to discuss their pathway to return to dermatology. Thematic analysis divided concepts into two categories – experiences of losing contact with dermatology and experiences of re-engagement with dermatology.

Results:

Themes related to leaving dermatology care included ineffectiveness of older treatments, toxicity of older treatments, attendance futility, dermatologist fatigue, and ‘fizzling out’.

“The ciclosporin would work for a few weeks but then I would have a flare, and my kidneys nearly gave out.”

“I could tell the dermatologist was sick of looking at me. Back then I thought I was the problem, but now I think he was embarrassed because he couldn’t help me.”

“I never decided I was going to stop going, it just ended up fizzling out and never going back.”

Themes related to re-engaging with dermatology care included social media influence, novelty, exasperation with quality of life, and the life-changing improvements seen with novel treatments.

“I saw someone on Facebook showing pictures after a few weeks on the injection and I went straight to my GP for a referral back to the dermatologist.”

“After 60 years with eczema I just wanted to try something new, even if it killed me!”

“A few days after starting the tablets I left like Lazarus, it was like standing up out of a wheelchair for the first time in my life.”

Conclusion:

This study highlights the reasons why adults with AD left dermatology services, explains why they re-engaged, and deeply explores the transformative effect that novel treatments have had on the AD landscape. As adults with AD
continue to return to dermatology care the implications of increasing patient numbers needing biologic and JAKi therapy should be factored into healthcare and finance planning.
Abstract N°: 2598

Real-World Treatment Patterns and Effectiveness of Upadacitinib in Patients With Moderate to Severe Atopic Dermatitis in Japan

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¹Iwate Medical University School of Medicine, Department of Dermatology, Japan, ²AbbVie Inc, North Chicago, United States, ³AbbVie GK, Tokyo, Japan, ⁴Genesis Research, Hoboken, United States, ⁵Gunma University Graduate School of Medicine, Department of Dermatology, Maebashi, Japan

Introduction & Objectives:

Upadacitinib (UPA), an oral Janus kinase (JAK) inhibitor with greater inhibitory potency for JAK1 than JAK2, JAK3, or tyrosine kinase 2, is approved for the treatment of moderate-to-severe atopic dermatitis (AD). Clinical trials have demonstrated the efficacy and safety of UPA in AD; however, real-world data are limited. This study evaluated real-world treatment patterns for UPA and the related impact on healthcare resource utilization in Japan.

Materials & Methods:

This retrospective analysis used payer-based administrative claims data from the Japan Medical Data Center database (JMDC), which mainly represents employed individuals and their dependents. Eligible patients were aged ≥ 12 years with ≥ 1 prescription of UPA 15 or 30 mg between August 1, 2021 to October 31, 2022 (date of first UPA prescription claim was defined as index date), ≥ 1 diagnosis of AD (International Classification of Disease, 10th edition codes L20.0, L20.9, L20.81, L20.89) in the year preceding the index date, and had continuous enrollment in the health plan for at least 1 year prior and 6 months post index date. Outcomes included descriptions of initial UPA dose patterns and dose modifications, proportion of days covered (PDC), and adherence (defined as PDC ≥ 80%) during the 6 months of follow-up. Healthcare resource utilization (all-cause and AD-related inpatient/outpatient visits) and use of systemic or topical corticosteroids were compared 6 months before and after UPA initiation using McNemar’s tests.

Results:

A total of 149 patients were identified in the study cohort; 77.9% were male, and the mean (SD) age was 27.6 (14.9) years. The majority (n = 107, 71.8%) of patients did not receive targeted therapies 1 year prior to UPA use, while 19.5% and 12.1% had previously used dupilumab and baricitinib (not mutually exclusive), respectively. Baseline use of other AD-related medications 1 year prior to UPA use was 16.8% for oral immunosuppressants (solely cyclosporine), 43.6% for systemic corticosteroids, 32.9% for topical calcineurin inhibitors, and 73.2% for topical corticosteroids. Most patients (n = 142, 95.3%) initially received UPA 15 mg, and among them, the majority (n = 129/142, 90.8%) continued with the same dose in the 6-month post-index period. Median (interquartile range) PDC was 100% (79% to 100%) during 6 months of follow-up, with 74.5% of patients adherent to treatment. The proportion of all-cause and AD-related inpatient visits 6 months before vs after UPA initiation decreased from 8.1% to 0.7% (P = .006) and 3.4% to 0% (P = .025), respectively. No differences in proportions of all-cause or AD-related outpatient visits were observed. The utilization of systemic corticosteroids decreased from 34.2% to 24.2% (P = .033). A decreasing trend was also observed with topical corticosteroid use (62.4% vs 57.1%), though not statistically significant (P = .200).

Conclusion:
In Japan, UPA treatment was mostly used in patients without prior use of targeted therapies. PDC was high, with about 75% of patients adherent to UPA treatment. Significant reductions in inpatient visits and systemic steroid use were observed 6 months post UPA initiation.
Abstract N°: 2608

The beneficial effects of dupilumab on comorbid asthma in pediatric AD patients treated with dupilumab

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Introduction & Objectives: Dupilumab, a human monoclonal antibody, inhibits signaling of interleukine (IL)-4 and IL-13, type 2 cytokines which play a key role in both atopic dermatitis (AD) and asthma. In clinical trials in children with moderate-to-severe asthma, dupilumab has been shown to improve lung function, but real-world evidence on the use of dupilumab in pediatric patients is limited. In addition, although asthma is a common comorbidity in pediatric patients treated with dupilumab for moderate-to-severe AD, knowledge on the impact of dupilumab on asthma in this population is yet unknown. Therefore, this study aimed to investigate the effect of dupilumab on asthma in pediatric patients treated with dupilumab for AD in daily practice.

Materials & Methods: This study consecutively included pediatric AD patients aged 3 to 17 years, starting dupilumab therapy between August 2019 and April 2023. All patients participated in the BioDay registry and provided informed consent. Starting dupilumab, all patients were screened by a pediatric pulmonologist for presence of asthma, including the assessment of Forced Expiratory Volume in 1 second (FEV1) and Fractional exhaled Nitric Oxide (FeNO). In patients diagnosed with asthma, measurements were repeated at 16- and 52-weeks of treatment. AD severity scores and laboratory measurements including thymus and activation-related chemokine (TARC), eosinophil levels, sIgE inhalation levels and total IgE were assessed during follow-up. A covariance pattern model was used to assess the primary effectiveness endpoints; mean change from baseline in FEV1 and FeNO at 16- and 52-weeks.

Results: Data of approximately 80 patients during at least 16 weeks and 25 patients during at least 52 weeks of treatment with dupilumab will be presented. At the moment, preliminary results of 68 pediatric AD patients are shown, of whom 64 were treated with dupilumab for at least 16 weeks. In total, 42 patients (61.8%) were diagnosed with asthma and were included in follow-up. AD severity scores were comparable between patients with and without asthma at baseline. In patients diagnosed with asthma, mean FEV1 baseline was 2.53 L (95%CI:2.18-2.88; n=42) at baseline and significantly improved over time with 0.18 L (95%CI:0.07-0.28, p= <0.00; n=30) at week 16 (Figure 1). Mean FeNO was 42.74 ppb (95%CI:28.14-57.35; n=29) at baseline, and significantly decreased to 12.55 (95%CI:8.91-16.20, p=0.01; n=18) at week 16. There was no significant change in eosinophil levels during treatment.

Conclusion: This is the first study that provides multidisciplinary physician-reported diagnoses and real world evidence of asthma in pediatric AD patients treated with dupilumab. The preliminary results of this study indicate that dupilumab provides an additional advantage in pediatric AD patients with comorbid asthma, and may be of importance for clinicians when selecting systemic therapy.
Figure 1. Effectiveness outcomes for asthma status during 52 weeks of dupilumab treatment for AD in pediatric patients with comorbid asthma. (A) Absolute change in FEV1. Bars represent mean and 95% CI. (B) Absolute change in FeNO per ppb. Bars represent median and 95% CI. Abbreviations: CI, Confidence Interval; FEV1, Forced Expiratory Volume in 1 s; FeNO, Fractional exhaled Nitric Oxide; Ppb, parts per billion. *p < 0.05.
Abstract N°: 2611

Treatments in chronic hand eczema: A systematic literature review of randomised controlled trials

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Introduction & Objectives:

Chronic hand eczema (CHE) is an inflammatory skin condition that can negatively impact all aspects of daily living. The impairment in health-related quality of life (HRQoL) for patients with moderate to severe CHE is similar to that in patients with moderate to severe atopic dermatitis or psoriasis (Capucci S et al. 2020, Dermatitis; 31 (3): 178-184).

The overall aim of this study was to perform a systematic literature review (SLR) to identify, summarise and contrast randomised controlled trial (RCT) evidence for the treatment of moderate to severe CHE in adults who had an inadequate response to topical corticosteroids, or for whom such treatments were not advisable.

Materials & Methods:

Searches were conducted in Embase, MEDLINE, and the Cochrane Library on July 25th, 2022, supplemented by searches of conferences, publication bibliographies and clinical trial websites. Search strategies incorporated subject heading and free-text terms for CHE with an RCT search filter. Two independent reviewers screened titles and abstracts followed by included full-texts, whilst a third reviewer resolved disputes and conducted quality checks. Inclusion and exclusion criteria were defined using the PICO (population, intervention, comparator and outcomes) framework. For included studies, data were collected on study design, patient characteristics, and outcomes. A feasibility assessment was conducted to determine whether an indirect treatment comparison was feasible and appropriate.

Results:

Search results: Overall, 61 articles (32 trials) met the predefined eligibility criteria, of which 32 articles (11 trials) recruited at least 50 patients and are summarised further below and in Figure 1.

Summary of trials: Five drug classes covered seven CHE treatments: alitretinoin, methotrexate, pimecrolimus, delgocitinib, clobetasol propionate + azathioprine and PUVA (bath and oral). The duration of CHE ranged from six weeks to >1 year. Study duration ranged from <3 to 24 weeks. Disease severity was moderate (n=6 trials), severe (n=6) or unclear in some trials (n=3). Six trials reported on the prior use of TCS use or failure as part of their inclusion criteria. Six trials excluded participants with concomitant atopic dermatitis. Studies also varied in terms of their comparators (i.e., the inclusion of an active treatment [n=4] or a control arm [n=7]) and the outcomes measured and reported (i.e., varying aspects relating to efficacy, HRQoL and safety). Risk of bias varied considerably, with only one study reporting low risk across domains.

Efficacy outcomes: The most commonly reported efficacy outcome was the Investigator Global Assessment (IGA)/Physician Global Assessment (PGA). Results are presented in Figure 2. Alitretinoin (30 mg) and delgocitinib
(20 mg/g) had similar relative efficacy compared to their control arms for percentage of patients achieving PGA 0/1 (40.0–47.7% vs 15.0–16.6% at week 24 and 37.7% vs 8% at week 16, respectively). However, there was substantial heterogeneity in terms of IGA/PGA responder definitions, timepoints and control treatments across studies.

**Conclusion:**

Of the 11 trials that recruited at least 50 patients, there were substantial differences in trial duration, CHE severity, comparators and in outcome definitions and reporting. Additionally, few trials had low risk of bias. At present, these challenges likely preclude an indirect comparison of efficacy outcomes for CHE treatments using RCT data.
<table>
<thead>
<tr>
<th>Trial ID</th>
<th>Interventions</th>
<th>Timepoint</th>
<th>N</th>
<th>ISA/PGA</th>
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<th>0</th>
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<tr>
<td>BACH 2004</td>
<td>Alitretinoin 10mg</td>
<td>24 weeks</td>
<td>418</td>
<td>ISA</td>
<td>115 (27.9)</td>
<td>39 (9.3)</td>
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<td></td>
<td>Alitretinoin 10mg</td>
<td>4 weeks</td>
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<td>135 (7.7)</td>
<td>50 (24.0)</td>
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<td>Placeto</td>
<td>24 weeks</td>
<td>206</td>
<td>ISA</td>
<td>31 (14.8)</td>
<td>9 (4.3)</td>
<td>NR (18.7)</td>
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<tr>
<td></td>
<td>Alitretinoin 10mg</td>
<td>24 weeks</td>
<td>290</td>
<td>ISA</td>
<td>118 (40.2)</td>
<td>56 (19.5)</td>
<td>80 (20.2)</td>
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<td>Placeto</td>
<td>12 weeks</td>
<td>296</td>
<td>ISA</td>
<td>44 (15.0)</td>
<td>14 (4.7)</td>
<td>30 (10.2)</td>
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<tr>
<td>Rusicka</td>
<td>Placebo</td>
<td>12 weeks</td>
<td>206</td>
<td>ISA</td>
<td>31 (15.0)</td>
<td>NR (4.0)</td>
<td>NR (18.7)</td>
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<tr>
<td></td>
<td>Alitretinoin 10mg</td>
<td>12 weeks</td>
<td>30</td>
<td>ISA</td>
<td>32 (10.0)</td>
<td>NR (4.0)</td>
<td>NR (18.7)</td>
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<tr>
<td>Placeto</td>
<td>12 weeks</td>
<td>206</td>
<td>ISA</td>
<td>44 (15.0)</td>
<td>14 (4.7)</td>
<td>30 (10.2)</td>
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### Topical calcineurin inhibitors

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<th>ISA/PGA</th>
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<th>0</th>
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<td>Bealito 2004</td>
<td>Pimecrolimus 1%</td>
<td>3 weeks</td>
<td>151</td>
<td>ISA</td>
<td>115 (27.9)</td>
<td>39 (9.3)</td>
<td>NR (18.2)</td>
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<tr>
<td></td>
<td>Cream vehicle</td>
<td>3 weeks</td>
<td>148</td>
<td>ISA</td>
<td>135 (7.7)</td>
<td>50 (24.0)</td>
<td>NR (20.7)</td>
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<tr>
<td>Hordinsky 2010</td>
<td>Pimecrolimus 1%</td>
<td>6 weeks</td>
<td>224</td>
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<td>97 (29.6)</td>
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<td></td>
<td>Vehicle cream</td>
<td>6 weeks</td>
<td>226</td>
<td>ISA</td>
<td>97 (29.6)</td>
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### Topical glucocorticosteroids

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<td>46 (24.0)</td>
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<td>Deltololene 1 mg/g</td>
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<td>11 (18.1)</td>
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<td>Deltololene 3 mg/g</td>
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<td>51</td>
<td>ISA</td>
<td>10 (16.0)</td>
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<td>Deltololene 8 mg/g</td>
<td>16 weeks</td>
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<td>ISA</td>
<td>10 (16.0)</td>
<td>NR (11.4)</td>
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<td>Deltololene 20 mg/g</td>
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<td>ISA</td>
<td>10 (16.0)</td>
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<td>Cream vehicle</td>
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<td>90</td>
<td>ISA</td>
<td>4 (6.0)</td>
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### Ultraviolet light therapy

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<td>UVA b.i.d.</td>
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<td>ISA</td>
<td>4 (11.4)</td>
<td>10 (28.6)</td>
<td>8 (22.8)</td>
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</table>

**Abbreviations:** b.i.d., twice a day; ISA, Investigator’s Global Assessment; ISA-CHET, Investigator’s Global Assessment for chronic hand eczema treatment success; mg, milligram; N, number of patients analyzed; n, number of participants in response; NR, not reported; PDA, Physician’s Global Assessment; PDPA, physician-dermatologist-assessed; UVB, ultraviolet B; UVB, ultraviolet B. *PDA treatment success defined as achieving clear or almost clear skin with at least 2-point improvement from baseline.

**References:**
Abstract N°: 2717

A global, observational, cohort study of patients with atopic dermatitis to evaluate tralokinumab real-world clinical use (TRACE): baseline characteristics from the first 100 patients in Germany

Diamant Thaçi1, Andreas Kleinheinz2, Dimitra Maria Anastasiadou3, John Stinson4, April Armstrong5

1University Luebeck, Institute and Comprehensive Center for Inflammation Medicine, Germany, 2Elbe Medical Center, Department of Dermatology, Buxtehude, Germany, 3LEO Pharma A/S, Ballerup, Denmark, 4LEO Pharma, Dublin, Ireland, 5University of Southern California, Keck School of Medicine, Los Angeles, United States

Introduction & Objectives:

Tralokinumab is a high-affinity, fully human IgG4 monoclonal antibody that specifically targets interleukin-13, a key driver of atopic dermatitis (AD) disease progression. Clinical trials have shown that tralokinumab is efficacious in patients with moderate-to-severe AD and has a favorable safety profile, including a low frequency of adverse events such as conjunctivitis. Management of patients in routine clinical practice differs from those enrolled in clinical trials due to strict protocol criteria, and there is a lack of clinical data on tralokinumab use in the real-world setting. TRACE is a real-world study in patients with AD, aiming to better understand the effectiveness, safety, and clinical use of tralokinumab in daily practice. Here, we describe baseline characteristics from the first patients enrolled into TRACE in Germany.

Materials & Methods:

TRACE is an observational, prospective, single-cohort study of adult patients with moderate-to-severe AD who are treated with tralokinumab, according to national approved labels. Eleven countries are participating in the study across Europe, North America and the Middle East. The primary objective is to assess changes in clinical signs and symptoms of AD in tralokinumab-treated patients. Secondary objectives are to investigate safety, quality of life, patient-reported outcomes and treatment adherence, among others.

Results:

Of the first 100 patients initiated on tralokinumab, the mean age (standard deviation [SD]) was 44.7 years (17.9) and 58% were male. Most patients had moderate-to-severe AD with a mean Investigator’s Global Assessment (IGA) score of 3.5 (SD 0.7) and mean Eczema Area and Severity Index (EASI) of 22.5 (SD 12.9). Patients reported heavy symptomatic burden of disease; the mean eczema-related sleep numerical rating scale (NRS) was 5.6 (SD 2.9) and mean worst daily pruritus NRS was 6.2 (SD 2.7). Patients also reported a substantial impact on quality of life, demonstrated by a mean Dermatology Life Quality Index of 15.6 (SD 6.9). Overall, 79 patients were biologic-naïve and 19 were biologic-experienced (data missing; n=2). All biologic-experienced patients were previously treated with dupilumab, of whom most experienced one or more treatment failures. Reasons for switching from dupilumab included lack or loss of effectiveness, and adverse events, which most commonly included conjunctivitis.

Conclusion:

Initial findings showed that most adult patients with moderate-to-severe AD who were treated with tralokinumab were biologic-naïve, indicating tralokinumab is prescribed as first-line systemic treatment in real-world clinical practice, in line with European Dermatology Forum guidelines. The main reasons for switching from dupilumab were lack or loss of effectiveness, and adverse events, such as conjunctivitis, indicating the need for alternative biologic treatments such as tralokinumab.
Abstract N°: 2718

APG777, a high-affinity humanized IgG1 mAb targeting IL-13, demonstrates prolonged half-life in non-human primates

Eric Zhu1, Jason Oh1, Carl Dambkowski2, Hussam Shaheen1

1Paragon Therapeutics, 2Apogee Therapeutics

APG777, a high-affinity humanized IgG1 mAb targeting IL-13, demonstrates prolonged half-life in non-human primates

Eric Zhu1, Jason Oh1, Carl Dambkowski2, and Hussam Shaheen1

1 Paragon Therapeutics, Inc.
2 Apogee Therapeutics, Inc.

Introduction & Objectives:

Interleukin-13 (IL-13) is a cytokine shown to play a role in the pathogenesis of atopic dermatitis, asthma, and other inflammatory and immunologic conditions. APG777 is a high-affinity humanized IgG1 mAb that binds IL-13 and subsequently blocks its ability to form the full signalling complex of IL-13/IL-13Rα1/IL-4Rα, preventing heterodimerization and downstream signalling. APG777 also contains YTE amino acid substitutions in the fragment crystallizable region designed to extend the half-life of monoclonal antibodies in nonhuman primates (NHPs) and humans by increasing binding to neonatal Fc receptor (FcRn) under acidic pH conditions.

Materials & Methods:

The pharmacokinetics (PK) of APG777 and lebrikizumab were studied in female cynomolgus monkeys following a single bolus dose of 3 mg/kg, given either IV or SC. Blood samples were collected serially starting with a sample pre-dose and subsequently at 0.167, 1, 4, 8, 24, 48, 96, 168, 336, 504, 674, 840, 1334, 1680, and 2160 hours post-dose. PK parameters included: maximum observed serum concentration, time to maximum observed serum concentration, area under the serum concentration versus time curve from time 0 extrapolated to infinity, clearance, volume of distribution at steady-state, half-life and absolute subcutaneous bioavailability were calculated.

Results:

APG777 exhibited an average half-life of 27.6 days and clearance rate of 1.45 (mL day⁻¹ kg⁻¹) in NHPs. The steady-state volume of distribution was observed to be 55.65 (mL kg⁻¹). APG777 was well-absorbed, with subcutaneous bioavailability determined to be 81.22%. Lebrikizumab exhibited an average half-life of 18.0 days and clearance rate of 2.93 (mL day⁻¹ kg⁻¹) in NHPs. The steady-state volume of distribution was observed to be 52.10 (mL kg⁻¹). Lebrikizumab was well-absorbed, with subcutaneous bioavailability determined to be 75.70%.

Conclusion:

APG777 demonstrated a substantial increase in half-life compared to lebrikizumab in NHPs. APG777 was engineered to have this extended half-life, due to the YTE amino acid substitutions in the Fc region of APG777, which have been shown to prolong the half-life of IgGs by increasing binding to FcRn under acidic pH conditions. FcRn-bound IgG is recycled via lysosomal salvage, resulting in the IgG returning to the circulation. APG777’s
prolonged half-life may enable less frequent dosing compared to currently available treatments, which could reduce injection burden and increase compliance for patients living with atopic dermatitis and other IL-13-driven diseases.
Abstract N°: 2722

Circadian Metabolome of Atopic Dermatitis

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Introduction & Objectives:

Atopic dermatitis (AD) is a chronic inflammatory skin disease characterized by dry, pruritic skin. Several studies have described nocturnal increases in itching behavior, suggesting a role for the circadian rhythm in modulating symptom severity. However, the circadian rhythm of metabolites in the skin and serum of patients with AD has yet to be described. This study sought to assess circadian patterns of skin and serum metabolism in healthy controls compared to patients with AD.

Materials & Methods:

12 adults with AD and 5 healthy volunteers were monitored for 28 hours in a controlled environment. Serum was collected every 2 hours and tape strips every 4 hours from both lesional and non-lesional skin in participants with AD and location matched, non-lesional skin in controls. We then performed an untargeted metabolomics analysis, examining the circadian features of metabolism in AD.

Results:

Distinct metabolic profiles were observed in control and AD samples. The serum metabolic pathways with the greatest differences between AD and controls were lacto- and neolacto-glycosphingolipid biosynthesis and one carbon pool by folate. We identified 42 circadian features in either AD or control samples in the serum and 17 in the skin. Pathway enrichment and serum-skin metabolite correlation varied throughout the day. Differences were most evident in the late morning and the time immediately following sleep onset.

Conclusion:

Our findings suggest that accounting for sample collection time could improve biomarker detection studies in AD and highlight that nocturnal differences in symptom severity might be associated with metabolic changes.
APG777, a humanized IgG1 mAb, binds to IL-13 with high affinity and potently blocks IL-13 signalling in multiple in vitro assays

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APG777, a humanized IgG1 mAb, binds to IL-13 with high affinity and potently blocks IL-13 signalling in multiple in vitro assays

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Introduction & Objectives:

Interleukin-13 (IL-13) is a cytokine that is primarily produced by activated T helper type 2 cells. IL-13 has been shown to play a role in the pathogenesis of atopic dermatitis and other inflammatory and immunologic conditions. APG777, a humanized IgG1 mAb, was engineered to have high affinity for IL-13 block the full signalling complex of IL-13/IL13Rα1/IL-4Rα, preventing heterodimerization and downstream signalling to a similar or greater extent compared to currently available therapies.

Materials & Methods:

Multiple in vitro assays APG777 was compared to dupilumab, lebrikizumab, and tralokinumab. Affinity for IL-13 was measured by surface plasmon resonance (SPR). Multiple assays were used to assess blockade of the full signalling complex of IL-13/IL13Rα1/IL-4Rα and downstream signalling. Cell-line-based assays included: inhibition of phosphorylation of STAT6 in HT-29 cells, inhibition of release of TARC in A549 cells, and inhibition of proliferation of TF-1 cells. Primary human lymphocyte-based assays included: inhibition of phosphorylation of STAT6 and inhibition of CD23 expression.

Results:

As measured by SPR, APG777 had an affinity of 77 pM compared to 131 pM and 116 pM for lebrikizumab and tralokinumab, respectively. In cell-line-based assays, APG777 exhibited an IC50 of 0.89 nM inhibiting IL-13 binding on an IL-13Rα1/IL-4Rα overexpression cell line compared to 1.11 nM for lebrikizumab; an IC50 of 0.28 nM inhibiting phosphorylation of STAT6 in HT-29 cells compared to 0.16 nM for dupilumab, 0.23 nM for lebrikizumab, and 0.41 for tralokinumab; an IC50 of 0.86 nM inhibiting release of TARC in A549 cells compared to 1.11 nM for dupilumab, 0.74 nM for lebrikizumab, and 4.14 for tralokinumab; and an IC50 of 0.16 nM inhibiting proliferation of TF-1 cells compared to 0.19 nM for dupilumab, 0.20 nM for lebrikizumab, and 0.59 nM for tralokinumab. In primary human lymphocytes, APG777 blocked IL-13 activity as exhibited by an IC50 of 0.44 nM inhibiting phosphorylation of STAT6 compared to 0.38 nM for lebrikizumab and an IC50 0.85 nM in inhibiting CD23 expression compared to 0.81 nM for lebrikizumab.

Conclusion:

APG777 demonstrated similar affinity for IL-13 as compared to lebrikizumab and tralokinumab and similar potency
in multiple assays as compared to dupilumab and lebrikizumab. These data provide preclinical evidence that APG777’s clinical potential in a variety of diseases where IL-13 signalling is the main driver of the inflammatory response, including atopic dermatitis. APG777 also contains YTE amino acid substitutions designed to extend its half-life in humans by increasing binding to neonatal Fc receptor, which may further enhance its potential benefits.
Abstract N°: 2734

**Patient satisfaction: a factor to consider for improving adherence**

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**Introduction & Objectives:**

Patient satisfaction is important as it can improve motivation and the ability to follow treatment instructions, which may lead to better long-term health outcomes.

Dry skin remains one of the most common reasons for dermatological consultations.

The *Objectifs Peau* project suggests that 23.83% of the French have dry skin: 20% in people with no related skin condition and 32.5% in those with one.

**Materials & Methods:**

In the context of patient centricity, we wanted to better understand patients’ expectations in order to evaluate their level of satisfaction. Satisfaction can be objectively described as the difference between the expected and the observed.

All 300 GPs who agreed to take part in the evaluation gave a two-part questionnaire to patients who had been prescribed an emollient [a dermocosmetic containing shea butter, niacinamide, LRP thermal spring water (TSW), APF (a biomass of VF grown in TSW) and microresyl] for xerosis and informed of the diagnosis that prompted the treatment. One questionnaire focused on patients’ expectations: the second concentrated on patients’ experiences.

**Results:**

The study included 2,723 patients, of whom 2,386 completed questionnaire 1 and 1,348 questionnaire 2. To evaluate their satisfaction, the patients had to complete both questionnaires, giving 1,009 evaluable responses.

The patients’ priority expectations identified in questionnaire 1 were clear: 99% wanted the product to be effective, 96% to provide rapid relief for their skin and 92% to reduce itching.

Following 15 days of use, the study’s results can be summarized as follows: 98% of the patients felt that the product was effective, 97% that it was easy to use, and 96% that it reduced sensations of tightness and itching.

87% of the patients also reported an improvement in the intensity of their skin’s dryness, 84% in the intensity of the itching and 77% in the intensity of the redness.

**Conclusion:**

This study made it possible to:

- suggest that the emollient is effective at relieving the symptoms of skin dryness, itching and redness, thereby meeting patients’ priority expectations.
- better understand xerosis patients’ expectations of treatment and measure their level of satisfaction after 15 days of using an emollient prescribed by their doctor.
Furthermore, the results show that patients have clear expectations of treatment efficacy, rapidity of action and reduction of itching sensations. The patients also expressed a high level of satisfaction with the prescribed emollient, with significant improvements in their skin’s dryness, itching and redness.

These results emphasize the importance of considering patients’ expectations when prescribing treatments and working to maintain a high level of satisfaction in order to improve treatment adherence and long-term health outcomes.
Abstract N°: 2756

Validity, reliability, responsiveness, and interpretability of the Recap of atopic eczema (RECAP) questionnaire

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Introduction & Objectives: The Recap of atopic eczema (RECAP) has been recommended by the Harmonising Outcome Measures for Eczema (HOME) initiatives as a core outcome instrument for measuring eczema control in both clinical trials and clinical practice. However, despite its potential utility, limited research has been conducted on the measurement properties of the RECAP. While its validity and reliability have been investigated to some extent, there is a lack of knowledge on the interpretability of individual RECAP score or the extent to which changes in scores can be considered as clinically relevant. Therefore, we aimed to investigate the validity, reliability, responsiveness, and interpretability of the RECAP in adults with atopic dermatitis.

Materials & Methods: We conducted a prospective study in a Dutch tertiary hospital where adults with atopic dermatitis, regardless of disease severity and treatment, as diagnosed by a dermatologist according to the U.K. Working Party Criteria, were recruited between June 2021 and December 2022. Patients completed the RECAP questionnaire, reference instruments, and anchor questions at three time points: baseline, after 1-3 days and after 4-12 weeks. Clinical severity was assessed by dermatologists based on the Eczema Area and Severity Index and the validated Investigator Global Assessment for Atopic Dermatitis. Hypotheses-testing was used to investigate single-score validity and responsiveness. Reliability was reported with standard error of measurement (SEMagreement) and intraclass correlation coefficient (ICCagreement). An anchor-based approach was used at baseline to determine possible cut-off points of the RECAP scores, and a linear weighted kappa coefficient of agreement was calculated to determine the final banding with the highest level of agreement. Smallest detectable change (SDC) and minimally important change (MIC) scores were also determined. Four different anchor-based methods were used to determine MIC values, including the mean change method, 95% limit cut-off point, receiver operating characteristic curve, and predictive modeling.

Results: In total 200 participants were included (57.5% male, mean age 38.5 years). Of the a priori hypotheses, 82% (single-score validity) and 59% (responsiveness) were confirmed. Known-group analyses showed difference in the RECAP scores between patient groups based on disease severity and impairment on the quality of life. The SEMagreement was 1.17 points, and the ICCagreement was 0.988. The final banding was: 0-1 (completely controlled); 2-5 (mostly controlled); 6-11 (moderately controlled); 12-19 (a little controlled); 20-28 (not at all controlled). Moreover, a single cut-off point of ≥6 was determined to identify patients whose AD is not under control. The SDC was 3.2 points. MIC values obtained from four methods is shown in Figure 1, and the one from the predictive modeling was 3.9 points. Neither floor or ceiling effects were seen.

Conclusion: The RECAP has good sing-score validity, moderate responsiveness and excellent reliability. This study fills a gap on the interpretability of the RECAP. Our results indicate a threshold of ≥6 points to identify patients whose AD is ‘not under control’, while an improvement of ≥4 points represents a clinically important change. Given its endorsement by HOME, the results of this study support the integration of RECAP into both routine clinical practice and research settings.

Figure 1.
Limited health literacy and its associated health outcomes among adults with at least two atopic diseases

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Introduction & Objectives: Health literacy is essential for patients with multiple atopic diseases to improve their health, given the complexity of their disease and treatment regimens. However, there is a lack of knowledge on the health literacy status and its associated health outcomes in this vulnerable group. Thus, we aimed to estimate the proportion of adults with multiple atopic diseases (at least two of atopic dermatitis (AD), asthma, allergic rhinitis, and food allergy) in the Dutch general population, and to evaluate the prevalence of limited health literacy, and its association with socioeconomic status (SES), lifestyle factors, and health-related quality of life (HR-QoL) in this patient population.

Materials & Methods: This cross-sectional study was conducted within the Lifelines Cohort Study via sending an add-on digital questionnaire, including (among others) questions on AD, to all adult participants (n=135,950) between February and May in 2020. Data on asthma, allergic rhinitis, lifestyle factors, HR-QoL, and SES were extracted from baseline assessment between 2006 and 2013. Functional, communicative, and critical health literacy was measured by validated items from Chew and the Dutch Functional Communicative and Critical Health Literacy questionnaires between 2012 and 2016. Food allergy was measured by the Food Allergy Questionnaire between 2014 and 2016. Binary logistic regression models were used.

Results: In total, 11.8% of the overall study population reported ever having multiple atopic diseases; of those 23.6% reported having limited functional health literacy, with a higher prevalence among those with a low SES, especially lower educational attainment. Moreover, limited functional health literacy showed positive associations with smoking, obesity, chronic stress, a low diet quality, and decreased HR-QoL among subjects with multiple atopic diseases. In addition, (more than) one-third of subjects with multiple atopic diseases were likely to report signs of limited communicative and critical health literacy.

Conclusion: We identified a health literacy deficit, and its association with a low SES and poor health outcomes among patients with multiple atopic diseases. Further research is warranted to utilize a more extensive assessment to measure health literacy and include more health outcomes, such as treatment adherence and disease control.
Abstract N°: 2768

**Drug survival analysis of dupilumab in moderate to severe atopic dermatitis patients: A retrospective study**

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**Introduction & Objectives:**

Dupilumab is a human monoclonal antibody that inhibits signaling of both IL-4 and IL-13, key inflammatory cytokines in the pathogenesis of atopic dermatitis (AD). It is proven to be effective and safe for long-term treatment of AD, but several patients discontinue with various reasons. We investigated the drug survival of dupilumab, reasons of discontinuation, and compared clinical characteristics between dupilumab withdrawing patients and continuing patients.

**Materials & Methods:**

This retrospective analysis included moderate to severe AD patients treated with dupilumab from March 2019 to April 2023. Patients demographics, laboratory findings, EASI and multiple reasons for each withdrawing patient were collected.

**Results:**

Total of 102 patients was included in the study. Among them, 23 patients (22.5%) had discontinued dupilumab after a mean time of 30.7 weeks. Significantly in 23 withdrawing patients, female rate (56.5% vs 20.2%) was higher, total IgE level (1871.15 vs 5163.11, IU/mL) was lower and disease onset (13.04 vs 16.30, years) was earlier than 79 continuing patients. There was no significant difference in baseline EASI. Reasons for withdrawing dupilumab were primary inefficacy (n=10), follow up loss (n=6), adverse effect such as conjunctivitis or head and neck flare (n=5), cost burden (n=4), pregnancy (n=2) and clinical remission (n=1). Few of them changed to other systemic treatment such as cyclosporine (n=4), baricitinib (n=5) and received improvement on itching and adverse effects.

**Conclusion:**

Female, low total IgE level, and younger disease onset age are at higher risk of discontinuing dupilumab in AD patients for a various reason. Common reasons for withdrawing dupilumab is due to ineffectiveness and adverse effects.
Abstract N°: 2791

**Efficacy of Abrocitinib and Dupilumab in Patients With Moderate-to-Severe Atopic Dermatitis With Severe Itch at Baseline and in Subgroups by Baseline Thresholds of Severe Itch: A Post Hoc Analysis of the JADE COMPARE and JADE DARE Clinical Trials**

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**Introduction & Objectives:** Abrocitinib, an oral, Janus kinase 1-selective inhibitor, and dupilumab, an anti-interleukin 4 receptor-α monoclonal antibody, have been approved for patients with moderate-to-severe atopic dermatitis (AD). Abrocitinib provided more rapid and significantly greater itch relief compared with dupilumab in phase 3 clinical trials. In addition, improvements in itch corresponded to clinically meaningful improvements in patients’ quality of life (QoL). Here, we examined the efficacy of abrocitinib versus dupilumab in an overall group of patients with moderate-to-severe AD who had severe itch at baseline (BL) and in individual subgroups by various BL thresholds of severe itch.

**Materials & Methods:** This post hoc analysis included pooled data from patients treated with abrocitinib 200 mg (once daily) or dupilumab 300 mg (subcutaneous every 2 weeks) from the phase 3 trials JADE COMPARE (NCT03720470) and JADE DARE (NCT04345367). Patients with severe itch at BL, defined as a Peak Pruritus Numerical Rating Scale (PP-NRS) score of ≥ 7, and individual subgroups by BL PP-NRS scores of 7 (BL PP-NRS7), 8 (BL PP-NRS8), 9 (BL PP-NRS9), and 10 (BL PP-NRS10) were assessed for achievement of ≥4-point improvement in PP-NRS (PP-NRS4) and PP-NRS 0/1 (no itch/very little itch). Individual subgroups were also assessed for achievement of Patient Oriented Eczema Measure (POEM) score ≤ 2 (indicating clear or almost clear AD) in patients with a BL POEM score > 2, and Dermatology Life Quality Index (DLQI) score of 0 or 1 (indicating no disease effect on dermatology-specific QoL).

**Results:** This analysis comprised a total of 875 patients (453 abrocitinib; 422 dupilumab) with severe itch at BL. The median (Q1, Q3) BL score for PP-NRS was 8.0 (7.0, 9.0) in the abrocitinib treatment arm and 8.0 (7.0, 9.0) in the dupilumab arm, 22.0 (19.0, 26.0) and 22.0 (19.0, 27.0) for POEM, and 16.0 (11.0, 20.5) and 16.0 (11.0, 20.0) for DLQI. In the overall group with severe itch, PP-NRS4 responses were greater with abrocitinib versus dupilumab as early as week 2 (56% vs 32%) and sustained through week 16 (73% vs 69%; Figure). Stringent responses of PP-NRS 0/1 were also greater with abrocitinib versus dupilumab at week 2 (15% vs 3%) and week 16 (35% vs 21%). Similarly, across the individual subgroups by BL PP-NRS scores of 7, 8, 9, and 10, a greater proportion of patients achieved PP-NRS4 and PP-NRS 0/1 responses with abrocitinib versus dupilumab at week 2 and week 16 (Figure). A greater proportion of patients across the individual subgroups achieved a POEM score of ≤ 2 with abrocitinib compared with dupilumab at week 16 (BL PP-NRS7, 33% vs 10%; BL PP-NRS8, 29% vs 20%; BL PP-NRS9, 39% vs 16%; BL PP-NRS10, 31% vs 23%). In the overall group with severe itch, a greater proportion of patients achieved DLQI 0/1 responses with abrocitinib versus dupilumab at week 2 (19% vs 6%) and week 16 (38% vs 27%). Across the individual subgroups, DLQI 0/1 responses with abrocitinib were generally greater than dupilumab at week 2 and at week 16 (Figure).

**Conclusion:** In patients with moderate-to-severe AD who had severe itch at BL, abrocitinib provided more rapid
and complete/near complete itch relief as well as improved quality of life that was substantially greater than dupilumab as early as 2 weeks after initiating treatment. These results were consistent across the individual subgroups of patients at various BL thresholds of severe itch.

Figure. Efficacy of abrocitinib and dupilumab in the overall group of patients with severe itch and subgroups by various thresholds of severe itch at baseline.

DLQI 0/1, Dermatology Life Quality Index score of 0 or 1; PP-NRS, Peak Pruritus Numerical Rating Scale (used with permission from Regeneron Pharmaceuticals, Inc., and Sanofi); PP-NRS4, 4-point improvement in PP-NRS score; QD, once daily; Q2W, once every 2 weeks.
Predicting Abrocitinib Efficacy at Week 12 in Patients With Moderate-to-Severe Atopic Dermatitis Based on Their Week 4 Response: A Post Hoc Analysis of 4 Randomised Studies

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Introduction & Objectives: Abrocitinib is an oral, once-daily, Janus-kinase 1-selective inhibitor approved for the treatment of moderate-to-severe atopic dermatitis (AD). Abrocitinib may be initiated at 100 mg orally once daily; however, some patients may not achieve an adequate response with the 100 mg dose and may benefit from increasing the dosage to 200 mg once daily. At week 4 of clinical trials, patients receiving abrocitinib 100 mg achieved approximately 50% to 75% of their week 12 efficacy responses. Prediction of response at week 12 based on week 4 assessments could improve the management of individual patients, as earlier dose increase could be suitable for patients who are expected to be nonresponders at week 12, if clinically appropriate and permitted by local product information. The objective of this post hoc analysis was to formulate a method to aid this prediction at 4 weeks of treatment.

Materials & Methods: Data pooled from patients with moderate-to-severe AD who received abrocitinib once-daily as monotherapy (JADE MONO-1 [NCT03349060]; JADE MONO-2 [NCT03575871]) or in combination with background topical therapy (JADE COMPARE [NCT03720470]; JADE TEEN [NCT03796676]) were evaluated. In the training phase of this analysis, data from 70% of the pooled population was examined to identify predictors of response. In the validation phase, identified predictors of response were tested using the remaining 30% of patient-level data from the pooled population. We chose ≥75% improvement in Eczema Area and Severity Index (EASI-75) and Investigator’s Global Assessment (IGA) response, defined as an IGA score of 0 (clear) or 1 (almost clear) and ≥2-point improvement from baseline at week 12, as the dependent variables. Predictor variables included week 4 scores for EASI, IGA, and Peak Pruritus Numerical Rating Scale (PP-NRS), changes from baseline to week 4 in EASI, IGA, and PP-NRS, and percent change in EASI from baseline at week 4. We calculated the probability of each variable to predict EASI-75 and IGA 0/1 at week 12 and estimated sensitivity and specificity of the prediction. Only patients randomised to abrocitinib 100 mg and with observed week 4 predictor values were included in this analysis.

Results: Data of 647 patients were analysed (training cohort, n=453; validation cohort, n=194). In the training cohort, EASI-75 response at week 12 was achieved by 72% of EASI-50 responders at week 4 and by 16% of nonresponders; for IGA response attainment at week 12, those values were 48% and 6%, respectively. In the validation cohort, 69% of EASI-50 responders at week 4 attained EASI-75 response at week 12 compared with 23% of EASI-50 nonresponders; for IGA response achievement at week 12, those values were 41% and 12%, respectively. Achievement of EASI-50 at week 4 predicted attainment of EASI-75 at week 12 with sensitivity of 0.90 and specificity of 0.60. For the prediction of IGA response at week 12, sensitivity was 0.94 and specificity 0.48.

Conclusion: These data suggest that an EASI-50 threshold of clinical improvement at week 4 may be a useful predictor of response at week 12. Thus, patients who failed to reach EASI-50 at week 4 may be considered for a dose increase to 200 mg to optimise efficacy response.
Abstract N°: 2794

Abrocitinib Long-Term Efficacy for up to 2 Years in Patients With Moderate-to-Severe Atopic Dermatitis: An Interim Analysis of JADE EXTEND, a Long-Term Extension Study

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Introduction & Objectives:

Abrocitinib, an oral Janus kinase 1-selective inhibitor approved in the European Union for the treatment of moderate-to-severe AD in adults, demonstrated efficacy and safety in short-term studies (12-16 weeks). The efficacy and safety of long-term abrocitinib treatment is being investigated in the ongoing phase 3 extension study, JADE EXTEND (NCT03422822). This interim analysis of JADE EXTEND evaluated the long-term efficacy of abrocitinib treatment up to approximately 2 years.

Materials & Methods:

This analysis included pooled data from eligible adolescents and adults with moderate-to-severe AD who had previously received once-daily abrocitinib (200 mg/100 mg) or placebo in qualifying parent studies as monotherapy (JADE MONO-1 [NCT03349060], JADE MONO-2 [NCT03575871], and JADE MOA [NCT03915496]), and in combination with background topical medicated therapy (JADE COMPARE [NCT03720470], JADE TEEN [NCT03796676], and JADE DARE [NCT04345367]), and who subsequently enrolled in JADE EXTEND. Patients who received abrocitinib at either dose in the qualifying parent studies continued to receive the same dose in JADE EXTEND (blinding maintained); patients who received placebo in the qualifying parent studies were randomly assigned to double-blind abrocitinib treatment at either dose in JADE EXTEND. JADE EXTEND did not have any efficacy-based entry criteria. Patients enrolled in the JADE REGIMEN (NCT03627767) trial or those randomly assigned to dupilumab in JADE DARE or JADE COMPARE were excluded. Efficacy assessments included the proportion of patients achieving an Investigator’s Global Assessment score of 0 (clear) or 1 (almost clear) with ≥2-grade improvement from parent study baseline (IGA 0/1, ≥75%, ≥90%, and 100% improvement from parent study baseline in Eczema Area and Severity Index (EASI-75/90/100), ≥4-point improvement from parent study baseline in Peak Pruritus Numerical Rating Scale score (PP-NRS4; used with permission from Regeneron Pharmaceuticals, Inc., and Sanofi), and PP-NRS score of 0 or 1 (no to very little itch) with ≥2-point reduction from parent study baseline (PP-NRS 0/1) at week 112. All data are reported as observed, with any missing data excluded. Baseline value was defined as the last pre-dose assessment in the qualifying parent study. Timepoints were relative to the first dose of abrocitinib, regardless of the qualifying parent study. Data cutoff date: September 5, 2022.

Results:
Of 955 and 753 patients who received abrocitinib 200 mg and abrocitinib 100 mg, 403 (42%) and 425 (56%) reached ≥112 weeks of treatment at data cutoff, respectively. At week 112 after the first abrocitinib dose, the proportion of patients who achieved efficacy responses in the abrocitinib 200 mg and 100 mg groups were 57% (181/317) and 52% (154/294) for IGA 0/1, 84% (308/368) and 78% (297/381) for EASI-75, and 69% (216/311) and 58% (167/290) for PP-NRS4. Responses at the higher thresholds of efficacy in the abrocitinib 200 mg and abrocitinib 100 mg groups were 61% (226/368) and 54% (204/381) for EASI-90, 26% (96/368) and 21% (81/381) for EASI-100, and 43% (138/319) and 33% (97/294) for PP-NRS 0/1.

**Conclusion:**

In this interim analysis of JADE EXTEND, up to 2 years of abrocitinib treatment was observed to provide clinically meaningful improvements in the signs and symptoms of AD in patients with moderate-to-severe AD. Substantial proportions of patients were observed to achieve complete to near-complete itch relief and/or skin clearance.
Baseline Use of Oral Contraceptives or Hormone Replacement Therapy in Patients With Moderate-to-Severe Atopic Dermatitis Treated with Abrocitinib in the Phase 2 and Phase 3 JADE Clinical Trial Program and Reported Venous Thromboembolic Outcomes

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Introduction & Objectives: Oestrogen-containing oral contraceptive pills (OCP) and hormone replacement therapies (HRT) pose a risk for venous thromboembolism (VTE), most frequently deep venous thrombosis (DVT) and pulmonary embolism (PE). DVT and PE have been reported in patients (pts) treated with Janus kinase (JAK) inhibitors including abrocitinib, an oral, once-daily, JAK 1-selective inhibitor approved for moderate-to-severe atopic dermatitis (AD). In the abrocitinib phase 2b and phase 3 JADE clinical trial program, all female pts of childbearing potential were required to use highly effective methods of contraception, including hormonal contraceptives. Here, we assessed the use of OCP and HRT therapy at baseline (BL) in female pts with moderate-to-severe AD who received treatment with abrocitinib; VTE outcomes during treatment were reported.

Materials & Methods: This post hoc analysis included pooled data from female pts receiving abrocitinib (100 mg or 200 mg) in the phase 2b (NCT02780167) and the phase 3 JADE trials MONO-1 (NCT03349060), MONO-2 (NCT03575871), REGIMEN (NCT03627767; pts who were not randomised into the maintenance period), COMPARE (NCT03720470), TEEN (NCT03796676), DARE (NCT04345367), and the ongoing long-term extension trial, JADE EXTEND (NCT04322822; data cutoff date: September 25, 2021). Subgroups of abrocitinib-treated pts with BL use of medications identified as OCP-only, HRT-only, or those identified as either OCP or HRT (referred as OCP and HRT-only) were assessed and VTE outcomes in these subgroups were reported. BL use was defined as OCP/HRT use starting on/before Day 1 of abrocitinib initiation (or if start date was missing) with a stop date on/after Day 1. Non-oral hormonal contraceptives (ie, patches, implants) were excluded from this analysis. Pts with VTE risk factors were not excluded.

Results: Of 1384 female pts who received either abrocitinib 200 mg (n=920) or abrocitinib 100 mg (n=464) in the pooled trials, 405 (29%) used oestrogen- or progesterone-containing medications at BL. Of those, most pts (261 [19%]) used OCP-only (abrocitinib 200 mg: 162; abrocitinib 100 mg: 99), 15 (1%) used OCP and HRT-only (200 mg: 7; 100 mg: 8), 12 (1%) used HRT-only (200 mg: 7; 100 mg: 5), and 117 (8%) used other hormonal contraceptives (200 mg: 91; 100 mg: 26). One nonfatal bilateral PE occurred in a 69-year-old White female in the HRT-only group who received abrocitinib 200 mg in the qualifying trial and continued to receive the same dose in JADE EXTEND (blinding maintained); pt had a history of treatment with oral oestradiol (0.5 mg dose). Onset of PE was on day 13 of JADE EXTEND and led to discontinuation of treatment with abrocitinib 200 mg (total exposure time: 112 days); oestradiol was also discontinued. The event was considered by the investigator to be unrelated to abrocitinib and likely related to oestradiol use. No VTE events occurred in the OCP- or the OCP and HRT-only groups.

Conclusion: In this exploratory analysis of 1384 female pts, a third (n=405) received oestrogen- or progesterone-containing medications. In the subgroups evaluated for VTE outcomes, 1 case of VTE was reported. Despite limited
data, these findings still provide useful information, given that many women with moderate-to-severe AD who are of childbearing age require highly effective contraception. Potential risk factors for VTE events need to be explored further, and it remains to be determined whether nonhormonal or low oestrogen contraceptives are preferred in some pts.
Abstract N°: 2805

Benefits of a gel cream in atopic dermatitis through lipid replenishing and reducing itching

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Introduction & Objectives:

Atopic dermatitis (AD) is a complex, chronic relapsing skin condition. It frequently manifests in erythema and xerosis, goes along with pruritus, desquamation, and sleep loss contributing to reduced quality of life (QoL). The present abstract reports results from 3 different clinical studies that assessed the lipid replenishing, hydrating, anti-itching and clinical benefit of a novel gel cream containing an enoxolone derivative that soothes the skin, reduces inflammation and itching, as well as vitamin B3 that helps to restore the natural skin barrier, and which improves its tonicity and radiance in subjects with AD.

Materials & Methods:

Two open-labelled, intraindividual clinical studies in healthy volunteers and one prospective, observational study in AD subjects were conducted. The first study assessed the lipid replenishing and hydrating effect of the gel cream using confocal micro-spectroscopy Raman and corneometry in 12 subjects with dry or very dry skin and who applied on one of the forearms the gel cream for 28 days. The 2nd study assessed its anti-itching benefit in 22 adult subjects with dry or very dry skin and an itching score ≥4 (from 0=none to 10=very severe) on designated areas of the face and body after 21 days. The third study assessed the clinical benefit, local tolerance, quality of life (QoL) and user perception of the gel cream after 28 days of use during summer season in 161 AD subjects aged above 3 months presenting a xerosis score ≥4 (from 0=none to 10=very severe).

Results:

After 28 days, thickness and hydration of the stratum corneum of the treated forearm had increased by 21% and 17%, respectively (p<0.05) compared to the control forearm; so did the lipid-protein ratio (5% increase, p=0.001). Corneometry confirmed the increase in skin hydration (15%).

The itching score decreased by 18% immediately after the 1st application as reported by 86% of the subjects; 24h after, the decrease was 46% as reported by 91% of the subjects. After 21 days of application of the gel cream, the decrease was 70% as reported by 95% of the subjects. All changes were statistically significant (p<0.001).

In total, 81% of the children, 72% of the adults and 78% of the global study population had their skin dryness significantly (p<0.001) improved with the gel cream after 28 days. Functional signs including desquamation, roughness, feeling of dryness, tightness, itching and sleep disturbance had significantly (p<0.001) improved in all populations; so did QoL. Subjects highly appreciated the efficacy and cosmetic properties of the gel cream. Moreover, the gel cream was very well tolerated.

Conclusion:

The gel cream significantly relipidates and hydrates the skin, and reduces itching and dryness in subjects with AD. Subjects highly appreciated the efficacy and cosmetic properties of the product which was very well tolerated.
Rapid, Substantial, and Sustained Reduction of Itch in Adults With Atopic Dermatitis Applying Ruxolitinib Cream — Clinical and Translational Results From the Open-Label Phase 2 SCRATCH-AD Study

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Introduction & Objectives:

A cream formulation of the selective Janus kinase (JAK) 1/JAK2 inhibitor ruxolitinib has received US approval for the short-term and non-continuous chronic treatment of mild to moderate atopic dermatitis (AD) in patients (pts) aged ≥12 y whose disease is not adequately controlled with topical prescription therapies or when those are not advisable. Results from the two pivotal phase 3 trials (TRuE-AD1 and TRuE-AD2) in adolescents and adults with AD reported significant improvement in itch with ruxolitinib cream 1.5% versus vehicle cream, as early as 12 h after initial application. The phase 2, open-label, single-site SCRATCH-AD study (NCT04839380) evaluated short-term clinical and translational effects of ruxolitinib cream on control of itch and reduction of disease severity in pts with AD.

Materials & Methods:

Pts (aged 18–65 y) with AD for ≥6 mo, chronic AD-related itch for ≥3 mo, 1–20% affected body surface area (BSA), Investigator’s Global Assessment (IGA) ≥2, and a peak pruritus numerical rating scale (PP-NRS) score ≥4 at baseline (BL) were eligible. Pts applied ruxolitinib cream 1.5% twice daily to all lesions identified at BL and any new lesions for 28 days. Primary endpoint was change from BL in PP-NRS at Day 2 (24 h after first application of ruxolitinib cream). Other endpoints/assessments included changes from BL in modified PP-NRS (mPP-NRS; current itch intensity), weekly average PP-NRS (WAPP-NRS), and total affected BSA; IGA-Treatment Success (IGA-TS; score of 0/1 with ≥2-grade reduction from BL); EASI-75 (≥75% improvement from BL in Eczema Area and Severity Index [EASI] score); global satisfaction on the Treatment Satisfaction Questionnaire for Medication (TSQM-9); and change in selected serum protein biomarkers.

Results:

The primary analysis included 46 pts in the modified intent-to-treat (mITT) population (median [range] age: 30 [18–64] y; 69.6% female; 89.1% White); mean (SD) 7-day average PP-NRS score during the run-in period was 6.7 (1.36); mean (SD) BL mPP-NRS score was 6.4 (1.72); 89.1% had an IGA of 3; affected BSA was 9.5% (4.94%); EASI score was 6.9 (2.94). Mean (SD) disease duration was 27.3 (16.01) y; 67.4% of pts previously received treatment for AD, most commonly a corticosteroid (63.0%). Mean (SE) change from BL in PP-NRS on Day 2 was −3.4 (0.28). Mean (SE) change from BL in mPP-NRS at 15 min post-treatment was −2.3 (0.35), peaking at −4.2 (0.31) at 4 h, and −3.1 (0.31) at 12 h. Mean (SE) change in WAPP-NRS was −4.2 (0.22), −5.1 (0.24), −5.4 (0.24) and −5.5 (0.23) at Wk 1, 2, 3 and 4. IGA-TS was achieved by 45.5%, 71.1% and 77.3% of pts on Days 8, 15 and 29. At Day 15 and 29, EASI-75 was achieved by 84.4% and 95.5% of pts, and mean (SE) change in affected BSA was −9.0 (0.70) and −9.3 (0.76). At Day 29, mean (SE) global satisfaction TSQM-9 score was 86.7 (2.24). Several serum proteins associated with AD and reduced barrier function were downregulated at Day 29 vs BL, including (but not limited to) IL22, IL19, and DEFB4 (adjusted P≤0.001).

Conclusion:
Pts with AD applying ruxolitinib cream 1.5% experienced rapid, substantial and sustained improvement in itch as early as 15 min and over a period of 4 weeks, and reduction in severity and extent of AD. Pt global satisfaction with treatment was also high. These results are aligned with reductions in serum protein biomarkers associated with disease severity and/or barrier defects, and provide further confirmation of the effectiveness of ruxolitinib cream for the topical treatment of AD.
Introduction & Objectives:

Hand eczema is one of the most common dermatological diseases with a chronic course. Data on the burden of chronic hand eczema (CHE) and effect on quality of life of patients in France are lacking. The objective of this study was to determine the perceived stress, disease burden, and quality of life of patients with CHE in France.

Materials & Methods:

The French Eczema Association, a patient association founded in 2011, sent an online survey in 2022 to CHE patients over 18 years-old with questions regarding the effect of their CHE on stress levels and quality of life. Their stress level was assessed using the perceived stress scale (PSS) and the quality of life using the dermatology life quality index (DLQI) and the burden of hand eczema (BoHEM) score.

Results:

In total, 407 patients responded. There were 326 women (79.7%), and the mean age was 36 ±11.

High level of stress (295/409, 72.1%) was not associated with any specific location on the hand: back of hands (148/295 vs 14/114, p=0.1), palms (137/295 vs 54/114, p=0.8), or fingers (219/295 vs 90/114, p=0.32). It was not associated with any particular symptom: pruritus (203/295 vs 70/114, p=0.15), burning sensation (191/295 vs 75/114, p=0.84), or pain (148/295 vs 52/114, p=0.4). It was not associated with the any signs on the hands either: dryness (222/295 vs 79/114, p=0.2), edema (80/295 vs 26/114, p=0.3), cracking (149/295 vs 50/114, p=0.2), thickening (50/295 vs 23/114, p=0.44).

Our study results show that the mean score of PSS in patients with CHE is not proportional to the severity of the disease (POEM score). However, patients with higher self-diagnosed severity of HE have significantly higher PSS. No relationship was found between PSS and age, sex, or number of hands involved. Higher levels of stress were not related to a particular location on the hand, or a specific symptom or sign. While previous studies show no difference in DLQI between males and females, our study shows that DLQI was significantly higher in males. This is in contrast to atopic dermatitis which seems to have a higher DLQI in females. Moreover, higher DLQI was significantly associated with a higher POEM score and higher self-diagnosed severity of HE. Our results also show that patients with a unilateral involvement have a higher DLQI. This can be explained by the fact that these patients, by worry of having their other hand affected, might limit their daily tasks or leisure activities, which ends up affecting their quality of life. Another explanation can be that unilateral involvement is usually more visible, which can result in a higher social impact. The BoHEM score was also proportional to the severity of the disease according to the POEM score and the self-diagnosed severity of HE. While no relation was noted with age, a higher BoHEM score was significantly associated with a longer duration of the disease, a unilateral involvement, and the male gender.

Conclusion:
CHE is a severely distressing dermatosis that adversely influences the psychological, occupational, and sex life of patients. While not associated with higher stress levels, our study demonstrates a higher disease burden and lower quality of life in male patients and those with unilateral involvement. To better meet the needs of patients, it is important to investigate the possible reasons behind these associations. Besides focusing on the treatment,
Benzyl benzoate induced contact dermatitis complicated by a necrotizing fasciitis of the perineum

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Introduction & Objectives:

Benzyl benzoate remains one of the most commonly prescribed agents for scabies in many parts of the world and compares favorably with other topical agents and oral ivermectin. Inappropriate use can be complicated by contact dermatitis. Here, we report a case of benzyl benzoate-induced contact dermatitis complicated by necrotizing fasciitis of the perineum.

Materials & Methods:

Results:

A 44-year-old man with no medical history was admitted to the urology department for a necrotizing inflammatory plaque of the perineum that had been evolving for three days. The medical interview revealed a history of generalized pruritus, predominantly at night and with a familial character. The patient reported applying benzyl benzoate 10% three times a day for two weeks, which worsened the pruritus and led to the appearance of vesicular lesions and erosions on the penis and scrotum. The patient’s condition worsened when severe swelling of the penis and scrotum appeared, accompanied by fever and general malaise. Clinical examination found edema of the external genital organs, more marked in the scrotum, accompanied by an inflammatory plaque and erosions. Blood tests showed a leukocytosis of 19,550/mm³, a C-reactive protein level of 250 mg/L, and renal insufficiency with a creatinine level of 22.2 mg/L. The diagnosis of Fournier’s gangrene was established, and the patient underwent necrosectomy and received triple intravenous antibiotic therapy with good recovery.

Conclusion:

Irritant contact dermatitis may occur in anyone who is exposed to an irritating substance for a significant duration or in significant concentrations, such as chronic or frequent water exposure, abrasive cleansers, detergents, and soaps. Benzyl benzoate, a topical insecticide for scabies, is applied in a diluted solution with a concentration between 10% and 25% and is known to cause skin irritation and contact dermatitis. Contact dermatitis may lead to skin barrier damage and provide an ideal environment for bacteria or fungi to develop. In our patient, the frequent and repetitive use of benzyl benzoate on sensitive skin caused a disruption in the skin barrier, resulting in a serious infection. Hence, it is important to raise awareness among the population regarding the appropriate use of benzyl benzoate.
Abstract N°: 2950

Dupilumab provides sustained effectiveness in patient-reported outcomes and favorable safety in patients with moderate-to-severe atopic dermatitis: up to 5-year results from the daily practice Bioday Registry

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Introduction & Objectives: Previous studies have demonstrated the long-term effectiveness of dupilumab for up to 4 years in patients with moderate-to-severe atopic dermatitis (AD) in open-label studies. Long-term daily practice data particularly those encompassing a range of patient-reported outcome measures (PROMs) is lacking, which could be helpful to fully capture the disease burden and gain further insight into the effectiveness of dupilumab from patients’ perspectives. In the present study, we aimed to assess PROMs and safety profile for up to 5 years in patients with AD of all ages treated with dupilumab in daily practice.

Materials & Methods: Data were extracted from the prospective, multicenter BioDay registry of patients with moderate-to-severe AD treated with dupilumab (October 2017-2022). Several (proxy) PROMs were captured every 3-6 months, including Patient-Oriented Eczema Measure (POEM), Dermatology Life Quality Index (DLQI), Numeric Rating Scale (NRS) weekly average itch and pain, Work Productivity and Activity Impairment (WPAI), Patient Global Assessment of Disease Status (PGADS). Clinical phenotype of AD was defined using NRS-Itch combined with Eczema Area and Severity Index (EASI) with the cutoff value of 4 and 21, respectively, as follows: mild-moderate itch and lesions (MI-ML), mild-moderate itch and severe lesions (MI-SL), severe itch and mild-moderate lesions (SI-ML), and severe itch and lesions (SI-SL). Adverse events (AEs) were also evaluated.

Results: A total of 1223 pediatric, 1108 adult and 115 pediatric patients, were included (mean±standard deviation (SD) 38.5±17.2 years, 56.8% males, 2281 patient-years (PY)), with up to 5 years of follow-up for the adult population (n=2), and 2.75 years for the pediatric population (n=2). For adult patients at year 4 (n=131), mean±SD POEM, DLQI, NRS-Itch, NRS-pain, overall work impairment was 8.7±6.2, 3.8±4.1, 2.9±2.2, 1.2±1.9 and 15.4±23.5, respectively, with 80.6% reporting ‘good/very good/excellent’ disease status. Taken together, 68.1% of adult patients at year 4 achieved ≥2 of the following absolute cut-off scores: POEM≤7, DLQI≤5, and NRS-Itch≤4, with being males and clinical responders at week 4 more likely to achieve it using the multivariate binary logistic regression model. Concomitant systemic treatments was reported by 2.4% of adult patients at year 4. For pediatric patients at year 1 (n=46), mean±SD POEM, DLQI, NRS-Itch, and NRS-pain was 10.9±7.8, 6.4±5.6, 3.7±2.5, 1.7±2.2, respectably, with 45.7% reporting ‘good/very good/excellent’ disease status. In total 50.0% of pediatric patients at year 1 achieved ≥2 of the following cut-off values: POEM≤7, DLQI≤5, and NRS-Itch≤4. Only one pediatric patient had concomitant systemic treatment at year 1. Moreover, most patients had MI-ML, followed by SI-ML after 1-year until 5-year of treatment, regardless of ages. There were 1696 AEs being reported (74.4/100 PY) and 66.8% of patients reporting at least one AE. The most reported AE was conjunctivitis in 33.7% of patients; of those 69.2% had moderate-to-severe conjunctivitis.

Conclusion: In addition to favorable safety, dupilumab provides a long-term efficacy based on a range of PROMs
in both adult and pediatric populations, including disease-specific symptoms, improvement on quality of life, work productivity and activity impairment, and patients’ assessment of disease status. This underscore the benefit of dupilumab treatment from patients’ perspectives.
Abstract N°: 2997

**Efficacy of lebrikizumab in moderate-to-severe atopic dermatitis based on Australian reimbursement criteria for severe atopic dermatitis**

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**Introduction & Objectives:** Lebrikizumab (LEB), a novel monoclonal antibody that binds with high affinity and slow off-rate to interleukin (IL)-13, thereby blocking the downstream effects of IL-13 with high potency, previously demonstrated clinical efficacy in patients with moderate-to-severe atopic dermatitis (AD) in Phase 3 trials. Here we evaluate 16-week efficacy outcomes of LEB based on the Australian reimbursement criteria used for currently approved systemic agents in the treatment of chronic severe AD from 3 randomized, double-blind, placebo (PBO)-controlled Phase 3 trials; ADVocate1, ADVocate2 and ADhere.

**Materials & Methods:** To align with Australian reimbursement criteria, eligible patients (≥12 years old) had a baseline Eczema Area and Severity Index (EASI) of ≥20 despite prior use of topical therapy, and an age-appropriate Dermatology Life Quality Index (DLQI) baseline score (of any value) measured following treatment with daily topical therapy for ≥28 days. Patients must have had AD for ≥6 months prior to the date of assessment per reimbursement criteria, and ≥12 months per study enrolment criteria.

Patients were randomised 2:1 to subcutaneous LEB (loading doses of 500 mg at Baseline and Week 2 followed by 250 mg every 2 weeks) or PBO in ADvocate1&2 as monotherapy, and in combination with topical corticosteroids (TCS) in ADhere. Efficacy analyses at Week 16 included Investigator’s Global Assessment (IGA) of 0 or 1 with ≥2-point improvement, EASI 50, EASI 75, EASI 90, and DLQI ≥4-point improvement. Per reimbursement criteria, responders must have achieved an adequate response of EASI 50 and DLQI ≥4-point improvement within the first 16 weeks of treatment and maintain this response at biannual evaluations thereafter.

Data from ADvocate1&2 were pooled and ADhere data were analysed separately. ADvocate2 and ADhere analyses were performed on a modified population (mITT), excluding 35 patients (from a single site) whose eligibility could not be confirmed. The Cochran-Mantel-Haenszel test was stratified by study (for pooled ADvocate1&2 data), geographic region, age, and disease severity at baseline. Missing data due to use of rescue medication or treatment discontinuation due to lack of efficacy were imputed with non-responder imputation (NRI). Other missing data were imputed with multiple imputation (MI).

**Results:** Significant differences in efficacy for all populations and quality of life outcomes for the ADvocate population were observed for patients who received LEB compared to PBO. Pooled 16-week results from ADvocate1&2 (LEB [N=432] vs. PBO [N=225]) were: IGA (0,1) with ≥2-point improvement from baseline 37.0% vs. 9.4% (p≤0.001); EASI 50 70.4% vs. 28.2% (p≤0.001); EASI 75 55.4% vs. 13.4% (p≤0.001); EASI 90 35.8% vs. 6.6% (p≤0.001); DLQI ≥4-point improvement from baseline 70.1% vs. 33.1% (p≤0.001), respectively. The corresponding proportions in ADhere (LEB + TCS [N=104] vs. PBO + TCS [N=43]) were IGA (0,1) with ≥2-point improvement from baseline 41.1% vs. 16.2% (p≤0.01); EASI 50 82.1% vs. 52.1% (p≤0.001); EASI 75 72.7%
vs. 40.1% (p≤0.001); EASI 90 44.2% vs. 15.8% (p≤0.01); DLQI ≥4-point improvement from baseline 80.5% vs. 58.4% (p=0.09), respectively.

**Conclusion:** LEB demonstrated statistically significant efficacy on all scales specific for AD disease severity when used both as monotherapy and with adjuvant TCS according to Australian reimbursement criteria used for currently approved systemic agents in the treatment of chronic severe AD.

Time-course Response Rates for EASI 50 and DLQI ≥4-point Improvement from Baseline in Pooled ADVocate 1&2 and ADhere Patients

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Percentage of patients (%) achieving EASI 50 in pooled ADVocate 1 and ADVocate 2 (A) and ADhere studies (B); percentage of patients (%) achieving DLQI ≥4-point improvement from baseline in pooled ADVocate 1 and ADVocate 2 studies (C) and ADhere studies (D).

**Abbreviations:** DLQI = Dermatology Life Quality Index; EASI = Eczema Area and Severity Index; EASI 50 = 50% reduction in EASI; LEB = LediStat® capsules; PRO = patient; TCS = topical corticosteroids.

* p<0.05; ** p<0.01; *** p<0.001 vs. PRO based on the Cochran-Mantel-Haenszel test stratified by study (pooled ADVocate 1&2 patients), geographic region, age group, and baseline GAG score. Missing data as a result of use of rescue medication or treatment discontinuation due to loss of efficacy were imputed with non-responder imputation (NRI). Other missing data were imputed with multiple imputation (MI).

**Notes:**
- Patients ≥18 years old with DLQI ≥4 at baseline.
- Patients ≤18 years old were not included in the DLQI analysis. DLQI measured at baseline and Weeks 4, 8, 12, and 16.
Abstract N°: 3005

First cross-border analyses of 5341 atopic dermatitis patients treated with systemic treatment or phototherapy enrolled in 7 European registries united in the TREatment of ATopic eczema (TREAT) Registry Taskforce

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Introduction & Objectives:

The TREatment of ATopic eczema (TREAT) Registry Taskforce is an international network of independent multi-centre registries and aims to generate reliable real-world data on long-term effectiveness, cost-effectiveness and safety of systemic immunomodulating treatments and phototherapy in atopic dermatitis (AD) patients. We aimed to provide an overview of the demographics, clinical characteristics and disease burden of patients enrolled in 7 TREAT registries across Europe.

Materials & Methods:
We collected baseline sociodemographic data, treatment characteristics and history, AD disease severity and burden (using physician- and patient-reported outcomes) of patients that were included between the date of first inclusion (variable) and October 31st 2022 in the following 7 established registries in the TREAT registry Taskforce: A-STAR registry (United Kingdom and Ireland), AtopyReg registry (Italy), Biobadatop registry (Spain), SCRATCH registry (Denmark), SwedAD registry (Sweden), TREATgermany registry (Germany) and TREAT NL registry (the Netherlands and Belgium).

**Results:**

A total of 5341 patients (mean age 39.2 years, 54.4% male) were included into this analysis. 4321 patients had received systemic treatment in the past, of whom most had received systemic corticosteroids (51.6%), followed by methotrexate (31.1%). 1212 patients received any type of phototherapy prior to enrolment. Dupilumab was the most commonly prescribed medication at enrolment (76.1%) in the registries, followed by methotrexate (9.1%). 4.3% of patients started treatment with a Janus Kinase inhibitor (JAKi) at the time of enrolment. Phototherapy was infrequently (1.5%) initiated at baseline. Most patients suffered from moderate (39.5%) to severe (28.3%) AD measured with the Validated Investigator Global Assessment (vIGA) scale for AD and had a mean Eczema Area and Severity Index (EASI) score of 17.4 (±12.1). The mean Patient-Oriented Eczema Measure (POEM) was 17.0 (±7.8), corresponding with severe disease. The mean pruritus past 24 hours Numerical Rating Scale (NRS) was 6.4 (±2.9) and mean Dermatology Life Quality Index (DLQI) score was 13.6 (±8.4).

**Conclusion:**

This pooled analysis is the largest cross-European sample with real-world baseline data of AD patients starting with systemic immunomodulating treatment and/or phototherapy. We have demonstrated the TREAT Registry Taskforce’s ability to join forces, and we have taken an important step toward future collaborative analyses for key (cost-)effectiveness and safety outcomes.
Abstract N°: 3006

Efficacy of lebrikizumab in severe atopic dermatitis based on the Korean reimbursement criteria for treatment of severe atopic dermatitis

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Introduction & Objectives:

Lebrikizumab (LEB) is a novel monoclonal antibody that binds with high affinity and slow off-rate to interleukin (IL)-13, thereby blocking the downstream effects of IL-13 with high potency. LEB previously demonstrated clinical efficacy in patients with moderate-to-severe atopic dermatitis (AD) in Phase 3 trials. Here we evaluate the 16-week efficacy outcomes of LEB based on the Korean reimbursement criteria in patients with severe AD from 2 randomized, double-blind, placebo (PBO)-controlled Phase 3 trials: ADvocate1 (ADv1; NCT04146363) and ADvocate2 (ADv2; NCT04178967).

Materials & Methods:

In ADv1&2, patients were randomized 2:1 to subcutaneous LEB (loading doses of 500 mg at baseline and week 2 followed by 250 mg every 2 weeks) or PBO. Efficacy analyses at week 16 included Investigator Global Assessment (IGA) of 0 or 1 with ≥2-point improvement, 50% reduction in the Eczema Area and Severity Index (EASI 50), 75% reduction in EASI (EASI 75), 90% reduction in EASI (EASI 90), and Dermatology Life Quality Index (DLQI) ≥4-point improvement.

Eligible patients were required to present with an EASI score ≥16 at baseline, chronic AD present for ≥1 year before screening, and a history of inadequate response to treatment with topical medications or determination that topical treatments were otherwise medically inadvisable. To align with the Korean reimbursement criteria, this analysis includes patients who presented with an EASI score ≥23 at baseline and history of disease onset of ≥3 years. Korean reimbursement criteria also require patients to have a documented history of previous therapy with either cyclosporine or methotrexate, however, due to the low number of patients who met these criteria in ADv1&2, this analysis is restricted to patients with any prior systemic therapy use.

Patients who received topical or systemic rescue medication or discontinued treatment due to lack of efficacy had values set to their baseline value through Week 16; multiple imputation was used to handle the remaining missing data. DLQI is only reported in patients >16 years of age with a baseline score ≥4. The common risk difference is the difference in proportions adjusted for the following stratification factors: study (ADv1 vs. ADv2), geographic region (US vs. EU vs. rest of world), age (adolescent patients ≥12 to <18 vs. adults ≥18 years), and disease severity (IGA 3 vs. 4). Confidence intervals are calculated using Mantel-Haenszel-Sato method. The relative risk
and odds ratio are also adjusted for the same stratification factors.

Results:

At baseline for LEB and PBO, the mean (standard deviation) values were: age in years 36.0 (15.8) and 35.3 (16.7); EASI 36.0 (11.3) and 37.8 (11.6); duration since AD onset in years 25.7 (14.2) and 25.0 (16.2); and DLQI 16.9 (6.6) and 17.8 (7.3), respectively.

Pooled 16-week results from ADv1&2 (LEB [N=201] vs. PBO [N=121]) were: 29.3% vs. 4.2% (p<0.001) for IGA (0,1) with ≥2-point improvement from baseline; 64.8% vs. 21.0% (p<0.001) for EASI 50; 48.4% vs. 7.8% (p<0.001) for EASI 75; and 29.5% vs. 2.6% (p<0.001) for EASI 90. The proportions of patients achieving DLQI ≥4-point improvement from baseline for LEB (N=161) and PBO (N=97) were 66.6% vs. 20.5% (p<0.001), respectively.

Conclusion:

In two, large phase 3 trials studying patients with moderate-to-severe AD, LEB demonstrated statistically significant efficacy versus placebo at Week 16 in a subpopulation of patients with severe AD who met the Korean reimbursement eligibility criteria.
Abstract N°: 3026

**Moderate to severe atopic dermatitis resistant to Baricitinib: a case report successfully treated with Dupilumab.**

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**Introduction & Objectives:**

Atopic dermatitis (AD), is a multifaceted skin condition that results from a complex interplay between genetic, environmental, and immunological factors. The dermatosis is characterized by recurrent episodes of pruritus, erythema, and scaling involving the skin. Timely and consistent treatment of AD is crucial to prevent disease exacerbations and manage symptoms. Nonetheless, a subset of patients may display refractory symptoms despite the use of topical and systemic therapies. In this context, we report a case of an 18-year-old female with moderate to severe AD treated unsuccessfully with topical and systemic drugs including Baricitinib. However, a marked improvement in her condition was observed when she was treated with Dupilumab.

**Materials & Methods:**

An 18-year-old female with a long-term history of AD was selected for this case report. The patient presented with a history of erythema, itching, and dry skin, which resulted in excoriations over the flexor surfaces of her limbs, trunk, neck, and face. The patient reported using multiple topical and systemic treatments, such as steroids, antihistamines, phototherapy, and Cyclosporine for the past few years, without any successful improvement. The patient also complained of a poor quality of life due to persistent itching, sleep disturbance, depression, and social isolation. On examination, the patient had erythematos, scaly, and lichenified skin on the neck, face, trunk, and limbs. The lesions showed signs of excoriations and crusting. Laboratory investigations including complete blood count, liver and renal function tests, chest radiography, PPD skin test were within the normal range as well as a negative HIV and hepatitis screening. Her DLQI was 20, BSA 14 and SCORAD 45.

The patient had been treated with Baricitinib for six months without any clinical response. We opted to introduce Ciclosporin until Dupilumab was available. The patient was closely monitored for the development of adverse events.

**Results:**

After six months of treatment with Dupilumab the patient’s symptoms had significantly improved. Ciclosporine was gradually removed. The itching was reduced, and the patient reported an improvement in her quality of life. Her DLQI improved to 14, BSA decreased to 5, and SCORAD to 15. The patient presented signs of a temporary mild conjunctivitis resolved with conservative management. Baricitinib, a Janus kinase inhibitor, is an oral medication that is commonly used for the treatment of rheumatoid arthritis. Recent studies have shown that Baricitinib may be beneficial for patients with AD by inhibiting the JAK/STAT signaling pathway which plays a crucial role in the pathogenesis of AD. However, in this patient’s case, there was no improvement after the use of Baricitinib. Dupilumab, a monoclonal antibody that targets the interleukin-4 receptor alpha subunit, has been approved by the FDA for the treatment of moderate to severe AD in adults. Dupilumab inhibits the downstream inflammatory signaling of interleukin-4 and interleukin-13, two cytokines that have been implicated in the pathogenesis of AD. Our patient showed significant improvement after the use of Dupilumab, indicating its effectiveness in severe and refractory AD.
Conclusion:

This case highlights the complexity of AD and the relevance of a multidisciplinary approach for its management. Dupilumab is an effective treatment option for patients with moderate to severe AD who have failed to respond to conventional therapies.
Abstract N°: 3075

The current trajectories for treatment of atopic dermatitis: results of a national study in France

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Introduction & Objectives:

Atopic dermatitis (AD) is one of the most common skin disorders in Europe. In the US, most healthcare visits for AD occur with primary care physicians (PCPs), with fewer visits to dermatologists. Data on the care pathway patterns in France is lacking. The aim of our study was to assess the current care pathway and patient satisfaction of AD management in France.

Materials & Methods:

The French Eczema Association sent an online survey in 2022 to AD patients over 18 years old with questions regarding symptoms, visited physicians and satisfaction regarding their AD management. The severity of AD was assessed via the POEM score. Treatment satisfaction (TS) was defined as the proportion of patients who declared being satisfied with their AD management.

Results:

In total, 1251 patients with AD responded to the survey, of whom 455 (36%) with an additional dermatosis were excluded. Therefore, 796 patients were included in the study. Among the patients consulting a hospital-based dermatologist, 24.2% consulted on their own (27.3% mild AD (MAD) and 22.7% moderate-to-severe AD (MSAD) patients), 50% were referred by a general physician, and 25.8% by a dermatologist in private practice (22.7% of MAD and 27.3% of MSAD). The referral purpose was to improve management in 62% of cases (50% of MAD and 67.7% of MSAD), and to change treatments in 32% of cases (43.8% of MAD and 26.5% of MSAD). The mean number of consultations per year with a general physician was 4±2.4, 2.1±2 with a hospital dermatologist, and 1.8±1 with a private dermatologist. For patients who declared to have been doctor shopping (n=501), 54.3% of them declared that it was the dermatologist who prescribed the suitable treatment: hospital dermatologist in 10.8% (7.5% MAD vs MSAD 13.4%) and private dermatologist in 43.5% (45.1% MAD vs 42.2% MSAD) of cases. On the other hand, 36.4% of these patients declared that it was the general physician that prescribed the suitable treatment (40.4% MAD vs 32.2% MSAD). As in the US, the most visited physician by AD patients is the general practitioner. For both, MAD and MSAD, the visited dermatologists are mostly those in private practice rather than those in hospitals. For those who have been doctor shopping, the type of visited physician has an impact on MAD and MSAD patients’ satisfaction Surprisingly, for MSAD, it is highest with PCPs. While MSAD patients’ needs seem to be met upon consulting PCPs, with a breadth of management options available, more complex or problematic AD should seek a specialist’s opinion for optimal results.

Conclusion:

Exploring AD care pathway and patients’ satisfaction in France should promote reinforcement of PCPs’ skills in diagnosing and treating this condition. In France as in the US, PCPs are allowed to prescribe systemic immunosuppressants but have a high level of discomfort in doing so. Initiation of immunosuppressants by PCPs can be validated through tele-expertise, and renewal can subsequently be done under joint supervision. Given the shortfall in dermatology workforce, pathway schemes in atopic dermatitis can rest on the efficacy of teledermatology in designing these models. Finally, European clinical practice guidelines for referral patterns can
help optimize patients’ access to new biologics when needed.
Patient beliefs on atopic dermatitis from a Baricitinib Treatment Satisfaction Survey in France, Germany and the United Kingdom

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Introduction & Objectives: Atopic dermatitis (AD) is an inflammatory skin disease that imposes a considerable burden on patients’ lives requiring a patient-centered therapeutic approach as recommended by the updated European AD guidelines [1, 2]. Recently, new treatments including biologics and oral Janus kinase inhibitors (JAKi) have become available. Amongst these, baricitinib was the first once daily oral JAKi approved for treating moderate-to-severe AD in adult patients in Europe [3]. This analysis aims to understand how the emotional and social aspects of patients’ beliefs around their AD may change with baricitinib treatment, as well as understanding patient beliefs about the disease itself.

Materials & Methods: This study is a protocol-driven analysis of data collected in a multi-country, cross-sectional, online survey conducted using a market research questionnaire completed by patients. It included adult patients with moderate-to-severe AD treated with baricitinib in routine clinical practice for at least four weeks in France, Germany, and the UK. Amongst others, the survey recorded patient-reported demographics, disease characteristics (Itch Numerical Rating Scale [NRS]) and patient beliefs around their AD on a 10-point Likert scale.** Descriptive analyses on observed data were employed.

Results: The survey was completed by 170 patients with moderate-to-severe AD treated with baricitinib (France=48, Germany=53, UK=69) with median treatment duration of 4 months. Mean patients’ age was 39 years (standard deviation [SD]=13.5), 59% (n=101) were female, and mean time since AD diagnosis was 20.9 years (SD=14.0). At the time of the survey, 96% (n=164) of patients reported less than 10% of body surface area affected by AD, and patients reported a mean itch of 2.7/10. The proportion of patients describing their AD currently as almost clear/mild was 56% (n=95). Amongst the surveyed patient beliefs, the statement “I feel more able to participate in my daily activities” obtained the highest rate of agreement with 82% (n=139) of patients agreeing with being more able to participate in daily activities. Over 20% of patients either completely agreed (score 10/10) with the belief that since starting baricitinib they were more able to participate in daily activities or rated their agreement with score 9/10 (Figure 1). Regarding being less embarrassed by their AD, the proportion of patients agreeing with this belief was 68% (n=115). 63% (n=106) of patients agreed with avoiding social situations less and agreed they were more in control of their emotions. 38% (n=66) of patients agreed at least to some extent with the belief that their AD can be completely cured.

Conclusion: Across the beliefs examined, baricitinib-treated patients were optimistic about aspects of their everyday life, particularly their ability to go about their daily activities and felt less embarrassed in everyday life.


3. Radi, G., et al., Baricitinib: The First Jak Inhibitor Approved in Europe for the Treatment of Moderate to Severe...
Figure 1: Patients beliefs concerning their atopic dermatitis since starting treatment.
Raising the Bar of Efficacy in Atopic Dermatitis: Lebrikizumab Provides Sustained Deep Skin and Itch Relief Up to 52 Weeks

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Introduction & Objectives:
Recent data suggest patients with atopic dermatitis (AD) who reach higher levels of improvement in measures of skin clearance and itch reduction experience greater improvements in quality of life above and beyond that reached by standard response thresholds currently proposed as treatment targets. Lebrikizumab (LEB) is a novel monoclonal antibody that binds with high affinity and slow off-rate to interleukin (IL)-13, thereby blocking the downstream effects of IL-13 with high potency. ADvocate1 (ADv1; NCT04146363) and ADvocate2 (ADv2; NCT04178967) are identically designed phase 3 trials evaluating LEB for the treatment of moderate-to-severe AD. In both studies, LEB administered every 2 weeks (Q2W) was statistically superior vs placebo across all primary and key secondary outcomes at week 16. During the maintenance period, most per protocol responders treated with LEB Q2W or LEB every 4 weeks (Q4W) maintained an Investigator Global Assessment (IGA) 0/1 (71% and 77%, respectively), a 75% improvement in the Eczema Area and Severity Index from baseline (EASI 75; 78% and 82%, respectively), and a Pruritus Numeric Rating Scale (NRS) ≥4-point improvement (85% and 85%, respectively) up to week 52. Most per protocol responders treated with LEB Q2W or LEB Q4W also achieved and maintained a 90% improvement in EASI from baseline (EASI 90; 64% and 66%, respectively). The objective of this analysis is to present LEB’s long-term maintenance of deep response, defined as IGA 0 (clear skin), EASI 100, or Pruritus NRS 0/1 (no or minimal itch), a significant unmet need in patients with moderate-to-severe AD.

Materials & Methods:
52-week results are reported for LEB Q2W, LEB Q4W, and placebo (LEB withdrawal) for IGA 0 (from the number of patients who achieved IGA 0/1 at week 16), EASI 100 (from the number of patients who achieved EASI 75 at week 16), and Pruritus NRS 0/1 (calculated by averaging daily scores from the previous 7 days with at least 1 nonmissing value and rounding the weekly score to the nearest integer). Intermittent use of topical rescue medications (any potency) for AD was permitted during the maintenance period. Patients who received systemic rescue medication, discontinued treatment due to lack of efficacy, or transferred to the escape arm were considered nonresponders for binary endpoints and had subsequent values set to their baseline value for continuous endpoints. Patients who received topical rescue medication (any potency) or discontinued treatment for other reasons had subsequent values set to missing, with missing data imputed with multiple imputation.

Results:
In week 16 responders of ADv1 and ADv2, the IGA 0 response, EASI 100 response, and Pruritus NRS 0/1 response achieved with LEB Q2W at week 16 was maintained or improved to 44.4% (LEB Q2W), 39.1% (LEB Q4W), and
22.6% (LEB withdrawal) at week 52 (IGA 0; Figure 1), 31.5% (LEB Q2W), 27.1% (LEB Q4W), and 19.2% (LEB withdrawal) at week 52 (EASI 100; Figure 2), and 39.1% (LEB Q2W), 40.7% (LEB Q4W), and 24.0% (LEB withdrawal) at week 52 (Pruritus NRS 0/1; Figure 3).

**Conclusion:**

ADv1 and ADv2 52-week results demonstrate long term maintenance of deep response with LEB, with approximately 30 and 40% of LEB-treated patients sustaining total skin clearance (EASI 100 and IGA 0, respectively) and approximately 40% of LEB-treated patients reporting no or minimal itch. Lebrikizumab treatment allows patients and providers to elevate their expected treatment goals in atopic dermatitis beyond EASI 75 and IGA 0/1 response.
Abstract N°: 3230

**Characterisation of GSK1070806, an anti-IL-18 monoclonal antibody**

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**Introduction:**

Interleukin 18 (IL-18) is a pleotropic pro-inflammatory immune modulator that functions in a highly context dependent manner depending on the local cytokine environment. Levels of IL-18 are elevated in a wide range of human diseases (including atopic dermatitis, inflammatory bowel disease, and rheumatoid arthritis) suggesting that neutralising IL-18 activity has considerable therapeutic potential in many indications.

In vivo, the functional activity of IL-18 is regulated by an endogenous antagonist - the IL-18 binding protein (IL-18 BP) – that circulates at higher levels than the cytokine and regulates its activity by inhibiting the interaction of IL18 with its cognate receptor, the IL-18Ra. Levels of IL-18BP are also altered in many disease states, making assessment of the contribution of IL-18 bioactivity to pathophysiology challenging.

**Results:**

GSK1070806 is a humanised IgG1 monoclonal antibody that binds to IL-18 with high affinity in surface plasmon resonance studies (42pM). GSK1070806 blocked production of interferon-γ (IFNγ) and IFNγ-mediated downstream signalling from IL-18 stimulated KG-1 cells confirming that it is a neutralising antibody.

In surface plasmon resonance experiments, the affinity of the interaction between IL-18BP and free IL18 was the same as the affinity of the interaction between IL-18BP and the IL18-GSK1070806 complex. Hydrogen deuterium exchange mass spectrometry confirmed that the binding sites on IL18 for the IL-18 BP and for GSK1070806 are independent and not overlapping.

GSK1070806 did not interfere with the binding of IL-18 to the IL-18Rα, which is consistent with the lack of impact on IL-18 BP binding. GSK1070806 therefore appears to neutralise IL-18 activity by preventing activation of the signalling chain of the receptor, the IL-18Rβ.

**Conclusion:**

GSK1070806 is therefore a potent neutralising anti-IL18 antibody with considerable therapeutic potential in a range of inflammatory disease. The antibody has been previously evaluated in healthy and obese subjects, patients with type 2 diabetes and patients undergoing renal transplantation. GSK1070806 has been recently assessed in a Phase 1B clinical study in patients with moderate-to severe atopic dermatitis.

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Abstract N°: 3342

Longitudinal EASI response with lebrikizumab through week 52 in initial week 16 partial responders

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Introduction & Objectives:

Lebrikizumab (LEB) is a novel monoclonal antibody under development for moderate-to-severe atopic dermatitis (AD) that binds with high affinity and slow off-rate to interleukin (IL)-13. ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) Phase 3 trials evaluated the efficacy and safety of LEB monotherapy in moderate-to-severe AD. Here we report the Eczema Area and Severity Index (EASI) response through the maintenance phase of ADvocate1 and ADvocate2 in those patients who did not achieve the protocol definition of response at Week 16.

Materials & Methods:

Patients were randomized 2:1 to LEB 250 mg or placebo (PBO) every 2 weeks (Q2W) during the Week 16 induction period. Patients were considered responders if they achieved a 75% reduction in the EASI from baseline (EASI 75) or an Investigator Global Assessment (IGA) 0/1 with a ≥2-point improvement from baseline at Week 16, without rescue medication use. At the end of the induction period, responder patients were re-randomized 2:2:1 to receive LEB 250 mg Q2W, LEB 250 mg every 4 weeks (Q4W) or PBO Q2W during the 36 weeks maintenance period. Non-responder patients to LEB at Week 16 were assigned to the escape arm and continued to receive LEB 250 mg Q2W up to Week 52. Low- and mid-potency topical corticosteroids (TCS) use was permitted during this period. This post-hoc analysis reports the proportion of LEB Week 16 non-responders achieving the following EASI cut-offs through Week 52: EASI<50, EASI ≥50 to <75, EASI ≥75 to <90 and EASI ≥90. Data is presented as observed results with no imputation for missing data.

Results:

Pooled results for patients who did not achieve the per protocol response at Week 16 (n=215) and continued to receive LEB 250 mg Q2W up to Week 52 show that 64.0% and 18.7% achieved EASI ≥75 and EASI ≥90, respectively, at Week 24 and 75.5% and 42.4% of patients achieved EASI ≥75 and EASI ≥90, respectively, at Week 52. Results are displayed in the table.
Conclusion:

These results suggest that patients who did not achieve the protocol defined response at Week 16 can progressively respond and therefore benefit from continuing long-term treatment with LEB +/- TCS.

References:

Abstract N°: 3350

Efficacy of lebrikizumab at week 52 in patients initially randomized to placebo from ADvocate1 and ADvocate2

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Introduction & Objectives:
Lebrikizumab (LEB) is a novel monoclonal antibody for moderate-to-severe atopic dermatitis (AD) that binds with high affinity and slow off-rate to interleukin (IL)-13. In ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) phase 3 trials, LEB monotherapy has demonstrated short-term (at Week 16) and durable maintenance of response (at Week 52) in patients with moderate-to-severe AD1. Here, we report the pooled efficacy results at Week 52 of patients initially randomized to placebo who did not respond at Week 16 and were moved to the escape arm, where they received LEB 250 mg Q2W for 36 consecutive weeks.

Materials & Methods:
During the Week 16 induction period, 851 patients were randomized 2:1 to LEB 250 mg or placebo every 2 weeks (Q2W). At the end of the induction period, patients who did not achieve a 75% reduction in the Eczema Area and Severity Index from baseline (EASI 75) or an Investigator Global Assessment (IGA) 0/1 with a ≥2-point improvement, or who received rescue medication use, were assigned to the escape arm and received LEB 250 mg Q2W up to Week 52. Low- and mid-potency topical corticosteroids (TCS) use was permitted during this maintenance period. This post-hoc analysis reports the data of patients initially randomized to placebo who did not respond at week 16. The proportion of these patients achieving EASI 75, EASI 90, IGA (0/1) with a ≥2-point improvement from baseline and ≥4-point pruritus improvement from baseline (assessed using an 11-point Pruritus Numeric Rating Scale, NRS)2 at Week 52 was reported. Data are presented as observed results with no imputation for missing data.

Results:
At Week 52, after 36 weeks of continuous LEB Q2W treatment, 83.7% of patients achieved EASI 75, 60.4% achieved EASI 90, 51.9% achieved IGA (0/1) with ≥2-point improvement from baseline and 65.5% reported ≥4-point improvement from baseline in Pruritus NRS.

Conclusion:
These results demonstrate the efficacy of LEB 250 mg Q2W in improving signs and symptoms of moderate-to-severe AD up to 36 continuous weeks.
References:

Abstract N°: 3387

Patients Maintain Stable Response with No or Minimal Fluctuations During Treatment with Lebrikizumab up to Week 52

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Introduction & Objectives: Lebrikizumab is a monoclonal antibody that binds with high affinity and slow off-rate to interleukin (IL)-13, thereby blocking the downstream effects of IL-13 with high potency. At Week (W) 16, lebrikizumab (LEB) 250mg every two weeks (Q2W) showed statistically significant improvements in measures of skin clearance and patient reported outcomes in ADvocate1 (ADv1) and Advocate2 (ADv2). In patients who met the protocol-defined criteria for response to LEB at W16, most patients treated with LEB Q2W and LEB every 4 weeks (Q4W) maintained an Investigator’s Global Assessment (IGA) 0/1 response (71% and 77%, respectively) and a 75% improvement in the Eczema and Severity Index from baseline (EASI 75; 78% and 82%, respectively) up to W52. The objective of this analysis is to determine the proportion and the individual efficacy trajectory of LEB-treated patients who exhibited a stable response with no or minimal fluctuations of efficacy from W16 to W52 in W16 responders.

Materials & Methods: Patients who responded to LEB at the end of the 16-week induction period were re-randomized 2:2:1 to receive LEB Q2W, LEB Q4W, or placebo Q2W (withdrawal) for 36 additional weeks. W16 responders were those achieving an EASI 75 or IGA 0/1 with a ≥2-point improvement and without rescue medication use. We defined no or minimal fluctuations as maintaining EASI 75 for at least 80% of the study visits from W16 to W52. EASI 90 was analyzed similarly. We also analyzed the proportion of patients who achieved each endpoint at all maintenance period study visits. ADv2 analyses were performed on a modified population, excluding 17 patients who entered the maintenance period (from a single study site) and whose eligibility could not be confirmed. Thus, analyses were performed on the modified pooled population of ADv1 and ADv2. All analyses were performed post-hoc.

Results: In ADv1 and 2, 291 patients met the criteria for response at W16 (EASI 75 or IGA 0/1 with a ≥2-point improvement and without rescue medication use) and were re-randomized to receive LEB Q2W (N=113), LEB Q4W, (N=118), or withdrawal (N=60) from W16 to W52. The proportions of patients who maintained EASI 75 for at least 80% of the maintenance period were 71% (LEB Q2W and Q4W each) and 60% (withdrawal). The proportions of patients who maintained EASI 75 at all study visits were 53% (LEB Q2W), 55% (LEB Q4W), and 38% (withdrawal). The proportions of patients to achieve and maintain EASI 90 for at least 80% of study visits were 45% (LEB Q2W), 51% (LEB Q4W), and 35% (withdrawal).

Conclusion: In ADv1 and 2, approximately 7 out of 10 of patients who continued treatment with LEB maintained at least an EASI 75 response with no or minimal fluctuations. The data show that most patients treated with monotherapy LEB Q2W and Q4W maintain a stable response with no or minimal fluctuations of efficacy up to
Previously presented at RAD-5th Annual Conference; April 29 - May 1, 2023; Washington, DC, USA.

**Figure 1. EASI Percent Change from Baseline Individual Patient Trajectory**

EASI, Eczema Area and Severity Index; LEB, lebrikizumab; Q2W, every 2 weeks; Q4W, every 4 weeks
Maintenance of efficacy and safety with lebrikizumab up to one year of treatment in patients with moderate-to-severe atopic dermatitis with or without topical corticosteroids

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Introduction & Objectives: ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) are phase 3 trials evaluating induction and maintenance treatment with lebrikizumab (LEB) monotherapy in patients with moderate-to-severe atopic dermatitis (AD). ADhere (NCT04250337) evaluated induction treatment with LEB plus topical corticosteroids (TCS) in patients with moderate-to-severe AD. Patients completing ADhere could roll over into ADjoin (NCT04392154), a long-term extension for five LEB parent studies. Here, we describe maintenance treatment results of ADvocate1 and ADvocate2 (Weeks 16 to 52; pooled data) and ADjoin (Weeks 0 to 40; patients rolling over from ADhere) in patients who achieved IGA 0/1 or EASI-75 after 16 weeks of LEB treatment without use of rescue therapy. This analysis evaluated the maintenance of efficacy and safety in Week 16 responders when administered LEB with or without TCS every 2 weeks (Q2W) or every 4 weeks (Q4W) in patients with moderate-to-severe AD for up to one year.

Materials & Methods: Non-responder imputation was used to handle missing data due to lack of efficacy (ADvocate1, ADvocate2, and ADjoin) or data after systemic rescue medication usage (ADvocate1 and ADvocate2 only; intermittent TCS use was allowed). Multiple imputation was used for other missing data.

Results: In ADvocate1 and ADvocate2 pooled results, most patients treated with LEB Q2W and Q4W maintained an IGA 0/1 response (71.2% and 76.9%, respectively) and EASI-75 response (78.4% and 81.7%, respectively) at Week 52. Similarly, most patients treated with LEB plus TCS Q2W and Q4W in ADjoin maintained an IGA 0/1 response (75.4% and 86.8%, respectively) and EASI-75 response (85.6% and 81.2%, respectively) at Week 40. Across studies, most LEB-treated patients also maintained EASI-90. Safety results were consistent with those previously published.

Conclusion: Following a 16-week induction, patients maintained a similarly durable response in the signs and symptoms of moderate-to-severe AD when treated with LEB Q2W and Q4W with or without TCS.

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Lebrikizumab provides long-term clinically meaningful responses in patients with moderate-to-severe atopic dermatitis

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Introduction & Objectives:

Lebrikizumab (LEB) is a novel monoclonal antibody for moderate-to-severe atopic dermatitis (AD) that binds with high affinity and slow off-rate to interleukin (IL)-13. Treatment response in AD is assessed by improvements in signs, symptoms and in quality of life (QoL) as recommended by Harmonizing Outcome Measures in Eczema (HOME) committee. The clinically meaningful response provided by LEB at week 16 in adult patients in monotherapy has been previously reported. Here, we report the clinically meaningful response provided by LEB at week 52 among week 16 responders of ADvocate1 (NCT04146363) and ADvocate2 (NCT04178967) clinical trials (pooled data).

Materials & Methods:

ADvocate1 and ADvocate2 were two identically designed, randomized, placebo-controlled, monotherapy Phase 3 trials assessing efficacy and safety of lebrikizumab in patients with moderate to severe AD. Responders at week 16 were defined as patients achieving a 75% reduction in the EASI from baseline (EASI 75) or an Investigator Global Assessment (IGA) 0/1 with a ≥2-point improvement from baseline, without rescue medication use. Patients who responded to LEB 250 mg every two weeks (LEB Q2W) at the end of the 16-week induction period were re-randomized 2:2:1 to receive LEB 250 mg every Q2W, LEB 250 mg every 4 weeks LEB (Q4W), or placebo (LEB withdrawal) for 36 additional weeks (maintenance period). Clinically meaningful responses were defined as follows: for signs by EASI ≤7, for symptoms by Pruritus Numeric Rating Scale (PNRS) ≤4, and for QoL by Dermatology Life Quality Index (DLQI) ≤5. This post-hoc analysis reports the proportion of adult patients achieving one or more of these three clinically meaningful responses, and the proportion of adult patients achieving all three clinically meaningful responses, which can be representative of minimal residual AD. The Maintenance Primary Population (MPP) was used for efficacy analyses. Adult patients with baseline DLQI>5 and PNRS>4 were selected. Data after systemic rescue medication or missing data due to lack of efficacy were imputed with non-responder imputation. Other missing data and data after topical corticosteroid usage were imputed with multiple imputation.

Results:

At week 52, 89.6% of patients in LEB Q4W, 84.3% of patients in LEB Q2W and 72.9% of patients in LEB withdrawal
achieved one or more of the clinically meaningful AD responses in signs, symptoms or QoL. 57.6% of patients in LEB Q4W, 60.7% of patients in LEB Q2W and 45.8% of patients in LEB withdrawal achieved all 3 endpoints at week 52.

Conclusion:

At week 52, LEB provides clinically meaningful responses for signs, symptoms, and QoL in adults with moderate-to-severe AD. In addition, more than half of the patients achieve response in all three domains (signs, symptoms and QoL), which represents a status of minimal disease.
Abstract N°: 3403  

**Efficacy and safety of lebrikizumab in combination with topical corticosteroids in patients with moderate-to-severe atopic dermatitis not adequately controlled or non-eligible for cyclosporine: a placebo-controlled, randomized phase 3 clinical study (ADvantage)**

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**Introduction & Objectives**

Lebrikizumab (LEB) is a novel monoclonal antibody that binds with high affinity and slow off-rate to interleukin (IL)-13, thereby blocking the downstream effects of IL-13 with high potency. LEB has previously demonstrated clinical efficacy and safety in adults and adolescents with moderate-to-severe atopic dermatitis (AD) in 3 randomized, placebo (PBO)-controlled, phase 3 trials.¹⁻³ Cyclosporine A (CsA) is approved in the EU for treatment of severe AD, but its efficacy may not be optimal in some patients and its safety limits longer-term use. Here, we report 16-week efficacy and safety of LEB combined with low- or mid-potency topical corticosteroids (TCS) in patients with moderate-to-severe AD not adequately controlled or non-eligible for CsA in the phase 3 ADvantage study (NCT05149313).

**Materials & Methods**

ADvantage is a 52-week study with a 16-week, randomized, double-blind, PBO-controlled, parallel-group period followed by a 36-week open-label maintenance period. Eligible patients were adults and adolescents (≥12 to <18 years) with an Eczema Area and Severity Index (EASI) ≥16, Investigator’s Global Assessment (IGA) ≥3, and ≥10% body surface area of AD involvement who were not adequately controlled or were non-eligible for CsA. Patients were randomized 2:1 to LEB 250 mg with a loading dose of LEB 500 mg at baseline and week 2, or PBO every two weeks (Q2W). All patients were to receive concomitant mid-potency TCS through week 16; dosage could be tapered to low-potency TCS once lesions were controlled and stopped after 7 days. The primary efficacy endpoint was the percentage of patients who achieved 75% reduction from baseline in EASI (EASI 75) at week 16. Secondary efficacy endpoints included percentage of patients achieving EASI 90, IGA 0/1, and ≥4-point improvement in pruritus Numeric Rating Scale (NRS) at week 16. Safety endpoints included treatment-emergent adverse events (TEAE), serious adverse events (SAE) and TEAE leading to discontinuation. Missing data due to lack of efficacy or data after rescue medication usage (high-potency TCS or systemic treatment) were imputed using non-responder imputation. Other missing data were imputed using multiple imputation.

**Results**
331 patients were randomized (220 LEB+TCS and 111 PBO+TCS) and 212 and 100, respectively, completed the 16-week period. Treatment groups had similar baseline characteristics. At week 16, a significantly higher proportion of LEB+TCS vs PBO+TCS patients achieved EASI 75 (68.4% vs 40.8%, p<0.001) and EASI 90 (42.9% vs 20.8%, nominal p<0.001). Moreover, a higher percentage of patients achieved IGA 0/1 (42.0% vs 24.5%, nominal p<0.01) and a ≥4-point improvement in pruritus NRS (49.9% vs 29.7%, nominal p<0.05) at week 16. Incidence of TEAE was 61.8% LEB+TCS vs 53.2% PBO+TCS with nasopharyngitis (12.7% vs 12.6%) and conjunctivitis (11.4% vs 1.8%) being the most common TEAE. Overall, SAE and TEAE leading to discontinuation were low and similar in LEB+TCS and PBO+TCS (1.4% vs 0.9% and 0.9% vs 1.8%, respectively).

**Conclusion**

At week 16, LEB 250 mg Q2W administered with TCS significantly improved signs and symptoms of AD in adults and adolescents with moderate-to-severe AD and history of inadequate response to CsA, or for whom CsA was not medically advisable. Safety was consistent with the known profile of lebrikizumab.

**References**


Abstract N°: 3406

Treatment Efficacy in Patients With Moderate-to-Severe Atopic Dermatitis Who Switched From Dupilumab to Abrocitinib in JADE EXTEND, a Phase 3 Long-Term Extension Study

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Introduction & Objectives: Abrocitinib, an oral, once-daily, Janus kinase 1–selective inhibitor, and dupilumab, an anti–interleukin 4 receptor α monoclonal antibody, have been approved for the treatment of patients with moderate-to-severe atopic dermatitis (AD). The efficacy of abrocitinib and dupilumab as monotherapy or in combination with medicated topical therapy has been demonstrated in multiple phase 3 clinical trials. As is the case with many therapies, some patients with AD may need to discontinue treatment with dupilumab (due to inadequate efficacy, intolerable side-effects, patient choice, or other reasons) and switch to other systemic therapies. This post hoc analysis evaluated the long-term treatment response in patients with moderate-to-severe AD who switched from dupilumab to abrocitinib, as it is valuable information for prescribers and patients to consider when making treatment decisions.

Materials & Methods: The phase 3 JADE COMPARE trial (NCT03720470) evaluated the efficacy of abrocitinib (100 mg or 200 mg once daily) and dupilumab (300 mg every 2 weeks) versus placebo in combination with topical medicated therapy in patients with moderate-to-severe AD through week 16. After a wash-out period, dupilumab-treated patients from JADE COMPARE who enrolled in the ongoing long-term extension trial JADE EXTEND (NCT03422822; clinical data cutoff: Sept 25, 2021) were randomised to receive double-blinded treatment with abrocitinib 100 mg or 200 mg. This analysis evaluated the response to dupilumab through week 16 in JADE COMPARE and thereafter in JADE EXTEND following a switch to abrocitinib through week 104 of total treatment duration/week 84 of abrocitinib treatment. Assessments included Investigator’s Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement from baseline (IGA 0/1), ≥75% or ≥90% improvement from baseline in Eczema Area and Severity Index (EASI-75 or EASI-90), ≥4-point improvement from baseline in Peak Pruritus Numerical Rating Scale score (PP-NRS4; PP-NRS used with permission from Regeneron Pharmaceuticals, Inc., and Sanofi), and a PP-NRS score of 0 or 1 (PP-NRS 0/1). JADE EXTEND data are presented as observed; patients with missing data at a visit were excluded. Analyses included both dupilumab responders and non-responders.

Results: Overall, 242 patients were treated with dupilumab in JADE COMPARE (mean age: 37 years; IGA score 4: 33%). Of those, 203 enrolled in JADE EXTEND and received abrocitinib 200 mg (n=73) or abrocitinib 100 mg (n=130). After 16 weeks of treatment with dupilumab in JADE COMPARE, the proportion of responders was 39% for IGA 0/1, 66% for EASI-75, 39% for EASI-90, 57% for PP-NRS4, and 24% for PP-NRS 0/1 (Figure). As early as 2 weeks after switching to abrocitinib 200 mg or 100 mg in JADE EXTEND, the proportion of responders was observed to increase in a dose-dependent manner for IGA 0/1 (61%; 51%), EASI-75 (90%; 85%), EASI-90 (60%; 54%), PP-NRS4 (81%; 72%), and PP-NRS 0/1 (47%; 37%). Long-term efficacy was observed out to week 84 (Figure).
**Conclusion:** In patients with moderate-to-severe AD who received prior treatment with dupilumab, switching to abrocitinib resulted in dose-dependent increases in the proportion of responders as early as week 2 after treatment with abrocitinib. This efficacy continued to be observed long-term through week 84 of abrocitinib treatment.

**Figure.** Treatment response with dupilumab in JADE COMPARE and after switching to abrocitinib in JADE EXTEND

- EASI-75, ≥75% Improvement in Eczema Area and Severity Index; EASI-90, ≥90% Improvement in Eczema Area and Severity Index; IGA 0/1, Investigator’s Global Assessment score of 0 (clear) or 1 (almost clear) with a ≥2-point improvement; NRI, non-responder imputation; PP-NRS4, 24-Point Improvement in Peak Pruritus Numerical Rating Scale score; PP-NRS 0/1, Peak Pruritus Numerical Rating Scale score of 0 or 1; Q2W, once every 2 weeks; QD, once daily; wk, week.

The NRI analysis set was used in JADE COMPARE. If a patient withdrew from the study, the patient was considered a non-responder after that point (Bieber T, et al. N Engl J Med. 2021 Mar 25;384[12]:1101-1112).

JADE EXTEND data are presented as observed (JADE EXTEND is an ongoing study and not all patients reached week 84 visits at the clinical data cutoff [September 25, 2021]).
Abstract N°: 3474

Assessing Imputation Methods with the Lebrikizumab Clinical Trial Program

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Introduction & Objectives: In ADvocate1 (ADv1) and ADvocate2 (ADv2), two randomized, double-blinded, placebo-controlled Phase 3 trials evaluating the efficacy and safety of lebrikizumab monotherapy in adolescent and adult patients with moderate-to-severe atopic dermatitis, a combined non-responder/multiple imputation (NRI/MI) approach was applied on the primary and key secondary endpoints. The analysis** illustrated the NRI/MI method using individual patient examples and to present Week 16 study results from ADv1 and ADv2 with NRI/MI and single imputation methods, NRI and last-observation carried forward (LOCF).

Materials & Methods: In the combined NRI/MI method, data from patients after initiating rescue medication or discontinuing treatment due to lack of efficacy were imputed with NRI, and missing data for other reasons were imputed with MI, which uses a statistical model based on all available patient data to impute missing values. The MI method considers each patient’s trajectory and leverages information from other patients within the same treatment arm to impute the missing data. With NRI alone, the cause leading to the missing data is not considered and missing data for any reason are imputed as nonresponse. With LOCF, missing data are replaced with the last available measurement; LOCF assumes that the patient response would be stable over time and does not consider the reason for missing data. We determined the amount of missing data in ADv1 and ADv2, and assessed patient-level imputed IGA scores to illustrate NRI/MI, NRI, and LOCF. With these missing data handling methods, we evaluated the percentage of patients achieving the co-primary endpoints of ADv1 and ADv2: an Investigator’s Global Assessment score of 0 or 1 (IGA [0,1]; clear or almost clear) with ≥2-point improvement from baseline or 75% improvement in Eczema Area and Severity Index (EASI 75) at Week 16.

Results: With the NRI/MI method, most missing data at Week 16 were imputed with NRI (ADv1: 73%, ADv2: 82%) compared with MI (ADv1: 27%, ADv2: 18%). Example imputed IGA scores based on patient-level data will be presented to demonstrate the missing data handling methods. For NRI/MI, NRI, and LOCF, respectively, the percentage of patients achieving IGA 0,1 were 12.7%, 11.3%, and 12.8% for placebo in ADv1 and 10.8%, 9.6%, and 11.0% for placebo in ADv2; 43.1%, 41.0%, and 42.4% for lebrikizumab in ADv1 and 33.2%, 31.3%, and 33.5% for lebrikizumab in ADv2. The percentage of patients achieving EASI 75 were 16.2%, 14.2%, and 16.3% for placebo in ADv1 and 18.1%, 17.1%, and 19.2% for placebo in ADv2; 58.8%, 56.5%, and 60.1% for lebrikizumab in ADv1 and 52.1%, 50.2%, and 55.5% for lebrikizumab in ADv2.

Conclusion: When using the NRI/MI method, we determined most missing data in ADv1 and ADv2 were handled with NRI. This analysis suggests that the NRI/MI method may provide a realistic estimation of response rate in ADv1 and ADv2.
Figure: Summary of the percentage of patients achieving SII, S, and AHI 1 in ambulatory and unobstructed sleep. The data was collected using the M-ANAGE.com system for monitoring sleep.
Abstract N°: 3476

Lebrikizumab does not impact vaccine-induced immune responses: results from a phase 3 study in adult patients with moderate-to-severe atopic dermatitis

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Introduction & Objectives: Lebrikizumab (LEB) is a monoclonal antibody (Ab) that has shown efficacy and safety in patients with moderate-to-severe atopic dermatitis (AD) in Phase 2/3 trials. LEB targets IL-13 and inhibits signaling of the IL-4Rα/IL-13Rα1 complex. The potential immunomodulator effect of LEB necessitates investigating its impact on immune responses.

Materials & Methods: ADopt-VA was a US Phase 3, 16-week (W) randomized, double-blind, placebo-controlled study to assess LEB impact on vaccine immune responses in adult patients with moderate-to-severe AD. The primary endpoint was the immune response to 2 vaccines, the Tdap (Diphtheria/Tetanus Toxoids/Pertussis) vaccine and MCV (Meningococcal Groups A, C, Y, and W-135) vaccine. LEB was given as a 500 mg loading dose at baseline and W2, followed by 250 mg LEB Q2W. At W12, both vaccines (Tdap and MCV) were administered to all patients, LEB group N=107, Placebo (PBO) group N=81. Immune responses were determined by Ab level differences between W12 and W16. Secondary efficacy endpoints at W16 were Investigator Global Assessment (IGA) and Eczema Area and Severity Index (EASI 75) scores.

Results: For Tdap, 73.6% of LEB patients had a positive Ab response vs 73.4% for PBO, 90% CI, 0.3 (-10.2, 11.2). For MCV, LEB patients had an 86.9% positive Ab response vs 75.0% for PBO, 90% CI, 12.2 (2.5, 22.0). IGA (0,1) was achieved by 40.6% of LEB patients vs 18.9% receiving PBO (p<0.001); EASI 75 was achieved by 58.0% and 32.7% (p<0.001), respectively. The safety profile was consistent with previous LEB trials.

Conclusion: These data show that LEB does not negatively impact immune responses for Tdap or MCV vaccines in adults with moderate-to-severe AD.

Previously presented at International Societies for Investigative Dermatology - 1st; 10 - 13 May 2023; Tokyo, Japan.
Abstract N°: 3523

Dupilumab Reduces Inflammatory Biomarkers in Patients Aged 6 Months to 17 Years With Moderate-to-Severe or Severe Atopic Dermatitis

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Introduction & Objective: Elevated levels of inflammatory biomarkers are observed in atopic dermatitis (AD). Dupilumab is associated with reduction of type 2 inflammatory biomarkers in adults, but data from adolescent and pediatric patients are lacking.

Materials & Methods: We report type 2 and general inflammatory biomarker serum levels (TARC/CCL17, LDH, total IgE, eosinophils) from patients with moderate-to-severe or severe AD (the latter in patients aged 6–11 years) enrolled in randomized, double-blind, placebo-controlled phase 3 studies receiving: dupilumab 200/300 mg every 4 weeks (q4w) + topical corticosteroids (TCS; n = 83), or placebo + TCS (n = 79) (0.5–5 years; NCT03346434 part B); dupilumab 100/200 mg q2w + TCS (n = 122), or 300 mg q4w + TCS (n = 122), or placebo + TCS (n = 123) (6–11 years; NCT03345914); and dupilumab 200/300 mg q2w (n = 82), or dupilumab 300 mg q4w (n = 84), or placebo (n = 85) (12–17 years; NCT03054428).

Results: Median percentage reduction from baseline in TARC/CCL17 (pg/mL) and LDH (U/L) was significantly greater in all dupilumab-treated arms across age groups ($P < 0.0001$ at Week 16). Greater reduction in median change from baseline to Week 16 in total IgE (kU/L) was observed in dupilumab-treated patients vs placebo for ages 0.5–5 (difference in median change [95% CI]: $-2201.1$ [−4497, −902.8], $P < 0.0001$); 6–11 ($-2338$ [−3391, −1473] and $-1888$ [−2949, −1038], both $P < 0.0001$) and 12–17 years ($-2524$ [−3579, −1783.6] and $-1996.6$ [−3260, −1308], both $P < 0.0001$). Median change (Q1–Q3) from baseline at Week 16 in eosinophil levels ($x$ 10\textsuperscript{9}/L) in patients aged 0.5–5 years was $0.01$ (−0.3−0.3) for placebo + TCS and $-0.01$ (−0.3−0.5) for dupilumab 200/300 mg q4w + TCS; in patients 6–11 years, it was $0.0$ (−0.2−0.2) for placebo + TCS, $0.0$ (−0.3−0.4) for dupilumab 300 mg q4w + TCS and $0.2$ (−0.2−0.5) for dupilumab 100/200 mg q2w + TCS; and in patients 12–17 years, it was $0.04$ (−0.2−0.3) for placebo, $-0.03$ (−0.3−0.3) for dupilumab 200/300 mg q2w and $-0.04$ (−0.3−0.2) for dupilumab 300 mg q4w.

Conclusions: Dupilumab treatment for 16 weeks in patients aged 6 months to 17 years with moderate-to-severe or severe AD reduces levels of type 2 and general inflammatory biomarkers TARC/CCL17, LDH, and total IgE, reflecting reduction of systemic general and type 2 inflammation. No changes in eosinophil levels were observed.
Clinically normal appearing skin in remission displays unique features before atopic dermatitis relapse

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Introduction & Objectives:

Atopic dermatitis (AD) is a widespread chronic relapsing skin disease that is characterized by lesions at specific body sites, which are typically driven by a type 2 immune response. While the active state is well-researched and a wide variety of treatment options exists, lesions often recur after treatment cessation. Recent research suggests that clinically healed AD skin is still distinguishable from healthy skin through increased subclinical inflammation. However, we currently do not know what characterizes the skin shortly before new relapses and therefore aimed at understanding the pathophysiology of relapses in this study.

Materials & Methods:

To this end, we conducted a clinical study involving 22 patients with recently successfully treated AD and monitored the donors’ subsequent time to relapse. Using single-cell RNA sequencing, we compared samples from donors relapsing within the first weeks with those that did not. Samples of healthy and active AD skin were used for additional reference.

Results:

Interestingly, we found that differentially expressed genes in many cell types of the pre-relapsing skin differed strongly from the active disease state, suggesting that the molecular processes in relapsing and active atopic dermatitis are dissimilar.

Conclusion:

These findings provide new insights into early disease pathology and potentially pave the way for new therapeutic treatment approaches to prolong lesion-free periods in atopic dermatitis.
Real-world efficacy and tolerability of tralokinumab in patients with moderate to severe atopic dermatitis

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Atopic dermatitis (AD) is one of the most common chronic inflammatory skin diseases with an estimated prevalence of 2-3% in adults worldwide. Recently, tralokinumab, an anti-IL-13 antibody has been licenced for the treatment of moderate-severe atopic dermatitis, but data on real-life use is still missing.

Patients with moderate to severe AD were treated with tralokinumab and the clinical real life efficacy was evaluated by assessments of the SCORing Atopic Dermatitis (SCORAD), body surface area (BSA), the Dermatology life Quality Index (DLQI) and visual analogue scales for pruritus and sleep loss at baseline (V1) and after 3 (V2) and 6 months (V3). Adverse events were documented at every visit.

We report on a cohort of 45 adult AD patients (62.2% male, 37.8% female) with a mean (SD) age of 41.2 years (15.6 years), who received tralokinumab (2x300 mg loading dose followed by 300 mg every 2 weeks s.c.). The mean (SD) SCORAD significantly decreased from 46.7 points (19.6) at V1 to 29.8 points (15.1) after 3 months and to 21.2 points (11.3) after 6 months of treatment. A similar reduction was seen for the mean (SD) BSA: At V1, the mean BSA was 31.6% (17.9%) and significantly decreased to 21.2% (17.4%) after 3 months and to 8.1% (9.1%) after 6 months of tralokinumab treatment. The mean DLQI decreased from 13.0 points (V1) to 8.0 points at V2 and remained stable with 8.8 points at V3. The mean reported pruritus on a 0-10 VAS decreased from 5.7 points at baseline to 3.6 points after 3 months and reached 3.8 points after 6 months. The mean reported sleep loss on a 0-10 VAS declined from 5.1 points at baseline to 2.4 points after 3 months and 2.1 points after 6 months. No safety signals were observed, eye related symptoms e.g. conjunctivitis were reported by one patient.

Taken together our data demonstrate the clinical efficacy of tralokinumab in AD patients. The clinical responsiveness was associated with an improvement of patient related outcomes and an excellent safety profile underpinning its real world efficacy and safety.
Efficacy Outcomes by Age and Race: A Post Hoc Analysis of Patients With Mild-to-Moderate Atopic Dermatitis Treated with Twice-Daily Crisaborole During the 8 Week Open-Label Period of the CrisADe CONTROL Trial

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Introduction & Objectives: Atopic dermatitis (AD) is a chronic immuno-inflammatory skin disease characterized by recurring flares of eczematous lesions and pruritus. Crisaborole ointment, 2%, is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild-to-moderate AD. In the double-blind, vehicle-controlled, randomized, 52-week, phase 3 CrisADe CONTROL trial (NCT04040192), comprising participants aged ≥3 months with mild-to-moderate AD who responded to a twice-daily (BID) treatment up to 8 weeks, participants treated with once-daily (QD) crisaborole as a maintenance treatment showed a longer median duration without flares, more flare-free days, and fewer flares versus vehicle and was well tolerated. This post hoc analysis evaluated efficacy outcomes for 497 participants in the open-label period who received crisaborole BID up to 8 weeks. Outcomes were stratified by age and race.

Materials & Methods: In CrisADe CONTROL, 497 participants received crisaborole BID during an open-label run-in period of up to 8 weeks for responder qualification. Responders (n=260; 52.3%) achieved both success per Investigator’s Static Global Assessment (ISGA) score of 0 [clear] or 1 [almost clear] with a ≥2-grade improvement and ≥50% improvement in Eczema Area and Severity Index total score from baseline. Age subgroups were participants aged 3 months to <7 years (n=140), 7 to <12 years (n=82), 12 to <18 years (n=105), and ≥18 years (n=170). Race subgroups comprised White (n=204), Black (n=161), Asian (n=101), or Other race (n=31) participants.

Results: The proportion of responders (%; 95% CI) up to Week 8 of the open-label run-in period was numerically greatest among participants aged ≥18 years (56.5; 48.2-64.0), followed by participants aged 12 to <18 years (52.4; 42.4-62.2), 3 months to <7 years (52.1; 43.5-60.7) and 7 to <12 years (43.9, 33.0-55.3). The proportion of responders was numerically greatest among Asian participants (58.4; 48.2-68.1), followed by Other race (54.8; 36.0-72.7), Black (52.8; 44.8-60.7), and White (48.5; 41.5-55.6) participants. A trend of improvement in patient/observer-reported outcomes was seen in responders to crisaborole BID across age and race subgroups. From the Work Productivity and Activity Impairment Questionnaire plus Classroom Impairment Questions, mean change from baseline (standard deviation [SD]) for percent activity impairment was −13.3 (23.4) for participants 12 to <18 years and −15.9 (28.2) for participants ≥18 years. Between race subgroups, mean change from baseline (SD) for percent activity impairment for participants of Other races, Black, Asian and White participants was -20.0 (22.7), -18.3 (28.3), -17.7 (26.1), and -8.4 (24.0), respectively. There were no safety concerns for all subgroups.

Conclusion: Overall, crisaborole BID has similar efficacy and safety outcomes across age and race subgroups. Sample sizes were small for some subgroups; ongoing evaluation of the safety and efficacy of crisaborole BID across diverse age and race populations is essential to ensure this treatment can be used effectively and safely to manage AD in all patients.
Flare-Free Maintenance and Safety Outcomes at 52 Weeks by Age and Race: A Post Hoc Analysis of Once-Daily Crisaborole as a Long-Term Maintenance Treatment in Participants With Mild-to-Moderate Atopic Dermatitis (CrisADe CONTROL)

Lawrence Eichenfield1, Linda Stein Gold2, Charles Lynde3, Paul Sanders4, Chuanbo Zang5, Juliana Machado Canosa6, Amy Cha7, Shoshana Greenberger8, Lin MA9, Roni Adiri10

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Introduction & Objectives: Treatments for atopic dermatitis (AD), a chronic immuno-inflammatory skin disease, often fail to achieve long-lasting disease control, with safety concerns limiting the long-term use of many AD therapies. Crisaborole ointment, 2%, is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild-to-moderate AD. In the double-blind, vehicle-controlled, randomized, 52-week phase 3 CrisADe CONTROL trial (NCT04040192), treatment with once-daily (QD) crisaborole was effective and well tolerated for long-term maintenance treatment in adult and pediatric participants with mild-to-moderate AD who responded to twice-daily (BID) treatment up to 8 weeks. This post hoc analysis was designed to evaluate flare-free maintenance and safety outcomes at week 52, stratified by age and race.

Materials & Methods: In CONTROL, 270 participants were randomly assigned 1:1 in the double-blind maintenance period to receive either crisaborole or vehicle QD for 52 weeks. For this analysis, age subgroups were participants aged 3 months to <7 years (n=72), 7 to <12 years (n=35), 12 to <18 years (n=53), and ≥18 years (n=94). Race subgroups were participants who were White (n=99), Black (n=83), Asian (n=55), or Other race (n=17).

Results: Among participants who received crisaborole QD, median time of flare-free maintenance until first flare was 111 days (95% CI, 56-224), overall, and longest for the 12 to <18 years subgroup (278; 54-not evaluable [NE]), followed by the 7 to <12 years (111; 28-NE), ≥18 years (110, 56-365), and 3 months to <7 years (54; 28-168) subgroups. Median time of flare-free maintenance until first flare (days; 95% CI) was longest for Black participants (365; 33-NE), followed by Asian (230; 69-NE) and White (56; 30-111) participants and participants in the Other race category (56; 14-NE). Both median time of flare-free maintenance until first flare and mean total flare-free days were numerically greater for participants who received crisaborole compared with participants who received vehicle for all subgroups except for participants in the Other race subgroup, who had more flare-free days with vehicle. The limited sample size of the Other race subgroup (n=17) may have contributed to this finding, which should be interpreted with caution. Mean number of flares was lower for participants who received crisaborole versus vehicle for all subgroups. Among participants treated with crisaborole, 1 Asian participant aged 12 to <18 years and 1 Asian participant aged ≥18 years experienced treatment-related, treatment-emergent adverse events. None of the participants treated with crisaborole experienced application site pain. In participants who received vehicle, application site pain was present in 1 participant aged 3 months to <7 years and 1 participant aged 12 to <18 years.

Conclusion: Overall, crisaborole QD was effective for long-term maintenance treatment with no safety concerns for all subgroups. The sample sizes of some subgroups were small; therefore, further exploration of crisaborole QD efficacy and safety among different age and race subgroups is necessary to ensure that all patients with AD can be
safely and effectively treated using this approach.
First and Second Flare-Free Maintenance at 52 Weeks: A Post Hoc Analysis of Once-Daily Crisaborole as a Long-Term Maintenance Treatment in Patients With Mild-to-Moderate Atopic Dermatitis (CrisADe CONTROL)

Lawrence Eichenfield1, Linda Stein Gold2, Charles Lynde3, Paul Sanders4, Chuanbo Zang5, Amy Cha6, Shoshana Greenberger7, Lin MA8, Juliana Machado Canosa9, Roni Adiri10

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Introduction & Objectives: Achieving effective and lasting management of atopic dermatitis (AD), a chronic immuno-inflammatory skin disease, remains an important clinical challenge. Crisaborole ointment, 2%, is a nonsteroidal phosphodiesterase 4 inhibitor for the treatment of mild-to-moderate AD. In the double-blind, vehicle-controlled, randomized, 52-week, phase 3 CrisADe CONTROL trial (NCT04040192), treatment with once-daily (QD) crisaborole was effective and well tolerated for long-term maintenance treatment in participants aged ≥3 months with mild-to-moderate AD who responded to twice-daily (BID) crisaborole during the run-in period up to 8 weeks. This post hoc analysis evaluated flare-free maintenance until first and second flare through week 52 of the double-blind maintenance period.

Materials & Methods: In the CrisADe CONTROL trial, 497 participants received crisaborole BID during an open-label run-in period of up to 8 weeks for responder qualification. Responders (N=254) were randomly assigned 1:1 in the double-blind maintenance period to receive either crisaborole QD or vehicle QD for 52 weeks. 254 and 136 participants were evaluable for first and second flares, respectively. For this post hoc analysis, incidence of flares and median duration until onset of flares were stratified by age (3 months to <12 years [n=107] and ≥12 years [n=147]), Investigator’s Static Global Assessment (ISGA) score at randomization (0 [clear, n=104] or 1 [almost clear, n=150], and run-in duration (≤4 weeks [n=77] or >4 weeks [n=177]).

Results: Numerically fewer crisaborole QD-treated participants vs vehicle QD-treated participants experienced a first flare in the total population (81/125; 64.8% vs 96/129; 74.4%) and all subgroups. There was a decreased risk (hazard ratio [HR; 95% CI] of experiencing a first flare with crisaborole QD vs vehicle QD for the overall population (HR, 0.646; 0.477-0.875), for participants aged ≥12 years (0.638; 0.423-0.963), participants with ISGA score 1 at randomization (0.592; 0.403-0.869), and participants treated with crisaborole BID for >4 weeks during the run-in period (0.657; 0.455-0.949). Overall, median duration of flare-free maintenance (days; 95% CI) until first flare was significantly longer with crisaborole QD (111 days; 56-224) vs vehicle QD (30 days; 28-56; P=0.0034) and numerically longer with crisaborole QD vs vehicle QD for all subgroups. Numerically fewer crisaborole QD-treated participants vs vehicle QD-treated participants experienced a second flare in the total population (26/60; 43.3% vs 45/76; 59.2%) and all subgroups, except among participants aged 3 months to <12 years (8/31; 26.2% vs 21/37; 61.5%). The risk (HR; 95% CI) of experiencing a second flare was similar with crisaborole QD vs vehicle QD (0.777; 0.475-1.273) and lower for participants aged ≥12 years (0.425; 0.186, 0.968). Median duration of flare-free maintenance (days, 95% CI) until second flare was similar between crisaborole QD (111 days; 56-224) vs vehicle QD (30 days; 28-56; P=0.0034) in the total population and between subgroups.

Conclusion: Compared with vehicle QD-treated participants, crisaborole QD-treated participants experienced fewer first and second flares in almost all subgroups and had more flare-free days until first flare in all subgroups.
Some subgroups were small; ongoing exploration of crisaborole QD as a maintenance therapy is warranted to ensure this approach is effective for all AD patients.
Abstract N°: 3578

Assessing the similarities and differences in the advanced therapeutics offered, and chosen, among atopic dermatitis patients

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Introduction & Objectives:

The recent expansion in the number of advanced therapeutics (biologics/oral JAK inhibitors) available to treat atopic dermatitis (AD) has enabled physicians to further tailor the prescribing options provided to patients¹. The objective of this study was to draw comparisons between the advanced therapy options provided, and chosen, among moderate-severe AD patients across the EU4&UK and USA.

Materials & Methods:

A multi-centre online medical chart review study of patients with AD was conducted between September – December 2022 among dermatologists from the UK, FR, DE, IT & ES and December 2022 – January 2023 among dermatologists and allergists in the USA. Physicians were screened for practice duration, patient volume and ability to prescribe advanced therapies. Charts of patients with moderate-severe AD were included in the analysis.

Results:

211 physicians in the EU4&UK and 108 physicians in the USA abstracted charts for 865 (EU4&UK) and 438 (USA) moderate-severe AD patients currently treated with an advanced therapy. Whilst similar reported usage of oral JAK inhibitors is evident across both reported patient cohorts, penetration of the biologic class is greater in the EU4&UK group (see Table 1).

Table 1. % reported moderate-severe AD patients receiving a biologic vs JAK inhibitor

<table>
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<th>EU4&amp;UK (n=857)</th>
<th>USA (n=552)</th>
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<tbody>
<tr>
<td>% currently treated with a biologic</td>
<td>81%</td>
<td>69%</td>
</tr>
<tr>
<td>% currently treated with an oral JAK inhibitor</td>
<td>11%</td>
<td>10%</td>
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When analysing options provided by sampled physicians at the commencement of patient’s current treatment, reported advanced therapy treated patients in the EU4&UK who have switched treatment (n=802 EU4&UK; n=351 USA) were less likely to be provided with multiple options to choose from, versus the USA (31% vs 59%). Instead, prescriptions of an advanced therapy in the EU4&UK cohort were more likely to arise as a result of physician-led decisions the patient agreed to (54% vs 25%).

In cases where multiple options were provided to advanced therapy treated patients, biologics were consistently more frequently offered over an oral JAK inhibitor in both cohorts (see Table 2). Whilst biologic therapies were offered to the patients in a similar frequency across both cohorts, oral JAK inhibitors were offered in a directionally greater frequency in the EU4&UK, in comparison to the USA.

Table 2. % reported moderate-severe advanced therapy treated AD patients offered a biologic vs JAK inhibitor
A similar trend is also observed when considering the proportion of advanced therapy treated patients who chose a biologic or oral JAK inhibitor, when offered. Once again across both cohorts a greater proportion of the patients are more likely to choose a biologic when offered. However, whilst biologic therapies were more frequently offered by sampled physicians in the EU4&UK, they are more frequently chosen by the patients in the USA (see Table 3).

<table>
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<th>EU4&amp;UK (n=246)</th>
<th>USA (n=206)</th>
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<tbody>
<tr>
<td>% offered a biologic</td>
<td>96%</td>
<td>94%</td>
</tr>
<tr>
<td>% offered an oral JAK inhibitor</td>
<td>57%</td>
<td>47%</td>
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Table 3.

Frequency therapeutic classes were chosen by moderate-severe advanced therapy treated AD patients who were offered the associated treatment

**Conclusion:**

Comparisons in this study cohort suggest the decision to commence an advanced therapy treatment is more likely to be physician-led in the EU4&UK, with patient choice from a list of physician-provided options a more frequent scenario taking place in the USA. Across both regions, in cases where options are provided, biologic therapies are offered by physicians, and chosen by patients, in a higher frequency than oral JAK inhibitors. Further exploration is warranted to understand additional factors that may affect the decision to provide certain options to patients.
Abstract N°: 3591

Real-life Effectiveness and Safety of Upadacitinib in Patients with moderate to severe Atopic Dermatitis naïve to any advance therapy: a multicentre, ambispective study

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Introduction & Objectives: The efficacy and safety of upadacitinib in atopic dermatitis (AD) have been defined in clinical trials, but real-world data are still lacking. We aimed to assess the safety and effectiveness of upadacitinib in a real-world AD patient cohort that included patients who have not previously received any the advanced systemic therapies (dupilumab, tralokinumab, or another anti-JAKs inhibitors).

Materials & Methods: We conducted an ambispective, real-life observational study. Data were collected from patients treated with upadacitinib from sixteen hospitals in Madrid, Spain. All patients had not received advanced therapies and completed at least 16 weeks of treatment with upadacitinib. A descriptive analyses of these cohort were performed to assess effectiveness and safety.

Results: Sixty-one patients showed rapid and marked response to upadacitinib with significant reduction of all disease severity scores since the first follow-up visit. At week 16, Eczema Area and Severity Index (EASI) 75, EASI 90 and EASI 100 response was observed in 78,3%, 45,6% and 21,7% of patients, respectively. Patients’ quality of life improved as suggested by the achievement of DLQI 0/1 by 38.5% of patients at week 4, and by 76.9% at week 16.

2 patients had herpes zoster, 4 herpes simplex, 2 nausea, 1 astenia, 2 patient increased CPK, 1 mild neutropenia, 1 mild hypertransaminasemia and 10 acne/foliculitis. 2 patients discontinued upadacitinib (1 due to acne and 1 due to eczema herpeticum).

Conclusion: Elevated effectiveness and favorable safety of upadacitinib were confirmed in patients previously naïve to advanced systemic therapies.
Long-Term Efficacy of Dupilumab for up to 5 Years in an Open-Label Extension Study of Adults With Moderate-to-Severe Atopic Dermatitis

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Introduction & Objectives: Moderate-to-severe atopic dermatitis (AD) is a chronic inflammatory skin disease often poorly controlled by topical therapies, thus requiring long-term management. Here we assess the long-term efficacy and safety of dupilumab in adult patients with moderate-to-severe AD up to 5 years at the end of this open-label extension (OLE) study.

Materials & Methods: The OLE study (NCT01949311) enrolled adults with moderate-to-severe AD up to 5 years who had participated in any dupilumab parent study (phase 1 through phase 3). During the OLE, patients were treated with 300 mg dupilumab weekly. 226 patients transitioned to 300 mg every 2 weeks to align with approved dosage. Concomitant topical treatments were permitted. Data are presented as observed for the overall study population (N = 2,677).

Results: Of the 2,677 patients who enrolled, 2,207 completed treatment up to Week 52, 362 up to Week 172, and 334 up to Week 260. Just over half of withdrawals (51.3%) were due to dupilumab approval/commercialization. 50 (1.9%) patients withdrew due to lack of efficacy. At the end of the study period, a 91.3% mean percentage reduction in Eczema Area and Severity Index (EASI) score was reported with 96.9%/88.9%/76.2% of patients achieving 50%/75%/90% decreases, respectively, in EASI from parent study baseline (PSBL). At the end of the OLE study period, 67.5% of patients achieved an Investigator Global Assessment score of 0 or 1. At Week 260, a 66.6% mean percentage reduction in Peak Pruritus Numerical Rating Scale (PP-NRS) score was reported with 76.4%/66.5% of patients achieving a ≥ 3/≥ 4-point decrease in PP-NRS from PSBL. Dupilumab had an acceptable safety profile over 5 years of treatment.

Conclusion: In this long-term (5-year/260-week) OLE, dupilumab demonstrated continued efficacy substantiated by sustained improvement of AD signs and symptoms in adult patients with moderate-to-severe AD. The safety profile was acceptable and consistent with the known safety profile observed in previous dupilumab placebo-controlled studies.
Abstract N°: 3673

Black and Indigenous Representation in Atopic Dermatitis Clinical Trials: a 10-year Cross-sectional Analysis

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Introduction & Objectives:

Atopic dermatitis (AD) is the most common chronic inflammatory dermatosis in the general population. Black and Indigenous people experience a disproportionate burden of the disease. The prevalence of AD is almost twice higher in Black children than in White children. In addition, Black children are likely to present with severe disease. Similarly, Canadian Indigenous youth have a high burden of AD and are more likely to present with moderate to severe disease. Recent scientific advancements have improved our understanding of the pathophysiology of AD, including its considerable genetic components. Filaggrin (FLG) loss-of-function mutation is the strongest risk factor for AD. This mutation results in suboptimal skin barrier function, including regulation of skin pH and hydration. Studies have indicated that FLG mutations play a less pathogenic role in individuals of African descent. While FLG mutations are less frequent among these patients, they are more likely to present with AD. This genetic conundrum makes racial and ethnic representation in AD clinical trials a critical consideration. Despite the development of new medications to treat AD, racial and ethnic health disparities have worsened. We explore the representation of Black and Indigenous participants in AD clinical trials over a 10-year period.

Materials & Methods:

We obtained data from the U.S. National Library of Medicine clinical trials database. A search was conducted on May 8, 2023, to identify completed clinical trials relating to AD. We limited our analyses to trials with completion years from 2013 to date. Our search yielded 151 trials with 34,877 participants.

Results:

The trials mostly consisted of phases: 2 (49.7%), 3 (29.8%), and 1 (7.3%); 8.6% of the trials did not explicitly identify a phase. While 49.3% of the trials had several international sites, 29.3% and 7.3% of the trials occurred exclusively in the United States and Japan, respectively. Of the 151 trials identified over the 10-year period, 41 (27.2%) did not report the race of participants. Of the trials that reported the race of participants (n = 28,444), Black and Indigenous participants made up 14.1% and 0.8% of enrollees. Respectively, White and Asian participants made up 58.9% and 23.3% of enrollees. Representation was met if trial participant demographics were equal to or greater than the US patient population. Only 42.0% of the 112 trials that reported race data met the benchmark for adequate representation of Black participants. Black participants were overrepresented in phase 1 trials (22.3% of participants), in which little therapeutic benefit is expected. Similarly, only 25.9% of trials met the benchmark for adequate representation of Indigenous participants.

Conclusion:

Our analyses show Black and Indigenous participants are underrepresented in AD clinical trials. The lack of representation is not limited to clinical trials; it is equally low in academia. The lack of diversity among investigators involved in clinical trials is a contributing factor to the low participation of Black and Indigenous populations in clinical trials. Conducting research with Indigenous populations necessitates cultural humility, competence, and sensitivity to the injustice inflicted by the medical field on Indigenous peoples. Clinical trial acceptance among Indigenous populations may be facilitated by involving Indigenous scholars, leaders, and
communities in the clinical trial process.
Abstract N°: 3810

Impact of feeling of stigmatization on the lives of adult patients with hand dermatitis: Data from the All Skins-All Colors-All Dermatoses: the ALL PROJECT

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Introduction & Objectives

Chronic hand eczema (CHE) is an inflammatory dermatosis that results in a significant psychological burden. People with chronic hand eczema (CHE) experience social embarrassment and shame around the appearance of their hands, resulting in a feeling of stigmatization (FS).

There is little information about the importance and consequences of FS on daily life. The objective of this study was to investigate the prevalence and impact of CHE-associated FS on social, professional and family life and to explore the impact of stigma on treatment adherence.

Material and methods

The ALL PROJECT involves individual’s representative of the adult populations of 20 countries spread over all five continents, which together account for over 50% of the world’s population. In each of the 20 countries surveyed, we conducted a population-based study on representative and extrapolable samples of the general population aged 16 years or more. 50552 individuals was recorded.

Results

Of this 50552, 1736 CHE confirmed by a Doctor was identified, including 843 (48.6%) males and 893 (51.4%) females. A total of 983 (56.6%) CHE respondents reported FS, of which 713 (41.1%) felt ostracized or rejected by others, 680 (39.2%) felt looked at with disgust, 662 (38.1%) reported that people avoided touching them, and 638 (36.8%) reported that people avoided approaching them because of their HS. A total of 753 CHE (43.4%) respondents were considered to have no FS.

The FS population was on average younger than the non-FS population (mean age 35.80 ± 10.92 years vs 41.54 ± 13.87 years; P = 1.624e-21). Signs/symptoms of HS, such as burning sensations [45,40% vs 29,10%, p0,036371] and skin pain (43,80% vs 23.90%, p 0,003525), were all significantly more frequent in patients with reported FS.

There were significant consequences for self-perception, relationships, daily life, sleep, and social and work life in subjects with reported FS. Poor adherence to therapy was associated with feelings of stigma (76.8% vs. 43.4%, P = 9,09E-39)

Discussion

FS affected 56.6% of patients with CHE. Our study established that FS was more frequent in young patients with signs/symptoms such as burning sensations and skin pain. Our study confirms that stigmatization in patients with CHE is associated with consequences in social interactions and dysfunction in interpersonal relationships but also in professional life.
The place of the hands as a functional organ but also as a tool for communication and expression is fundamental.

In our study, FS was associated with poor adherence to therapy, which can lead to a vicious cycle of mutually reinforcing negative conditions. Efforts to reduce FS in patients who live with CHE can include public education campaigns, increased access to healthcare and support services, and challenging stereotypes and prejudices through advocacy and activism. It is important to promote a message of empathy and understanding toward those affected by CHE rather than fear and rejection.
Abstract N°: 3866

**Long-term efficacy and safety of Dupilumab in patients with atopic dermatitis: a single-centre retrospective study.**

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**Introduction & Objectives:** Dupilumab is a monoclonal antibody that inhibits IL4/IL13 interleukin signaling indicated for moderate-to-severe atopic dermatitis (AD) with an important impact on signs and symptoms with good safety, but few long-term efficacy and safety data are available. However, there are few long-term efficacy and safety data.

The aim of this study is to evaluate efficacy and safety of dupilumab for up to three years after treatment initiation.

**Materials & Methods:** We collected data from patients ≥12 years with moderate-to-severe AD who started dupilumab at the Dermatology Clinic of the Turin December 2018 and October 2022 and evaluated them for up to 3 years. MeanEASI score at baseline, EASI75, EASI90, meanNRSpp, meanNRSsd, meanPOEM, meanDLQI were evaluated at baseline (T0), at 16 weeks (T1), at 32 weeks (T2), at one year (T3), at two years (T6), at three years (T9).

**Results:** At baseline out of 418 patients collected 226 were male (53.94%), the mean age was 39.2 years (sd ± 17.43), the mean age of onset of AD was 13.5 years (sd ± 20.6). 226 (53.94%) were males, mean age was 39.2 (sd ± 17.43) years old and mean age of onset of AD was 13.5 (sd ± 20.6) years old.

271 patients of 418 (65.9%) have childhood onset, 149 (37.9%) patients have family history of atopy, 25 patients (8.8%) had manifestation of prurigo escoriata, 96 patients (23.0%) had history of allergic conjunctivitis, 79 patients (19.2%) had recurrent herpetic infections, 8 patients (1.9%) had parasitic infections, and 3 patients (0.73%) had diagnosis of ichthyosis.

All patients performed topical steroid, 46.6% topical immunomodulator, 10.2% phototherapy, 96% systemic steroid, 84% cyclosporine and 9% performed omalizumab.

A progressive decrease in the EASI value is observed: 23.64 at baseline (T0) (ds 10.44), 3.69 (ds 4.95) at T1, 2.31 at T9 (ds 3.18). Similar trends are observed in the analysis of the mean DLQI value: 14.83 (ds 7.16) at baseline (T0), 4.71 (ds 4.96) at T1 and 2.31 (ds 3.18) at three years (T9).

Achievement of EASI75 and EASI90 was also assessed: at T1 75.58% of patients achieved EASI75 and 53.49% EASI90; at T2 80.26% achieved EASI75 and 53.72% EASI90; at T9 92.55% achieved EASI75 and 80.85% EASI90.

As for quality of life, DLQI 0/1 was achieved at T1 in 68.06% of patients (228 of 335 patients) and at T9 in 61.7% (58 out of 94 patients).

Mean NRSpp ≤ 4 was achieved at T1 in 71.3% of patients (236 out of 331 patients) and at T9 in 91.5% (86 out of 94 patients).

The most common adverse event was conjunctivitis occurring in 13% of patients on average at each timepoints analyzed.
**Conclusion:** Strength of this study is definitely the sample size and the results based on continuous treatment with Dupilumab for up to 3 years.

This real-world study shows that the efficacy of dupilumab is maintained and improves over time, with an excellent safety profile and without an increase in adverse effects with long-term treatment, supporting the long-term continuous use of Dupilumab in this chronic and debilitating disease.
Abstract N°: 4045

Differences in atopic dermatitis risk according to urban/rural areas: A systematic review and meta-analysis of observational studies

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Introduction & Objectives:

Atopic dermatitis is the most common chronic inflammatory skin disease affecting children. Some studies have reported a higher risk of atopic dermatitis in urban areas than in rural areas. In this study, we systematically reviewed and carried out a meta-analysis of previous studies to investigate the differences in the development of atopic dermatitis between urban and rural areas.

Materials & Methods:

This systematic review was conducted in accordance with the PRISMA guidelines and Embase and Medline were searched on April 19, 2021. Two authors independently evaluated studies that met the inclusion criteria. The meta-analysis was performed using random- or fixed-effect methods, and funnel plots were used to assess publication bias.

Results:

We identified 2,115 studies, of which 49 were finally included. Combining all included studies, urban residency was associated with an increased risk of atopic dermatitis (odds ratio, 1.55; 95% confidence interval [CI], 1.42-1.70). A significantly increased risk of atopic dermatitis was observed only in children (OR, 1.54; 95% CI, 1.38-1.72) but not in adults (odds ratio, 1.29; 95% CI, 0.99-1.67). Additionally, the risk of atopic dermatitis has been higher in the last decade than in the past (OR, 1.78 vs 1.44), and in developing countries than in developed countries (OR, 1.89 vs 1.35).

Conclusion:

To the best of our knowledge, this is the first meta-analysis to investigate differences in AD prevalence between urban and rural areas. We directly investigated the uncertainty in observational studies by calculating previous data for an association between AD and urban and rural areas. Our study found that people living in urban areas were 55% more likely to develop AD than those living in rural areas were.

One of the strengths of our study is that we included subgroup studies based on important factors, such as age, year of publication, and developed/developing countries. Subgroup analysis by age showed that children had a higher risk of AD than adults did. Subgroup analysis by year showed that there was a tendency to increase the risk of AD in recent years compared to the past. Additionally, developed and developing countries have shown a tendency to increase this risk more recently than in the past.

The results of this study provide evidence of an association between AD and urban/rural living. Our analysis also
found that urban children had a higher risk of developing AD than rural children, but there was no statistically significant difference in adults. Further research is needed to explore the factors associated with AD in children living in urban areas.
Abstract N°: 4054

Initial rather than cumulative ultraviolet irradiation dose determines Narrow-Band ultraviolet phototherapy efficacy

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Introduction & Objectives: The efficacy of narrow-band ultraviolet phototherapy in patients with atopic dermatitis varies greatly and could be influenced by different factors that are not currently fully understood. In this study, we aimed to evaluate the efficacy of whole-body NB-UVB-phototherapy in patients with atopic dermatitis depending on initial and cumulative UV doses.

Materials & Methods: Forty patients, 21 females and 19 males, with moderate-to-severe atopic dermatitis were enrolled in the study. The median age was 27.5 years (range 18–49). Disease severity was evaluated by Eczema Area and Severity Index (EASI). All patients were treated with narrow-band UVB four times weekly for 5 weeks using the light cabin equipped with 311-nm lamps. Efficacy of NB-UVB therapy was evaluated in patients depending on initial and cumulative doses. The initial UV dose ranged from 0.05 to 0.3 J/cm² (mean 0.19±0.08 J/cm²). 24 patients had initial dose ≥0.2 J/cm², 16 patients had initial dose <0.2 J/cm².

Results: EASI value in patients whose treatment had been started with high initial dose ≥0.2 J/cm² significantly reduced from 15.6±8.2 to 3.3±3.6 (p<0.05). In patients with low initial dose <0.2 J/cm² EASI value reduced from 12.5±4.9 at baseline to 5.3±4.4 (p<0.05) after NB-UVB treatment. EASI value decreasing in patients with initial dose 0.2–0.3 J/cm² amounted 75.6% and was much more pronounced than 58.7% improvement of EASI in group with initial dose <0.2 J/cm² (p<0.05). EASI75 was reached in 75.0% of patients with initial dose 0.2 or more J/cm² and in 37.5% of patients with initial dose 0.2 or less J/cm² (p=0.041).

Mean cumulative dose was 10.9±2.6 J/cm² (from 5.8 to 18.4 J/cm²). Patients were divided into two groups: patients with cumulative dose from 5.8 to 10.5 J/cm² (mean – 9.0±1.5 J/cm²) and patients with cumulative dose from 10.6 to 18.4 J/cm² (mean 12.8±1.9 J/cm²). In patients with the higher cumulative dose 12.8±1.94 J/cm² EASI value decreasing was 68.6% and in patients with cumulative dose 9.0±1.54 J/cm² EASI improvement was 69.1% (p>0.05). 55% of patients with cumulative dose 12.8±1.92 J/cm² and 65% of patients with cumulative dose 9.02±1.49 J/cm² reached EASI75 (p>0.05).

Conclusion: Our investigation shows that NB-UVB has definitely higher efficacy in the case it is started with an initial dose 0.2–0.3 J/cm² in comparison with an initial dose <0.2 J/cm². Cumulative dose has no impact on the efficacy of narrow-band ultraviolet phototherapy in patients with atopic dermatitis.
Abstract N°: 4075

Dupilumab shifts the gut microbiome to a healthy state in patients with atopic dermatitis

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Dupilumab shifts the gut microbiome to a healthy state in patients with atopic dermatitis

Introduction & Objectives:

Gut microbiome is likely to involve in the development of atopic dermatitis (AD). As the second genome of human body, growing evidence suggests that it could possibly further regulate the host response to treatments. However, little is known about the association between therapies and gut microbiome in AD patients. Therefore, this study aims to identify the differences in intestinal microbiome between patients with AD and healthy controls (HC) among Asian ethnicity, and the changes of gut microbiome and underlying function after dupilumab treatment.

Materials & Methods:

48 HC and 44 AD patients demographically matched were enrolled in this study (baseline). 27 out of 44 AD patients successfully received a course of 16 weeks of dupilumab treatment (endpoint). Fecal samples of the participants at baseline and endpoint were subjected to 16s rRNA gene sequencing. Bioinformatics methods were used to analyze the microbial diversity, dominant bacterial genera, bacterial network between groups. Combining PICRUSt2 with KEGG database, differential metabolic pathways of AD patients before and after dupilumab were predicted, and further validated via targeted metabolome sequencing.

Results:

We confirmed the previously shown lower alpha-diversity and changed beta-diversity of the gut microbiome and identified increased Firmicutes/Bacteroidetes ratio among the Asian AD population compared to HC. After 16 weeks of Dupilumab treatment, improved alpha-diversity, reversed beta-diversity and increased colonization of bacterial genera negatively correlated with AD severity indices, including Bifidobacterium, Ruminococcus gnavus, Coprococcus, were observed, largely independant from the degree of clinical improvement. Bacterial co-occurrence analysis indicated a more robust bacterial network configuration and ecological restoration after Dupilumab treatment in contrast to before treatment. Gene prediction showed significantly increased expression of genes involved in indole pathway of tryptophan metabolism after Dupilumab treatment, which was further validated by quantitative UHPLC-MS/MS analysis.

Conclusion:

The microbial community with respects to alpha, beta diversities, and dominant bacterial genus differed significantly between AD patients and HC. Dupilumab treatment tends to shift this gut microbial dysbiosis in AD patients to a healthy state, along with improved intestinal tryptophan metabolism, suggesting the gut flora might mediate some of the synergistic therapeutic effects on the host.
Study design

Healthy control (n=8)  AD (n=44)  Dupilumab (n=27)

Dietary sampling
DNA extraction
16S rDNA gene sequencing

Dupilumab effects

Dissociation

Dupilumab therapy shifts the microbiome towards a healthy state

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<th>Dupilumab</th>
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Pediatric Patients with Atopic Dermatitis Have a High Burden of Co-existing Type 2 Inflammatory Diseases:  
German Results from a Global Survey

Stephan Weidinger1, Andreas Pinter2, Alexander Zink3, 4, Christina Schnopp3, Tarek Mnif5, Jason Wang6, Kerry Noonan7, Mario Hubo7, Mike Bastian8

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Introduction & Objectives: To report the prevalence of co-existing type 2 inflammatory diseases in pediatric patients with atopic dermatitis (AD) in Germany.

Materials & Methods: This cross-sectional, web-based survey of pediatric patients aged 6 months to 17 years with diagnosed AD (International Study of Asthma and Allergies in Childhood [ISAAC] criteria [itchy rash for ≥ 6 months plus itchy rash in the past 12 months plus flexural dermatitis] plus self-report of a physician diagnosis of eczema) was conducted in 18 countries. We report results from Germany, where the survey was conducted during 06 November 2018 to 13 January 2019. Caregivers (of children aged < 12 years) or adolescents (aged ≥ 12 years) were asked whether their child/they had ever suffered from asthma or hay fever (other type 2 inflammatory diseases). They were also asked whether they had been told by a healthcare provider (HCP) that their child/they had ever had various comorbidities and whether they were currently receiving treatment for these. Results are stratified by patient age (< 6, 6 to < 12, and ≥ 12 years).

Results: Among 223 patients with AD in Germany, 59 were aged < 6 years (47% male), 76 were aged 6 to < 12 years (50% male), and 88 were aged ≥ 12 years (52% male). Most patients with AD had a family history of eczema, asthma, or hay fever: 76%, 89%, and 70% across age groups. The majority of patients with AD had ≥ 1 co-existing type 2 inflammatory disease or attention deficit hyperactivity disorder: 75%, 93%, and 86% across age groups. Ever suffering from hay fever was reported for/by 34%, 73%, and 46%, respectively (Figure 1). The most common HCP-diagnosed co-existing type 2 inflammatory disease was seasonal allergies (15%, 42%, and 45% across age groups; Figure 1). Most patients with HCP-diagnosed co-existing type 2 inflammatory diseases were receiving treatment for these at the time of the survey, although this varied by condition and by age (Figure 2).

Conclusion: Most of the German pediatric patients with AD included in this survey had at least one comorbidity (mainly type 2 inflammatory disease), contributing to the disease burden in these patients. Treatments that could effectively treat a range of type 2 inflammatory diseases could be highly beneficial for pediatric patients with AD.

Figure 1. Co-existing type 2 inflammatory diseases among pediatric patients with AD.
*Parent/adolescent report of ever suffering from hay fever or asthma.

†Parent/adolescent report of being told by an HCP that their child/they had the atopic comorbidity.

**Figure 2. Treatment for HCP-diagnosed co-existing type 2 inflammatory diseases among patients with AD.**
Abstract N°: 4103

Demographic, clinical characteristics and treatment patterns of adult patients initiating dupilumab: Real-world data from a healthcare provider in Israel

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Introduction & Objectives: Patients with atopic dermatitis (AD), especially with moderate-to-severe disease, often present treatment challenges. Dupilumab has been available in Israel as a third-line treatment of moderate-to-severe AD since 2018, and from 2019 as a second-line treatment after systemic immunosuppressants. The objective of this analysis was to describe the characteristics of adult patients with AD initiating dupilumab and their treatment patterns.

Materials & Methods: A retrospective cohort study was performed using the Maccabi Healthcare Services database in Israel. Patients diagnosed with AD with at least 2 dispensed dupilumab prescriptions in 2018–2019 (index date = first prescription) and continuous enrolment from 12-months pre- through 12-months post-index, and ≥ 18 years at index, were included. Follow-up data were collected through 31 December 2020. Data were obtained on demographic and clinical characteristics, including diagnosed type 2 comorbidities and AD-related treatments dispensed pre- and post-index (topical corticosteroids [TCS]; other topicals [OT] including topical calcineurin inhibitors and crisaborole; systemic corticosteroids [SCS]; other systemic immunosuppressants [SI; cyclosporin A, azathioprine, mycophenolate mofetil, methotrexate]; phototherapy [PT]). Persistence was defined as the cumulative percent of patients who did not discontinue treatment at a given time point.

Results: The study included 135 adult patients (39.3% female), with a median age of 43.3 (interquartile range: 27.9–54.3) years. The median time to dupilumab since AD diagnosis was 14.9 years. Most (71.9%) had a history of asthma, allergic rhinitis or food allergy. Persistence on dupilumab remained high at 6 months (95.6%; 95% confidence interval [CI]: 92.1–99.1) and 1 year (91.9%, 95% CI: 87.4–96.6). Use of other AD treatments was lower in the 12-months post- vs pre-index for TCS (64.4% vs 88.1%), OT (22.2% vs 29.6%), SCS (16.3% vs 37.8%), SI (8.1% vs 60.7%), and PT (4.4% vs 20.0%).

Conclusion: As expected, the majority of patients prescribed dupilumab had longstanding disease with atopic comorbidities. The proportion of patients using different concomitant treatments decreased substantially in the 12 months after dupilumab initiation, although a significant proportion of patients continued to use topicals. However, the study design did not compare the quantity of topical medication use pre- to post-dupilumab. Once initiated, dupilumab persistence remained high after 1 year. Further research may provide insight into longer-term treatment patterns and predictors for treatment persistence in AD patients treated with dupilumab in Israel.
Nemolizumab modulates prurigo nodularis-associated skin pain and markedly improves patient reported outcomes in patients with moderate-to-severe prurigo nodularis in a phase 3 study (OLYMPIA 2)

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Introduction & Objectives: Prurigo nodularis (PN) is a chronic, debilitating and severely pruritic neuroimmune skin disease. In addition to chronic itch, the majority of patients experience skin pain, burning or stinging sensations. Nemolizumab significantly improved itch intensity and skin lesions with a positive safety and tolerability profile in a phase 3, multicentre, double-blind study (OLYMPIA 2; NCT04501679) in patients with moderate-to-severe PN. Here we report additional outcomes such as PN-associated pain, Patient Global Assessment of Disease (PGAD) and Patient Global Assessment of Treatment (PGAT).

Materials & Methods: Adults (≥18 years old) with PN presenting ≥20 nodules, Investigator’s Global Assessment score ≥3 (range: 0–4) and weekly average Peak Pruritus Numerical Rating Scale (PPNRS) score ≥7.0 (range: 0–10) were randomized (2:1) to receive nemolizumab monotherapy (N=183) or matching placebo (N=91). The primary and key secondary endpoints were reported elsewhere. Other secondary endpoints included change in PN-associated pain frequency (6-point scale, range: ‘0’ [never] to ‘5’ [everyday]) and intensity (11-point NRS, range: ‘0’ [no pain] to ‘10’ [the worst unbearable pain]) from baseline through Week (W) 16; proportion of patients reporting low disease activity in PGAD (5-point scale from ‘0=clear’ to ‘4=severe’) and ‘good’, ‘very good’ or ‘excellent’ response to study treatment in PGAT (5-point Likert scale where ‘0=poor’ and ‘4=excellent’) at W16.

Results: Primary and key secondary endpoints were met (P<0.0001; reported elsewhere). At baseline, 63.4% of nemolizumab- vs 70.3% of placebo-treated patients reported having PN-associated pain every day; the mean (standard deviation [SD]) PN-associated pain intensity was 7.7 (2.4) vs 7.8 (2.3) in the nemolizumab vs placebo group; 69.4% of nemolizumab- vs 72.5% of placebo-treated patients reported severe disease based on PGAD. At W16, a substantially lower proportion of patients having PN-associated pain everyday (18.6% vs 53.8%; with proportion difference [95% confidence interval [CI]]: -35.3 [-47.0, -23.6]), and a higher reduction in PN-associated pain intensity from baseline (mean [standard error], -4.5 [0.3] vs -1.6 [0.4]; with mean difference [95% CI]: -2.9 [-3.7, -2.1]) were observed in Nemolizumab vs placebo; a higher proportion of patients receiving nemolizumab vs placebo reported ‘clear’, ‘almost clear’ or ‘mild’ disease status based on PGAD (64.2% vs 19.1%; P<0.0001) and some improvements in key secondary endpoints (P<0.05). Additionally, a higher proportion of patients reported that their PN-associated pain improved or was no longer a problem in Nemolizumab vs placebo (P<0.0001).
‘good’, ‘very good’ or ‘excellent’ status to study treatment based on PGAT (72.2% vs 25.8%; \(P<0.0001\)). Adverse events occurring in \(\geq 5\%\) of patients (nemolizumab vs placebo) were worsening of PN (3.8% vs 11.0%), headache (6.6% vs 4.4%) and atopic dermatitis (5.5% vs 0%).

**Conclusion:** Nemolizumab monotherapy resulted in substantial improvement in PN-associated pain in patients with moderate-to-severe disease at baseline, and patients reported lower disease severity and better response to study treatment with nemolizumab vs placebo.
Introduction & Objectives:
Atopic dermatitis (AD) is a multifactorial, inflammatory, skin disease with a chronic relapsing course. Dysregulation of the immune system is a major hallmark in the development of this disease, in which immune response cells (such as T helper cells [Th] 2 and Th22) and consequently the cytokines released by them (such as interleukin [IL]-4, IL-13 and IL-22) play a crucial role in AD pathophysiology. Nevertheless, the specific contribution of each cytokine on the epidermal physical and immune barrier has been poorly investigated in the literature.

Thus, in view of this consideration, the aim of this study was to investigate the influence of Th2 proinflammatory cytokines IL-4 and IL-13, IL-22, and IL-23, on (i) the epidermal immune barrier, and (ii) the epidermal physical barrier, in a 3D model of normal human skin.

Materials & Methods:
A 3D model of normal human skin biopsies (n = 7) at the air-liquid interface for 24 and 48 h was used to assess the effect of proinflammatory cytokines IL-4, IL-13, IL-22, and IL-23 on epidermal barrier. The expression of (i) claudin-1, and zonula occludens (ZO)-1 for the physical barrier and (ii) Toll-like receptor (TLR)2, 4, 7, 9, human beta-defensin 2 (hBD-2) for the immune barrier, was investigated by immunofluorescence qualitative/quantitative analysis. The measurement of intercellular distances (as spongiosis index) was performed by transmission electron microscopy (TEM).

Results:
This study revealed that the Th2 cytokine profile strongly affected the TLR-mediated innate immune barrier with a greater extent than IL-22. The expression of hBD2 was early inhibited by IL-4, whereas IL-22 and IL-23 influenced
its distribution. On the other hand, Th2 cytokines induced spongiosis and failed to impair the epidermal physical barrier (tight junction composition), whereas IL-22 reduced, and IL-23 induced claudin-1 expression.

**Conclusion:**

In conclusion, this experimental 3D model has proved to be useful in understanding the pathophysiology of AD through the early evaluation of the alteration of epidermal proteins of the physical and immune barrier. Thus, this 3D model of normal human skin, might be able to pave the way for new concepts and improvements in targeted therapy for each patient, underlining, once again, the importance of the epidermal barrier in the pathogenesis of AD.
Abstract N°: 4253

Lebrikizumab Improves POEM with and without TCS in Patients With Moderate-to-Severe Atopic Dermatitis

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Introduction & Objectives: Lebrikizumab (LEB) is a novel monoclonal antibody that binds with high affinity and a slow off-rate to interleukin (IL)-13, thereby blocking the downstream effects of IL-13 with high potency. LEB has been shown to provide clinician-assessed improvement for patients with moderate-to-severe atopic dermatitis (AD) in the Phase 3 trials ADvocate1, ADvocate2 (ADv1&2) and ADhere. Here, we report the impact of LEB with and without topical corticosteroid (TCS) on patient-reported symptoms of moderate-to-severe AD as assessed by the Patient-Oriented Eczema Measure (POEM) tool.

Materials & Methods: ADv1&2 compared LEB 250 mg every 2 weeks (LEBQ2W) versus placebo (PBO) for 16 weeks. At Week 16, LEB responders (achieved IGA (0,1) or at least EASI 75 at Week 16, without use of topical rescue) were rerandomized to LEBQ2W, LEB 250 mg every four weeks (LEBQ4W) or PBO (LEB withdrawal) for 36 more weeks, with optional TCS. ADhere compared combination therapy LEB and TCS every 2 weeks (LEBQ2W+TCS) versus PBO and TCS (PBO+TCS) for 16 weeks. AD symptoms were collected using POEM, a patient reported questionnaire that assesses symptoms of AD over the previous week, from baseline to Week 16 and Week 52 in ADv1&2 results for LEB responders at Week 16, mean absolute score at Week 16 was 8.6 (n=101) in LEBQ2W, 7.7 (n=104) in LEBQ4W and 8.8 (n=50) LEB withdrawal. At Week 52, absolute POEM total score was 5.8 (n=65) in LEBQ2W, 7.0 (n=75) in LEBQ4W, 8.8 (n=27) LEB withdrawal; LEM change from baseline was -13.5 in LEBQ2W, 13.1 in LEBQ4W and -10.1 LEB withdrawal; and 59.1% of patients in LEBQ2W, 58.3% in LEBQ4W and 36.8% LEB withdrawal reported ≥4 point-improvement in POEM score from baseline.
In ADhere (+ TCS), baseline mean absolute POEM score was 19.5 (n=145) in LEBQ2W+TCS vs. 19.5 (n=66) PBO+TCS. At Week 16 absolute POEM total score was 9.5 in LEBQ2W+TCS vs. 13.3 PBO+TCS; LSM change from baseline was -10.23 in LEBQ2W+TCS vs. -6.24 PBO+TCS; and 61.7% of patients in LEBQ2W+TCS vs. 41.3% PBO+TCS reported ≥4 point-improvement in POEM score from baseline. In all three studies, nominal p-values were p<0.001 at Week 16, except for ≥4 point-improvement in POEM score in ADhere (p=0.008).

**Conclusion:** LEB treatment with and without TCS showed clinically meaningful improvements of POEM measures in patients with moderate-to-severe AD at Week 16 and improvements were maintained after an additional 36 weeks of LEB treatment and LEB withdrawal.

**Reference:**

Abstract N°: 4262

Chronic hand eczema clinical features and severity: a French study

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Introduction & Objectives:

Data on chronic hand eczema and severity of hand eczema in the general population is scarce.

The aim of this study was to investigate the clinical characteristics and severity of CHE in a sample from the French population. The questionnaire collected clinical and sociodemographic characteristics.

Materials & Methods

This was an observational, cross-sectional questionnaire-based study. Survey participants were recruited between October 2022 and January 2023, through the French eczema patient association. Patients were asked to self-evaluate the clinical severity of their CHE. Clinical severity was also assessed by the patient using the Patient-Oriented Eczema Measure (POEM).

Results

A total of 409 adult participants with a mean age of 36.5 (SD 11.5) years responded to the questionnaire. The sex distribution was as follows: 79.7% (n=326) female and 20.3% male (n=83). According to the POEM scores of the respondents, 111 (27.1%) presented mild CHE, 171 (41.8%) moderate CHE, and 127 (31.1%) severe CHE (The proportion of males and females were similar within each POEM severity class. Age distribution, economic activity, occupation, geographic location, and family/social situation did not differ across the three CHE severity classes as defined by the POEM score (p=0.4659, p=0.4853 p=0.7689, p=0.5187 and p=0.4195). The mean age at onset of first symptoms was 18.1 (SD 13.3) years and did not differ across the three CHE severity classes (p=0.6588). Most participants (303/409, 74.1%) reported having CHE on both hands. The most commonly reported location of CHE was fingers (75.6%). Dry hands were the most commonly reported clinical manifestation (73.6%). Unpleasant sensations, stinging and pulling, pruritus and burning sensations were reported by 94.6%, 93.6%, 93.4%, 84.8% and 74.1% of participants respectively.

Conclusions

In this French cross-sectional questionnaire-based study performed in partnership with the eczema patient association (Association Française de l’Eczema) we explored the clinical features and symptoms of patients with CHE. Our study gives a broad assessment of CHE signs, symptoms and severity in a large sample from the French population. Describing this population is the first step towards providing a comprehensive account of CHE in France. Our future research work will focus on the impact and burden of CHE on patients’ health-related quality of life, as well as identifying the current care pathways patients go through to uncover potential unmet medical needs.
Interpreting the Relationships Among Abrocitinib Treatment, Itch, Skin Pain, and Health-Related Quality of Life: A Mediation Modeling Analysis of JADE MONO-1 and JADE MONO-2

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Introduction & Objectives:

Itch and skin pain are burdensome symptoms of atopic dermatitis (AD) that have significant adverse impacts on patients’ health-related quality of life (HRQoL). Abrocitinib, an oral, once-daily, Janus kinase 1−selective inhibitor, rapidly improved itch, skin pain, dermatology-specific QoL, and general HRQoL in patients with moderate-to-severe AD in 2 phase 3 trials (JADE MONO-1 [NCT03349060]; JADE MONO-2 [NCT03575871]). A previous mediation modeling analysis suggested that improvements in dermatology-specific QoL with abrocitinib are mostly mediated indirectly via reduction in skin pain and less so by itch relief (Silverberg JI et al. Br J Dermatol. 2023;188 [suppl 3]: ljac140.043). This analysis aims to characterize the relationships amongst reductions in itch and skin pain alongside improvements in general HRQoL with abrocitinib treatment in patients with AD.

Materials & Methods:

Data were pooled from adults with moderate-to-severe AD who received abrocitinib monotherapy (200 mg or 100 mg) or placebo over 12 weeks in JADE MONO-1 and JADE MONO-2. Mediation modeling was applied post hoc in a supplemental analysis to assess the relationships among abrocitinib treatment (predictor), general HRQoL (outcome variable), and itch and skin pain (mediator variables). Itch and skin pain were assessed using the itch numerical rating scale (NRS) item (How itchy was your skin over the past 24 hours?) and the skin pain NRS item (How painful was your skin over the past 24 hours?) of the Pruritus and Symptoms Assessment for Atopic Dermatitis instrument (©2016 Pfizer Inc., all rights reserved), respectively; data were average values of daily observations during week 12. HRQoL was assessed using the Short Form-36 Health Survey Acute version 2 (SF-36v2®) at week 12, measuring 8 health domains (bodily pain, general health, mental health, physical functioning, role emotional, role physical, social functioning, and vitality). Treatment was represented by a binary variable (abrocitinib vs placebo). Effects with P<0.05 were considered statistically significant.

Results:

The initial mediation analysis indicated that none of the direct paths from treatment to SF-36 domains were statistically significant (Figure 1A). Moreover, the initial model implied that the paths from itch to all SF-36 domains, except the general health domain, were also not significant (Figure 1A). The initial model was therefore respecified to include only significant and logical paths. In this respecified model, the effect of abrocitinib on the bodily pain, mental health, physical functioning, role emotional, role physical, social functioning, and vitality domains of the SF-36 was fully mediated via skin pain (Figure 1B). The indirect effect of abrocitinib on the SF-36 general health domain was estimated to be 65% (P<0.0001) as mediated via skin pain and the remaining 35%
Conclusion:

Most of the effect of abrocitinib on generic health status (as assessed by SF-36) is mediated indirectly via reductions in skin pain, while reduction of itch contributes to improvements in the general health domain of the SF-36. These findings are consistent with the prior mediation modeling analysis evaluating the effect of abrocitinib treatment via itch and skin pain on dermatology-specific HRQoL, underscoring the importance of skin pain as a fundamental symptom in AD.
IL-9 sensitizes human pathogenic Th2 cells to pro-inflammatory IL-18 signals in atopic dermatitis

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Introduction & Objectives: Pathogenic CRTh2+ T helper 2 (pTh2) cells are crucial contributors to the pathogenesis of atopic dermatitis (AD) by secreting high levels of interleukin (IL-)13 and IL-22. Yet, the upstream regulators of pTh2 cells in AD skin remain incompletely understood. IL-18 is one such putative regulator and is linked to AD pathogenesis by multiple lines of evidence raising intriguing questions regarding its role in the activation of pTh2 cells in AD skin. Here, we sought to decipher the role of IL-18 in human Th2 responses in AD.

Materials & Methods: We analysed pTh2 cells from AD patients, as well as used \textit{ex vivo} skin explants of human healthy and lesional AD skin.

Results: We first investigated the signals that induce interleukin 18 receptor (IL-18R) expression on Th2 cells. Of all the cytokines for which pTh2 cells express the receptor, only IL-9 was able to induce high levels of IL-18R. Consistently, IL-9R+/IL-18R+ pTh2 cells were strongly increased in the peripheral blood of AD patients. Functionally, stimulation of circulating pTh2 cells with IL-18 induced secretion of IL-13 and IL-22, an effect that was significantly enhanced by co-stimulation with IL-9. Mechanistically, IL-18 induces rapid and strong activation of both NF-κB and AP-1 signaling in pTh2 cells. In human skin explants from lesional AD skin, neutralization of IL-18 rapidly downregulated both IL-13 and IL-22 secretion from pTh2 cells. Finally, IL-18 protein levels correlated positively with \textit{IL13} expression and disease severity in lesional AD skin.

Conclusion: Collectively, our data reveal a previously underappreciated role of IL-9 and IL-18 as positive regulators of Th2 cell responses in human AD. These findings may guide future therapeutic approaches aiming at inhibiting aberrant activation of pTh2 cells in human skin.
Abstract N°: 4304

Efficacy, Safety, and Tolerability of GSK1070806, an Anti-IL-18 Monoclonal Antibody, in Patients with Moderate to Severe Atopic Dermatitis: A Phase 1b, Randomised, Double-Blind, Parallel Group, Placebo Controlled Study

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Introduction & Objectives:
Atopic dermatitis (AD) is a chronic, relapsing, inflammatory skin disease characterised by eczematous lesions and intense pruritus, and is associated with skin barrier dysfunction and immune dysregulation. AD heterogeneity is likely a result of the varying contributions from both T-helper cell (TH)2/TH22-skewing and TH1/TH17.

Interleukin-18 (IL-18), a pleiotropic cytokine, may play a role in the pathophysiology of AD. This study compared the clinical effect and patient reported outcomes (PROs) of a single IV infusion of GSK1070806, a novel, first-in-class, highly potent anti-IL-18 monoclonal IgG1 antibody, versus placebo in patients with AD.

Materials & Methods:
This was a multicentre, randomised, double-blind, parallel-group study to investigate the efficacy, safety, and tolerability of GSK1070806 in participants with moderate-to-severe AD.

Eligible patients were adults (≥18 years) with a confirmed diagnosis (≥6 months) of moderate-to-severe AD (Eczema Area and Severity Index [EASI] ≥16; Investigator’s Global Assessment [IGA] score ≥3), for whom topical therapies were ineffective or not recommended. Two groups were recruited: patients naïve to biologic treatment and Janus kinase (JAK) inhibitors (BN group), and patients who were inadequate responders (after ≥16 weeks treatment), or intolerant, to dupilumab (Dupi-IR group). Participants were randomised 2:1 (BN group) or 5:1 (Dupi-IR group) to receive a single, one-hour IV infusion of 2mg/kg GSK1070806 or placebo.

The primary endpoint was the percent change from baseline in the EASI score in the BN group at Week 12. PRO measures included worst itch (Peak Pruritis Numerical Rating Scale [PP-NRS]) and quality of life (QoL; Dermatology Life Quality Index [DLQI]). Endpoints were assessed at Week 12 using a Bayesian repeated measures model. Safety assessments included anti-drug antibodies.

Results:
Overall, 34 participants were randomised: 30 in the BN group (GSK1070806 n=20, placebo n=10) and 4 in the Dupi-IR group (GSK1070806 n=3, placebo n=1). Demographics were balanced across subgroups and treatment arms (mean age 44.8 years, 53% female). At baseline, 22 participants (65%) had moderate disease and 12 (35%) had severe disease as assessed using the EASI.

In the BN group, the percent reduction in EASI score was greater in participants treated with GSK1070806 than in those administered placebo (posterior median of difference -33.2% [95% credible interval 51.0, −14.8]) (Table). Participants who received GSK1070806 had clinically meaningful improvements in itch (PP-NRS) and QoL (DLQI) until at least Week 12 compared with those who received placebo (posterior median of difference [95% CrI]: PP-NRS -4.10 [-5.63, -2.55]; DLQI -6.13 [-11.41, −0.90]) (Table). Outcomes in the Dupi-IR group are not shown due to
Across the combined groups, 10 participants (43%) receiving GSK1070806 and 6 (55%) receiving placebo experienced \( \geq 1 \) adverse event; most were mild in intensity, none were serious, and none resulted in withdrawal from the study. There was no safety signal of concern. No anti-drug antibodies were observed.

Conclusion:

A single 2mg/kg IV infusion of GSK1070806 demonstrated a positive treatment effect on the EASI score and PRO measures of itch and QoL, which was sustained for at least 12 weeks. There were no safety concerns. GSK1070806 may be a promising future treatment option for patients with AD for whom topical therapies are not effective or appropriate.

Table, Primary and exploratory PRO endpoints in the BN group

<table>
<thead>
<tr>
<th>Week 12 outcome</th>
<th>GSK1070806 2mg/kg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCFB in EASI (primary endpoint)</td>
<td>n=19</td>
<td>n=9</td>
</tr>
<tr>
<td>Posterior median (95% CI)</td>
<td>-86.1% (-78.7, -53.5)</td>
<td>-32.8% (-46.6, -20.3)</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>(-33.2% (-51.0, -14.8))</td>
<td></td>
</tr>
<tr>
<td>CFB in PP-NRS score (itch)</td>
<td>n=12</td>
<td>n=7</td>
</tr>
<tr>
<td>Posterior median (95% CI)</td>
<td>-4.61 (-5.58, -3.65)</td>
<td>-0.52 (-1.73, 0.67)</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>(-4.10 (-5.63, -2.55))</td>
<td></td>
</tr>
<tr>
<td>CFB in DLQI score (QoL)</td>
<td>n=8</td>
<td>n=4</td>
</tr>
<tr>
<td>Posterior median (95% CI)</td>
<td>-6.06 (-8.86, -3.29)</td>
<td>0.05 (-4.08, 4.22)</td>
</tr>
<tr>
<td>Difference (95% CI)</td>
<td>(-6.13 (-11.41, -0.90))</td>
<td></td>
</tr>
</tbody>
</table>

CFB, change from baseline; CI, credible interval; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; PCFB, percent change from baseline; PP-NRS, Peak Pruritis Numerical Rating Scale; PRO, patient reported outcome; QoL, quality of life.
Abstract N°: 4317

High-threshold responses for skin clearance and itch are associated with additional quality of life benefits in patients with moderate-to-severe atopic dermatitis treated with abrocitinib or dupilumab: A post hoc analysis of the head-to-head phase 3 JADE DARE study

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Introduction & Objectives:

Abrocitinib is an oral, once-daily, Janus kinase 1-selective inhibitor, approved for the treatment of patients with moderate-to-severe atopic dermatitis (AD). In JADE DARE trial (NCT04345367), a 26-week head-to-head study of abrocitinib 200 mg vs dupilumab, the high-threshold response in skin clearance (EASI-90) was achieved by 55% of participants treated with abrocitinib and 48% of those treated with dupilumab (Reich K et al. Lancet. 2022;400:273-282). The goal of this post hoc analysis of JADE DARE was to assess whether the attainment of higher-threshold efficacy responses was associated with greater quality of life (QoL) benefits compared to conventional thresholds, and whether this additional QoL benefit differed between abrocitinib and dupilumab.

Materials & Methods:

JADE DARE was a randomized (1:1), double-blind, double-dummy, active-control, phase 3 trial of adult patients with moderate-to-severe AD who received oral abrocitinib 200 mg once daily (QD) or subcutaneous dupilumab 300 mg every 2 weeks (Q2W) for 26 weeks, on the background of topical therapy. We analyzed commonly used efficacy responses for skin clearance (<50%, 50%-74%, and 75%-89% improvement from baseline in Eczema Area and Severity Index [EASI <50, EASI 50-74, and EASI 75-89]) and itch (score <4 or ≥4-point improvement from baseline in Peak Pruritus Numerical Rating Scale [PP-NRS <4 or PP-NRS4]; PP-NRS used with permission from Regeneron Pharmaceuticals, Inc., and Sanofi) as well as higher threshold responses (EASI 90-99, EASI-100, and PP-NRS score of 0 or 1 [PP-NRS 0/1]). Achieving common and high-efficacy responses at weeks 12, 16, and 26 was analyzed in the context of absence or presence of skin-related impact on patient QoL, as assessed via the Dermatology Life Quality Index (DLQI; score 0-1, absence of impact; score 2-30, presence of impact).

Results:

We analyzed data of all 727 individuals enrolled in JADE DARE (abrocitinib, n=362; dupilumab, n=365). At week 26, DLQI 0/1 was achieved by 7 (18%) and 19 (43%) of EASI 50-74 responders and 16 (24%) and 26 (28%) of EASI 75-89 responders to abrocitinib and dupilumab, respectively. In addition, DLQI 0/1 was achieved by 52 (45%) and 48 (37%) of EASI 90-99 responders and by 65 (79%) and 24 (48%) of EASI-100 responders, respectively (Figure 1A). For the most stringent EASI categories (EASI 90-99 and EASI-100), and at all 3 visits, this effect was more pronounced with abrocitinib than with dupilumab. A similar pattern was observed with itch responses (Figure 1B).
Conclusion:

This post hoc analysis suggests that attainment of high-threshold responses in skin clearance or itch severity (eg, skin lesion clearance or absence of itch) over a 26-week treatment period with systemic therapies is associated with notable improvements in quality of life for patients with moderate-to-severe AD. In addition, this effect appears to be more pronounced with abrocitinib than with dupilumab.
Abstract N°: 4392

Efficacy and Safety of Upadacitinib Through 140 Weeks in Adolescents and Adults with Moderate-to-Severe Atopic Dermatitis: Phase 3 Randomized Clinical Trial Results

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Introduction & Objectives: Upadacitinib (UPA) is an oral Janus kinase 1 (JAK1) inhibitor approved in multiple countries for the treatment of adolescents and adults with moderate-to-severe atopic dermatitis (AD). Here, we present the efficacy and safety of UPA administered over 140 weeks in an ongoing randomized, double-blinded, multicenter phase 3 study (Measure Up 1, NCT03569293).

Materials & Methods: Patients (12–75 years) with moderate-to-severe AD were randomized 1:1:1 to receive UPA 15 mg (UPA15), UPA 30 mg (UPA30), or placebo (PBO) once daily at baseline. At week 16, PBO-treated patients were re-randomized 1:1 to receive UPA15 (PBO/UPA15) or UPA30 (PBO/UPA30) once daily. Co-primary endpoints were the proportion of patients achieving ≥75% reduction in EASI (EASI 75) from baseline and vIGA-AD of clear (0) or almost clear (1) with ≥2 grades of reduction from baseline (vIGA-AD 0/1) at week 16. A meaningful improvement in itch, defined as a ≥4-point reduction in Worst Pruritus Numeric Rating Scale (ΔWP-NRS≥4), was assessed among patients with baseline WP-NRS≥4. All efficacy endpoints were summarized using the Observed Cases (OC) approach, and no missing data imputation was applied. Safety was assessed by monitoring of serious adverse events (SAEs), treatment-emergent adverse events (TEAEs), and treatment-emergent adverse events of special interest (AESIs), which were analysed as exposure-adjusted rates per 100 patient-years (PY).

Results: Efficacy results were sustained up to week 140 since week 16. Proportions of patients in the UPA15 (205), UPA30 (206), PBO/UPA15 (91), and PBO/UPA30 (94) groups achieving EASI 75 at week 140 were 88.8% (182), 90.3% (186), 83.5% (76), and 89.4% (84), respectively, and for vIGA-AD 0/1 was 63.4% (130), 65.5% (135), 60.4% (55), and 75.5% (71), respectively. Proportions of patients achieving an improvement (reduction) in WP-NRS≥4 from baseline at week 140 were 68.0% (136), 70.5% (146), 71.3% (62), and 81.3% (74) respectively. Overall, the rates of AESIs were similar across treatment groups (Table 1), which aligned with prior reports at earlier time points. Both UPA15 and UPA30 were well-tolerated in all patients, and no new safety signals were observed compared to the known safety profile of UPA. Data from two additional pivotal studies will be available at the time.
Conclusion: In this interim analysis, sustained skin clearance and itch and a consistent safety profile were observed with UPA 15 mg and UPA 30 mg across 140 weeks in adolescent and adult patients with moderate-to-severe AD.

Table 1. Treatment-Emergent Adverse Events (TEAEs) During Administration of Upadacitinib Through Week 140 for Patients Receiving UPA 15 mg or UPA 30 mg in Measure Up 1.

<table>
<thead>
<tr>
<th>Events [events/100 PY]</th>
<th>UPA15 (N=457)</th>
<th>UPA30 (N=427)</th>
<th>Total (N=884)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AEs in [%]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any AEs</td>
<td>2522 (203.7)</td>
<td>3187 (251.6)</td>
<td>5719 (278.0)</td>
</tr>
<tr>
<td>Severe AEs</td>
<td>137 (11.1)</td>
<td>205 (16.1)</td>
<td>342 (13.0)</td>
</tr>
<tr>
<td>Serious AEs</td>
<td>67 (5.4)</td>
<td>101 (7.5)</td>
<td>168 (6.7)</td>
</tr>
<tr>
<td>AEs leading to discontinuation of study drug</td>
<td>40 (3.2)</td>
<td>56 (4.6)</td>
<td>96 (3.9)</td>
</tr>
<tr>
<td>Deaths</td>
<td>0</td>
<td>2 (0.2)</td>
<td>2 (&lt;0.1)</td>
</tr>
<tr>
<td>AEs by</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious infections</td>
<td>24 (1.9)</td>
<td>43 (3.4)</td>
<td>67 (2.7)</td>
</tr>
<tr>
<td>Opportunistic infections excluding tuberculosis and herpes zoster</td>
<td>1 (&lt;0.1)</td>
<td>3 (0.2)</td>
<td>4 (0.2)</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>1 (&lt;0.1)</td>
<td>4 (0.3)</td>
<td>5 (0.3)</td>
</tr>
<tr>
<td>Active tuberculosis</td>
<td>1 (&lt;0.1)</td>
<td>0</td>
<td>1 (&lt;0.1)</td>
</tr>
<tr>
<td>Non-melanoma skin cancer (NMSC)</td>
<td>1 (&lt;0.1)</td>
<td>0</td>
<td>1 (&lt;0.1)</td>
</tr>
<tr>
<td>Malignancy other than NMSC</td>
<td>4 (0.3)</td>
<td>6 (0.5)</td>
<td>10 (0.4)</td>
</tr>
<tr>
<td>Lymphoedema</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hepatic disorder</td>
<td>0</td>
<td>1 (&lt;0.1)</td>
<td>1 (&lt;0.1)</td>
</tr>
<tr>
<td>Adjudicated gastrointestinal perforation</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Anemia</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lymphopenia</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CPK elevation</td>
<td>1 (&lt;0.1)</td>
<td>0</td>
<td>1 (&lt;0.1)</td>
</tr>
<tr>
<td>Renal dysfunction</td>
<td>0</td>
<td>1 (&lt;0.1)</td>
<td>1 (&lt;0.1)</td>
</tr>
<tr>
<td>Adjudicated MACE</td>
<td>2 (0.2)</td>
<td>0</td>
<td>2 (&lt;0.1)</td>
</tr>
<tr>
<td>Adjudicated VTE</td>
<td>2 (0.2)</td>
<td>1 (&lt;0.1)</td>
<td>3 (0.1)</td>
</tr>
</tbody>
</table>
Abstract N°: 4397

**Treatment of Chronic Palmoplantar Eczema with Dupilumab: Retrospective Multicenter Cohort Study**

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**Introduction & Objectives:**

Chronic eczema of the hands and/or feet is a chronic skin condition that can have a significant impact on patients’ quality of life. Despite the wide variety of available treatments, such as topical products, phototherapy, or systemic medications, they are not entirely effective, and many patients continue to experience persistent and limiting symptoms. Dupilumab, a monoclonal antibody targeting interleukin-4 and interleukin-13, has shown efficacy in treating patients with atopic dermatitis (AD) as well as its various phenotypes or related disorders, such as nodular prurigo or chronic palmoplantar eczema. In this study, we present the current evidence on the use of dupilumab in real clinical practice from hospitals in the Comunidad Valenciana, Spain.

**Materials & Methods:**

Retrospective multicenter observational study that included adult patients diagnosed with chronic eczema of the hands and/or feet with or without AD lesions in other anatomical regions who received dupilumab treatment at recommended doses in several hospitals in our area.

**Results:**

A total of 11 patients were included, with 82% being women and 18% men, with a mean age of 50.35 years. Five patients (45%) had a history of AD. Six patients (54%) presented exclusive involvement of the palms of the hands and/or soles of the feet. Two patients (18%) had a phenotype of dyshidrotic eczema, while the remaining (82%) had hyperkeratotic eczema. The mean baseline Dermatology Life Quality Index (DLQI) was 18.2, and the mean pruritus visual analog scale (VAS) score was 9.3 out of 10. The median follow-up duration was 68 weeks. All patients reported improvement in their lesions within the first 4 weeks of treatment, and 8 of them (72%) achieved complete clearance of lesions within the first 4 months of treatment. At week 16, mean DLQI a was 4 and mean pruritus VAS was 1. During the follow-up, one patient had treatment intensification to every 10 days due to partial response, and one patient discontinued treatment at 16 weeks due to inefficacy. The remaining patients (80%) continued with the medication, with one of them having treatment de-intensification to every 21 days. None of the patients reported adverse effects.

**Conclusion:**

The efficacy of dupilumab in palmoplantar eczema has been reported in several case series in Europe, with results similar to ours. The reported experience has led to the initiation of the randomized, double-blind, phase 3 clinical trial LIBERTY-AD-HAFT (NCT04417894), which is evaluating the efficacy and safety of dupilumab in adults and adolescents with AD on the hands and feet. Longer follow-up of patients and a greater number of cases are needed to further support the use of this medication as a treatment for these patients.
Abstract N°: 4421

Dupilumab is an effective and safe therapy in the treatment of moderate to severe atopic dermatitis in real clinical practice: a series of 40 patients.

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Introduction & Objectives: Dupilumab is a monoclonal antibody directed against the interleukin 4 receptor α, which acts mainly decreasing Th2 lymphocyte activation and positioning itself as one of the reference treatments for atopic dermatitis (AD). The aim of this work was to study the effectiveness and safety of dupilumab in patients with moderate-severe AD, under real clinical practice conditions.

Materials & Methods: It was an observational, retrospective, single-center study, that included 40 adult patients with a diagnosis of moderate-severe AD [Investigator’s Global Assessment (IGA) greater than or equal to 3]. Recruitment period was from January 2018 to December 2021, with a minimum follow-up of 12 months. Sociodemographic data, clinical comorbidities (both atopic and non-atopic), severity and effectiveness scales [Eczema Area Severity Index (EASI), IGA], quality of life [Dermatology Life Quality Index (DLQI), Patient-Oriented Eczema Measure (POEM)] and adverse events of special interest were collected before starting treatment and at 4, 6 and 12-month visits.

Results: Our series showed an increase in the proportion of males and a lower prevalence of food allergies compared to other similar series. Treatment with dupilumab resulted in a statistically significant improvement in all parameters of effectiveness and quality of life at 4 months of treatment, which was maintained at the rest of the successive visits. The percentage of patients achieving an EASI 75 after 16, 26, and 52 weeks of treatment was 74%, 89%, and 97%, respectively. The most important adverse events were facial erythema and dupilumab-induced ocular surface disease (DIOSD), in 15% and 25%, respectively. No serious adverse events were registered and none necessitated discontinuation of dupilumab treatment.

Conclusion: Dupilumab has proven to be an effective drug in the treatment of our patients with moderate-severe AD, achieving a remarkable clinical response at 4 months of treatment which was maintained at 6 and 12 months. We have found no major safety problems to date, with the most frequent adverse events being facial erythema and DIOSD, in percentages similar to those described in other real practice studies.
Treatment satisfaction of adult patients with moderate-to-severe atopic dermatitis treated with baricitinib in Germany: final results from a cross-sectional patient survey

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Introduction & Objectives:

Baricitinib (BARI) was the first European Medicines Agency licensed once-daily oral Janus kinase inhibitor (JAKi) approved for treating adults with moderate-to-severe atopic dermatitis (AD). AD is an inflammatory skin condition that imposes a heavy burden on patients’ lives and requires a holistic approach to treatment according to European AD guidelines. Successful long-term AD management can be improved by understanding patients’ perspectives and contributors to treatment satisfaction.

Objective: To describe real-world patient experiences with BARI, including treatment satisfaction and other patient-reported outcomes (PROs) in adults with AD receiving BARI in Germany.

Materials & Methods:

This cross-sectional online survey using market research methodology included adult patients with moderate-to-severe AD receiving BARI in routine clinical practice for ≥4 weeks in Germany, France and the United Kingdom. This abstract focuses on data from patients in Germany. Patients answered questions related to demographics, disease characteristics, treatment information, patient’s perspectives on treatment satisfaction (4-point Likert scale) and other PROs. Data were analysed and presented descriptively.

Results:

In Germany, survey data were collected from 53 participants; 47% (n=25) were male, mean (standard deviation [SD]) age of 50.2 (12.2) years, age at AD diagnosis of 31.7 (21.7) years and disease duration of 18.5 (15.3) years. At BARI initiation (at a 2mg dose for 43%), 32% of patients reported ≥10% body surface area (BSA) affected by AD, 53% described AD as severe and 42% as moderate, and mean (SD) itch Numeric Rating Scale score was 5.7 (2.7). Systemic therapy (corticosteroids, immunosuppressants, biologics) was used prior to starting BARI by 25% of patients (Table 1). At the time of survey, 87% reported being very satisfied/satisfied with the overall effect of BARI treatment. Specifically, patients were very satisfied/satisfied with BARI for improvements in skin lesions (87%), rapid symptom improvement (83%), reduced itch (81%), reduced skin pain (72%) and improved sleep quality (68%) (Figure 1). Most patients had rapid skin lesion improvement by 1 week (53%). At the time of survey, 4% reported ≥10% BSA affected and AD was described as clear by 9%, almost clear by 38% and mild by 26%. Since starting BARI, improvements in skin lesions, itch and sleep were reported by 96%, 83% and 79% of patients, respectively, and 72% of patients reduced/stopped use of topical corticosteroids (Figure 2).
Conclusion:
The surveyed adult patients in Germany receiving BARI for moderate-to-severe AD in real-world practice reported high BARI treatment satisfaction scores across a range of disease symptoms including speed of improvement. They achieved high rates of clear/almost clear skin clearance, concomitant with reduced/stopped topical medication use. Possible limitations include selection and recollection bias, and bias of a participatory patient population.

### Table 1. Treatments for AD received immediately prior to starting baricitinib treatment

<table>
<thead>
<tr>
<th>Treatments</th>
<th>Number of patients (N=53)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Emollients</td>
<td>36 (68%)</td>
</tr>
<tr>
<td>Topical corticosteroids</td>
<td>35 (66%)</td>
</tr>
<tr>
<td>Topical calcineurin inhibitors</td>
<td>22 (42%)</td>
</tr>
<tr>
<td>Systemic antihistamines</td>
<td>20 (38%)</td>
</tr>
<tr>
<td>Phototherapy</td>
<td>16 (30%)</td>
</tr>
<tr>
<td>Systemic corticosteroids</td>
<td>9 (17%)</td>
</tr>
<tr>
<td>Alternate therapy</td>
<td>7 (13%)</td>
</tr>
<tr>
<td>Systemic immunosuppressants</td>
<td>6 (11%)</td>
</tr>
<tr>
<td>Biologic</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>No prior treatments</td>
<td>4 (8%)</td>
</tr>
<tr>
<td>Systemic retinoids</td>
<td>1 (2%)</td>
</tr>
</tbody>
</table>

*Figure 1. Patient satisfaction with baricitinib treatment for moderate-to-severe atopic dermatitis*

*Figure 2. Changes in treatments since starting baricitinib for moderate-to-severe atopic dermatitis*
Continuous tralokinumab treatment over 4 years in adults with moderate-to-severe atopic dermatitis provides long-term disease control

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Introduction & Objectives: There is a need for additional long-term treatment options for patients with moderate-to-severe atopic dermatitis (AD) that provide sustained disease control with a favorable safety profile. Tralokinumab, a monoclonal antibody that specifically neutralizes interleukin-13, is approved for the treatment of moderate-to-severe AD in multiple countries. Clinical trials of up to 52-wk duration showed that tralokinumab was effective and well tolerated as monotherapy and in combination with topical therapy. ECZTEND (NCT03587805) is an ongoing open-label, 5-yr extension trial investigating the long-term safety and efficacy of tralokinumab ± optional topical corticosteroids (TCS). To assess the efficacy of long-term tralokinumab treatment, we conducted a post hoc interim subgroup analysis restricted to the largest, most homogenous patient population, with the longest treatment duration.

Materials & Methods: Adult patients with moderate-to-severe AD who were continuously treated with tralokinumab ± optional TCS for 52 wks in the parent phase 3 trials ECZTRA 1 (NCT03131648) or ECZTRA 2 (NCT03160885) and for up to 152 wks in ECZTEND as of data cutoff April 30, 2022 were included. Endpoints included proportion of patients achieving Investigator’s Global Assessment (IGA) score of 0/1 (clear/almost clear skin), at least 75% or 90% improvement in Eczema Area and Severity Index (EASI) relative to parent trial baseline (EASI-75 or EASI-90), EASI ≤ 7, worst weekly pruritus Numeric Rating Scale (NRS) ≤ 4, and Dermatology Life Quality Index (DLQI) ≤ 5. Results are presented using observed data. Sensitivity analyses on patients who completed Wk 152 in ECZTEND (or who withdrew, but were enrolled in the study at least 152 wks prior to the study cutoff) were performed using last observation carried forward (LOCF; missing data imputed) and modified non-responder imputation (mNRI; discontinuation due to AEs or lack of efficacy imputed as non-responders and LOCF for other missing data).

Results: 347 adult patients with a mean age (SD) of 42.2 (14.5) yrs and a mean EASI (SD) of 30.8 (13.7) at parent trial baseline were included in this analysis. After 4 yrs of total tralokinumab treatment (at Wk 152 in ECZTEND), IGA 0/1 [% (n/N)] was observed in 52.6% (92/175) of patients, EASI-75 in 84.5% (147/174), and EASI-90 in 64.4% (112/174) of patients. Additionally, EASI ≤ 7 (mild disease) was observed in 84.5% (147/174) of patients, worst
weekly pruritus NRS ≤ 4 (no to mild itch) in 68.0% (119/175), and DLQI ≤ 5 (no to small effect of AD on quality of life) in 79.0% (128/162) of patients. Results of the sensitivity analyses for IGA 0/1 and EASI-75 are presented in Table 1A and B. The safety profile was favorable and consistent with earlier analyses, with no new safety signals arising with continued tralokinumab use.

**Conclusion:** Continuous use of tralokinumab ± optional TCS provided long-term disease control over 4 yrs in adult patients with moderate-to-severe AD.

**Table 1A: Proportion of patients achieving IGA 0/1.**

<table>
<thead>
<tr>
<th>Week</th>
<th>Number of patients observed</th>
<th>Responders (%)</th>
<th>Number of patients observed/impacted</th>
<th>Responders (%)</th>
<th>Number of patients observed/impacted</th>
<th>Responders (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>16</td>
<td>347</td>
<td>93 26.8</td>
<td>347/10</td>
<td>93 26.8</td>
<td>347/10</td>
<td>93 26.8</td>
</tr>
<tr>
<td>52</td>
<td>159</td>
<td>153 44.1</td>
<td>159/10</td>
<td>153 44.1</td>
<td>159/10</td>
<td>153 44.1</td>
</tr>
</tbody>
</table>

**Table 1B: Proportion of patients achieving EASI-75.**

<table>
<thead>
<tr>
<th>Week</th>
<th>Number of patients observed</th>
<th>Responders (%)</th>
<th>Number of patients observed/impacted</th>
<th>Responders (%)</th>
<th>Number of patients observed/impacted</th>
<th>Responders (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>347</td>
<td>153 45.8</td>
<td>347/10</td>
<td>153 45.8</td>
<td>347/10</td>
<td>153 45.8</td>
</tr>
<tr>
<td>52</td>
<td>347</td>
<td>251 73.0</td>
<td>347/10</td>
<td>251 73.0</td>
<td>347/10</td>
<td>251 73.0</td>
</tr>
</tbody>
</table>
Abstract N°: 4553

Safety of tralokinumab for the treatment of atopic dermatitis in patients with up to 4.5 years of treatment: an updated integrated analysis of eight clinical trials

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Introduction & Objectives: Tralokinumab, a monoclonal antibody that specifically neutralizes interleukin-13, is indicated for the treatment of patients (pts) with moderate-to-severe AD. Clinical trials of up to 52 weeks’ duration, showed that tralokinumab was efficacious and well tolerated as monotherapy and in combination with topical therapy. Here, the objective was to evaluate the long-term safety of tralokinumab in an integrated analysis of seven phase 3 parent trials of up to 52 weeks’ duration (NCT03131648, NCT03160885, NCT03363854, NCT03562377, NCT03526861, NCT03761537, NCT04587453), and the ongoing, up to 5-year extension study (ECZTEND; NCT03587805).

Materials & Methods: Two datasets were analyzed: a placebo-controlled (PC) dataset from the initial 16-wk period of the parent trials and an all-tralokinumab (AT) dataset combining the parent trials with the subsequent ECZTEND trial including pts from first dose of tralokinumab until end of tralokinumab exposure or data cut-off (April 30th, 2022). Exposure was defined over the active treatment periods. For the AT dataset, periods on placebo were disregarded. All treatment-emergent adverse events (AEs) were recorded. AEs of special interest (AESIs) were predefined. Proportions of pts with events and incidence rates (IR) per 100 patient-years of exposure (PYE) were calculated. PYE was defined as the time until the first event or exposure end, whichever came first, and incidence was defined as the first event.

Results: In total, 2693 pts (≥12 years) received tralokinumab for up to 238.5 weeks (≈4.5 years) with a median exposure time of 76.5 weeks in the AT dataset. Total exposure time was 5320.2 patient years. Median age at baseline was 33.0 years (min-max: 12-92). 10.4% of pts were 12-17 years. Overall, 2307 pts experienced an AE (IR=202.0), most (97.3%) of which were mild-to-moderate. Serious AEs (SAEs) were reported in 226 pts (IR=4.5); SAEs were considered possibly or probably related by the investigator in 50 pts (IR=0.9). No SAEs at the preferred term level were reported with an IR≥0.1. Discontinuation of treatment due to AEs was low (IR=2.8). AEs leading to drug withdrawal with an IR>0.1 were dermatitis atopic (IR=0.5) and injection site reaction (ISR) (IR=0.2). The most
frequently reported AEs in the AT dataset were consistent with the PC dataset, including nasopharyngitis (IR=18.4), upper respiratory tract infection (IR=6.9), conjunctivitis (IR=5.0), ISR (IR=3.6), conjunctivitis allergic (IR=2.7), and injection site pain (IR=1.5). AESIs, including eye disorders, skin infections requiring systemic treatment, eczema herpeticum, and malignancies, were observed in the AT dataset at rates similar to or lower than reported in the PC dataset.

**Conclusion:** Long-term use of tralokinumab, for up to 4.5 years, was well tolerated, and the pattern of AEs was consistent with the initial placebo-controlled treatment period and with no new safety signals identified.
Abstract N°: 4580

Efficacy and safety of baricitinib treatment in pediatric patients with atopic dermatitis aged 2 to less than 18 years (up to 3.6 years of exposure)

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Introduction & Objectives:

Baricitinib (Bari) is approved in many countries for moderate-to-severe atopic dermatitis (AD) in adult patients (pts) who are candidates for systemic therapy. Here, we describe the efficacy (through 52 weeks) and safety (up to 3.6 years) results from the Phase 3 study (BREEZE-AD-PEDS; NCT03952559) evaluating Bari in pediatric pts (2 to <18 yrs [yrs] of age) with moderate-to-severe AD.

Materials & Methods:

Data are from 1 phase 3, randomized, blinded, placebo-controlled study. Efficacy analyses were conducted on the intent-to-treat population with results presented using mLOCF (modified last observation carried forward) imputation or observed case. Efficacy results are presented by treatment groups (PBO, BARI low, BARI medium, BARI high dose) across the entire pt population (2 to <18 yrs), using the instrument measuring AD severity, vIGA-AD®. Response (vIGA-AD® score of 0/1) at Week 52 was assessed for partial responders and responders (vIGA-AD® of 0, 1, or 2) at Week 16 who remained on the same treatment, and for non-responders (vIGA-AD® of 3-4) at Week 16 who transitioned to BARI high dose at Week 16. Safety analyses are summarized for all randomized pts who received ≥1 dose of study treatment and are reported for 2 populations: Bari extended (patients continuously treated from baseline with baricitinib low, medium, or high dose [1-mg, 2-mg, or 4-mg exposure equivalents, respectively] and censored after dose change) and All-bari (patients receiving any baricitinib dose at any time during the study). Data cut-off was 20 January 2023. Proportions of patients with events and incidence rates (IR)/100 patient-years at risk were calculated.

Results:

467 patients received baricitinib for 750.7 patient-years (maximum exposure 3.6 yrs). Among Week 16 responders and partial responders (IGA 0, 1, or 2 with no prior rescue) who remained on double-blind study drug, the proportion of pts achieving an IGA 0 or 1 response at Week 52 was greater for pts receiving BARI high dose compared with all other treatment groups. Among Week 16 non-responders (IGA 3 or 4 or having previous rescue) who transitioned to open-label BARI high dose at Week 16, all groups showed improvement at Week 52 in the proportion of pts achieving an IGA 0 or 1 response. The majority of treatment-emergent adverse events (TEAEs) were mild to moderate in severity and the discontinuation rate due to adverse events was low (IR=1.7).
Overall, 6.6% (n=31) of the All-Bari population reported ≥1 serious adverse event (IR=4.2), with worsening AD (n=3), asthma (n=2), herpes simplex (n=2), and ophthalmic herpes simplex (n=2) most frequently reported. Overall, 60.8% (n=284) of the All-Bari population reported ≥1 TEAE of infection (IR=64.4) with COVID-19, nasopharyngitis, and upper respiratory tract infection most frequently reported. One opportunistic infection (herpes zoster) was reported. Growth assessments showed patients maintained a growth velocity consistent with their baseline height, weight, or body mass index percentile. No deaths, pulmonary embolisms, deep vein thromboses or arterial thrombotic events, major adverse cardiovascular events, malignancies, tuberculosis events, or gastrointestinal perforations were reported.

**Conclusion:**

Patients continued to show improvement in signs and symptoms of AD to 52 weeks, and the safety profile was generally consistent with that established for baricitinib in adults with moderate-to-severe AD. No new safety signals were identified.

**Table 1. Efficacy Endpoints at Week 52**

<table>
<thead>
<tr>
<th>vIGA-AD® 0/1 at Week 52 n/N (%)</th>
<th>Placebo</th>
<th>†BARI Low dose (1-mg equivalent)</th>
<th>†BARI Medium dose (2-mg equivalent)</th>
<th>†BARI High dose (4-mg equivalent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 16 responders and partial responders (IGA 0, 1, or 2 with no prior rescue)</td>
<td>23/58  (39.7%)</td>
<td>31/65  (47.7%)</td>
<td>27/64  (42.2%)</td>
<td>46/81  (56.8%)</td>
</tr>
<tr>
<td>Data are censored after permanent discontinuation of treatment or transition to open-label BARI high dose, and mLOCF imputation is used.</td>
<td>††Placebo/ BARI High (4-mg equivalent)</td>
<td>††BARI Low/ BARI High (4-mg equivalent)</td>
<td>††BARI Medium/ BARI High (4-mg equivalent)</td>
<td>††BARI High/ BARI High (4-mg equivalent)</td>
</tr>
<tr>
<td>Week 16 non-responders (IGA 3 or 4 or having previous rescue)</td>
<td>16/50  (32.0%)</td>
<td>15/41  (36.6%)</td>
<td>11/43  (25.6%)</td>
<td>5/30  (16.7%)</td>
</tr>
</tbody>
</table>

† 10 to <18 yrs: BARI low (1 mg), BARI medium (2 mg), and BARI high (4 mg);
2 to <10 yrs: BARI low (0.5 mg), BARI medium (1 mg), and BARI high (2 mg)

†† Patients transitioned from initial treatment group to open-label BARI high dose (4-mg equivalent) at Week 16.

BARI=baricitinib, IGA= Investigator Global Assessment, mLOCF=modified last observation carried forward
### Table 2. Patient Disposition and Safety Summary

<table>
<thead>
<tr>
<th></th>
<th>Placebo N=123 n (%)</th>
<th>Placebo N=120 n (%)</th>
<th>Placebo n (%)</th>
<th>Placebo IR</th>
<th>Extended BARI* N=467 n (%)</th>
<th>Extended BARI* N=467 n (%)</th>
<th>Extended BARI* IR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td>99.4</td>
<td>103.6</td>
<td>122.6</td>
<td>750.7</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Patient-Years of Exposure</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any TEAE</td>
<td>76 (61.8)</td>
<td>76 (63.3)</td>
<td>69 (57.5)</td>
<td>78 (55.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>(150.2)</td>
<td>(148.3)</td>
<td>(135.1)</td>
<td>(133.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>TEAE severity</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>35 (28.5)</td>
<td>45 (37.5)</td>
<td>39 (32.5)</td>
<td>38 (31.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>(46.1)</td>
<td>(51.3)</td>
<td>(40.2)</td>
<td>(40.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate</td>
<td>34 (27.6)</td>
<td>28 (23.3)</td>
<td>26 (21.7)</td>
<td>35 (29.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>(40.2)</td>
<td>(30.5)</td>
<td>(40.2)</td>
<td>(35.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>7 (5.7)</td>
<td>3 (2.5)</td>
<td>4 (3.3)</td>
<td>5 (4.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>(7.0)</td>
<td>(3.9)</td>
<td>(4.3)</td>
<td>(3.9)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serious adverse events</td>
<td>7 (5.7)</td>
<td>2 (1.7)</td>
<td>3 (2.5)</td>
<td>4 (3.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>(7.1)</td>
<td>(2.0)</td>
<td>(2.9)</td>
<td>(3.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Study discontinuation</td>
<td>2 (1.6)</td>
<td>2 (1.7)</td>
<td>0</td>
<td>2 (1.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>because of an AE</td>
<td>(1.9)</td>
<td>(2.0)</td>
<td>(1.7)</td>
<td>(1.7)</td>
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<tr>
<td><strong>TEAEs reported in ≥5% of All BARI</strong></td>
<td></td>
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<td></td>
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<td></td>
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<tr>
<td>COVID-19</td>
<td>6 (4.9)</td>
<td>8 (6.7)</td>
<td>12 (10.0)</td>
<td>14 (11.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>(6.1)</td>
<td>(8.4)</td>
<td>(12.9)</td>
<td>(12.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>9 (7.3)</td>
<td>9 (7.5)</td>
<td>7 (5.8)</td>
<td>9 (7.5)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>(9.3)</td>
<td>(9.4)</td>
<td>(7.2)</td>
<td>(7.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acne</td>
<td>6 (4.9)</td>
<td>6 (5.0)</td>
<td>5 (4.2)</td>
<td>12 (10.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>(6.0)</td>
<td>(6.6)</td>
<td>(5.1)</td>
<td>(10.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Headache</td>
<td>10 (8.1)</td>
<td>7 (5.8)</td>
<td>12 (10.0)</td>
<td>12 (10.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>(9.9)</td>
<td>(7.4)</td>
<td>(12.7)</td>
<td>(10.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Upper respiratory tract</td>
<td>4 (3.3)</td>
<td>5 (4.2)</td>
<td>7 (5.8)</td>
<td>7 (5.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>infection</td>
<td>(3.9)</td>
<td>(5.2)</td>
<td>(7.0)</td>
<td>(5.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyrexia</td>
<td>2 (1.6)</td>
<td>5 (4.2)</td>
<td>6 (5.0)</td>
<td>4 (3.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>(1.9)</td>
<td>(5.1)</td>
<td>(6.0)</td>
<td>(3.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>4 (3.3)</td>
<td>3 (2.5)</td>
<td>7 (5.8)</td>
<td>8 (6.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N (%)</td>
<td>(3.9)</td>
<td>(3.1)</td>
<td>(7.1)</td>
<td>(7.0)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* 10 to <18 yrs: BARI low (1 mg), BARI medium (2 mg), and BARI high (4 mg); 2 to <10 yrs: BARI low (0.5 mg), BARI medium (1 mg), and BARI high (2 mg)

†Nausea was reported <2% of pts in All BARI [3 [2.4%], 1 [0.8%], 2 [1.7%], 2 [1.7%], 9 [1.9] of pts in the PBO, BARI low, BARI medium, BARI high doso, and All BARI respectively]

BARI=boricatab, IGA= investigator Global Assessment, IR=incident rate, mLOCF=modified last observation carried forward, TEAE=treatment-emergent adverse event
Efficacy and safety of IL-22RA1 inhibition in patients with moderate-to-severe atopic dermatitis: results from a Phase 2a monotherapy trial

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Abstract N°: 4607

Introduction & Objectives: Atopic dermatitis (AD) is a chronic, inflammatory skin disease in which IL-22 expression is increased and thought to contribute to epidermal hyperplasia and barrier defects. Previous data have shown that targeting the IL-22 cytokine benefits a subset of AD patients. LEO 138559 is a monoclonal antibody that specifically targets the IL-22 receptor subunit alpha-1 (IL-22RA1). Here we evaluate the efficacy and safety of IL-22RA1 inhibition in a Phase 2a study in adult patients with moderate-to-severe atopic dermatitis. As IL-20 and IL-24 partially signal via the IL-22RA1, we used an in vitro system to further understand how targeting the IL-22RA1 influences not only IL-22, but also IL-20 and IL-24 signaling.

Materials & Methods: A phase 2a, randomized, double-blind, placebo-controlled, multi-site, proof of concept trial (NCT04922021) was conducted in which patients were randomized 1:1 to receive LEO 138559 or placebo every 2 weeks for 16 weeks with an additional dose at Week 1, followed by an additional 16 weeks of safety follow-up. The primary endpoint was change in EASI from baseline to Week 16. In vitro experiments were conducted assessing the effect of LEO 138559 on IL-20, IL-22, and IL-24 signaling using HEK293 cells transfected with IL-22 receptor complex or IL-20 receptor type 2 complex.

Results: Baseline and clinical characteristics were similar between the LEO 138559 (N=29) and placebo (N=29) groups. Mean change in EASI from baseline to Week 16 was significantly greater for LEO 138559 compared with placebo (-15.3 vs. -3.5; P=0.003). The benefit of LEO 138559 with respect to EASI was evident by Week 4. At Week 16, greater proportions of patients receiving LEO 138559 relative to placebo achieved EASI-75 (41.6% vs. 13.7%; P=0.011), EASI-90 (30.8% vs. 3.5%; P=0.003), EASI-100 (20.9% vs. 0%; P=0.006), and vIGA-AD 0/1 (27.3% vs. 7.0%; P=0.035). LEO 138559 was well-tolerated with no safety signals observed. LEO 138559 was shown in vitro to not only block IL-22 signaling, but also IL-20 receptor type 2-dependent IL-20 and IL-24 signaling.

Conclusion: In this Phase 2a study, targeting IL-22RA1 with LEO 138559 for 16 weeks improved the signs and symptoms of AD compared to placebo and was well-tolerated. These data are the first to demonstrate the efficacy and safety of an IL-22RA1 targeting antibody for the treatment of moderate-to-severe AD. In vitro data showing LEO 138559 blocked IL-20 receptor type 2-dependent IL-20 and IL-24 signaling, in addition to IL-22 signaling, suggest that the mechanism of action of LEO 138559 in AD goes beyond inhibition of IL-22-mediated skin inflammation.
Comorbidities in Atopic Dermatitis

Didem Dizman¹, Melisa Ozay¹, Gullu Gencebay¹, Ozlem Su Kucuk*¹

¹Bezmialem Vakıf University, Dermatology, İstanbul, Türkiye

Introduction & Objectives:

Atopic dermatitis is one of the most common inflammatory disorders which affects all ages with complex and multifactorial etiological factors. Allergic comorbidities associated with atopic dermatitis is well known, but the associations between atopic dermatitis and non-allergic comorbidities are less known. This study aimed to evaluate the distribution of comorbidities associated with atopic dermatitis.

Materials & Methods:

We screened patients with atopic dermatitis admitted to the outpatient dermatology clinic between 2019 and 2023 years, from the database system of the hospital, retrospectively. Patients between 12 – 70 ages included in the study. Allergic and non-allergic comorbidities, laboratory anomalies of Total IgE and anti-TPO, and other diseases were recorded. Data on patient populations were evaluated by the Excel Sofware system.

Results:

Our study population consisted of 200 atopic dermatitis patients, 97(48.5%) male and 103(51.5%) female. In laboratory tests performed, 102(51%) patients increased Total IgE, 13 (6.5%) anti-TPO, 2(1%) anti-TG, 1 (0.5%) positive ANA, 29(14.5%) patients had type 1 hypersensitivity results confirmed by a positive prick test or specific anti-IgE antibody. Atopic comorbidities were detected in a total of 51(25.5%) patients as allergic asthma in 31(15.5%), allergic rhinitis in 19(9.5%), allergic urticaria in 2(1%) allergic conjunctivitis in 1(0.5%) patient, respectively. Allergic asthma accompanied allergic urticaria in 2(1%) patients. Angioedema history was found in 2(1%) patients. One(0.5%) patient had hereditary angioedema. Thyroid diseases were found in total of 12(6%) patients; hypothyroidism in 6(3%), hyperthyroidism in 3(1.5%), Hashimoto tiroiditis in 2(1%), thyroiditis in 1(0.5%). Diabetes mellitus was detected in a total of 3(1.5%) patients, 2(1%) of them had type II DM, and the remaining one had type I DM(0.5%). Psychiatric comorbidities were seen in 4(2%) patients. Celiac disease was seen in 1(0.5%) patient. Two patients had gluten hypersensitivity. In our study population, hypertension, which is among the cardiovascular comorbidities in atopic dermatitis patients, was seen in 6(3%) and coronary artery disease in 2(1%) patients. There were prurigo nodularis in 6(3%), rosacea in 2(1%), lichen planus in 1(0.5%), morphea in 1(0.5%), alopecia areata in 1(0.5%), and scabies in 3(1.5%), epilepsy in 3(1.5%), sleep apnea in 1(0.5%), systemic lupus erythematosus in 1(0.5%), thalassemia minor carrier in 1(0.5%), ectodermal dysplasia in 1(0.5%) patient. The malignancy, as the diagnosis of T-cell lymphoma, was detected in 1(0.5%) patient.

Conclusion: Patient-specific comorbidities and simultaneous drugs used for these comorbidities are important in the selection and follow-up of newly developed treatment agents in atopic dermatitis. As our knowledge on this subject increases, the management of atopic diseases will be more successful and effective.
Abstract N°: 4733

Dupilumab survival in patients with atopic dermatitis

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¹Virgen de las Nieves University Hospital, Granada, Spain

Introduction & Objectives:

Dupilumab is a recombinant IgG4 monoclonal antibody that specifically binds to the α-subunit of the shared chain of interleukin-4 and interleukin-13 receptors. Blockade of the IL-4/IL-13 pathway by dupilumab decreases the type 2 inflammatory mediators present in atopic dermatitis (AD). The aim is to analyse the survival time of dupilumab treatment in patients with AD.

Materials & Methods:

A prospective observational study was designed. It was carried out in a tertiary level hospital which included patients who started treatment with dupilumab from 01/04/2020 and who had been on treatment for at least 30 weeks on 22/05/23. The variables collected were sex, age, start and end date of treatment and cause of treatment interruption, as well as the Eczema Area and Severity Index (EASI) and the Body Surface Assessment (BSA). A descriptive analysis of the data was performed, as well as a Kaplan-Meier survival analysis.

Results:

52 were included in the study. The mean age was 31.08 (SD: 13.08) years, being 48% (27/52) female. The baseline EASI was 29.57 (SD: 9.26) and the BSA was 40.49 (SD: 20.61). Treatment discontinuation was reported in 26.8% (15/52) of patients. The mean overall drug survival was 119.77 (SD: 8.68) weeks. The mean duration at the end of the study for patients who did not discontinue treatment was 87.50 (SD: 37.15), while the mean duration for patients who discontinued treatment was 42.13 (SD: 21.23) (p<0.001), being the main cause of discontinuation non-response to treatment. The reasons for treatment discontinuation were lack of response (87.5%, 14/16), adverse reactions (6.3%, 1/16) and treatment optimisation (6.3%, 1/16).

Conclusion:

Kaplan-Meier survival studies are useful for assessing treatment persistence, which would be useful for assessing the efficacy of biologic drugs. More studies are needed in this direction to compare persistence time with baseline parameters in order to identify those patients who would benefit most from these drugs.
Abstract N°: 4737

**Dupilumab Treatment Normalizes Skin Barrier Function and Improves Patient-Reported Outcomes in Children Aged 6 to 11 Years With Moderate-to-Severe Atopic Dermatitis**

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**Introduction & Objectives:** Atopic dermatitis (AD) is associated with significant skin barrier dysfunction mediated by type 2 inflammatory cytokines interleukin (IL)-4 and IL-13. This analysis reports the effect of dupilumab treatment in pediatric patients aged 6–11 years with moderate-to-severe atopic dermatitis (AD) on skin barrier function and patient-reported outcomes.

**Materials & Methods:** PELISTAD (NCT04718870) was an open-label, exploratory study in patients aged 6–11 years with moderate-to-severe AD. Patients received dupilumab based on baseline weight (≥ 15 kg to < 30 kg: 300 mg every 4 weeks; ≥ 30 kg to < 60 kg: 200 mg every 2 weeks for 16 weeks, with a 12-week off-treatment follow-up period). Transepidermal water loss (TEWL) was assessed longitudinally on AD lesional and non-lesional skin and on healthy skin of matched volunteers before skin tape stripping (STS). Daily sleep disturbance Numerical Rating Scale (NRS) and worst itch NRS were assessed over 16 weeks.

**Results:** 23 patients treated with dupilumab and 18 healthy volunteers were included in the study. Median basal TEWL before STS was significantly higher in lesional (48.2 [32.0, 64.3]) and non-lesional AD skin (25.3 [15.8, 34.8]) compared with healthy skin (13.5 [8.2, 18.8]) at baseline (P < 0.0001 and P < 0.001, respectively). After 16 weeks of dupilumab treatment, median TEWL (before STS) significantly improved in lesional skin (median [95% CI] TEWL before STS: 28.1 [21.4, 34.8]; P < 0.0001, versus baseline). At Week 16, the least squares (LS) mean TEWL in lesional skin (20.2 [4.0]) was comparable to that observed in healthy skin (28.2 [4.0]; P = 0.191). Similar improvement was obtained in non-lesional skin (19.1 [2.9]) which did not significantly differ from healthy skin (24.1 [2.9], P = 0.234). Mean (standard deviation [SD]) sleep disturbance NRS decreased from 6.9 (2.5) at baseline to 2.7 (1.4) at Week 16, while mean (SD) worst itch NRS decreased from 7.6 (2.1) at baseline to 3.0 (1.4) at Week 16. Of 23 patients with AD, 21 reported treatment-emergent adverse events. None were serious, severe, or led to treatment discontinuation.

**Conclusion:** Dupilumab treatment leads to normalization in skin barrier function and improvement in patient-reported outcomes in patients aged 6–11 years with moderate-to-severe AD.
Dupilumab treatment enhances keratinocyte differentiation in atopic dermatitis patients

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Introduction & Objectives: Skin cornified envelop (CE) consists of highly cross-linked insoluble proteins and the extracellular lipids anchoring on it. Filaggrin (FLG)-keratin (KRT) bundles determine the corneocyte structure and foundation of CE. Due to the ongoing type 2 inflammation the composition of CE is disrupted in atopic dermatitis (AD). The objective of this study was to evaluate the components of the CE in AD, and determine whether the 16-week (wk) of treatment with dupilumab, a fully human monoclonal antibody that blocks the shared receptor subunit for IL-4 and IL-13 (IL-4 receptor alpha), can improve CE structures and the epidermal differentiation in patients with moderate to severe AD.

Materials & Methods: Skin tape strips (STS) were collected longitudinally from lesional and non-lesional skin of 20 AD patients over the 16-wk course of dupilumab treatment. STS were also collected from 20 healthy volunteers (HV) that were followed for 16 wks. STS extracts were examined at baseline, wks 8 and 16 of treatment by liquid chromatography mass spectrometry for proteomic analysis.

Results: Proteomic analysis revealed significant redistribution of KRT expressions in AD skin samples at baseline, prior to dupilumab treatment. KRT1 and KRT10, KRTs that typically form FLG-KRT bundles in differentiated epidermis, were significantly (over 2-fold) inhibited in AD lesional skin (p<0.0001 for both as compared to HV skin), but normalized after dupilumab treatment (p<0.0001 for both as compared to AD lesional skin prior to treatment). KRT16, KRT6A and KRT6B, KRTs that outcompete KRT/KRT10 filaments, were significantly elevated at baseline in AD non-lesional (over 10-fold) (p<0.0001 for all as compared to HV skin), and more so in AD lesional skin (over 50-fold) (p<0.0001 for all as compared to HV skin). The expression of KRT16, KRT6A and KRT6B declined after 16 weeks of dupilumab treatment (p<0.001 for KRT16, p<0.0001 for KRT6A and KRT6B as compared to AD lesional skin prior to treatment). KRT14 and KRT5, KRTs typically present in undifferentiated basal epithelium, were increased in AD non-lesional and lesional skin at baseline (over 2-fold) (p<0.0001 as compared to HV skin), and dupilumab treatment significantly inhibited the expression of KRT14 in AD lesional skin (p<0.01 as compared to prior to treatment); a reduction in KRT5 was observed in AD non-lesional skin (p<0.05 as compared to prior to treatment).

Conclusion: The study revealed significant abnormalities in KRT distributions in AD skin. Proteomic analysis demonstrated that IL-4/IL-13 inhibition by dupilumab treatment resulted in significant normalization/improvements in KRTs associated with differentiated epidermis and inhibition of KRTs associated with hyperplastic and undifferentiated epithelia.
Abstract N°: 4752

Dupilumab Treatment in Girls and Boys with Moderate-to-Severe Atopic Dermatitis Increases Bone Alkaline Phosphatase, a Marker of Bone Mineralization

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Introduction & Objectives: Children with moderate-to-severe atopic dermatitis (AD) are at risk for lower bone mineral density (BMD) and levels of bone alkaline phosphatase (BALP), a marker of bone mineralization, compared with healthy children. Restricted nutrition, vitamin D deficiency, poor sleep, corticosteroid use, and chronic inflammation may contribute to low BMD and BALP, which could lead to a higher lifetime prevalence of fractures and osteoporosis. Although reference intervals for BALP vary, prepubescent girls demonstrate higher values earlier than boys, and plateau around 12 years of age, while boys’ BALP levels continue to increase until around 15 years of age. The objective of this analysis is to report the impact of dupilumab treatment on BALP levels in girls and boys aged 6–11 years with moderate-to-severe AD.

Materials & Methods: Analysis was performed retrospectively on sera from participants in LIBERTY AD PEDS, a phase 3, placebo-controlled trial of 16 weeks (NCT03345914) and LIBERTY AD PED-OLE (NCT02612454), an open-label extension trial where all eligible patients received dupilumab until Week 52. BALP levels were analyzed at baseline, and at 8, 12, 16, and 52 weeks.

Results: Dupilumab treatment led to a significant increase in geometric mean (standard error, SE) levels of BALP at 16 weeks, within reference intervals, compared with placebo in boys aged 6–<9 years (100/200mg q2w group n = 29, P<0.001; 300mg q4w group n = 25, P<0.001) and 9–11 years (100/200mg q2w group n = 36, P<0.05; 300mg q4w group n = 32, P<0.05). In girls aged 6–<9 years, dupilumab treatment also led to a significant increase in geometric mean (SE) levels of BALP at 16 weeks compared with placebo (100/200mg q2w group n = 29, P<0.05; 300mg q4w group n = 35, P<0.05). However, in girls aged 9–11 years only 100/200mg q2w led to a significant increase in geometric mean (SE) levels of BALP at 16 weeks compared with placebo (100/200mg q2w group n = 28, P<0.001; 300mg q4w group n = 30, P=0.36). At 52 weeks, BALP levels were significantly increased vs baseline in boys aged 6–<9 years (placebo transitioned to dupilumab n = 31, combined doses, P<0.01; 100/200mg q2w, P=0.0625; 300mg q4w, P<0.05) and 9–11 years (placebo transitioned to dupilumab n = 30, combined doses, P<0.01; 100/200mg q2w, P=0.0781; 300mg q4w, P<0.05). At 52 weeks, BALP levels were significantly increased vs baseline in girls aged 6–<9 years (placebo transitioned to dupilumab n = 26, combined doses, P<0.01; 100/200mg q2w, P<0.05; 300mg q4w, P<0.001), but not aged 9–11 years (placebo transitioned to dupilumab n = 36, combined doses, P=0.4375; 100/200mg q2w, P=0.0547; 300mg q4w, P=0.625).

Conclusion: Dupilumab treatment led to a significant increase in BALP levels compared with placebo in both genders at Week 16, with increased levels in girls 9–11 years treated with the q2w regimen only. In children who were in the placebo arm of the initial phase 3 trial and then transitioned at Week 16 to the OLE study, levels of BALP continued to increase over 52 weeks in both girls and boys aged 6–8 years, as well as boys 9–11 years, regardless of dupilumab treatment regimen. Levels of BALP appeared to rise, and then return to baseline in girls aged 9–11 years over 52 weeks. This return to baseline may reflect girls’ natural BALP curve, which tends to peak sooner than that for boys. Overall results suggest an increase in bone mineralization in girls and boys with AD
following dupilumab treatment, potentially restoring gender specific BALP increase during prepubescent growth.
Effects of tralokinumab treatment on quantitative and qualitative measures of skin barrier function and biology in patients with moderate to severe atopic dermatitis.

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Introduction & Objectives:

One of the key type cytokines driving atopic dermatitis (AD) is IL-13. IL-13 has pleiotropic functions that include downregulation of important epidermal barrier proteins and lipids. Tralokinumab is a fully human IgG4 monoclonal antibody that specifically neutralizes IL-13 and is approved for the treatment of moderate to severe AD in adults and adolescents. While tralokinumab was shown to be clinically efficacious in multiple trials, its specific impact on skin barrier function has not been examined so far.

Materials & Methods:

To investigate the impact of tralokinumab treatment on quantitative and qualitative measures of skin barrier function, an investigator-initiated single arm, open label, clinical trial was conducted. A total of 16 adult patients received 300 mg of tralokinumab subcutaneously every two weeks for a total of 16 weeks after an initial loading dose of 600 mg. The primary endpoint was the change in trans-epidermal water loss (TEWL, assessed with Tewameter TM300\(^\circledR\), Courage + Khazaka Electronic, Köln) at one non-lesional and one lesional marker skin area at week 16 compared to baseline. Secondary endpoints comprised changes of stratum corneum (SC) hydration (assessed with Corneometer CM 825\(^\circledR\), Courage + Khazaka Electronic, Köln), epidermal thickness (determined with QuPath open source software), microbiome composition, bacterial load and \(S.\) aureus abundance assessed by 16s rRNA analysis and RT-qPCR of skin swabs (Isohelix, Cell Projects Ltd, Harrietsham Kent, United Kingdom) and candidate SC biomarker levels assessed in tape strips (Standard D-Squame, Monaderm, Monaco, France) using Luminex.

Results:

All severity scores decreased significantly over time. At week 16, EASI 50, EASI 75 and EASI 90 response rates were 93.75%, 56.25% and 12.5%. A total of 32 adverse events (AE), either categorized as “mild” or “moderate”, were reported in 13 patients. There were no serious AE and no study drug discontinuations due to an AE. The most frequently reported AE were eye disorders (including conjunctivitis and blepharitis) and headache reported in 25.00% of the patients, respectively. The mean TEWL in AD marker lesions significantly decreased towards the levels seen at non-lesional skin areas from 25.44 \([\text{g/h/m2}]\) at baseline to 17.13 \([\text{g/h/m2}]\) at week 16, representing a 32.67% reduction \((p=0.01)\). In parallel, SC hydration increased by 36.68% \((p=0.004)\). Several Th2 mediators (MCP-4, MDC, CCL17), innate and adaptive immunity markers (IL-8, IL-18), and structural proteins associated with AD (S100A8/9, fibronectin) significantly decreased in marker lesions with highest foldchanges observed for IL-8 \((\log2FC: -2.15)\) and fibronectin \((\log2FC: -1.62)\), while epidermal thickness decreased \((p=0.001)\). Total bacterial load and \(S.\) aureus abundance showed a significant and early decrease in both lesional and non-lesional marker areas which was maintained throughout the observation period.

Conclusion:
In this small scale open clinical trial on adult patients with moderate to severe AD, tralokinumab demonstrated favorable clinical efficacy and safety, and led to significant improvements of skin barrier function parameters, improvement of microbial dysbiosis, and decreases of key SC AD biomarker expression.
Abstract N°: 4869

The Combination of Serum Total IgE and Blood Eosinophil Levels as a Predictor of Response to Phototherapy Treatment in Patients with Atopic Dermatitis

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Introduction & Objectives:

Atopic dermatitis (AD) is the most common chronic inflammatory skin disease affecting approximately 25% of all people worldwide at some point during their lifetime. Although total serum immunoglobulin E (IgE) and blood eosinophil levels are not elevated in all patients with AD, they have been shown associated with AD severity.

This study aimed to investigate whether IgE and blood eosinophil levels correlate with the response to phototherapy treatment, which is a second-line treatment for moderate to severe AD, and therefore could be considered a readily available and reliable biomarker that could guide patient management.

Materials & Methods:

Eighty-two patients with AD who received phototherapy were retrospectively evaluated for the following: demographic characteristics, serum IgE levels, blood eosinophils count, hospitalization duration, response to phototherapy, and requirement for systemic treatment. Response to phototherapy treatment was assessed by comparing the pre- and post-treatment Investigator’s Global Assessment score for each patient in relation to the aforementioned factors.

Results:

The total IgE and eosinophil levels were found significantly higher in patients who did not respond to phototherapy (p=0.018 and p=0.002, accordingly). Serum values of 1780 IU/mL for IgE and 225.0 cells/μL for eosinophils showed maximum sensitivity and specificity as predictive values for treatment response.

Conclusion:

This study found that high total serum IgE levels and eosinophilia correlated with a low response to phototherapy. These results suggest that escalating treatment is recommended for patients presenting these clinical features.
Efficacy and safety of UVA-1 phototherapy in moderate-to-severe atopic dermatitis: a single-center prospective study

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Introduction & Objectives:

Atopic dermatitis (AD) is a widespread chronic recurrent genetically determined inflammatory skin disease characterized by eczematous rashes, accompanied by severe itching, which significantly reduces the quality of life of patients. AD is a major related social problem due to its increasing incidence and prevalence in various countries. One of the leading treatments for moderate-to-severe AD, as recognized by the global dermatology community, is phototherapy, particularly long-wavelength UVA-1 phototherapy. Evaluate the efficacy and safety of UVA-1 phototherapy for moderate-to-severe atopic dermatitis.

Materials & Methods:

The study was conducted with the participation of 42 patients with moderate-to-severe atopic dermatitis receiving UVA-1 phototherapy in the period from 2022 till 2023, following the method 3-5 exposures per week for 4 weeks (up to 20 procedures), with wavelength of 350-400 nm and emission peak of 370 nm. For the II skin phototype the initial dose of irradiation was 1.0-5.0 J/cm² with subsequent increase of the dose by 1.0-5.0 J/cm² each 1-2 procedures up to the maximum single dose of 20-40 J/cm²; For skin phototype III the initial dose was 5.0-10 J/cm², with subsequent increase of 5.0-10 J/cm² every 1-2 sessions up to the maximum single dose of 20-40 J/cm² with screening of the eye area, genitalia, breast nipples, melanocytic nevi. To maintain objectivity, the severity of clinical manifestations and efficiency of therapy were evaluated by one dermatologist using SCORAD, EASI, IGA, and VAS indices at weeks 0, 1, 2, 3, and 4 of the study.

Results:

The 42 patients included 19 (45%) men and 23 (55%) women aged 18 to 68 years (32.5 ± 10.0) with Fitzpatrick skin phototype III (n=29; 69%) and II (n=13; 31%). The duration of AD averaged 30.3 ± 10.5 years. During the study, 32 patients received 20 sessions of UVA-1, with a mean cumulative dose of 367.21 J/cm² (145.2 J/cm² to 480 J/cm²), with a mean dose per session of 18.36 J/cm² (7.26 J/cm² to 24 J/cm²). The SCORAD index before and after 20 sessions of UVA-1 therapy decreased on average by 56% (from 50.5 to 22.2), EASI by 76.4% (from 20.2 to 4.8), IGA from 3.3 to 1.7, and VAS from 6.1 to 2.4 (p < 0.05). Of these, 19 patients had mild side effects (mild erythema, fever, itching), which were transient and resolved when additional emollients were added, allowing the patients to continue treatment according to the prescribed regimen. Due to developed moderate side effects or unwillingness to continue therapy, 10 (23.8%) patients dropped out of the study.

Conclusion:

Thus, long-wavelength UVA-1 phototherapy is a highly effective and safe treatment for moderate-to-severe atopic dermatitis, contributing to achieving clear and almost clear skin.
An indirect comparison of lebrikizumab, dupilumab, and tralokinumab in Japanese patients with moderate to severe atopic dermatitis by network meta-analysis methodology

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Introduction & Objectives:

Atopic dermatitis (AD) is a common chronic inflammatory skin disease with ethnic phenotype differences. In Japan, AD affects 2.5–10% of adults. Multiple systemic therapies have recently been approved and added to the dermatologists’ armamentarium. Lebrikizumab is a novel, high-affinity monoclonal antibody that selectively binds to interleukin-13 and demonstrated efficacy and safety in treating moderate to severe AD in global phase 2 and 3 clinical studies. In the absence of direct drug comparisons, it is important to describe how lebrikizumab compares to other advanced therapies in Japanese patients. This network meta-analysis (NMA) compared the relative effectiveness of the targeted biologics lebrikizumab, dupilumab, and tralokinumab in Japanese adult patients with moderate to severe AD.

Materials & Methods:

PubMed and trial registries were searched for double-blind, randomized, placebo-controlled trials. Eligible studies had comparable designs assessing the efficacy of biologics in combination with topical corticosteroids and included Japanese patients. Outcomes included the percentage of patients (response rate [RR]) at week 16 with (a) Investigator’s Global Assessment (IGA) of 0 or 1 and ≥2 point reduction from baseline, (b) ≥75% improvement in Eczema Area Severity Index (EASI-75), and (c) >4-point improvement in Itch Numeric Rating Scale (NRS-4) score. Bayesian NMA was applied.

Results:

Three eligible trials were retrieved: the dupilumab CHRONOS study (300 mg every 2 weeks [q2w]; Japanese subpopulation N=70; NCT02260986), tralokinumab ECZTRA 8 study (300 mg q2w; N=106; NCT04587453), and lebrikizumab ADhere-J study (250 mg q2w; N=205; NCT04760314).

All medications had higher RRs than placebo for IGA 0/1: 27% (95% credible interval 17–37%) for lebrikizumab, 15% (−5 to 35%) for dupilumab, and 6% (−11 to 23%) for tralokinumab. EASI75 RRs were also higher than placebo by 38% (27–49%) for lebrikizumab, 40% (14–66%) for dupilumab, and 15% (−3 to 33%) for tralokinumab. Itch NRS-4 RRs were higher than placebo by 30% (21–39%) for lebrikizumab and by 21% (−5 to 47%) for dupilumab, but lower by 4% (−22 to 14%) for tralokinumab. Only lebrikizumab differed statistically significantly from placebo in all outcomes (Table, Figure).

Based on the derivation of the posterior probability using a noninformative prior, the probability that lebrikizumab had a higher IGA 0/1 than dupilumab was 85%; than tralokinumab was 98%. The probability that lebrikizumab had higher EASI-75 than tralokinumab was 98%. The probability that lebrikizumab had higher Itch NRS than tralokinumab was >99.9%.
Conclusion:
Lebrikizumab showed superior efficacy relative to tralokinumab on all measures and to dupilumab on two measures. Lebrikizumab had a higher probability of yielding a higher RR and was the only medication superior to placebo on all measures. This was an indirect comparison limited by the small sample sizes in the dupilumab and tralokinumab trials.

Table. Mean response rate differences by endpoint and medication.

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Medication</th>
<th>Medication vs. placebo, mean RR difference (95% CrI)</th>
<th>Lebrikizumab vs. medication, mean RR difference (95% CrI)</th>
<th>Lebrikizumab vs. medication probability of higher RR</th>
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</thead>
<tbody>
<tr>
<td>IGA 0/1</td>
<td>Lebrikizumab</td>
<td>0.270 (0.173, 0.367)</td>
<td>NA</td>
<td>NA</td>
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<td></td>
<td>Dupilumab</td>
<td>0.151 (-0.047, 0.350)</td>
<td>0.119 (-0.103, 0.340)</td>
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<td></td>
<td>Tralokinumab</td>
<td>0.060 (-0.112, 0.233)</td>
<td>0.210 (0.010, 0.407)</td>
<td>0.980</td>
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<tr>
<td>EASI-75</td>
<td>Lebrikizumab</td>
<td>0.380 (0.266, 0.494)</td>
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<td>NA</td>
</tr>
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<td></td>
<td>Dupilumab</td>
<td>0.401 (0.138, 0.664)</td>
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<td>0.443</td>
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<td></td>
<td>Tralokinumab</td>
<td>0.150 (-0.030, 0.331)</td>
<td>0.230 (0.015, 0.442)</td>
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<tr>
<td>Itch NRS-4</td>
<td>Lebrikizumab</td>
<td>0.300 (0.209, 0.391)</td>
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<td>NA</td>
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<td>Dupilumab</td>
<td>0.211 (-0.052, 0.474)</td>
<td>0.089 (-0.188, 0.367)</td>
<td>0.736</td>
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<tr>
<td></td>
<td>Tralokinumab</td>
<td>-0.040 (-0.220, 0.141)</td>
<td>0.340 (0.137, 0.541)</td>
<td>&gt;0.999</td>
</tr>
</tbody>
</table>

Abbreviations: CrI, credible interval; EASI, Eczema Area Eczema Area Severity Index; IGA, Investigator’s Global Assessment; NA, not applicable; NRS, numeric rating scale; RR, response rate.

Figure. Forest plots of treatment differences from placebo in IGA 0/1, EASI-75, and Itch NRS-4 at week 16 by medication.
Abstract N°: 4905

Conception and Conduction of the German Atopic Dermatitis Registry ADBest-TREAT

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Introduction & Objectives:

Atopic dermatitis (AD) is a chronic inflammatory skin disease that occurs in episodes. It often affects the flexures, scalp, face and hands and is accompanied by distressing itching which can lead to significant psychosocial impairment and a severe reduction of quality of life. AD is associated with an increased rate of atopic and non-atopic comorbidities. The aim is to conceptualize and establish a web-based, large-scale AD patient registry for dermatology practices in Germany complementary to the academic registry TREAT.

Materials & Methods:

The registry was developed by experts from dermatology and methodology in collaboration with patients. The methods were aligned with the leads of the German academic TREAT registry. Multiple investigational sites in Germany will recruit 5000 patients with AD over a period of five years with no upper limit on the number of patients included (prolongation to 10 years possible). The registry provides real-world data on the efficiveness and safety of AD therapeutics and facilitates the development of predictive models.

Results:

A disease registry based on electronic, web-based data collection in a standardized eCRF was conceptualized and a core data set of variables assessed by both the physician (405 variables) and the patient (126 variables) was specified. The development was aligned with several dermatology offices. The IT solution permits multiple time points of documentation and largely visualized data recordings. Continuous analyses of recruitment status and baseline data are possible for each center. Consensus reports, expert recommendations, and annual updates from the registry are the communication tools.

Conclusion:

AD-TreatBest for AD is a novel registry designed especially shaped for office-based dermatologists. Such registries are important and scientifically accepted methods to obtain insights in a large number of clinical and epidemiological research questions.
Abstract N°: 4910

Real-World Treatment Outcomes in Disease Severity in Children < 12 Years of Age With Moderate-to-Severe Atopic Dermatitis: Interim Results From PEDISTAD Registry

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Introduction & Objectives:
Safe and effective treatments for atopic dermatitis (AD) in children are currently limited; immunosuppressants are mostly used off-label to treat AD in children. Dupilumab has been found to significantly improve disease severity in children with moderate-to-severe AD in phase 3 studies. However, the impact of this systemic treatment on children in real-world treatment settings is yet to be investigated.

Materials & Methods:
PEDISTAD (NCT03687359) is an ongoing, international, longitudinal, observational 5-year registry study in patients aged from 6 months to 11 years at enrollment with moderate-to-severe AD, whose disease is not adequately controlled by topical prescription therapies or for whom those therapies are medically inadvisable. This interim analysis evaluates the effect of dupilumab, methotrexate, and cyclosporine on Eczema Area and Severity Index (EASI) total score and %-affected body surface area (BSA) from therapy start to up to 3 years’ follow-up. Safety was also evaluated. This descriptive non-comparative analysis includes data from different cohorts of patients and treatment episodes, including those from within the same patient.

Results:
129 patients received dupilumab (mean [standard deviation] age: 7.4 [2.4] years; median treatment observation period: 17.0 months; accumulated 3-year discontinuation rate: 10.1%), 70 patients received cyclosporine (6.7 [2.5] years; 12.2 months; 40.0%), and 77 patients received methotrexate (7.1 [2.5] years; 21.3 months; 22.1%). The proportion of patients with clear/mild AD (EASI score < 7 [range 0–28]) increased for dupilumab (therapy start: 27.0%; last observation: 78.8%), cyclosporine (18.8%; 54.6%), and methotrexate (13.3%; 58.7%). The mean (± SE) EASI score improved with dupilumab (therapy start = 18.4 ± 1.3; last observation = 5.0 ± 0.7), cyclosporine (16.9 ± 1.4; 10.0 ± 1.4), and methotrexate (16.6 ± 1.3; 8.4 ± 1.1). The mean (± SE) BSA affected decreased with dupilumab (37.5 ± 2.2; 15.6 ± 2.3), cyclosporine (36.9 ± 2.8; 24.0 ± 2.8), and methotrexate (34.3 ± 2.3; 20.3 ± 2.5). The exposure-adjusted AE/serious AE rate per 100 patient-years was 29.2/1.5 for dupilumab; 43.5/0.9 for cyclosporine; and 30.7/0.6 for methotrexate.

Conclusion:
Dupilumab treatment was associated with numerically greater improvement in disease signs and symptoms compared with methotrexate and cyclosporine for patients aged from 6 months to less than 12 years old in real-world practice. Only dupilumab reached the minimal clinically important difference in EASI score. Dupilumab treatment was also associated with lower treatment discontinuation.

**Acknowledgments**

Research sponsored by Sanofi and Regeneron Pharmaceuticals Inc. ClinicalTrials.gov Identifier: NCT03687359. Medical writing/editorial assistance was provided by Eleanor Ewins, PhD, of Excerpta Medica and was funded by Sanofi and Regeneron Pharmaceuticals Inc., according to the Good Publication Practice guideline.
Introduction & Objectives: An increasing body of literature suggests clinical, epidemiologic, genetic, and endotypic variations in patients with skin of color (SOC) who have atopic dermatitis (AD). Patients with SOC with AD experience pigmentary and other sequelae that contribute to distinct variations in the impact of the disease. Despite this, no qualitative research has been published to date specific to this population, contributing to a limited understanding of the AD experience among patients with SOC.

Materials & Methods: This independent non-interventional study included adults and adolescents (≥12 years) with moderate-to-severe AD who had a Fitzpatrick skin type of IV–VI. Prior to study conduct, published qualitative studies were reviewed to understand the experience of AD among patients with SOC; results informed the development of a literature-based conceptual model (CM) depicting symptoms and impacts of AD as well as a discussion guide for the moderation of expert advice meetings (EAMs). Feedback from experts during the EAMs provided a more granular understanding of the patients with SOC experience with AD which was used to update the CM, and informed the development of an interview guide used to conduct N=15 concept elicitation (CE) interviews with patients. Each interview was conducted, transcribed verbatim, coded, and analyzed using thematic analysis by trained qualitative researchers until concept saturation was reached. Interviews were conducted in two waves to allow refinement of the guide and the resulting patient data was incorporated into the CM.

Results: Patient interviews elicited 19 AD disease sequelae and 42 impacts (organized across 15 domains: family activities, interpersonal relationships, social activities, recreational/leisure activities, household chores/responsibilities, physical functioning, emotional functioning, self image, cognition, personal hygiene, work/school, sleep, adaptive behaviors, and financial) (Table 1) which was reflected in the updated CM. The most frequent patient-reported (n [%]) disease sequelae were xerosis (15 [100%]), itchiness (15 [100%]), cracking skin (14 [93.3%]), skin roughness (13 [86.7%]), redness (12 [80.0%]), and hyperpigmentation (11 [73.3%]). Most frequently patient-reported impacts of AD were burden of treatment (12 [80.0%]), interrupted sleep (9 [60%]), self-consciousness (8 [53.3%]), hiding/covering skin (7 [46.7%]), and feeling annoyed/irritable (7 [46.7%]).

Conclusion: This is the first published study to conduct an in-depth exploration of experiences of patients with SOC and AD, providing a deeper understanding of the experience of living with AD for patients with SOC and which highlights the significant burden of disease. This study also provides an evidence base to inform outcomes to further evaluate treatment benefit in patients with SOC and AD.

Table 1. Disease sequelae and impacts.
<table>
<thead>
<tr>
<th>Symptom</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dry skin (xerosis)</td>
<td>15</td>
</tr>
<tr>
<td>Xerosis reported to be bothersome</td>
<td>15</td>
</tr>
<tr>
<td>Xerosis reported to be important</td>
<td>15</td>
</tr>
<tr>
<td>Skin darkening (hyperpigmentation)</td>
<td>11</td>
</tr>
<tr>
<td>Skin lightening (hypopigmentation)</td>
<td>8</td>
</tr>
<tr>
<td>Dyspigmentation reported to be bothersome</td>
<td>12</td>
</tr>
<tr>
<td>Dyspigmentation reported to be important</td>
<td>11</td>
</tr>
<tr>
<td>Itchiness</td>
<td>15</td>
</tr>
<tr>
<td>Cracking skin</td>
<td>14</td>
</tr>
<tr>
<td>Roughness</td>
<td>13</td>
</tr>
<tr>
<td>Redness</td>
<td>12</td>
</tr>
<tr>
<td>Skin bleeding</td>
<td>10</td>
</tr>
<tr>
<td>Skin peeling</td>
<td>10</td>
</tr>
<tr>
<td>Skin tightness</td>
<td>10</td>
</tr>
<tr>
<td>Skin hardness</td>
<td>9</td>
</tr>
<tr>
<td>Feeling irritated</td>
<td>8</td>
</tr>
<tr>
<td>Skin flaking</td>
<td>7</td>
</tr>
<tr>
<td>Skin thickening</td>
<td>7</td>
</tr>
<tr>
<td>Scaling</td>
<td>6</td>
</tr>
<tr>
<td>Skin oozing</td>
<td>5</td>
</tr>
<tr>
<td>Skin pain</td>
<td>4</td>
</tr>
<tr>
<td>Bumps</td>
<td>3</td>
</tr>
<tr>
<td>Warm/burning skin</td>
<td>2</td>
</tr>
<tr>
<td>Adaptive behaviors</td>
<td>n reporting each item</td>
</tr>
<tr>
<td>--------------------------------------------------------</td>
<td>-----------------------</td>
</tr>
<tr>
<td>Treatment burden (using lotion/cream/medicine)</td>
<td>12</td>
</tr>
<tr>
<td>Hiding/covering skin (e.g., clothes, band aids)</td>
<td>7</td>
</tr>
<tr>
<td>Impacted clothing choice (some fabrics snag on affected skin)</td>
<td>2</td>
</tr>
<tr>
<td>Restricted diet (to prevent symptoms)</td>
<td>2</td>
</tr>
<tr>
<td>Restricted use of soaps/lotions</td>
<td>1</td>
</tr>
<tr>
<td>Staying out of the sun</td>
<td>1</td>
</tr>
<tr>
<td><strong>Sleep</strong></td>
<td></td>
</tr>
<tr>
<td>Interrupted sleep</td>
<td>9</td>
</tr>
<tr>
<td>Difficulty falling asleep</td>
<td>3</td>
</tr>
<tr>
<td><strong>Self-image</strong></td>
<td></td>
</tr>
<tr>
<td>Self-conscious</td>
<td>8</td>
</tr>
<tr>
<td>Feeling judged by others</td>
<td>3</td>
</tr>
<tr>
<td>Reduced self-confidence</td>
<td>3</td>
</tr>
<tr>
<td>Feeling different from others</td>
<td>2</td>
</tr>
<tr>
<td>Lower body image</td>
<td>1</td>
</tr>
<tr>
<td><strong>Emotional</strong></td>
<td></td>
</tr>
<tr>
<td>Feeling annoyed/irritable</td>
<td>7</td>
</tr>
<tr>
<td>Embarrassed</td>
<td>4</td>
</tr>
<tr>
<td>Category</td>
<td>Count</td>
</tr>
<tr>
<td>----------------------------------</td>
<td>-------</td>
</tr>
<tr>
<td>Sadness</td>
<td>4</td>
</tr>
<tr>
<td>Emotionally tired</td>
<td>2</td>
</tr>
<tr>
<td><strong>Personal hygiene</strong></td>
<td></td>
</tr>
<tr>
<td>Impacted bathing/showering</td>
<td>5</td>
</tr>
<tr>
<td>Avoiding manicures</td>
<td>1</td>
</tr>
<tr>
<td><strong>Recreational/leisure activities</strong></td>
<td></td>
</tr>
<tr>
<td>Limited outdoor activities</td>
<td>4</td>
</tr>
<tr>
<td>Impaired ability to play sports</td>
<td>3</td>
</tr>
<tr>
<td>Reduced ability to go for walks</td>
<td>1</td>
</tr>
<tr>
<td>Avoiding swimming</td>
<td>1</td>
</tr>
<tr>
<td><strong>Social</strong></td>
<td></td>
</tr>
<tr>
<td>Avoiding social activities</td>
<td>4</td>
</tr>
<tr>
<td>Reduced desire to socialize</td>
<td>2</td>
</tr>
<tr>
<td>Increased comfort in dark places</td>
<td>1</td>
</tr>
<tr>
<td>Social isolation</td>
<td>1</td>
</tr>
<tr>
<td><strong>Physical function</strong></td>
<td></td>
</tr>
<tr>
<td>Physical discomfort</td>
<td>4</td>
</tr>
<tr>
<td>Limited mobility</td>
<td>2</td>
</tr>
<tr>
<td><strong>School</strong></td>
<td></td>
</tr>
<tr>
<td>Interrupted schoolwork</td>
<td>3</td>
</tr>
<tr>
<td>Reduced productivity</td>
<td>2</td>
</tr>
<tr>
<td><strong>Interpersonal relationships</strong></td>
<td></td>
</tr>
<tr>
<td>Impacted family/friend relationships</td>
<td>3</td>
</tr>
<tr>
<td>Being bullied</td>
<td>1</td>
</tr>
<tr>
<td>Impacted spousal relationships</td>
<td>1</td>
</tr>
<tr>
<td><strong>Work</strong></td>
<td></td>
</tr>
<tr>
<td>Reduced productivity</td>
<td>2</td>
</tr>
<tr>
<td>Inability to work</td>
<td>1</td>
</tr>
<tr>
<td>Job change</td>
<td>1</td>
</tr>
<tr>
<td><strong>Cognitive functioning</strong></td>
<td></td>
</tr>
<tr>
<td>Difficulty focusing</td>
<td>2</td>
</tr>
<tr>
<td>Impaired ability to problem-solve</td>
<td>1</td>
</tr>
<tr>
<td><strong>Family activities</strong></td>
<td></td>
</tr>
<tr>
<td>Decreased ability to participate in family events</td>
<td>1</td>
</tr>
<tr>
<td><strong>Financial</strong></td>
<td></td>
</tr>
<tr>
<td>Financial stress</td>
<td>1</td>
</tr>
<tr>
<td><strong>Household chores/responsibilities</strong></td>
<td></td>
</tr>
<tr>
<td>Impaired dishwashing</td>
<td>1</td>
</tr>
</tbody>
</table>
Introduction & Objectives:

Atopic dermatitis (AD), a chronic inflammatory skin disease, causes considerable burden to patients’ quality of life. This burden is impacted by the body location of AD lesions with visible body areas, specifically the head and neck, reported as most bothersome. In recent years, available systemic treatments for topically inadequately controlled AD has expanded to include biologics and oral Janus Kinase (JAK) inhibitors. Of which, baricitinib (BARI) was the first oral selective JAK1/2 inhibitor approved by the European Medicines Agency for treatment of adults with moderate-to-severe AD who are candidates for systemic therapy.

This analysis, of data from a cross-sectional patient survey, aims to assess which body areas affected by AD are most bothersome for patients and to understand patients’ perspectives on the impact of BARI treatment on lesion involvement in a real-world clinical setting.

Materials & Methods:

This is a protocol-driven analysis of data collected in a multi-country, cross-sectional, online patient survey using market research methodology. Adults (≥18 years) with moderate-to-severe AD treated with BARI in routine clinical practice for ≥4 weeks in France, Germany, and the United Kingdom were invited to participate in the survey by their treating dermatologist. Patient-reported demographics, disease characteristics including where on the body they experience AD and where is most bothersome, and treatment satisfaction (based on a four-point Likert scale) was recorded. Descriptive analyses were used to report observed data on predefined variables.

Results:

The survey was completed by 170 patients (France=48, Germany=53, UK=69) with moderate-to-severe AD who were treated with BARI for a median (IQR) duration of 4 (2.3-7.0) months. Mean age was 39.3 years (standard deviation=13.5), 59% were female. At BARI initiation, all patients reported experiencing AD symptoms on ≥1 body location with 4%, 49% and 47% on 1, 2-3 and 4-6 body locations, respectively. Patients reported AD symptoms most commonly on the arms/legs (85%; excludes hands/feet), trunk (74%), hands (71%) and head and neck (62%; includes scalp, face and neck; Table 1). Of these body areas, the head and neck area was reported as the single most bothersome (36%), followed by hands (23%) and arms/legs (14%). At the time of survey completion (while on BARI treatment), 11%, 26%, 52% and 10% of respondents reported AD on none, 1, 2-3 and 4-6 body locations, respectively. Patients reported AD symptoms on the arms/legs (59%), trunk (44%) and head and neck area (29%). Of those reporting AD on the head and neck at BARI initiation (n=106), 54% (n=57) experienced clearance while
on BARI treatment, most of whom (96%) were satisfied (n=39, 68%) or very satisfied (n=16, 28%) with their BARI treatment.

**Conclusion:**

Adult patients treated with BARI for moderate-to-severe AD in real-world clinical practice and who participated in this survey reported the head and neck area as the single most bothersome body area for their AD. By survey completion, AD symptoms were reported on fewer body areas than at BARI initiation. More than 50% of those who reported AD symptoms on the head and neck experienced clearance of AD symptoms in this specific area and reported high treatment satisfaction. Limitations of the survey include selection bias toward those who stay on BARI treatment, recall bias and potential bias for a more engaged patient population.


<table>
<thead>
<tr>
<th>Most bothersome body area for AD*</th>
<th>Body areas patients report experiencing AD symptoms*</th>
<th>N=170</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>At BARI initiation, n (%)</td>
<td>At time of survey completion, n (%)</td>
</tr>
<tr>
<td>Head and neck</td>
<td>106 (62%)</td>
<td>49 (29%)</td>
</tr>
<tr>
<td>Hands</td>
<td>120 (71%)</td>
<td>61 (36%)</td>
</tr>
<tr>
<td>Arms and legs</td>
<td>145 (85%)</td>
<td>100 (59%)</td>
</tr>
<tr>
<td>Trunk</td>
<td>126 (74%)</td>
<td>75 (44%)</td>
</tr>
<tr>
<td>Feet</td>
<td>69 (41%)</td>
<td>33 (19%)</td>
</tr>
<tr>
<td>Genitals</td>
<td>42 (25%)</td>
<td>16 (9%)</td>
</tr>
<tr>
<td>My skin was or is clear</td>
<td>NA</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

*AD, atopic dermatitis; BARI, barrier; N, total number of respondents; n, number of respondents per category; NA, not applicable.
Real-World Patient-Reported Outcomes in Children < 12 Years of Age With Moderate-to-Severe Atopic Dermatitis: Interim Results From PEDISTAD Registry

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1Trinity College Dublin, Dublin, Ireland, 2Hospital Vital Alvarez-Buylla, Asturias, Spain, 3University of Perugia, Perugia, Italy, 4NorthShore University Health System, Skokie, United States, 5The Hospital for Sick Children, Toronto, Canada, 6Ajou University Hospital, Suwon, Korea, Rep. of South, 7Osaka Habikino Medical Center, Osaka, Japan, 8Hospital Angeles Puebla, Puebla, Mexico, 9Sanofi, Cambridge, United States, 10Regeneron Pharmaceuticals Inc., Tarrytown, United States

Introduction & Objectives: Dupilumab has proven efficacy in improving patient-reported outcomes for atopic dermatitis (AD) in pediatric patients in randomized clinical trials. However, few real-world daily practice studies are available to show the treatment effect on patient-reported disease symptoms and quality of life (QoL) in children with moderate-to-severe AD. This interim analysis assessed the effect of dupilumab, cyclosporine, and methotrexate for up to 3 years.

Materials & Methods: PEDISTAD (NCT03687359) is an ongoing global, observational 5-year study of patients with moderate-to-severe AD, aged 6 months to 11 years at enrollment, whose disease is not adequately controlled by topical prescription therapies or for whom those therapies are medically inadvisable. Patient-reported disease severity is measured using Patient-Oriented Eczema Measure (POEM [range 0–28]) and the 0–10 Peak Pruritus Numerical Rating Scale (PP-NRS for worst itching during previous night/current day [self-assessed; children aged 6 to < 12 years]; worst scratching during previous 24 hours [caregiver-assessed; children aged < 6 years]). The effect on QoL of the family is measured using the Dermatology Family Impact questionnaire (DFI; range 0–30). Overall safety was also evaluated.

Results: 129 patients received dupilumab (median treatment observation period: 17.0 months; cumulative 3-year discontinuation rate: 10.1%), 70 patients received cyclosporine (12.2 months; 40.0%), and 77 patients received methotrexate (21.3 months; 22.1%). Mean (± SE) POEM scores decreased for dupilumab (therapy start: 17.2 ± 0.7; last observation: 8.3 ± 0.8), cyclosporine (17.4 ± 0.8; 11.9 ± 1.2), and methotrexate (17.7 ± 0.9; 11.7 ± 0.9). Mean (± SE) PP-NRS scores (previous night/current day) improved with dupilumab (5.4 ± 0.3; 3.0 ± 0.4/4.4 ± 0.3; 2.6 ± 0.4), cyclosporine (5.7 ± 0.4; 4.2 ± 0.7/4.4 ± 0.4; 3.0 ± 0.6), and methotrexate (4.2 ± 0.4; 3.4 ± 0.4/3.4 ± 0.4; 2.9 ± 0.4). Dupilumab use improved the mean (± SE) DFI score (12.7 ± 0.7; 7.5 ± 0.8), as did cyclosporine (12.3 ± 0.9; 8.5 ± 1.2) and methotrexate (11.9 ± 0.8; 7.1 ±0.9). The exposure-adjusted AE/serious AE rate per 100 patient-years was 29.2/1.5 for dupilumab; 43.5/0.9 for cyclosporine; and 30.7/0.6 for methotrexate.

Conclusion: Dupilumab improved patient-reported symptoms of AD and QoL in children aged 6 months to 11 years in real-world daily practice with numerically greater improvements in signs and symptoms compared with patients receiving cyclosporine and methotrexate.
Introduction & Objectives:

Atopic dermatitis (AD) is a chronic inflammatory skin disease with significant pruritus and phases of exacerbation and remission. Patients with AD present with reddened skin, swelling and oozing lesions, but also feel the debilitating effect it has on their daily lives, such as persistent itching, cracked, thickened and oozing skin.

This condition is associated with an increased risk of developing mental disorders such as sleep disturbances, depression, anxiety, isolation and suicidal ideation. In fact, according to the Spanish Society of Allergy and Clinical Immunology (SEAIC), AD can cause negative psychological effects in up to 50% of patients.

Type D personality is defined as the tendency to experience the consequences of chronic distress, characterized by the simultaneous presence and synergistic interrelation of its two components: negative affectivity (NA) and social inhibition (SI). Worse health-related quality of life (HRQoL) has been linked to type D personality in patients with AD.

Screening for type D personality in dermatology consultations might be beneficial to identify patients who are more psychologically vulnerable to the consequences of chronic skin diseases such as AD.

Materials & Methods:

A cross-sectional study was designed in which patients with AD of at least 6 months of evolution diagnosed by a dermatologist were included.

Type D personality was assessed with the Spanish version of Type D Scale-14 (DS14). Participants who did not answer at least 80% of the questions were excluded.

Results:
64 patients with AD were included. The DS14 results in 3 scores, the SI score, the NA score, and the overall DS14 score.

50% (32/64) of patients with AD showed NA; 43.8% (28/64) of patients with AD showed SI; 45.3% (29/64) of patients with AD showed overall DS14 score.

More specifically, 64.6% (42/64) of patients with AD show difficulty in establishing contact with other people, 55.4% (36/64) of patients with AD assert they do a world of unimportant things, and 53.9% (35/64) of patients with AD consider themselves a closed person.

**Conclusion:**

- These results showed that almost half of the patients with AD present type D personality. SI was more prevalent compared to AN.

- The SI of patients with AD may be associated with a feeling of self-consciousness due to their skin lesions, which is probably why they have limitations when having contact with other people and consider themselves to be closed people.

- The presence of type D personality could lead to dysfunctional coping strategies in patients, which would be responsible for worse quality of life, higher rates of psychological comorbidities and, in some cases, potentially worse disease control.

- Further studies are needed to determine whether the degree of severity of AD is correlated with the degree of SI, AN, or SD14 in our patients.
Abstract N°: 4995

**Dupilumab Improves Patient-Reported Symptom Control Among Adults with Moderate-to-Severe Atopic Dermatitis in Clinical Practice: 4-Year Follow-up Results From the RELIEVE-AD Study**

Jason Wang¹, Min Yang², Jingdong Chao¹, Bruno Martins², Gaelle Le Bagousse-Bego³, Brad Shumel¹, Debra Sierka⁴, Bruce Strober⁵, Alexa B. Kimball⁶

¹Regeneron Pharmaceuticals, Inc., Tarrytown, United States, ²Analysis Group, Inc., Boston, United States, ³Sanofi, Chilly-Mazarin, France, ⁴Sanofi, Cambridge, United States, ⁵Yale University and Central Connecticut Dermatology, Cromwell, United States, ⁶Harvard Medical School, Boston, United States

**Introduction & Objectives:** Atopic dermatitis (AD) is often perceived to be a childhood disease, but it can also have a highly detrimental impact among adults. Results from the RELIEVE-AD study, which included adults with moderate-to-severe AD who initiated dupilumab in real-world clinical practice showed significant, sustained improvements in disease control, flares, skin symptoms, sleep, quality of life, treatment satisfaction, and concomitant AD medications up to 3 years¹-³. The aim of this study is to report 4-year patient-reported symptom control from RELIEVE-AD.

**Materials & Methods:** RELIEVE-AD is a single-arm, prospective, longitudinal patient survey study of adults with moderate-to-severe AD who were prescribed dupilumab, enrolled in the US dupilumab patient support program, and agreed to participate in online surveys at baseline and Months 1, 2, 3, 6, 9, 12, 33, and 48. Outcomes presented here are: global change in itch since treatment initiation; absence of flares (increased itching/redness and/or new/spreading lesions) in the previous 4 weeks; skin symptoms (pain, hot/burning, sensitivity) severity in the past week (0 [no symptoms] to 10 [worst symptoms]); and AD-related sleep problems in the past week. Statistical significance was determined using generalized estimating equations to account for correlated data from the same patients. Normal distributions with an identity link function were used for continuous outcomes; binomial distributions with a logit link function were used for categorical outcomes.

**Results:** Among 698 patients who completed the baseline survey, 353 (50.6%) completed the Month 48 survey. At baseline, the mean age was 46.2 years, 61.7% were female, and common comorbidities included: non-seasonal allergies (36.0%), asthma (32.2%), and hypertension (26.9%). Over 75% of patients reported that their itch was “very much better” at Month 48 in comparison to baseline. Flare-free status over the previous 4 weeks increased from 3.0% at baseline to 33.8% at Month 1 and 43.5%, 45.9%, and 49.0% at Months 12, 33, and 48 (all p<0.001). Skin symptoms improved considerably from baseline to Month 1 and then continued to improve to Month 48 (Fig 1). Similarly, AD-related sleep problems in the past week were reported by 77.5% of patients at baseline, falling to 27.1% at Month 1, and 14.1%, 13.4%, and 12.7% at Months 12, 33, and 48, respectively (all p<0.001). Only 50.6% of patients were evaluable at Month 48.

**Conclusion:** Dupilumab treatment in real-world clinical practice led to rapid and sustained improvements in multiple patient-reported AD symptoms (itch, flares, skin symptoms, and sleep problems) over 4 years, with similar benefits at 4 years compared to those previously reported at 1 and 3 years.
References


*Vertical bars represent the range of imputed outcome values for the study follow-up period using pattern mixture models, for patients who completed the BL survey. BL, baseline; M, Month.
Abstract N°: 5011

Sustained Improvement in Atopic Dermatitis Disease Control and Treatment Satisfaction with Dupilumab in Clinical Practice: 4-Year Follow-up Results From the RELIEVE-AD Study

Jason Wang¹, Min Yang², Jingdong Chao³, Bruno Martins², Gaelle Le Bagousse-Bego³, Brad Shumel¹, Debra Sierka⁴, Bruce Strober⁵, Alexa B. Kimball⁶

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Introduction & Objectives: Although atopic dermatitis (AD) typically affects children, it can persist into, or start during, adulthood. In the RELIEVE-AD study, which included adults with moderate-to-severe AD who initiated dupilumab in real-world clinical practice, results up to 3 years showed significant, sustained improvements in disease control, flares, skin symptoms, sleep, quality of life, treatment satisfaction, and concomitant AD medications. This study aims to report 4-year disease control, treatment satisfaction, and concomitant medication results from RELIEVE-AD.

Materials & Methods: RELIEVE-AD is a single-arm, prospective, longitudinal patient survey study of adults with moderate-to-severe AD who were prescribed dupilumab, enrolled in the US dupilumab patient support program, and agreed to participate in online surveys at baseline and Months 1, 2, 3, 6, 9, 12, 33, and 48. Outcomes presented here are: disease control (assessed using the Atopic Dermatitis Control Tool [ADCT], with a score <7 on a scale of 0–24 indicating controlled disease); treatment satisfaction (7-point Likert scale from “extremely satisfied” to “extremely dissatisfied”); and use of concomitant treatment categories (topicals excluding crisaborole, crisaborole, systemic steroids, systemic immunosuppressants, and ultraviolet therapy). Statistical significance was determined using generalized estimating equations to account for correlated data from the same patients. Normal distributions with an identity link function were used for continuous outcomes; binomial distributions with a logit link function were used for categorical outcomes.

Results: Among 698 patients who completed the baseline survey, 353 (50.6%) completed the Month 48 survey. At baseline, the mean age was 46.2 years, 61.7% were female, and common comorbidities included: non-seasonal allergies (36.0%), asthma (32.2%), and hypertension (26.9%). Controlled disease (ADCT <7) was reported in 5.9% of patients at baseline, increasing to 61.0% at Month 1, then 77.4%, 80.7%, and 80.5% at Months 12, 33, and 48, respectively (all p<0.001). Patient satisfaction with AD treatments improved over time as shown in Fig 1 (p<0.0001 for all time points vs baseline). Similarly, the proportions of patients reporting use of concomitant therapies decreased as shown in Fig 2. At baseline, only 12.8% of patients reported no concomitant treatment category in the past 4 weeks, improving to 39.6% at Month 1 and 43.9%, 54.4%, and 58.1% at Months 12, 33, and 48, respectively (all p<0.001).

Conclusion: A majority of patients who responded to the survey at 4 years reported controlled disease and were satisfied with treatment in real-world clinical practice despite moderate-to-severe AD at baseline.
Figure 1. Patient Satisfaction with Current AD Treatment(s)

Figure 2. Concomitant Therapies by Category*

*Based on a 4-week recall. †Calcineurin inhibitors, steroid creams, or ointments. BL, baseline; M1, Month 1, etc.

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Dupilumab treatment in patients with hand and foot atopic dermatitis: Results from a phase 3, randomized, double-blind, placebo-controlled trial

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Introduction & Objectives: Atopic dermatitis (AD) of the hands and/or feet is often chronic, difficult to treat, and substantially impacts patient quality of life. We report the effect of dupilumab treatment on signs, symptoms, and quality of life in patients with atopic hand and foot dermatitis using dedicated clinical and patient reported instruments.

Materials & Methods: The phase 3, randomized, double-blind LIBERTY-AD-HAFT (NCT04417894) trial enrolled patients ≥12 years with moderate-to-severe (Investigator’s Global Assessment [IGA] 3/4) atopic hand and foot dermatitis. Patients were randomized to dupilumab monotherapy 300 mg q2w in adults; 200/300 mg every 2 weeks in adolescents, or placebo for 16 weeks. The primary endpoint was hand and foot IGA 0/1 score at Week 16. Safety/tolerability was assessed.

Results: The 133 patients enrolled were randomized to dupilumab (n=67) or placebo (n=66). At Week 16, the primary and all secondary endpoints were met. Significantly more patients in the dupilumab vs placebo group achieved hand and foot IGA 0/1 (40.3% vs 16.7%; P=0.003; primary endpoint) and ≥4-point improvement in the hand and foot Peak Pruritus Numerical Rating Scale (52.2% vs 13.6%; P<0.0001; a key secondary endpoint). Dupilumab-treated patients experienced significant improvement in percent change from baseline in the modified Total Lesion Sign Score for hand and foot lesions vs placebo (LS mean [SE] −69.4 [5.8] vs −31.0 [5.9]; P<0.0001) and Hand Eczema Severity Index (HECSI; LS mean [SE] −74.8 [6.3] vs −39.9 [6.2]; P<0.0001). At Week 16, treatment with dupilumab also significantly increased the proportion of patients achieving a 75% improvement in HECSI (46.9% vs 21.5%; P=0.0028) and improved Quality of Life in Hand Eczema Questionnaire scores (LS mean [SE] −40.3 [4.0] vs −16.2 [4.2]; P<0.0001). Treatment-emergent adverse events (TEAEs) were reported in 44 (65.7%) patients in the dupilumab group and 49 (74.2%) patients in the placebo group. The most common TEAEs (≥10%) were nasopharyngitis (dupilumab: 16% vs placebo: 11%) and dermatitis atopic (dupilumab: 5% vs placebo: 18%). Severe TEAEs were reported by 1 (1.5%) dupilumab treated patient and 3 (4.5%) placebo treated patients. Serious adverse events were reported by 2 patients (3%; post procedural infection, dizziness, and syncope) in the dupilumab group and 1 patient (1.5%; appendicitis) in the placebo group.

Conclusion: Dupilumab significantly improved signs, symptoms, and quality of life in patients with moderate-to-severe atopic hand and foot dermatitis and had an acceptable safety profile.
Abstract N°: 5023

Management of sensitive skin with Atopic Dermatitis: an extensive clinical program demonstrating the efficacy and safety of a flare-up relieve cream

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Introduction & Objectives:
Sensitive skin is defined by occurrence of unpleasant sensations in response to neuro-mediated inflammation and external stimuli that normally should not provoke such sensations. Atopic Dermatitis (AD) can affect sensitive skin leading to very unpleasant itchy, scratchy skin worsening burden and quality of life (QOL) in adults and children.

An innovative cream including colloidal oatmeal (w. 2% colloidal oat), a proprietary technology (sodium pyrrolidone carboxylic acid and arginine), niacinamide, and tocopherol acetate was specifically designed for sensitive skin. In vitro, this cream exhibited a positive impact on the regulation of the skin microbiome. Indeed, it: 1) tended to limit the growth of pathogenic Staphylococcus aureus to the benefit of commensal Staphylococcus epidermidis; 2) did not affect biofilm formation by S. aureus; and 3) reduced adhesion of S. aureus, while commensal strain prevails in reconstructed human epidermis. These beneficial effects might be interesting, especially in the case of dysbiosis, such as eczema. The aim of this extensive clinical research plan was to evaluate the safety and efficacy of the flare-up relieve cream in adults and children.

Materials & Methods:
In total, 558 subjects of different origins and age categories (babies, toddler, and adults) were included in 13 clinical studies. 297 subjects had sensitive skin. Six of the studies were specifically designed to assess the local tolerability of the cream, including the large-scale Flare-up study. In the Flare-up study (treatment vs vehicle, twice-daily application; 100 subjects with mild-to-moderate eczema/AD and with at least 2 flares in the past two months; 50 subjects per group, age 4–60 y.o), AD severity was evaluated using SCORing Atopic Dermatitis (SCORAD) and patient-oriented SCORAD. QoL was assessed using Dermatology Life Quality Index (DLQI) and Children’s Dermatology Life Quality Index (CDLQI). Skin sensitivity was measured using the Sensi Scale. Skin barrier (Trans-Epidermal Water Loss, TEWL) and hydration (Corneometer), as well as clinical dryness, scaling, redness, roughness, and skin sensitivity (SensiScale-10) were assessed under normal conditions of use.

Results:
The cream was very well tolerated with no adverse reactions reported. SCORAD and patient-oriented SCORAD decreased respectively by 57% (p=0.001) and 63% (p=0.001) and QoL was improved drastically as attested by a reduction of 75% of DLQI score (p<0.05) and by 61% of CDLQI (p<0.05) after 56 days. In the Flare-up study a reduction of 72% (p<0.05) in overall skin sensitivity was measured after 8 weeks of twice daily application. The cream also demonstrated very good emollient qualities with 8% significant improvement of skin hydration until 48h and skin barrier repairing effect of 39% at Timm (p=0.021) and full barrier recovery as of 5 days after a skin damaging by tape stripping.

Conclusion:
Through this extensive and thorough clinical research program involving 13 clinical studies and >500 subjects, it was demonstrated that this cream, which was specifically formulated to reduce SS and AD, was very well tolerated and efficient in addressing the different symptoms of those two conditions.
Abstract N°: 5024

Atopic dermatitis, associated psychological conditions and pruritus – an inquiry study

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Introduction & Objectives:

Atopic dermatitis (AD) is a chronic inflammatory skin disease, often with a substantial itching. Internal and external stimuli may affect the extent of the disease. AD causes a significant burden on patients, including decreased productivity due to work disruptions, reduced daily activity, higher direct medical costs, fatigue and daytime sleepiness due to sleep disturbance. Stress is known to worsen the disease.

We wanted to investigate, primarily stress and associated psychological conditions like anxiety and depression, in patients with AD, as well as symptoms connected to the disease like severity and character of pruritus.

Materials & Methods:

Adult patients diagnosed with AD were invited to take part in this inquiry study. The invitation was sent out via regular mail to 3395 patients and the questionnaire was accessed anonymously via an online platform. The topics were generated from several focus groups with AD-patients and thereafter also discussed with the patient organization. Further, validated forms to evaluate quality of life (Dermatology Life Quality Index, DLQI), chronic stress* (Karolinska Exhaustion Disorder Scale, KEDS), perceived stress (perceived stress scale, PSS) and anxiety and depression (hospital anxiety and depression scale, HAD) were used. Also, extent of disease using SCORAD (SCORing Atopic Dermatitis) was reported by the patients.

Results:

In total 609 patients (17.9%) answered the inquiry. Of these were 204 (32.9%) males and 412 (66.5%) females. The median age was 39 years (range 26-54 years). The patients reported debut of the symptoms at the age of 0-9 years (78.9%). Ongoing eczema was reported for 543 (87.2%) of the patients, while 80 (12.8%) reported no symptoms. Eighty-nine (14.3%), of the patients had systemic treatment, while 532 (85.7%) topical treatment.

Three hundred forty-six (55.7%) of the patients had at least once consulted a doctor for stress, anxiety, depression or exhaustion, the majority for stress. More than half, 50.3%, reported ongoing stress, anxiety, depression or exhaustion., the majority (62.4%) reported stress. The majority had no treatment, while 103 (16.6%) had treatment for these conditions.

The majority (82.5%) of the patients reported stress worsening of their eczema, work/study-related stress being the most important, followed by family problems and economic stress.

Of different worsening factors, psychological stress was rated the highest. Some of, (11%) the patients had some time been offered treatment for stress, anxiety, depression or exhaustion, and of them, most (67.2%), were treated with cognitive behavioral therapy (CBT) or mindfulness.

Correlations were found between the extent of disease measured with subjective SCORAD and quality of life as well as between SCORAD and chronic stress and SCORAD and anxiety and depression.

Fifty-one (72.5%) of the patients had had pruritus during the last 24 hours, and the majority scored 3 on a VAS
scale, median value 3.0. Regarding the localization of the pruritus the majority (45.7%) reported both superficial and deep type. The majority (85.1%) of the patients reported that the itch was worsened by stress.

**Conclusion:**

The importance of psychological triggers and psychiatric comorbidities should not be underestimated in patients with AD. The majority of patients reported worsening of their eczema by stress. One possible mechanism might be that stress triggers itch and starts the itch-scratch cycle.
Abstract N°: 5026

Remibrutinib demonstrates target engagement but does not suppress signs in patients with moderate to severe atopic dermatitis

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Introduction & Objectives:
Atopic dermatitis (AD) is a common chronic, relapsing, inflammatory, itchy skin disease affecting 1-3% of all adults. Often, AD is classified into allergic AD, which is characterized by elevated levels of Immunoglobulin E (IgE) and non-allergic AD, characterized by low or normal levels of IgE. Levels of IgE are thought to be correlated with disease severity. Blocking Bruton Tyrosine Kinase (BTK) downstream from the intracellular FcεR-pathway triggered by the interaction with IgE may be a novel therapeutic approach for diseases where IgE plays a role. Therefore, the aim of this study was to investigate the safety, pharmacokinetic and pharmacodynamic effects of remibrutinib in patients with moderate to severe AD.

Materials & Methods:
A double-blind, randomized, placebo-controlled 4-week multiple dose study was conducted wherein remibrutinib (100 mg) twice daily in 16 subjects with AD was administered to investigate safety, tolerability, pharmacodynamics, pharmacokinetics and efficacy. Eligible subjects participated in a 6-week screening period, a baseline visit, a 4-week treatment period and a 3-week follow-up. During the study visits safety assessments and pharmacodynamic assessments were performed including clinical scoring, multimodal imaging, and collecting skin punch biopsies.

Results:
Generally, remibrutinib was safe and well tolerated. Treatment with remibrutinib 100 mg bid resulted in a mean percent inhibition of stimulated basophils (CD63) above 97% and was near complete from 8h post-dose throughout the entire treatment period. No clinically meaningful differences were observed between placebo and remibrutinib for EASI, SCORAD and IGA. Although, no clear response of remibrutinib was present on the multi-faceted evaluation of the disease status, an effect on itch measured by numerical rating scale was observed in the remibrutinib group, with the largest difference in means at day 22 (difference -1.97 on a 11-point rating scale, 90% CI -4.62 – 0.68, p-value 0.221).

Conclusion:
Remibrutinib (100 mg bid) was safe and well tolerated in AD subjects. Clear target engagement was observed by BTK occupancy and blood basophil CD63 inhibition, however, a clear treatment effect on AD skin signs after 4 weeks of treatment was absent in this small cohort. A trend in itch reduction was observed in the remibrutinib treated group which is consistent to the observed effect in CSU.
Abstract N°: 5041

Long-term efficacy and safety of dupilumab treatment in children aged 6 months to 5 years with severe atopic dermatitis enrolled in an open label extension study

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Introduction & Objectives: Dupilumab is the only approved systemic treatment in the European Union for patients aged 6 months to 5 years with severe atopic dermatitis (AD) who are candidates for systemic therapy. Here we report the long-term efficacy and safety of dupilumab over 44 weeks from an open-label extension trial in this age group with severe AD at parent study (PS) baseline.

Materials & Methods: Patients aged 6 months to 5 years with inadequately controlled moderate-to-severe AD were enrolled in LIBERTY AD PRESCHOOL (NCT03346434 part B; parent study), a randomized, double-blind placebo-controlled phase 3 study. Patients were randomized to either dupilumab 200/300 mg every 4 weeks (200 mg if baseline weight 5 to < 15kg, 300 mg if 15 to < 30kg) or placebo for 16 weeks. All patients initiated standardized treatment with low-potency topical corticosteroids (TCS) from Day –14. After 16 weeks of treatment, patients were subsequently enrolled into the ongoing, long-term, LIBERTY AD PED-OLE trial (NCT02612454) and were treated with dupilumab 300 mg every 4 weeks + TCS. This analysis reports on the subgroup of children with severe AD (Investigator’s Global Assessment score [IGA] of 4) at the PS baseline that enrolled in the OLE. Endpoints include the proportion of patients achieving IGA 0/1, 75% reduction from baseline in the Eczema Area and Severity Index (EASI-75), and the mean percent change in EASI from the PS baseline. Data presented as observed. Safety was also assessed.

Results: Of the 162 patients in the PS, 125 patients with severe AD at baseline were randomized to dupilumab + TCS (n=63) or placebo + TCS (n=62). After 16 weeks of treatment, 104 patients with severe AD at PS baseline were subsequently enrolled in the OLE. At the OLE baseline, most patients were male (67 [64.4%]), aged 2 years or older (95.2%), and had a mean (SD) AD duration of 3.6 (1.2) years. At Week 28 of the OLE, 46% of patients achieved an IGA score of 0/1 and 62% of patients achieved EASI-75. At OLE study baseline, a mean percent (SE) change in EASI from the PS baseline of −52% (3.2) was noted. This improved to −73% (2.4) at Week 4, −83% (2.6) at Week 16, and −89% (3.6) at Week 28. Treatment-emergent adverse events (TEAEs) were reported in 55 (52.9%; nP/100PY: 171.6) patients with 7 (6.7%; nP/100PY: 21.8) patients reporting TEAEs related to treatment, 2 (1.9%; nP/100PY: 6.2) patients reporting severe TEAEs and 1 (1.0%; nP/100PY: 3.1) patient reporting a TEAE that lead to permanent discontinuation. Overall safety was consistent with the known dupilumab safety profile.

Conclusion: Long-term dupilumab treatment showed sustained improvement of AD signs in children aged 6 months to 5 years with severe AD. Consistent with results seen in adults, adolescents and children aged 6 years and older, long-term treatment with dupilumab in children aged 6 months to 5 years with severe AD showed an acceptable safety profile.
Relationship between the Topography of Atopic Dermatitis, Body Mass Index and Cardio-metabolic Comorbidities

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Introduction: Numerous comorbidities such as asthma, nasal polyps, hay fever, food allergies, eosinophilic esophagitis, alopecia areata, or ulcerative colitis are common in patients with atopic dermatitis (AD). In contrast, there are conflicting data on cardio-metabolic comorbidities. Following the data published on psoriasis, it can be assumed that the affection of certain localizations, such as the scalp, the intertriginous areas or the nails, are associated with an increased risk of cardio-metabolic comorbidities.

Objective: To establish clinical risk profiles of atopic dermatitis for cardio-metabolic comorbidities.

Methods: We performed a retrospective analysis of data from AtopicHealth2, a cross-sectional non-interventional cohort on health care characteristics and quality of care for atopic dermatitis in Germany in the years 2017, 2018 and 2019. Patients with AD were included in the study by dermatologists (n = 1261). AD history, clinical findings and distribution of eczema were collected with standardized questionnaires.

Results: Affection of intertriginous areas by AD is associated with** concomitant cardio-metabolic disease ($\chi^2(1) = 7.164, p = 0.007, \varphi = 0.076$). When cardiovascular and metabolic comorbidities were considered separately, the involvement of intertriginous areas was associated exclusively with cardiovascular ($\chi^2(1) = 5.282, p = 0.022, \varphi = 0.065$) and not metabolic disease ($\chi^2(1) = 2.519, p = 0.113, \varphi = 0.045$). In the regression model on 1,064 patients cardiometabolic comorbidities (if at least one of the two types of comorbidities, i.e. cardiovascular or metabolic, has been reported) are predicted by BMI and age.

Conclusion: The involvement of intertriginous skin areas in patients with AD may be a clinical indicator of cardiometabolic disease. Increased age and BMI are associated with a higher risk of cardio-metabolic comorbidities in patients with AD.
Efficacy of a Dermocosmetic containing neurosensine, sphingobioma and niacinamide in Atopic Dermatitis patients - achieving rapid symptom relief after one-day use and sustained improvement of Disease Severity and Quality of Life over time

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Introduction & Objectives:

Atopic Dermatitis (AD) is a chronic inflammatory skin disease associated with dysfunctional integrity of epidermal barrier, which frequently results in skin dryness, itching, burning sensations and inflammatory lesions. Maintaining and stabilizing the skin barrier is essential for preventing and treating AD. Everyday emollient therapy is the basis of AD treatment and helps to restore epidermal barrier functions.

The purpose of this clinical study was to evaluate the effects of a face skin care cream (DC) on skin barrier function, clinical symptoms, skin appearance, and quality of life in patients with AD.

Materials & Methods:

A total of 63 adult patients with mild to moderate AD without acute eczema on face, neck and décolleté were enrolled and applied the DC twice daily on their face, neck, and décolleté for two weeks. The following investigations were performed at baseline, after 24h and day 14: Clinical parameters such as general SCORAD (Scoring of Atopic Dermatitis), EASI (Eczema Area and Severity Index) scores and local SCORAD, skin physiological measurements such as TEWL, pH, corneometry, sebumetry, chromametry, and electrochemical impedance spectroscopy (EIS). Subjective and objective assessments of the skin as well as The Dermatology Life Quality Index (DLQI) questionnaire were evaluated at baseline and over time.

Results:

The study results indicate that the application of the DC led to significant improvements in both subjective and objective symptom assessment as early as day 1, with further improvements observed after 14 days. Patients reported a significantly (p<0.001) reduction in symptoms such as dryness, itching, redness, desquamation, burning and tightness feeling on the face, neck, and décolleté over time, with the strongest improvement observed in the facial area. Patients with previous eczema in face, neck and décolleté showed greater disease severity at baseline compared to those without. Disease severity, as measured by SCORAD and EASI, improved over time, particularly in the reduction of skin symptom intensity and subjective symptoms such as sleeplessness and pruritus intensity. Clinical examinations confirmed the high dermatological tolerance of DC. An improvement in quality of life (DLQI) was also observed.

Conclusion:

The study demonstrates the tolerability and rapid and sustained efficacy of a DC containing neurosensine, niacinamide and sphingobioma used twice a day in improving the signs and symptoms of AD. In light of the observed improvements in quality of life and disease severity, it can be inferred that the use of a facial cream
results in a broad enhancement of the patient’s condition. Despite eczema affecting several body parts, the use of a facial skin care cream alone resulted in an improvement in the general well-being of the patients. This finding confirms the importance of emollients to be used even on the facial, neck and décolleté areas in the management of AD.
Abstract N°: 5116

Healthy Lifestyle in Patients with Atopic Dermatitis: Mediterranean Diet and Physical Activity

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Introduction & Objectives:

Atopic dermatitis (AD) is a chronic, heterogeneous, inflammatory skin disorder characterized by recurrent, pruritic and eczematous lesions, excoriations, desquamation and skin dryness. AD can create significant disruptions in sleep and quality of life of patients.

Environmental factors, including diet, are associated with an increased risk of developing AD. Obesity, as well as smoking or unhealthy nutritional habits, are associated with AD. In this context, the Mediterranean Diet (MD) is an anti-inflammatory dietary regimen, and following a MD during pregnancy decreases the risk of atopy in newborns.

On the other hand, physical inactivity is one of the most prevalent modifiable risk factor related to inflammatory diseases. Physical activity (PA) can help patients with cutaneous inflammatory diseases improve disease severity, lose weight, and reduce emotional burden.

The identification of a modifiable risk factor contributing to an AD-affected population could generate large-scale preventive approaches. The aim of this study was to analyze adherence to MD and the PA level (PAL) in patients with AD.

Materials & Methods:

A cross-sectional study was designed in which patients with AD of at least 6 months of evolution diagnosed by a dermatologist were included. Adherence to MD was assessed with the PREDIMED (PREvención con DIeta MEDITerránea) questionnaire, and the PAL was assessed with the International Physical Activity Questionnaire (IPAQ) validated in the Spanish population. Participants who did not answer at least 80% of the questions were excluded.

Results:

65 patients with AD were included. Regarding nutritional habits, 4.6% (3/65) of the included patients presented low adherence to the MD, 76.9% (50/65) medium adherence to the MD, and 18.5% (12/65) high adherence to the MD. Regarding PA, 23.1% of the included patients presented a slow PAL, 44.6% (29/65) moderate PAL and 32.3% (21/65) vigorous PAL.

More specifically, 89.2 (58/65) of the included patients consume less than 3 portions of fish per week, 63.1% (41/65) consumes less than 3 portions of legumes per week, 47.7% (31/65) consumes less than 3 pieces of fruit per day, 67.7% (44/65) consumes less than 90 grams of nuts per week and 46.2% (30/65) consumes more than two commercial bakery products per week.

Conclusion:

- In our study, the majority of the participants included presented a medium adherence to MD and a moderate...
- The least consumed healthy foods were fish, legumes, fruit and nuts.
- There was a tendency to consume bakery products such as cookies or non-homemade pastries.
- In addition, it would be interesting to carry out a study with a larger number of participants from different geographical areas to determine if eating habits are associated with severity or response to the treatment of patients with AD.
Altered neurophysiology and intraepidermal neuroanatomy in patients with atopic dermatitis recovers upon dupilumab treatment

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Introduction & Objectives:

Chronic Pruritus is a cardinal symptom and major burden of patients with atopic dermatitis (AD). Biologicals such as dupilumab have revolutionised the therapy of AD, offering an effective, well tolerated treatment for patients.

We aim at identifying neurophysiologic and intraepidermal neuroanatomic changes during the treatment course with dupilumab in AD patients in order to improve understanding of effects of this anti-inflammatory therapy on skin nerve fibers.

Materials & Methods:

In a monocentric, open-label study, patients > 18 years with moderate to severe AD and pruritus lasting > 6 weeks received an in-label therapy with dupilumab (300mg s.c.) for 16 weeks. At baseline (BL) and after 16 weeks (W16), quality of life (via DLQI), anxiety and depression (via hospital anxiety and depression scale), and worst pruritus (WP) intensity in the past 24 h (via numeric rating scale (NRS)) were measured. Three skin biopsies were taken for analysis of intraepidermal nerve fiber density (IENFD) by PGP9.5 staining – two biopsies at BL (pruritic lesional (PL) and non-pruritic, non-lesional (NPNL)) and one at W16 (former pruritic lesional/healed (FPL)). Alloknesis testing (itch induced by mechanical stimuli; sign for neuronal sensitization) was performed at the biopsy sites before biopsy taking via cotton brush/paint brush at BL PL, NPNL and W16 FPL.

Results:

49 patients (16 females) were enrolled, with a mean age of 41.1 years (32; [19-78]). Treatment with dupilumab decreased WP-NRS ([0-10]) significantly from BL (8; [2-10]) to W16 (3; [0-9]) (p < 0.001), as well as the DLQI (p < 0.001) (BL: 11, [3-30]; W16: 3, [0-17]), both showing a highly significant correlation to another (p < 0.001). We found IENFD reduced at PL and NPNL at BL, improving significantly after 16 weeks of treatment (PL (5.62; [0.75-19.91]) vs. FPL (7.69; [1.13-15.47]), p = 0.002). Alloknesis was significantly more often detected at BL PL vs. NPNL (p = 0.021), improving significantly from BL to W16 (PL vs. FPL, p = 0.016). Both IENFD and alloknesis correlated significantly to another at BL PL (p = 0.019, r = 0.365). Alloknesis showed further a significant correlation to WP-NRS at BL NPNL (p = 0.011, r = 0.393), as well as at W16 FPL (p = 0.049, r = 0.345).

Conclusion:

This study demonstrated reduced IENFD in AD patients that recovered during treatment with dupilumab. Moreover, nerve fiber function was altered resulting in alloknesis, which significantly correlated with IENFD and accordingly also improved during dupilumab therapy.

In sum, treatment of AD patients with dupilumab seems to have not only a clinically beneficial, but neuroanatomical and neurophysiological measurable effect, demonstrating the therapeutic relevance in curing AD patients. In addition, IENFD may provide a corresponding neuroanatomic marker for clinically successful treatment.
Abstract N°: 5166

Long-term effectiveness of dupilumab in adults with moderate-to-severe atopic dermatitis: 2-year results from a national non-interventional study (PROLEAD)

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Introduction & Objectives: Dupilumab is the first biologic licensed for the treatment of patients with moderate-to-severe atopic dermatitis (AD) who require systemic therapy. Dupilumab has been shown to be efficacious in patients with moderate-to-severe AD in Phase 3 clinical trials and real-world evidence. Here we report the long-term effectiveness findings of PROLEAD, the largest prospective, non-interventional study to investigate the real-world effectiveness and safety of dupilumab in adults with moderate-to-severe AD in Germany.

Materials & Methods: PROLEAD was a national, multicentre, prospective, non-interventional study in Germany, with a 2-year observation period conducted from April 2018 to December 2022. The primary objective was to describe the real-world effectiveness of dupilumab in routine clinical practice as treatment for moderate-to-severe AD. Primary endpoints were change from baseline to Month 12 in SCORing Atopic Dermatitis (SCORAD; absolute values) and proportion of patients achieving a 75% improvement in Eczema Area and Severity Index (EASI-75) at Month 12. Secondary endpoints were improvement in Dermatology Life Quality Index (DLQI), patients achieving EASI-90 at Month 12. Clinically meaningful response (CMR) was defined as patients who achieved either EASI-50 or showed an improvement of a ≥3-point reduction from baseline in worst daily Peak Pruritus Numerical Rating Scale (NRS), or an improvement of a ≥4-point reduction from baseline in DLQI score. Optimal treatment response (OTR) was defined as an EASI score ≤7 or a worst Peak Pruritus NRS absolute score ≤4 or DLQI ≤5. Effectiveness assessments were analysed at Months 12 and 24 for the full analysis set (FAS, patients with baseline and ≥1 follow-up effectiveness assessment) as observed.

Results: The FAS comprised 780 patients in PROLEAD; of these, 12- and 24-month data were available for 614 and 393 patients, respectively. The mean (SD) [n] change from baseline to Months 12 and 24 in absolute SCORAD was -41.2 (20.3) [513] and -46.5 (19.6) [371], respectively. The proportion of patients achieving EASI-75 and -90 was 80.3% and 53.9% (Month 12), and 87.1% and 70.1% (Month 24). The mean (SD) [n] change from baseline to Months 12 and 24 in absolute DLQI was -10.1 (7.2) [529] and -10.8 (7.0) [366], respectively. The proportion of patients achieving EASI-75 was similar for patients with moderate AD (Month 12: 69.0% [n=60]; Month 24: 77.1% [n=61]) compared with severe AD (Month 12: 83.1% [n=315]; Month 24: 89.7% [n=292]). A similar proportion of patients achieving CMR and OTR at Months 12 and 24 was observed for patients with moderate AD severity (CMR: 92.2% [n=94] and 94.3% [n=66]; OTR: 95.9% [n=163] and 98.5% [n=127], respectively) compared with severe AD severity (CMR: 96.1% [n=417] and 97.8% [n=308]; OTR: 93.9% [n=309] and 97.5% [n=235], respectively).

Conclusion: PROLEAD was the first non-interventional study in Germany to investigate the long-term real-world effectiveness and safety of dupilumab in adults with moderate-to-severe AD. The long-term effectiveness findings
of PROLEAD confirm that the Phase 3 study efficacy data of dupilumab in this patient population are consistent with data seen in real-world practice, and show that treatment with dupilumab was effective in patients with moderate AD in addition to those with severe AD.
Cardiovascular disease-specific proteomics of Korean patients with atopic dermatitis reveal distinct proteomic signatures

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Introduction & Objectives: Cardiovascular diseases (CVDs) have been found to be associated with atopic dermatitis (AD) in Korean patients. This study aimed to characterize the blood proteomic signature in Korean patients with moderate to severe AD, by focusing on proteins related to CVDs.

Materials & Methods: A total of 78 patients with AD and healthy controls were enrolled. The patients were clinically assessed for eczema area and severity index (EASI) scores. Patient blood proteomics were collected using the Olink CVD II panel. The functions of the proteins were examined through gene ontology (GO) and pathway analyses. Protein expression levels were visualized on the heatmap. AD proteomics and control proteomics were compared using the principal component analysis (PCA). Correlation and multiple linear regression analyses were performed to examine correlations among protein expression levels and the association between the disease severity and the protein expressions, respectively.

Results: The CVD II panel incorporated proteins involved in PI3K-Akt, ERK1, and ERK2 pathways. The unsupervised hierarchical clustering and subsequent analyses yielded 39 upregulated and 10 downregulated proteins. Ninety-two proteins, as well as 39 upregulated and 10 downregulated proteins, could distinguish AD patients from healthy subjects in the PCA and clustering analyses. Twenty-five upregulated proteins, such as MMP12, CCL17, IL6, IL-1R2, and FGF21, were highly correlative in the correlation analysis. STK4, ITGB1BP2, and DECR1 were newly found to be upregulated in Korean patients with moderate to severe AD. A multiple linear regression model comprising CCL17 and FGF21 highly correlated with the EASI score (R = 0.619).

Conclusion: The blood proteomics of Korean patients with moderate to severe AD were readily distinguished from those of the healthy volunteers with the CVD II panel. Some CVD-related proteins were newly found to be upregulated in Korean AD patients.
Abstract N°: 5190

**efficacy and safety of narrowband phototherapy in the treatment of generalized eczema**

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**Introduction:**

Eczema is a common skin ailment, often chronic and relapsing. Narrow band ultraviolet B and ultraviolet A1 phototherapies are slowly getting recognized as an effective, safe and affordable alternative of treatment of eczema. However very few studies have been performed to evaluate the efficacy and safety of narrow-band ultraviolet B (NBUVB) therapy in Indian patients with generalised eczema.

**Objectives:**

We aimed to evaluate efficacy and safety of the Narrow band phototherapy in cases of chronic generalized eczemas using EASI (eczema area and severity index), SCORAD (scoring in atopic dermatitis ) score and physician global assessment score (PGA). Our secondary objective was to find the impact of eczema in quality of life of these patients and also to find the impact of phototherapy in quality of life of these group of patients by noting the changes in DLQI (dermatology life quality index) before and after the treatment.

**Materials & Methods:**

In this institute based prospective study, after signing informed consent, adult patients (more than 16 years of age) of generalized eczemas refractory to treatment with topical and short course of systemic steroids, were subjected to full body NB-UVB therapy twice weekly up to 24 weeks. Sample size was 30. Patients were allowed to use emollients and antihistaminics. The SCORAD, EASI, DLQI, PGA indices and visual analogue scale for pruritus and sleep were used to evaluate the therapeutic output.

**Results:**

During the study period January 2018 to December 2019, total of 30 patients (17 males and 13 females) were enrolled. Pre and post treatment SCORAD for 23 patients ranged from 52.1 to 80.0 (mean 52.33; severe grade) and 7.3 to 4.1 (mean 5.7; mild grade) respectively. EASI score for same patients pre and post treatment ranged from 21.6 to 42.1 (mean 29.14; severe grade) and 6 to 3.2 (mean 4.6; mild grade) respectively. Pre and post treatment EASI for 5 patients ranged from 10.1 to 18.3 (mean 12.95; moderate grade) and 0.0 to 2.0 (mean 0.5) respectively. SCORAD score pre and post treatment for these 5 patients ranged from 44.5 to 37.1 and 4.3 to 6.1 respectively. There was decline in DLQI from mean of 25.53 (at week 0) to 4.0 (at week 24th ), that showed a 85% decrease in the score. The PGA score has also fallen from mean of 3.6 (at week 0) to 1.2 (at week 24th ), that is 66% fall in the score post treatment.

This decrement in scores correlates with the clinical improvement of the patients in terms of extent of body surface area involvement, intensity of redness of lesions, thickness of lesions, scratching intensity and lichenification intensity.

Even the visual analogue scale for pruritus showed improvement in 30 patients after 6 months from mean equal to 9.8 (at week 0) to 1.16 (at week 24th ) i.e. 86.4 % improvement. There an improvement of 90% in the visual analogue scale for sleep loss from mean of 18.03 (at week 0) to 0( at week 24th ).
This phototherapy was found to be safe in 83.33% of our study patients, with rest 26.67% showing minor side effects like xerosis and erythema which managed with emollients and adjustments of NBUVB doses.

**Conclusion:**

Our study shows NB-UVB phototherapy could be a very safe and effective alternative to oral steroids and immunosuppressives in the management of refractory cases of generalized eczema.
Long-term improvement in patient-reported symptoms and quality-of-life in adults with moderate-to-severe atopic dermatitis receiving treatment with dupilumab in real-world clinical practice: results from a prospective non-interventional study (PROLEAD)

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Introduction & Objectives: Dupilumab, a monoclonal antibody that inhibits type 2 inflammation pathways via dual inhibition of interleukin (IL)-4 and IL-13 signalling, has been demonstrated to be effective in treating the signs, symptoms, and quality-of-life of atopic dermatitis (AD). However, there is a need to investigate the real-world effectiveness of dupilumab using patient-reported outcomes. Here we report the long-term patient-reported outcome (PRO) results from PROLEAD, the largest study in Germany to investigate the real-world effectiveness and safety of treatment with dupilumab in adults with moderate-to-severe AD in routine clinical practice.

Materials & Methods: PROLEAD was a national, multicentre, prospective, non-interventional study in Germany, with a 2-year observation period. The present analysis describes the patient-focused experience of dupilumab as treatment for moderate-to-severe AD. Outcome measures included Patient Oriented Eczema Measure (POEM; absolute values), Patient Benefit Index (PBI; calculated from Patient Needs & Benefit questionnaire), and Dermatology Life Quality Index (DLQI; minimally clinically important difference: ≥4-point improvement) at Months 12 and 24, Pruritus Numerical Rating Scale (NRS; average pruritus during past 24 hours from baseline to Months 12 and 24), and Medical Outcomes Study (MOS) Sleep Scale (duration of falling asleep during the last 4 weeks prior to baseline, Months 12 and 24; change from baseline to Months 12 and 24 in sleep disturbance). PROs were analysed for the full analysis set (FAS, patients with baseline and ≥1 follow-up effectiveness assessment) as observed.

Results: The FAS comprised 780 patients in PROLEAD; of these, 12-month and 24-month data were available for 614 and 393 patients, respectively. The mean (SD) POEM scores at Months 12 and 24 were 7.1 (6.1) [n=527] and 5.9 (5.6) [n=367], respectively. The mean (SD) PBI at Months 12 and 24 were 3.3 (0.7) [n=415] and 3.4 (0.7) [n=284], respectively. In the Patient Needs questionnaire, the most common needs that patients ranked as “very important” were “itch-free” (93%), “regain control of disease” (84%), “no burning sensation” (81%), and “skin gets better quickly” (80%); at Month 24, the percentage of patients who stated their goal was “very” or “quite” achieved was 87.7% (itch-free), 89.8% (regain control of disease), 85.4% (no burning sensation), and 89.8% (skin gets better quickly). The proportion of patients achieving a minimally clinically important difference in DLQI at Months 12 and 24 was 82.2% (n=435) and 82.8% (n=303), respectively. The average pruritus during the last 24 hours (Pruritus NRS [SD]) at Months 12 and 24 were 2.3 (2.1) [n=519] and 1.7 (1.8) [n=366], respectively. The proportion of patients who reported taking >30 minutes to fall asleep reduced from 52.7% (n=408) at baseline to 19.9% (n=106) at Month 12 and 14.5% (n=53) at Month 24. Mean (SD) change from baseline to Months 12 and...
24 in MOS Sleep Scale – disturbance was -27.1 (25.0) [n=530] and -30.5 (24.0) [n=360], respectively.

**Conclusion:** PROLEAD was the first non-interventional study in Germany to report the long-term PRO results of dupilumab in adults with moderate-to-severe AD. The findings of PROLEAD demonstrate that treatment with dupilumab achieves a rapid and durable improvement in the symptoms (including itching and burning sensation) and quality-of-life of patients with moderate-to-severe AD.
Abstract N°: 5258

Long-term safety and tolerability of treatment with dupilumab in patients with moderate-to-severe atopic dermatitis: real-world data from the prospective, non-interventional PROLEAD study

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Introduction & Objectives: Dupilumab is the first biologic licensed for the treatment of patients with moderate-to-severe atopic dermatitis (AD). Dupilumab has been shown to have a favourable safety and tolerability profile in this patient population over a period of 5 years, as reported in Phase 3 clinical trials. Here we report the 24-month real-world safety results from PROLEAD, the largest study in Germany to investigate the real-world effectiveness and safety of dupilumab in adults with moderate-to-severe AD in a clinical setting.

Materials & Methods: PROLEAD was a national, multicentre, prospective, non-interventional study in Germany conducted from April 2018 to December 2022, with a 2-year observation period. The primary objective was to describe the real-world effectiveness of dupilumab in routine clinical practice as treatment for moderate-to-severe AD. The present analysis assessed the 24-month safety of treatment with dupilumab, reported as adverse events (AEs), serious AEs (SAEs), treatment-emergent AEs (TEAEs), AEs leading to discontinuation and deaths, including those related to study treatment. Safety was assessed in the safety analysis set (SAS; all patients who received ≥1 dose of dupilumab), and study discontinuations were analysed in the full analysis set (FAS; patients with baseline and ≥1 follow-up effectiveness assessment).

Results: Overall, 818 and 780 patients were included in the SAF and FAS, respectively. At Month 24, 336 (41.1%) patients experienced AEs, with 58 (7.1%) experiencing SAEs. TEAEs were reported in 324 (39.6%) patients, with serious TEAEs reported in 53 (6.5%). Drug-related TEAEs were reported in 180 (22.0%) patients, two (0.2%) of which experienced serious drug-related TEAEs. The most frequently reported TEAEs were conjunctivitis (12.8%, n=105), eye pruritus (5.6%, n=46) and ocular hyperaemia (5.6%, n=46). A total of four deaths (0.5%) occurred, none of which were related to study drug. The reasons for death were cited as ‘breast carcinoma’ (n=1), ‘patient has died’ (n=1), ‘death of unknown cause’ (n=2). In the FAS, 313 (40.1%) patients discontinued the study prior to the end of observation period. The most common reasons for discontinuation were loss of contact (6.2%, n=48), occurrence of AEs (5.6%, n=44) and lack of efficacy (4.1%, n=32).

Conclusion: PROLEAD was the first study to report the long-term safety data over 2 years of treatment with dupilumab in clinical practice. The findings of PROLEAD confirm the established safety and tolerability profile of dupilumab in clinical trials is consistent with that observed in real-world conditions, with no new safety signals identified. The frequency of study discontinuation was predominantly unrelated to the study drug, and is a common observation in long-term, unmonitored, non-interventional studies.
Psoriasis and atopic dermatitis: two diseases or two poles of the same disease?

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Introduction & Objectives:

Psoriasis and Atopic Dermatitis (AD) are the most common inflammatory dermatitis. Even though traditionally have been considered as two different diseases, in the few last years many reports have described them as the two poles of the same disease. Patients with clinical and/or pathological characteristics of both diseases have been also published, and the concept of “overlap” or “PsEma” has been used to describe these patients with characteristics of both psoriasis and atopic dermatitis. This new disease, which has been described in paediatric patients, it has not been well characterized in adult patients.

Materials & Methods:

Observational, retrospective, multicentric study. We included patients aged 18 years or older, whose have been diagnosed of both psoriasis and atopic dermatitis somewhen during follow-up. Simultaneous diagnosis of psoriasis and atopic dermatitis was not required to include these patients.

Results:

We included a total of 12 patients. 10 of them presented an overlap diagnosis which began with psoriasis-like lesions (83.3%) and 2 of them with atopic dermatitis lesions (16.7%).

Only 2 of the patients presented atopic comorbidities (16.7%) (1 with allergic rinoconjuntivitis and eosinophilic esophagitis and 1 with allergic asthma), and 7 patients presented inflammatory arthritis (58.3%), axial arthritis in 3 patients (25%), peripheral arthritis in 3 patients (25%) and enthesitis in 1 patient (8.3%).

9 patients had received oral treatments previously (75%) (acitretin, methotrexate or cyclosporin), and 9 of them (75%) at least 1 previous biologic therapy (BT), 2 patients had received 1 BT (16.7%), 4 patients 2 BT (33.3%), 2 patients 3 BT (16.7%) and 1 patient 4 BT (8.3%). After being diagnosed of psoriasis-dermatitis overlap, treatment was replaced in all of the patients, in 6 patients with a janus kinase (JAK) inhibitor (50%), (5 patients upadacitinib (41.7%) and 1 patients baricitinib (8.3%)), an anti-interleukin-17 in 3 patients (25%), an anti-interleukin-23 in 2 patients (16.7%) and anti-tumor necrosis factor (TNF) in 1 patient. Response to treatment replacement was complete in 6 patients and partial in 6 patients (50%). Patients who received a JAK inhibitor presented complete response in 66.7% of them.

Conclusion:

Psoriasis-atopic dermatitis overlap syndrome, although being a poorly described syndrome, is becoming more frequent in dermatology consultations, and seems to have a complete and quick response to JAK inhibitors.
inhibitors. Immunopathogenesis of this syndrome should be described better in order to be able to develop better targeted therapies.
Complementary use of a next-generation emollient plus and pimecrolimus in atopic dermatitis: a case report

Tiago Torres*

Introduction & Objectives: Atopic dermatitis (AD) is a chronic skin disease characterised by inflammation, erythema, dryness and pruritic lesions. Due to the intermittent nature of AD, management strategies focus on preventing flares following remission. Recently, a next-generation emollient ‘plus’ cream (EC), containing active ingredients that specifically target AD pathophysiology, was released. Studies have demonstrated that EC is not only effective as maintenance therapy for AD, but it is also effective when used synergistically with anti-inflammatory pharmacological therapies, such as the topical calcineurin inhibitor, pimecrolimus.

Materials & Methods: A 24-year-old male patient, diagnosed with AD at the age of 3 years, visited the outpatient clinic after worsening of AD symptoms that were non-responsive to topical corticosteroids (TCS) and standard emollient therapy. Physical examination findings included severe lesions localised around the eyes and mild lesions on the upper limb flexures. The Investigator’s Global Assessment (IGA) score was 3, the Eczema Area and Severity Index (EASI) was 5.5, body surface area (BSA) was 5% and the Pruritus Numerical Rating Scale (Pruritus-NRS) was 7/10, indicating mild-to-moderate AD. The patient was prescribed pimecrolimus twice daily for 12 days and ongoing maintenance EC twice daily for AD-affected skin. He was advised to re-initiate pimecrolimus after the 12 days if the AD symptoms relapsed or worsened.

Results: At the 3-week follow-up visit, the AD lesions had improved and were categorised as very mild. The IGA score was 1, the EASI was 0.9, BSA was <1% and the Pruritus-NRS was 1/10. The patient reported that between Day 12 and Week 3, he applied only EC to AD-affected skin and did not use pimecrolimus. From Week 3 onwards, he continued to apply only EC to AD-affected skin. At the 8-week follow-up visit, the clinical signs of AD and the disease severity evaluation scores remained unchanged. Between Weeks 3 and 8, the patient confirmed that he continued to use only EC. At the 16-week follow-up visit, the severity of AD remained unchanged, similar to Weeks 3 and 8; however, the patient reported mild worsening of AD symptoms on his face at Week 12, resulting in the application of pimecrolimus twice daily for 5 days. Overall, the patient reported a flare-free period between Weeks 3 and 12 and between Weeks 13 and 16. Throughout the 16 weeks, no tolerability issues were reported.

Conclusion: This case report demonstrates the use of a complementary approach of daily administration of maintenance EC and intermittent application of pimecrolimus for flare management, which was effective for treating a patient with mild-to-moderate AD resistant to TCS and standard emollient therapy. Comparative studies are required to further understand the value of this treatment approach.

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**Abstract N°: 5328**

**Real-World Use and Effectiveness of Upadacitinib in Adults and Adolescents With Atopic Dermatitis: Preliminary Analysis of the Real-World Multicountry AD-VISE Study**

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**Introduction & Objectives:** Upadacitinib (UPA) 15 and 30 mg once daily is approved for moderate to severe atopic dermatitis (AD) in several jurisdictions, including, but not limited to, the European Union, Japan, Canada, and the United States, with indication/posology differences. Clinical studies have documented the safety and efficacy of UPA; however, real-world data on UPA are limited. The AD-VISE study objective is to characterize the real-world utilization patterns and effectiveness of UPA 15 and 30 mg in adults and adolescents with AD in clinical practice.

**Materials & Methods:** AD-VISE is an ongoing observational, prospective, multicountry study to assess the use of UPA in routine clinical practice for 2 years. Adult and adolescent patients (pts) receiving UPA for AD are being enrolled. Primary effectiveness outcome measures included validated Investigator Global Assessment for Atopic Dermatitis (vIGA-AD) 0/1 at month 4. Other outcome measures included Eczema Area and Severity Index (EASI), Worst Pruritus Numeric Rating Scale (WP-NRS), and Dermatology Life Quality Index (DLQI). This interim analysis (data cutoff February 27, 2023) reports baseline data and 2- and 4-month effectiveness data. Effectiveness analyses included pts that were enrolled at least 4 months by the data cutoff date or discontinued from the study; non-responder imputation with multiple imputation (NRI-MI) was used.

**Results:** Baseline analyses included 267 pts, of whom 21 (7.9%) were adolescents; effectiveness analyses included 209 patients (NRI-MI). Overall, 155 (58.1%) pts started on UPA 15 mg and 112 (41.9%) started on UPA 30 mg. Most pts in this analysis were from Canada (56.2%), followed by Russia (10.9%) and Australia (8.6%). Mean (SD) UPA exposure was 218.8 (±117.6) days; 5.6% of pts discontinued UPA and 3.7% discontinued the study. The most common reason for starting on UPA 15 mg was attempting lowest possible effective dose (42.9%) and on 30 mg, high disease burden/severity of skin symptoms (35.2%). More pts starting UPA 30 mg vs 15 mg were between 18 to <65 years old (96.4% vs 76.1%), male (61.6% vs 51.0%), had severe AD (vIGA-AD score 4: 53.6% vs 46.3%), had prurigo nodules (30.6% vs 18.4%), asthma (45.5% vs 24.5%), and prior biologic systemic therapy use (16.1% vs 10.3%) (Table 1). More than half of the pts (51.2%) achieved vIGA-AD 0/1 at month 2, and this proportion increased to 61.3% at month 4. Similarly, rate of achieving EASI 90 (month 2: 46.9%; month 4: 57.2%) and DLQI 0/1 (month 2: 35.1%; month 4: 41.3%) increased, whereas rates were maintained for ≥4-point WP-NRS improvement (month 2: 68.1%; month 4: 69.3%). Similar results were observed with other endpoints (Table 2).

**Conclusion:** Initial findings from the** AD-VISE study, the largest study to report multicountry real-world data on UPA treatment patterns and effectiveness in AD, suggest that most pts achieved clear/almost clear skin and clinically meaningful itch improvement by month 4. Because this is a real-world observational study, it was expected that physicians start with UPA dose per local label. The main reason for starting UPA 30 mg was high...
disease burden/severity of skin symptoms, whereas 15 mg was started to attempt the lowest possible effective dose. More pts starting UPA 30 mg vs 15 mg were adults, male, and had prior biologic systemic therapy use.

Table 1. Baseline demographics and disease characteristics by starting dose.

<table>
<thead>
<tr>
<th></th>
<th>UPA 15 mg</th>
<th>UPA 30 mg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years, mean (SD)</td>
<td>37.1 (18.1)</td>
<td>38.5 (13.7)</td>
</tr>
<tr>
<td>&lt;18 years, n (%)</td>
<td>21 (13.5)</td>
<td>0</td>
</tr>
<tr>
<td>18 to &lt;65 years, n (%)</td>
<td>118 (76.1)</td>
<td>108 (64.4)</td>
</tr>
<tr>
<td>≥65 years, n (%)</td>
<td>16 (10.3)</td>
<td>4 (3.6)</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>79 (51.0)</td>
<td>69 (61.6)</td>
</tr>
<tr>
<td>Duration of AD symptoms, years, mean (SD)</td>
<td>24.6 (16.7)</td>
<td>29.9 (16.0)</td>
</tr>
<tr>
<td>Asthma, n (%)</td>
<td>38 (24.5)</td>
<td>51 (45.5)</td>
</tr>
<tr>
<td>Food allergies, n (%)</td>
<td>20 (12.9)</td>
<td>17 (15.2)</td>
</tr>
<tr>
<td>Prurigo nodules, n (%)</td>
<td>28 (18.4)</td>
<td>34 (30.6)</td>
</tr>
<tr>
<td>Prior biologic systemic therapy, n (%)</td>
<td>16 (10.3)</td>
<td>18 (16.1)</td>
</tr>
<tr>
<td>Prior dupilumab use, n (%)</td>
<td>17 (11.0)</td>
<td>14 (12.5)</td>
</tr>
<tr>
<td>Prior non-biologic immunomodulating systemic therapy, n (%)</td>
<td>48 (31.0)</td>
<td>53 (47.3)</td>
</tr>
<tr>
<td>vIGA-AD, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Moderate (3)</td>
<td>73 (49.0)</td>
<td>47 (42.7)</td>
</tr>
<tr>
<td>Severe (4)</td>
<td>69 (46.3)</td>
<td>59 (53.6)</td>
</tr>
<tr>
<td>EASI, mean (SD)</td>
<td>23.6 (12.1)</td>
<td>22.0 (11.1)</td>
</tr>
<tr>
<td>WP-NRS, mean (SD)</td>
<td>7.2 (2.2)</td>
<td>7.3 (2.3)</td>
</tr>
<tr>
<td>POEM, mean (SD)</td>
<td>18.4 (6.5)</td>
<td>19.6 (6.9)</td>
</tr>
<tr>
<td>ADCT, mean (SD)</td>
<td>14.9 (6.0)</td>
<td>15.5 (6.4)</td>
</tr>
<tr>
<td>DLQI*, mean (SD)</td>
<td>14.3 (7.3)</td>
<td>15.9 (7.9)</td>
</tr>
</tbody>
</table>

ADCT Atopic Dermatitis Control Tool; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; POEM, Patient Oriented Eczema Measurement; UPA, upadacitinib; vIGA-AD, validated Investigator Global Assessment for Atopic Dermatitis; WP-NRS, Worst Pruritus Numeric Rating Scale.

*DLQI was assessed in patients ≥16 years old.
Table 2. Effectiveness endpoints at month 2 and month 4.

<table>
<thead>
<tr>
<th>Endpoint, n (%)</th>
<th>N</th>
<th>Month 2</th>
<th>Month 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>VIGA-AD 0/1</td>
<td>209</td>
<td>107 (51.2)</td>
<td>128 (61.3)</td>
</tr>
<tr>
<td>EASI 75</td>
<td>208</td>
<td>148 (71.1)</td>
<td>164 (78.8)</td>
</tr>
<tr>
<td>EASI 90</td>
<td>208</td>
<td>97 (46.9)</td>
<td>119 (57.2)</td>
</tr>
<tr>
<td>EASI ≤3</td>
<td>209</td>
<td>118 (56.6)</td>
<td>139 (66.7)</td>
</tr>
<tr>
<td>WP-NRS 0/1</td>
<td>209</td>
<td>77 (36.8)</td>
<td>86 (41.2)</td>
</tr>
<tr>
<td>WP-NRS ≥4-point reduction from baseline</td>
<td>200</td>
<td>136 (68.1)</td>
<td>138 (69.3)</td>
</tr>
<tr>
<td>DLQI* 0/1</td>
<td>196</td>
<td>69 (35.1)</td>
<td>81 (41.3)</td>
</tr>
<tr>
<td>DLQI ≥4-point reduction from baseline</td>
<td>183</td>
<td>148 (81.3)</td>
<td>160 (87.4)</td>
</tr>
<tr>
<td>POEM ≤2</td>
<td>209</td>
<td>65 (31.2)</td>
<td>66 (31.7)</td>
</tr>
<tr>
<td>POEM ≥4-point reduction from baseline</td>
<td>206</td>
<td>180 (87.4)</td>
<td>178 (86.6)</td>
</tr>
<tr>
<td>ADCT &lt;7</td>
<td>209</td>
<td>146 (69.8)</td>
<td>155 (73.9)</td>
</tr>
<tr>
<td>ADCT ≥5-point reduction from baseline</td>
<td>200</td>
<td>160 (80.0)</td>
<td>164 (81.8)</td>
</tr>
</tbody>
</table>

ADCT, Atopic Dermatitis Control Tool; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; POEM, Patient Oriented Eczema Measurement; UPA, upadacitinib; VIGA-AD, validated Investigator Global Assessment for Atopic Dermatitis; WP-NRS, Worst Pruritus Numeric Rating Scale.

*DLQI was assessed in patients ≥16 years old.
Real Life Efficacy of Upadacitinib for Moderate to Severe Atopic Dermatitis in Adolescents and Adults. Report of ten patients.

Ileana Afroditi Kleidona1, Michalis Bakakis1, Alexander Stratigos1, Stamatis Gregoriou1

1Andreas Sygros Hospital ; National and Kapodistrian University of Athens, 1st Dept. of Dermatology - Venereology , ATHENS, Greece

Introduction & Objectives: Atopic dermatitis is a complex chronic inflammatory dermatological disease. Despite the progress into the insight of pathophysiology and the new available therapies, managing moderate to severe atopic dermatitis remains an unmet medical need. Upadacitinib is an oral selective Janus Kinase-1 (JAK-1) inhibitor approved in Europe for the treatment of moderate to severe atopic dermatitis in patients aged 12 or older. The efficacy and safety of this molecule has been demonstrated in clinical trials. However, it is essential to evaluate the outcomes in real life settings because clinical studies include selected population under controlled situations. Herein, we present ten patients with moderate to severe atopic dermatitis who were treated with upadacitinib.

Materials & Methods: Among them nine were adults and one was adolescent. Four of them had moderate disease and six had severe disease. Three patients received upadacitinib 15 mg per day and seven patients received 30 mg per day. All of them previously failed therapy with cyclosporin. One patient also failed treatment with dupilumab (biologic agent) and baricitinib (JAK-1 and JAK-2 inhibitor) prior to commencement of upadacitinib. The effectiveness of therapy was evaluated at 16 weeks by the percentage of patients who achieved at least 75% improvement on the Eczema Area and Severity Index (EASI 75) and a validated Investigator’s Global Assessment for atopic dermatitis (vIGA-AD) of 0 or 1 (clear of almost clear).

Results: At baseline the EASI score ranged from 11 to 72 (median 31). At the end of 16 weeks follow-up all patients achieved EASI 75 and nine EASI 90. Moreover, seven patients achieved vIGA-AD of 0 and three vIGA-AD of 1. One patient is currently undergoing the 60th week of treatment, whereas two patients are undergoing the 52th week of treatment and still maintain the great response with clear skin. No severe adverse events (AE) were noted. Mild upper airway infections were reported by one patient. No AE led to discontinuation of therapy.

Conclusion: We report our daily practice experience of ten patients, which confirm disease control with upadacitinib in the treatment of moderate to severe atopic dermatitis recalcitrant to classical immunosuppressive agents. Furthermore, good outcomes were demonstrated with upadacitinib in one patient after failure with biological (dupilumab) and small molecule (baricitinib) treatment. We conclude that real life data confirm the effectiveness of upadacitinib in moderate to severe atopic dermatitis at 16 weeks of treatment which seems to remain durable through week 60. More data are required to further support these findings.
Burden of disease in adults diagnosed with moderate to severe atopic dermatitis in Greece (APOLO study)

Alexander Stratigos¹, Vasiliki Chasapi², Alexander Katoulis³, Efstratios Vakirlis⁴, Fotis Psarros⁵, Sophia Georgiou⁶, Dimitrios Vourdas⁷, Michael Makris⁸, Elizabeth Lazaridou⁹, Stamatis Gregoriou¹⁰, Ioannis Skiadas¹⁰, Magdalini Nakou¹⁰, Christopher Koulias¹⁰

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Introduction & Objectives:

Atopic dermatitis (AD) is a common, chronic, highly pruritic inflammatory skin disease with a substantial impact on the quality of life. However few data are available on the burden experienced by Greek patients suffering from moderate to severe AD (M2S-AD).

Materials & Methods:

The 9-month (September 2021-June 2022) cross-sectional study included patients with clinical diagnosis of M2S-AD attending for the first time 13 tertiary centers of reference experienced in the management of AD. Data on demographics, clinical characteristics, healthcare utilization, treatment patterns and burden of disease via patient reported outcomes (PROs), including Dermatology Life Quality Index (DLQI), EuroQol-5D (EQ-5D; Work Productivity and Activity Index (WAPI), Patient Oriented Eczema Measure (POEM), Peak Pruritus Numerical Rating Scale [PP-NRS©Regeneron Pharmaceuticals, Inc. and Sanofi (2017)] were recorded. We herein report the burden of disease experienced by M2S (as per Eczema Area Severity Index) adult Greek patients.

Results:

The study included 184 adult patients (51% female) with a median (Q25-Q75) age of 38.8 (24.7-52.7) years and a median EASI 16.9 (10.4-23.4). Current treatment (past 2 weeks), prior to expert consultation included topical corticosteroids (78.8% of patients), topical calcineurin inhibitors (36.4%), phototherapy (3.8%), antihistamines (56%), systemic steroids [26.1%, median course 15 days (5-30)], classical immunosuppressants (15.2%) and biologics (6.5%). Patients/disease characteristics and treatments used by severity subgroups are presented in table 1.

The median DLQI score of the patients was 12 (7.0-17.0) with 60.9% of them presenting with severe impact on their QoL. Highest impact involved the domains of symptoms and feelings [mean (SD) 4.1 (1.4)], followed by daily activity [mean (SD) 2.5(1.8)]. Median EQ-5D-3L utility index score was 0.7 (0.5-0.8) and the observed VAS 70 (50-80). Among 112 employed patients, WAPI scores for absenteeism, presenteeism, work productivity and activity
impairment were, mean (SD), 4.9% (12), 27.1% (26.3), 29.8% (27.3) and 34.2% (30) respectively. The median POEM score was 17 (12-21), while 51.6% of patients reported severe/very severe eczema. The median PP-NRS score was 7 (5-8). Interestingly, apart from pruritus, 80.4% of patients reported pain with a median intensity of 5 out of 10 (3-7), while about 30% experience pain daily. Moreover, 87.5% of patients reported sleep disturbances in the last 3 days. Controlling for baseline factors, the impact on quality of life as measured by the DLQI score was significantly associated (p<0.001), with sleep disturbances, itching intensity and pain intensity. PROs by severity subgroups are presented in Table 2.

**Conclusion:**

This is the first detailed report on the burden experienced by Greek patients with physician diagnosed M2S AD. Both patients with moderate and severe AD present with substantial itch, pain, sleep disturbances and severe impact on the quality of life, despite the use of available systemic treatments.

Table 1: Patient and disease characteristics and current treatment by severity subgroups

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Moderate AD (N=117)</th>
<th>Severe AD (N=57)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (Q25-Q75; Min-Max), y</td>
<td>39.2 (25.2-52.7; 18.1-90.2)</td>
<td>38.4 (24.3-52.5; 19.2-92.5)</td>
</tr>
<tr>
<td>BMI, median (Q25-Q75; Min-Max)</td>
<td>24.8 (21.5-27.9; 18.9-42.0)</td>
<td>26.8 (22.7-27.3; 18.4-42.2)</td>
</tr>
<tr>
<td>POEM score, median (Q25-Q75; Min-Max)</td>
<td>12.6 (8.9-16.2; 7.1-20.8)</td>
<td>26 (22.8-32.4; 21.1-60)</td>
</tr>
<tr>
<td>Age at onset, median (Q25-Q75; Min-Max), years</td>
<td>19.2 (6.3-37.4; 0.0-83.0)</td>
<td>16.4 (4.6-45.6; 0.0-71.4)</td>
</tr>
<tr>
<td>Disease duration (onset of symptoms to study entry) (Q25-Q75; Min-Max), y</td>
<td>12.1 (5.1-26.1; 0.1-62.0)</td>
<td>11.5 (4.1-22.3; 0.8-76)</td>
</tr>
<tr>
<td>BSA, median (Q25-Q75; Min-Max)</td>
<td>22 (15-40; 3-75)</td>
<td>40.0 (30-60; 20-90)</td>
</tr>
<tr>
<td>Current treatment (past 2 weeks) no. (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical corticosteroids (overall)</td>
<td>87 (75.6)</td>
<td>58 (86.6)</td>
</tr>
<tr>
<td>- protractive use (among users)</td>
<td>22 (19.3)</td>
<td>16 (27.0)</td>
</tr>
<tr>
<td>Topical calcineurin inhibitors</td>
<td>88 (83.2)</td>
<td>20 (34.4)</td>
</tr>
<tr>
<td>- protractive use (among users)</td>
<td>12 (10.8)</td>
<td>19 (32.8)</td>
</tr>
<tr>
<td>Phototherapy</td>
<td>5 (4.3)</td>
<td>2 (3)</td>
</tr>
<tr>
<td>Systemic steroids</td>
<td>26 (22.2)</td>
<td>22 (32.8)</td>
</tr>
<tr>
<td>- duration of current course, median (Q25-Q75; Min-Max)</td>
<td>14 (7-30; 1-135)</td>
<td>20 (5-50; 1-130)</td>
</tr>
<tr>
<td>Classical immunosuppressants</td>
<td>14 (12)</td>
<td>14 (20.9)</td>
</tr>
<tr>
<td>- Cyclosporin</td>
<td>14 (12)</td>
<td>13 (19.4)</td>
</tr>
<tr>
<td>Dupilumab</td>
<td>7 (6)</td>
<td>5 (7.9)</td>
</tr>
<tr>
<td>Antihistamines</td>
<td>66 (54.7)</td>
<td>39 (53.2)</td>
</tr>
</tbody>
</table>

Table 2: Patient reported outcomes in M2S AD patients by severity subgroups.
<table>
<thead>
<tr>
<th>Patient Reported Outcome</th>
<th>Severe</th>
<th>Moderate (Q25-Q75; Min-Max)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLQI score, median</td>
<td>14 (12-15; 2-29)</td>
<td>10 (5-16; 0-29)</td>
</tr>
<tr>
<td>- DLQI-10 (severe impact), no. (%)</td>
<td>50 (81.6)</td>
<td>50 (47.9)</td>
</tr>
<tr>
<td>EQ-5D-3L utility index score (Q25-Q75; Min-Max)</td>
<td>0.7 (0.6-0.8; 0.1-1)</td>
<td>0.7 (0.5-0.8; 0.1-1)</td>
</tr>
<tr>
<td>EQ-VAS score, median</td>
<td>75 (50-80; 0-100)</td>
<td>70 (50-90; 2-100)</td>
</tr>
<tr>
<td>WPAI-GH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Absenteeism, mean (SD)</td>
<td>4.7 (7.3)</td>
<td>4.3 (14.1)</td>
</tr>
<tr>
<td>Absenteeism, median (Q25-Q75; Min-Max)</td>
<td>0 (0-0; 0-28.6)</td>
<td>0 (0-6; 0-28.6)</td>
</tr>
<tr>
<td>Presenteeism, mean (SD)</td>
<td>29.5 (25.3)</td>
<td>28.8 (27)</td>
</tr>
<tr>
<td>Presenteeism, median (Q25-Q75; Min-Max)</td>
<td>20 (10-45; 0-90)</td>
<td>20 (0-40; 0-90)</td>
</tr>
<tr>
<td>Work productivity loss, mean (SD)</td>
<td>38.9 (81.1)</td>
<td>38.7 (53.1)</td>
</tr>
<tr>
<td>Work productivity loss, median (Q25-Q75; Min-Max)</td>
<td>20 (0-47; 0-100)</td>
<td>20 (0-47; 0-90)</td>
</tr>
<tr>
<td>Activity impairment, mean (SD)</td>
<td>42.4 (30.7)</td>
<td>29.3 (28.6)</td>
</tr>
<tr>
<td>Activity impairment, median (Q25-Q75; Min-Max)</td>
<td>40 (20-100; 0-100)</td>
<td>20 (0-50; 0-100)</td>
</tr>
<tr>
<td>POEM, median (Q25-Q75; Min-Max)</td>
<td>20 (15-24; 2-28)</td>
<td>16 (11-20; 1-28)</td>
</tr>
<tr>
<td>POEM-M16 (severe excursus) no (%)</td>
<td>40 (68.7)</td>
<td>49 (41.5)</td>
</tr>
<tr>
<td>PP-NRS, median (Q25-Q75; Min-Max)</td>
<td>8 (7-9; 0-10)</td>
<td>7 (4-8; 0-10)</td>
</tr>
<tr>
<td>Pain, presence no. (%)</td>
<td>51 (76.1)</td>
<td>57 (82.9)</td>
</tr>
<tr>
<td>Pain intensity (0-10 scale), median (Q25-Q75; Min-Max)</td>
<td>6 (4-8; 3-10)</td>
<td>4 (3-7; 0-10)</td>
</tr>
<tr>
<td>Frequency of pain=4 days a week</td>
<td>23 (45.1)</td>
<td>29 (29.5)</td>
</tr>
<tr>
<td>3-day Sleep VAS, presence of disturbances, no. (%)</td>
<td>64 (95.5)</td>
<td>97 (82.9)</td>
</tr>
<tr>
<td>3-day Sleep VAS, median (Q25-Q75; Min-Max)</td>
<td>5 (2.0-0; 0.2-10)</td>
<td>5 (2.7-1.10)</td>
</tr>
</tbody>
</table>
Abstract N°: 5563

Treatment and maintenance of xerotic skin using a once daily lipid replenishing cleanser and moisturizer

Chris Sibley¹, Diana Diao², Nour Dayeh³, Katie Beleznay⁴, Catherine Nicole Hawkins⁵

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Introduction & Objectives: Xerotic skin presents with dryness, scales, and flakes, which can lead to fissures, cracks and sometimes eczema. These signs and symptoms can negatively affect patients’ quality of life. The purpose of this open-label, multicentre cohort study was to evaluate the improvement of mild-to-moderate xerosis following the use of a once-daily gentle cleanser and moisturizer, over a duration of 28 days.

Materials & Methods: The study recruited subjects from 4 Canadian sites with a documented history of xerosis on the torso, arms, and/or legs. Clinical assessments were performed at baseline and end of study (Day 28 +/- 5 days) using the physician-assessed Dry Skin Classification Scale (DSCS) and the Global Aesthetic Improvement Scale (GAIS). The primary study endpoint was the proportion of subjects having at least a one-grade improvement in skin dryness, based on the DSCS.

Results: 48 Subjects were enrolled [8 males (16.67%); 40 females (83.33%)], with 47 subjects completing all study endpoints. The average age of the sample was 47.14 years (SD: 18.08). The population included Caucasian (n = 35; 72.92%), Asian (n = 8; 16.67%), other (n = 5; 10.41%) All subjects (100%) reported being entirely compliant with the once-daily application regimen. No product-related adverse events were reported. In addition, 91.49% (N = 43/47) of subjects in the per-protocol population met the primary endpoint, including: 51.06% (n = 24) of subjects demonstrating a multi-point decrease and 40.43% (n = 19) of subjects demonstrating a multi-point decrease in skin dryness. At the end of the study, 95.74% (45/47) of subjects at least “improved” based on the physician-assessed GAIS.

Conclusion: The once-daily regimen was very well tolerated in a cohort of subjects that are prone to skin irritation. The investigative cleanser and moisturizer significantly improved clinical signs of xerosis, including skin dryness.

C1 - Internal use
Efficacy and safety of tralokinumab for the treatment of moderate-to-severe atopic dermatitis in adult patients: a multicentre, real-life, retrospective study from AtopyReg® registry

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Introduction & Objectives:
Tralokinumab, a full human monoclonal antibody that specifically neutralizes interleukin (IL)-13, was recently approved for treatment of moderate-to-severe atopic dermatitis (AD). Currently, there is limited data regarding its real-life use. The aim of our study is to evaluate the efficacy and safety of tralokinumab treatment in adult patients with moderate-to-severe AD in a real-life setting.

Materials & Methods:
A multicentre, retrospective study was conducted including adult (≥18 years) patients with moderate-to-severe AD included in the Italian Atopic Dermatitis Registry (AtopyReg®) and starting tralokinumab treatment from February 2019 to May 2023. Tralokinumab was administered subcutaneously at an induction dose of 600 mg on day (D) 1 followed by 300 mg on D15 and then every two weeks. Demographic and disease characteristics, severity, and quality of life scales were collected at the baseline visit. Severity and quality of life scales, and adverse events (AEs) were registered at weeks 4 and 16. The primary endpoint was the percentage of patients achieving at least 75% improvement in Eczema Area and Severity Index (EASI) score from baseline to week 16 (EASI75). Secondary endpoints included the mean percentage reduction in both pruritus and sleep Numerical Rating Scale (P-NRS; S-NRS) and Dermatology Life Quality Index (DLQI), and the types and rates of AEs from baseline to week 16.

Results:
A total of 125 patients [75 males (60%); mean age 41.97±17.22 years] were included in the study. AD occurred since childhood (persistent AD) in 49/125 (39.2%) patients, while in 76/125 (60.8%) had directly started in adult age (≥18 years) (adult-onset AD). The most frequent AD phenotype was flexural dermatitis, observed in 89/125 (71.2%) patients. At baseline the mean of EASI score, P-NRS, S-NRS and DLQI were 23.12±2.61, 7.53±3.58, 5.24±3.58, and 15.28±8.55, respectively.
A statistically significant improvement in all endpoints was observed (p<0.0001). The safety profile was acceptable.

**Conclusion:**

This multicentre, retrospective, real-life study seems to confirm the effectiveness of tralokinumab in AD patients on all disease aspects; the safety profile was good. This data is in line with previous clinical trials.
Abstract N°: 5571

Impact of a Colloidal Oatmeal-infused Cream on Skin Microbiome and Barrier Function in Mild to Moderate Atopic Dermatitis: An Experimental Study

Alpana Mohta¹

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Introduction & Objectives: Atopic dermatitis is a common skin condition that causes dry, itchy and inflamed skin, often with a dysbiotic microbiota. The aim of this clinical research was to investigate the effects of a topical eczema cream containing 1% colloidal oat on the skin microbiome and skin barrier properties of individuals with mild to moderate eczema.

The primary objective was to evaluate the efficacy of 1% colloidal oat eczema cream compared to a standard moisturiser in improving skin microbiome and skin barrier properties. Secondary objectives included assessing changes in atopic dermatitis severity index, eczema area severity index, prevalence of Staphylococcus species and microbiome diversity at lesion sites.

Materials & Methods: Sixty-one patients were paired at random to receive either 1% colloidal oat eczema cream or a typical, unscented daily moisturiser. After a 14-day treatment phase, there was a 7-day recovery period. Skin microbiome and skin barrier properties were assessed at baseline, day 14 and day 21.

Results: At day 14, the 1% colloidal oat eczema cream significantly decreased mean scores for atopic dermatitis severity index and eczema area severity index by 55% and 59%, respectively. Treatment with 1% colloidal oat eczema cream was associated with trends towards decreased prevalence of Staphylococcus species and increased microbiome diversity at lesion sites, in contrast to treatment with the conventional moisturiser. The standard moisturiser increased hydration, but the 1% colloidal oat eczema cream significantly improved skin pH, skin barrier function and skin hydration from baseline to day 14.

Conclusion: This study demonstrates that topical treatments can have significant effects on the skin’s barrier functions and microbiota. The use of 1% colloidal oat eczema cream improves skin barrier deficiencies and enhances microbial composition, making it a promising treatment option for individuals with atopic dermatitis.
Abstract N°: 5593

Health literacy in individuals with atopic dermatitis: Revealing the extent of the problem both in the general and the clinical population

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¹University Medical Center Groningen, Groningen, Netherlands

Introduction & Objectives:

Health literacy is defined as the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions. As of today, patients are more and more considered to actively participate in their own health and health-related aspects. However, this can be complicated, especially among those with limited health literacy. When specifically looking into atopic dermatitis (AD), adequate health literacy is of major importance in understanding, treating, and managing this condition. The objective of this study was to investigate the proportion of patients with AD with limited health literacy, and the association between limited health literacy and socio-economic status (SES), quality of life (QOL) and lifestyle, in the Dutch general population and a tertiary referral center.

Materials & Methods:

Among the general population, participants with AD were identified by sending out a questionnaire in 2020 to the adult population of the Lifelines Cohort Study (n=135 950, response rate 42.8%). Functional health literacy was measured by three validated screening questions (Set of Brief Screening Questions (SBSQ)), and communicative and critical health literacy were assessed by three single questions from the validated Dutch Functional Communicative and Critical Health Literacy (FCCHL) questionnaire. Among the clinical population health literacy was measured by the Newest Vital Scale (NVS), a performance-based instrument assessing reading and numeracy skills, and by the European Health Literacy Survey Questionnaire (HLS-EU-Q16) a perception-based instrument including questions related to health care, disease prevention, and health promotion.

Results:

Of the 5 196 subjects (9.3%) with AD in the general population, 24.2% had limited functional health literacy. In addition, 48.2% and 37.2% never or occasionally talked or collected information about their condition, respectively. Among the clinical population, 322 (response rate 50.8%) patients were included. 8.0 % had a score of 0-1 on the NVS, which suggests a high likelihood of limited literacy, 12.3% scored 2 or 3 points, indicating a possibility of limited literacy. According to the HLS-EU-Q16, 32.4% had limited health literacy. Limited health literacy was associated with a lower QOL, smoking, a higher BMI, and a lower SES.

Conclusion:

A substantial proportion of the subjects with AD, both in the clinical and in the general population, reported signs of limited health literacy which was associated with a lower QOL, poor lifestyle behaviours and a lower SES. This emphasizes the need for more awareness of limited health literacy among this patient population. Further research should evaluate the influence of inadequate health literacy on health outcomes and focus on strategies to improve organizational health literacy to eventually improve patient-centered care.
Abstract N°: 5600

**Fluctuations of Skin Microbiome Throughout Treatment in Atopic Dermatitis Patients: clinical implications**

Alpana Mohta

1 Sardar Patel Medical College, DERMATOLOGY, VENEREOLOGY AND LEPROSY, Bikaner, India

**Introduction & Objectives:** Atopic dermatitis (AD) is characterized by an altered skin microbiome with S. aureus being the dominant colonizer. Treatment for AD includes emollients, anti-inflammatory drugs, and antiseptics. The aim of this study is to investigate changes in the skin microbiome during treatment for AD.

**Materials & Methods:** A longitudinal prospective study was conducted to investigate the skin microbiomes of children with moderate-to-severe AD and healthy children. Patients with AD were randomly assigned to standard treatment with emollients and topical corticosteroids or standard treatment with the addition of dilute bleach baths (DBB) and were sampled at four visits over a three-month period. The severity of AD was measured at each visit, swabs were taken from four body sites, and the composition of the microbiome at those sites was assessed using 16S rRNA amplification.

**Results:** The study included 14 healthy controls and 28 patients with AD. The patients showed high relative abundances of S. aureus, which correlated with AD severity and reduced alpha diversity. As the disease severity improved with treatment, the abundance of S. aureus decreased gradually and became similar to that of the healthy controls. After the treatment, patients who received DBB had significantly lower S. aureus abundance than those who received only standard treatment.

**Conclusion:** The skin microbiome of AD patients gradually normalizes during treatment. The addition of DBB to standard treatment significantly reduced S. aureus burden, indicating its use as a therapeutic option. Further double-blinded trials are necessary for a more in-depth study.
Investigating the Efficacy of Multistrain Synbiotic and Vitamin D3 Supplementation in Treating Atopic Dermatitis among Infants below the Age of One: A Double-Blind Randomized Clinical Trial

Alpana Mohta

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Introduction & Objectives: Atopic dermatitis (AD) is a common skin disease that frequently affects infants and is characterized by chronic and recurrent symptoms. This study aimed to evaluate the effect of multistrain synbiotic and vitamin D3 supplements on the severity of AD among infants under 1 year of age.

Materials & Methods: A randomized, double-blind clinical trial was conducted involving 70 infants diagnosed with AD. The subjects were randomly assigned to three groups: the synbiotic group, the vitamin D3 group, and the control group. The synbiotic group was given a daily dose of five drops of synbiotic in addition to routine treatment, while the vitamin D3 group received 1000 IU of vitamin D3 daily along with routine treatment. The severity of AD was evaluated using SCORing Atopic Dermatitis (SCORAD) at baseline and two months’ follow-up.

Results: The mean age of the subjects was 5.71 ± 3.4 months with 42 males and 28 females. The mean SCORAD scores were significantly reduced in both the synbiotic ($p < .001$) and vitamin D3 ($p = .001$) groups as compared to the control group after two months.

Conclusion: The results of this study suggest that multistrain synbiotic and vitamin D3 supplements may be an effective complementary treatment in reducing the severity of AD in infants, when administered in addition to routine treatments.
Abstract N°: 5626

Efficacy of Sublingual Immunotherapy using Dermatophagoides Pteronyssinus (House Dust Mite) Extract in the Treatment of Atopic Dermatitis: A Trial with Placebo Control

Alpana Mohta

1Sardar Patel Medical College, Bikaner, India

Introduction & Objectives: Atopic dermatitis (AD) is characterized by an altered skin microbiome with S. aureus being the dominant colonizer. Treatment for AD includes emollients, anti-inflammatory drugs, and antiseptics. The aim of this study is to investigate changes in the skin microbiome during treatment for AD.

Material and Method: A longitudinal prospective study was conducted to investigate the skin microbiomes of children with moderate-to-severe AD and healthy children. Patients with AD were randomly assigned to standard treatment with emollients and topical corticosteroids or standard treatment with the addition of dilute bleach baths (DBB) and were sampled at four visits over a three-month period. The severity of AD was measured at each visit, swabs were taken from four body sites, and the composition of the microbiome at those sites was assessed using 16S rRNA amplification.

Results: The study included 14 healthy controls and 28 patients with AD. The patients showed high relative abundances of S. aureus, which correlated with AD severity and reduced alpha diversity. As the disease severity improved with treatment, the abundance of S. aureus decreased gradually and became similar to that of the healthy controls. After the treatment, patients who received DBB had significantly lower S. aureus abundance than those who received only standard treatment.

Conclusion: The skin microbiome of AD patients gradually normalizes during treatment. The addition of DBB to standard treatment significantly reduced S. aureus burden, indicating its use as a therapeutic option. Further double-blinded trials are necessary for a more in-depth study.
Topical GZ21T attenuates skin lesions and pruritus in an atopic dermatitis preclinical model

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Introduction & Objectives:

Atopic dermatitis (AD) is a chronic inflammatory skin condition characterized by recurrent eczematous lesions, intense pruritus, and barrier dysfunction. Non-steroidal, topical therapies are needed in the management of AD.

Materials & Methods:

In this study, we evaluated GZ21T, a novel agent composed of curcumin, isovanillin, and haramine, in a murine model of AD. A total of 16 male C57BL/6 mice were initially separated into control (n=8) and GZ21T treatment (n=8) groups. Mice of both groups were treated daily for 12 days with MC903 (4 nmol in 20 ml ethanol) on the right ear and ethanol (20 ml) on the left ear. Each day, 4 hours after the application of MC903 and ethanol, mice of the control group received a vehicle cream, and mice of the GZ21T group received GZ cream.

Results:

We find that in both groups, the MC903-treated ears showed visible changes in ear appearance, including increased redness, dryness, swelling, and hypervascularity, starting on day 6. Ear thickness was measured daily, and scratching behavior was recorded every 4 days for 30 minutes. Percent change in ear thickness showed that GZ21T treatment significantly decreased the rate of ear thickening of the MC903-treated ear, starting on day 5 (p<0.001), with this reduction persisting at day 12 (p<0.0001) of the observation period. Assessment of scratching behavior showed that itch bouts were significantly reduced in the GZ21T treatment group by day 12 (p<0.001).

Conclusion:

These results indicate that GZ21T exhibits promising potential as a topical agent for the treatment of eczematous lesions and pruritus in AD.
Dupilumab for treatment of atopic dermatitis in children and adolescents: a systematic review and meta-analysis

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¹Federal University of Health Sciences of Porto Alegre (UFCSPA), ²Massachusetts General Hospital, United States, ³Universidade Federal do Amazonas (UFAL), Brazil, ⁴Universidade Federal de São Paulo - UNIFESP, Brazil, ⁵Universidade Federal do Rio de Janeiro - Macaé, Brazil, ⁶Universidade Federal de Pelotas (UFPEL), Brazil

Introduction & Objectives:

Dupilumab is a monoclonal antibody with action in the JAK-STAT pathway [1] that has been long used for the treatment of asthma in children and adolescents and has recently been approved by the U.S. Food and Drug Administration (FDA) for the treatment of atopic dermatitis (AD) in pediatric patients. In this single-arm meta-analysis, we assess the efficacy of dupilumab for severe-to-moderate AD in patients aged 0-18 years old.

Materials & Methods:

Clinical trials and observational studies that analyzed ≤18 years old patients with moderate-to-severe AD using dupilumab were searched on Pubmed, Embase, and Cochrane Central. Outcomes of interest were Eczema Area Severity Index (EASI) improvement ≥50% (EASI-50), EASI improvement ≥75% (EASI-75), Investigator’s Global Assessment score of 0 or 1 (IGA-0/1), and conjunctivitis. Subgroup analyses were performed for patients aged 0-5, 6-11, and 12-18 years. Statistical analysis was performed using OpenMeta. Heterogeneity was assessed using I² statistics.

Results:

A total of 19 studies comprising 905 patients were included. Ages ranged from 0 to 18 years. EASI-50 was achieved by 76.2% (95% CI 64.3%-88.1%; I²=94.17%) of patients. EASI-75 was achieved by 57.0% (95% CI 45.5%-68.4%; I²=85.57%) of patients. IGA-0/1 was achieved by 41.9% (95% CI 26.6%-57.1%; I²=92.36%) of patients. Conjunctivitis was observed in 9.5% (95% CI 7.7%-11.4%; I²=0) patients.

Conclusion:

The results statistically corroborate the already-known efficacy of the newly FDA-approved dupilumab for managing AD in children and adolescents. However, due to the small sample size and high heterogeneity, more studies are encouraged to confirm this hypothesis for the general population.
Abstract N°: 5645

Atopic dermatitis and psoriasis vulgaris as concurrent conditions - a case report

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Introduction & Objectives: Atopic dermatitis and psoriasis are recurrent, chronic inflammatory conditions, that are associated with significant burdens, strongly influencing the patient’s quality of life. Clinically, there are some clear differences between the two entities, but both are characterised by erythematous-squamous lesions that vary in intensity and distribution, according to severity. In addition, the immunopathogenic pathways found to underlie the two, the Th1/Th17 pathway in psoriasis, and the Th2,Th 22 and even Th1 and Th17 pathways in atopic dermatitis, have established a clear therapeutic distinction. However, in our day-by-day clinical practice, there are numerous cases of intersection between these two pathologies, increasing the difficulty of diagnosis, but especially of establishing an effective, sustainable and personalised treatment.

Materials & Methods:

Results: In this regard, we report the case of a 21-year-old female patient, presenting to our department with an intensely pruriginous, generalized truncal eruption, consisting of vaguely demarcated erythematous-squamous patches and plaques, on a background of cutaneous xerosis, associated with facial involvement, with edema, erythema and desquamation, cheilitis and right eye conjunctival hyperemia, arising after an upper respiratory tract infection. The patient states a childhood onset of these episodes, with repeated exacerbations from adolescence until now. Her personal pathological history includes an adenoidectomy during early years of childhood. The patient underwent 2 punch-biopsies, with the diagnosis of psoriatic dermatitis in 2017 and psoriasis vulgaris in 2020, followed numerous topical treatments, intermittent courses of corticotherapy, treatment with Methotrexate in doses of 7.5-10 mg/ML/week from December 2020 to June 2022, without sustained therapeutic success, and one month of treatment with Etanercept in March 2023, discontinued at the beginning of the current eruption. During hospitalization, it was decided to initiate therapy with Medrol 16mg/day and Cyclosporine 200mg/day, with favorable evolution and progressive improvement of her symptoms.

Conclusion: The paradoxical eczematous reactions during anti-TNF alpha therapy are now currently discussed regarding the possible Th1-interferone gamma involvement related event. The history of atopic dermatitis must be an indication for an appropriate therapy and cyclosporine can be chosen as a treatment for remission induction for both diseases.

Whilst the majority of patients diagnosed with psoriasis vulgaris have a well-defined course, cases of psoriasis vulgaris overlapping with atopic dermatitis have been reported. The intertwine of these two entities complicates therapeutic management and keeps the patient in a vicious circle of short remission periods and troublesome exacerbations.
The Benefits of a Ceramide-Containing Skincare Routine as Part of the Treatment of Atopic Dermatitis, Psoriasis, and Xerosis

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¹Hospital Universitario Ramón y Cajal, Madrid, Spain, ²L’Oreal España SA, Madrid, Spain

Introduction & Objectives: Atopic dermatitis (AD), psoriasis and skin xerosis are frequent reasons for consultation in dermatology. Skincare, as adjunctive or monotherapy, is often utilized to help address and manage the symptoms by hydrating the skin. However, underlying these conditions is an association with a disrupted skin barrier and altered barrier lipid composition, which simple hygiene and hydration products do not directly address. The implementation of adapted skincare products that restore and maintain the skin barrier has scientifically demonstrated its benefits in skin that presents with alterations in the skin barrier function. The main objective of this study was to evaluate the benefits of incorporating a skincare routine containing ceramides (1, 3, and 6-II) in the treatment plan of patients with AD, psoriasis and xerosis.

Materials & Methods: The multicenter, prospective intervention study in enrolled 312 adult patients with mild to moderate AD (n=109), psoriasis (n=97) and xerosis (106). Physicians evaluated skin condition at baseline using the appropriate scale and enrolled those meeting the inclusion criteria SCORAD <40 for AD, PASI < 10 for chronic plaque psoriasis and VAS <4 for xerosis. Physicians assessed condition severity using the relevant scale, symptom including itching, stinging/burning, and pain, quality of life assessment (DLQI), tolerability, and patient satisfaction at the baseline (D0) visit and final visit (D4 weeks). During the study period, patients were instructed to use the ceramide-containing Moisturizing Cleanser 1/day and Body Cream at least 1/day in addition to previously prescribed treatments (if relevant).

Results: Of the 312 patients enrolled, 42.6% were previously prescribed treatment (56.0% for AD; 56.7% for psoriasis; 16.0% for xerosis) and continued use during the study complemented with the ceramide-containing daily routine. At week 4, subjects showed significant improvement in condition severity: SCORAD (n=91) -19.38 points (D0 31.65 (SD12.32)/D4 12.27 (SD10.81); p < 0.001); PASI (n=71), -2.77 points ( D0 4.43 (SD4.74)/D4 1.66 (SD2.11), p < 0.001); Xerosis (n=94) improvement in all parameters (p<0.001): dryness, desquamation, roughness, pruritus, burning/stinging, pain and erythema. Overall, (n=203) an improvement in quality of life was observed by 3.22 points (p<0.001). 96.23% of the patients (n=292) found the routine satisfactory or highly satisfactory.

Conclusion: This study demonstrates the ceramide-containing skincare routine (hygiene + daily hydration) is effective and well tolerated as a monotherapy or as a complement to the treatment of AD, psoriasis, and xerosis, all conditions associated with barrier disruption. Patients experienced a significant reduction in the signs and symptoms with a high degree of satisfaction and an improvement in their quality of life.
**Abstract N°: 5701**

**Sensitive areas in atopic dermatitis: is Dupilumab less effective on head and neck? A single-centre retrospective study.**

Gabriele Perego¹, Italo Francesco Aromolo¹, Martina Zussino², Luca Valtellini¹, Angelo Valerio Marzano¹, ², Silvia Ferrucci*²

¹University of Milan, Department of Pathophysiology and Transplantation, Milan, Italy, ²Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Dermatology Unit, Milan, Italy

**Introduction & Objectives:**

Atopic dermatitis (AD) is an inflammatory disease of the skin with a chronic-recurrent course. Dupilumab is an all-human monoclonal antibody that binds the IL-4Rα receptor subunit, resulting in inhibition of IL-4 and IL-13 signaling. It is approved for the treatment of moderate to severe AD. Real-life data published in the literature suggest a varied response to the drug depending on the affected body sites, highlighting difficulties in achieving a response in the head-and-neck region. AD in sensitive areas negatively impacts quality of life (QoL).

Our study aimed to evaluate sensitive areas involvement in a cohort of patients with moderate-to-severe AD, Dupilumab effectiveness in their treatment and the impact of sensitive areas AD in terms of QoL.

**Materials & Methods:**

We conducted a retrospective single-centre study, selecting 616 patients treated with Dupilumab 300 mg q2w who had AD in at least one sensitive area (head and neck, hands, genital region). We carried out a dynamic follow-up of the patients, distinguishing cases of continuous AD since the start of treatment from cases of AD relapse after initial resolution. The impact on QoL was assessed using the Dermatology Life Quality Index (DLQI) and the Atopic Dermatitis Control Tool (ADCT) questionnaires.

**Results:**

Results showed that at baseline (T0), 552 (89.6%) patients had facial involvement, 484 (78.6%) had hand involvement, and 187 (30.4%) had genital involvement. The prevalence of AD in specific sensitive areas at T0 was consistent with previous literature.

Dupilumab demonstrated good effectiveness in resolving AD on the hands and genital area, with rapid response observed as early as the first follow-up after 4 months of treatment. The non-responder rate averaged around 15% for AD on the hands and 2.5% for AD in the genital area. However, Dupilumab was less effective in the head-and-neck region (figure 1). Approximately 25% of patients responded within 4 months of therapy, and around 40% experienced facial AD resolution within 12 months. A plateau in facial involvement was reached from the second year, with about half of the patients maintaining clinical signs of localized AD on the face and neck. From the second year of follow-up, the number of patients experiencing AD relapse gradually increased among those with facial involvement (figure 2). Similar trends were observed in non-responding patients with hand involvement.

Comparing average DLQI and ADCT scores between responder and non-responder groups, significantly higher scores were observed in the non-responder group at 4, 12, and 24 months, indicating a greater impact on QoL (table 1).

**Conclusion:**
Our study confirms the low effectiveness of Dupilumab in treating AD on the head and neck, which can be considered a difficult-to-treat area. It provides clinically relevant data for determining the appropriate timing of potential therapeutic switches to emerging AD treatments as alternatives to Dupilumab. Additionally, the study prompts consideration of appropriate first-line therapies for moderate-to-severe AD with facial involvement in patients unresponsive to traditional systemic treatments. Using small molecules like JAK inhibitors instead of anti-IL4 and anti-IL13 monoclonal antibodies may be worth considering, especially for patients with a long-standing history of facial involvement.

![Figure 1](image1.png)

![Figure 2](image2.png)

### Table 1

<table>
<thead>
<tr>
<th>Atopic Dermatitis Impact on Quality of Life</th>
<th>Head and neck</th>
<th>Hands</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLQ</td>
<td>ADCT</td>
<td>DLQ</td>
</tr>
<tr>
<td>Responder M4</td>
<td>3.67 (±4.07)</td>
<td>4.04 (±4.10)</td>
</tr>
<tr>
<td>Non-responder M4</td>
<td>5.46 (±5.15)</td>
<td>6.45 (±5.99)</td>
</tr>
<tr>
<td>p R-M4 vs NR-M4</td>
<td>0.0001</td>
<td>0.0001</td>
</tr>
<tr>
<td>Responder M12</td>
<td>2.82 (±3.63)</td>
<td>3.43 (±4.05)</td>
</tr>
<tr>
<td>Non-responder M12</td>
<td>4.11 (±4.44)</td>
<td>5.25 (±4.32)</td>
</tr>
<tr>
<td>p R-M12 vs NR-M12</td>
<td>0.0005</td>
<td>0.0001</td>
</tr>
<tr>
<td>Responder M24</td>
<td>2.10 (±2.73)</td>
<td>3.06 (±3.59)</td>
</tr>
<tr>
<td>Non-responder M24</td>
<td>3.21 (±3.22)</td>
<td>4.64 (±3.09)</td>
</tr>
<tr>
<td>p R-M24 vs NR-M24</td>
<td>0.0012</td>
<td>0.0002</td>
</tr>
</tbody>
</table>
Pregnancy outcome in patients with atopic dermatitis treated with dupilumab - clinical experience of three centres

Joana Xarà1, Pedro Farinha2, Ana Maria Lé3, Bruno Duarte2, Tiago Torres3, 4, Margarida Gonçalo1, 5

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Introduction & Objectives:
Atopic dermatitis (AD) typically worsens during the second and third trimesters of pregnancy and systemic therapy is presently restricted to corticosteroids, cyclosporine and azathioprine. Dupilumab, a highly effective and safe drug for the treatment of AD, has been used only in few cases of pregnant/breastfeeding women. Although there is evidence of transplacental diffusion of monoclonal antibodies especially during the third trimester of pregnancy, no maternal or fetal adverse outcomes have been reported with dupilumab.

This study aims to describe the use of dupilumab during pregnancy and breastfeeding in AD.

Materials & Methods:
We conducted a retrospective study of severe AD treated with dupilumab during pregnancy and breastfeeding in three tertiary medical centres, evaluating demographic and clinical data from patients and their newborns.

Results:
Five women (mean age 31.8 ± 6.1 years) with moderate-to-severe AD (mean EASI score 29.1 ± 13.9) non-responsive to several classical therapies and with very good response to dupilumab (EASI score ≤ 5 at onset of pregnancy) became pregnant after 4-31 months of therapy (mean 15 ± 11.5 months). Two patients maintained dupilumab throughout the full course of their pregnancy, whereas two were exposed only during the first and/or second trimester. Good control of AD obtained with Dupilumab was maintained during pregnancy with no additional adverse events.

There were 2 full-term non-eventful pregnancies, with vaginal eutocic deliveries of healthy newborns one with normal length and weight (3600g) and the other with a low weight (2170g). Both have been breastfed for an average of 6.5 months, with a proper development and weight gain, while the mothers continued dupilumab treatment. Another woman exposed to dupilumab during the first and second trimesters had a dystocic delivery (vacuum-assisted) at week 38, giving birth to a healthy baby with normal length and weight. One patient, currently on week 29 of pregnancy, was on dupilumab during the second trimester with no complications and normal routine ultrasounds.

One woman with epilepsy and an unplanned pregnancy under treatment with sodium valproate suffered a miscarriage at week 9.

Conclusion:
Apart from a miscarriage in a patient also medicated with a well-known teratogenic agent, pregnancy progressed...
normally in 4 other patients under dupilumab, with no worsening of AD even though one patient stopped therapy in the third trimester. Full term-pregnancies with delivery of normal healthy babies occurred in the 3 patients who completed their pregnancy, and 2 newborns have a normal development with breastfeeding under dupilumab. These results support other data that have shown the safety of dupilumab use during pregnancy and breastfeeding.
Abstract N°: 5807


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Introduction & Objectives: Dupilumab is a monoclonal antibody that inhibits IL4/IL13 interleukin signaling indicated for moderate-to-severe atopic dermatitis (AD) with an important impact on signs and symptoms with good safety, but few long-term efficacy and safety data are available. However, there are few long-term efficacy and safety data.

The aim of this study is to evaluate efficacy and safety of dupilumab for up to three years after treatment initiation.

Materials & Methods: We collected data from patients ≥12 years with moderate-to-severe AD who started dupilumab at the Dermatology Clinic of the Turin December 2018 and October 2022 and evaluated them for up to 3 years. MeanEASI score at baseline, EASI75, EASI90, meanNRSpp, meanNRSsd, meanPOEM, meanDLQI were evaluated at baseline (T0), at 16 weeks (T1), at 32 weeks (T2), at one year (T3), at two years (T6), at three years (T9).

Results: At baseline out of 418 patients collected 226 were male (53.94%), the mean age was 39.2 years (ds 17.43), the mean age of onset of AD was 13.5 years (ds 20.6). 226 (53.94%) were males, mean age was 39.2 (sd ± 17.43) years old and mean age of onset of AD was 13.5 (sd ± 20.6) years old.

271 patients of 418 (65.9%) have childhood onset, 149 (37.9%) patients have family history of atopy, 25 patients (8.8%) had manifestation of prurigo escoriata, 96 patients (23.0%) had history of allergic conjunctivitis, 79 patients (19.2%) had recurrent herpetic infections, 8 patients (1.9%) had parasitic infections, and 3 patients (0.73%) had diagnosis of ichthyosis.

All patients performed topical steroid, 46.6% topical immunomodulator, 10.2% phototherapy, 96% systemic steroid, 84% cyclosporine and 9% performed omalizumab.

A progressive decrease in the EASI value is observed: 23.64 at baseline (T0) (ds 10.44), 3.69 (ds 4.95) at T1, 2.31 at T9 (ds 3.18). Similar trends are observed in the analysis of the mean DLQI value: 14.83 (ds 7.16) at baseline (T0), 4.71 (ds 4.96) at T1 and 2.31 (ds 3.18) at three years (T9).

Achievement of EASI75 and EASI90 was also assessed: at T1 75.58% of patients achieved EASI75 and 53.49% EASI90; at T2 80.26% achieved EASI75 and 53.72% EASI90; at T9 92.55% achieved EASI75 and 80.85% EASI90.

As for quality of life, DLQI 0/1 was achieved at T1 in 68.06% of patients (228 of 335 patients) and at T9 in 61.7% (58 out of 94 patients).

Mean NRSpp ≤ 4 was achieved at T1 in 71.3% of patients (236 out of 331 patients) and at T9 in 91.5% (86 out of 94 patients).

The most common adverse event was conjunctivitis occurring in 13% of patients on average at each timepoints analyzed.
Conclusion: Strength of this study is definitely the sample size and the results based on continuous treatment with Dupilumab for up to 3 years.

This real-world study shows that the efficacy of dupilumab is maintained and improves over time, with an excellent safety profile and without an increase in adverse effects with long-term treatment, supporting the long-term continuous use of Dupilumab in this chronic and debilitating disease.
The impact of molecular diagnostics in hand dermatoses

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Introduction & Objectives:

It has always been challenging to diagnose psoriasis and eczema of the hands. Fortunately, molecular disease classifier (MC) have been introduced in dermatology. This cohort study with occupational dermatology patients was started in 2020 and is the largest collective of patients receiving MC for differentiation of both diseases. The aim is to investigate the influence of MC on disease severity and course, quality of life (QoL), therapies and occupational status.

Materials & Methods:

285 patients were included in the study. The probability of psoriasis vs. eczema was determined based on the expression of the genes NOS2 and CCL27. RNA is extracted from formalin-fixed paraffin embedded tissue and the method is therefor applicable in addition to conventional histopathological analyses. Studies showed a test sensitivity of 92% and specificity of 100%. Patients are then being followed-up over 3 years and data on clinical (e.g. severity, therapies) and patient reported outcomes (e.g. quality of life, sick leave) are collected. To determine the influence of MC it will then be compared to an existing cohort without use of MC.

Results:

As of May 2023, 153 men and 132 women from 62 departments of dermatology and dermatological practices throughout Germany were included. The mean age was 50.5 ±12.3 years. Skin disease had persisted for a mean of 7.2 years with a high range (0.5-48 years). In 90% the hands were affected, mainly the palms (69%), interdigital spaces (40%) and backs (28%).

The MC decided in 2/3 in favor of eczema (n=192), ¼ (n=69) in favor of psoriasis; 6.6% (n=19) remained ambiguous. Clinicians diagnosed eczema in 35% (n=101) and psoriasis in 23% (n=67). In 106 cases (39%), the diagnosis was clinically unclear at study entry. By using MC, 95% of these cases received a diagnosis. Clinical and molecular diagnoses were concordant in only 36% of participants (Cohen’s k = .04 (95%-confidence interval (CI): -0.02-0.1)). A weak statistically correlation can be seen ($\chi^2$(4)=11.47, p=.02, Cramers V=.15, n=272).

Histopathological results were available for half of the patients and diagnosed eczema in 49% (n=73), psoriasis in 28% (n=42); 22% (n=34) were unclear. Concordance was slightly higher but at the same time showed a higher dispersion (Cohen’s k = .04 (95%-CI: 0.01-0.24). Correlations were again weak ($\chi^2$(4)=10.46, p=.03, Cramers V=.19, n=146).

Conclusion:

The use of molecular diagnostics reduced the number of unclear cases significantly and helped to confirm a diagnosis in occupational dermatology. Weak associations with existing diagnostics such as histopathology speak for the novelty of this approach.
Abstract N°: 6004

Absolute EASI improvements over 16 weeks in patients with moderate-to-severe atopic dermatitis treated with lebrikizumab

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Introduction & Objectives:

Lebrikizumab (LEB) is a monoclonal antibody that binds with high affinity and slow off-rate to interleukin (IL)-13, thereby blocking the downstream effects of IL-13 with high potency. The efficacy of LEB monotherapy for patients with moderate-to-severe atopic dermatitis (AD) as the percentage of improvement in the Eczema Area and Severity Index score (EASI) (EASI 75 and EASI 90) has been established in previous studies [1]. However, attainment of absolute EASI thresholds indicative of mild disease or clear/almost clear skin may provide additional clinically meaningful information for patients and physicians about the response to LEB treatment. This post-hoc analysis examined the percentage of patients in the ADvocate1 (ADv1) and ADvocate2 (ADv2) trials achieving absolute EASI scores of ≤7 (mild) or ≤1 (clear/almost clear) in the overall population and stratified by different baseline EASI severity subgroups (16–21 [moderate], 21.1–50 [severe], and >50 [very severe]) [2].

Materials & Methods:

Adults (≥18 years of age) and adolescents (12 to <18 years of age, weighing ≥40 kg) were randomized 2:1 to LEB monotherapy (N=564) or placebo (PBO; N=287) for 16 weeks. LEB was given as a 500 mg loading dose at baseline and Week 2, followed by 250 mg LEB every 2 weeks (Q2W). Eligible patients had moderate-to-severe AD, with an EASI score of ≥16 at baseline. ADv1 analyses were performed on the intent-to-treat population. ADv2 analyses were performed on a modified population, excluding 18 patients (from a single study site) whose eligibility could not be confirmed. Therefore, analyses were performed on the pooled modified population of ADv1 and ADv2 patients. The proportion of patients who achieved an EASI score of ≤7 or ≤1 over 16 weeks was assessed for the overall pooled ADv1&2 population, and subgroups with baseline EASI of 16–21 [moderate], 21.1–50 [severe], and >50 [very severe] [2].

Results:

In the overall ADv1&2 populations, a significantly greater proportion of patients treated with LEB achieved EASI ≤7 at Week 16 compared with PBO (54% [n=307] vs 18% [n=52], p<0.001; Fig 1A). Of the 163 patients on LEB with moderate baseline EASI (16–21), 64% (n=104) achieved EASI ≤7 by Week 16 compared with 38% PBO (n=27, p<0.001; Fig 1B). For patients with severe baseline EASI (21.1–50), 52% of patients treated with LEB (n=185) achieved EASI ≤7 at Week 16 compared with 13% PBO (n=25, p<0.001; Fig 1C). For patients with very severe baseline EASI (>50), 43% of LEB patients (n=18) achieved EASI ≤7 compared with 0% PBO (p<0.001; Fig
1D). For all groups, a significant difference was seen as early as Week 4. A significantly greater proportion of patients treated with LEB also achieved EASI ≤1 at Week 16 compared with PBO (20% [n=113] vs 4% [n=10], p<0.001; Fig 2A). Similar proportions of patients treated with LEB in each baseline severity subgroup achieved EASI ≤1 at Week 16 (moderate 20% [n=33] vs 9% [n=6], p<0.05; severe 20% [n=73] vs 2% [n=4], p<0.001; very severe 17% [n=7] vs 0%, p<0.05; Fig 2C-D).

**Conclusion:**

Regardless of baseline severity, over 50% of patients treated with LEB 250 mg Q2W monotherapy for 16 weeks achieved an EASI score indicating mild AD and approximately 20% achieved an EASI score indicating clear/almost clear skin.

**References:**

Introduction & Objectives:
Cutaneous warts are benign proliferative lesions that occur at any ages in human lives and are caused by human papilloma virus. In immunocompetent people, warts are harmless and resolve as a result of natural immunity within months or years.

Materials & Methods:
A 45-year-old male with no medical history presented for an oval erythematous-squamous pruritic plaque present for a fortnight from no evident cause. On clinical examination, an erythematous vesicular plaque, excoriated in places and measuring 2 cm in length, was noted on the palmar surface of the first interdigital commissure of the left hand. this lesion was centred by a keratotic skin tumour with a papillomatous surface.

Results:
A skin biopsy was performed revealing a wart associated with perilesional eczematous remodelling and therefore the diagnosis of Meyerson phenomenon arising around a wart was made.

Conclusion:
Meyerson’s phenomenon is an uncommon clinical condition that consists of an eczematous reaction occurring around a preexisting melanocytic nevus.

This condition is typically seen in the trunk, the root of the limbs (and more rarely on the extremities) of healthy young (average age 25 years) males.

The perilesional eczema is clinically typical, with a scaly appearance of the nevus surface and a peri-lesional inflammatory halo, with a very variable pruritus.

The etiology of this condition is unknown. Some suggest that the mechanism is due to the interaction between CD4 T lymphocytes and increased expression of intercellular cell adhesion molecule 1 (ICAM-1).

This phenomenon has been reported in relation to melanocytic lesions in more than 50 cases. However Meyerson phenomenon is not limited to benign melanocytic nevi, it has also been described around atypical nevi and nonmelanocytic lesions on a few occasions such as seborrheic keratosis, molluscum contagiosum, dermatofibromas, stucco keratosis, lentigo, keloid, and insect bites, as well as basal cell and squamous cell carcinomas.

Meyerson phenomenon is rarely mentioned in the dermatology literature especially in nonmelanocytic lesions.

To the best of our knowledge, meyerson’s phenomenon has never been reported in warts.
Abstract N°: 6083

McGill Adult Atopic Dermatitis Digital Outcomes (MAADD) Study: Development and Usability Testing of the EczemaQ Mobile Application

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Introduction & Objectives:
The challenge of atopic dermatitis (AD) management is compounded by the brevity of dermatology appointments and the complexity of information exchange. Limited resources at points of care lead patients to resort to unvalidated digital resources. To improve healthcare delivery, clinicians and patients co-developed EczemaQ, a mobile health application. The objective is to integrate stakeholder feedback in the development and usability testing of EczemaQ.

Materials & Methods:
EczemaQ was developed based on patient-identified themes using a participatory research approach. A mixed methods convergent study is being used to optimize and validate EczemaQ with patients; quantitative and qualitative data are collected in parallel and used for triangulation. The Technology Acceptance Model (TAM) framework is used to evaluate user acceptance of EczemaQ quantitatively with 31 questionnaire items on a 5-point Likert scale; achieving at least 70% of the maximum score indicates high agreement. Qualitative data collected through focus groups is inductively coded using themes from the data and structured by the five stages of Framework Analysis.

Results:
In the development phase, key themes identified by the patient committee included the need for reliable and up-to-date information on AD, a tool to track medications and flare symptoms, and the lack of resources in French or with skin-of-colour representation. Accordingly, EczemaQ presents evidence-based, interactive, and digestible bilingual educational content (English and French) through multimedia forms to facilitate AD self-management. Disease tracking is achieved through a comprehensive approach that includes the use of photos, notes, clinic visit documentation, a personalized body map, and patient-reported outcomes.

The first iterative user testing round included 14 participants meeting the U.K. Working Party’s AD diagnostic criteria. The age range was between 19 and 65 years, with a median Patient-Oriented Eczema Measure (POEM) score of 12.5, indicating moderate AD. The median Dermatology Life Quality Index (DLQI) score was 11, indicating significant impacts on the patients’ lives. As measured by TAM 2, user acceptance of EczemaQ was medium-high (mean±SD) in the areas of perceived ease of use (3.70±0.73), usefulness (3.73±0.66), content satisfaction (3.83±0.74), enjoyment (3.65±0.75), satisfaction and tendency to recommend (3.92±0.83), with an overall score of 3.92±0.82 on 5-point Likert scales. Most participants showed relatively high Patient Activation Measure® levels for AD management. Recurring comments from semi-structured focus groups suggest the following themes: 1) appreciation of having abundant information in one place; 2) desire for a more specific design for self-monitoring and management; 3) a preference for the BodyMap feature to track flares; 4) the importance of personal...
treatment and disease duration (thus varying information needs), in determining the app’s usefulness. Using the “following a thread” method, the findings suggest exploring EczemaQ further among newly diagnosed patients as a potential bridging tool between primary care and dermatology.

Conclusion:

The ongoing iterative development of EczemaQ will optimize this tool based on user needs, provide insights into patient activation and technology acceptance, and improve the quality of patient care.
Introduction & Objectives:

Atopic dermatitis (AD) is a chronic, inflammatory and pruritic skin disease, with a prevalence of 1-3% among the adult population. Its therapeutic approach can be really challenging. The appearance of new therapies in the market allows a high percentage of patients to achieve a significant control, however, not all of them reach that goal. The different options we currently have allow us different approaches, either doing a specific inhibition with biologics or a more broad one with jak inhibitors.

Long-term real world data on efficacy and safety with the latter, namely Upadacitinib, is lacking in the literature.

The objective of this study is to assess the effectiveness and safety of upadacitinib, at long term, in a real clinical setting.

Materials & Methods:

We present a series of 15 moderate-to-severe AD patients from 11 Spanish hospitals who started Upadacitinib as compassionate use, and have been treated for at least 24 months. Data collected included age, time of evolution of the disease, personal history (comorbidities), and previous systemic/biological treatments. Disease severity was measured by SCORAD, EASI, BSA and Pruritus VAS scores at the baseline visit, and at follow up weeks 4 and 16. Quality of life was assessed with DLQI. Adverse effects related to the drug and the following analytical parameters were collected: haemoglobin, eosinophils, total IgE, CPK, cholesterol, LDH, GGT, GOT and GPT

Results:

The mean age of our series was 28.67 (SD=12.36) years old (12-56). 60,00% of the patients were male. The median time of evolution of the disease was 19.67 (SD=8.63) years (4-40). The mean weight was 66.16kg (SD = 15.53) and the BMI was 23.22 (SD = 4.65). Concomitantly atopic diseases were present in the following proportions: nasal polyps 0%, conjunctivitis 33,33%, asthma 46,67%, allergic rhinitis 46,67% and food allergies 40,00%. 100% of the patients had received previous systemic corticosteroids, 93,33% cyclosporine, and 80,00% Dupilumab. The mean baseline SCORAD was 57.75 (SD=17.87), EASI 26.16(SD=7.63), DLQI 19.17 (SD=5.64), PGA 3.79 (71,42%)
PGA 4) and the pruritus VAS was 7.60 (SD=1.40).

At week 104, EASI diminished to 1.2 (SD=2.1), SCORAD to 4.56 (SD=5.78) and pruritus VAS reduced to 1.3 (SD=2.74). 98% of the patients reached an EASI 75 at week 104 and 75% an EASI 90. The safety profile was favourable. 4 patients (26.67%) reported some mild adverse events. There was discontinuation of the drug in 3 cases. No laboratory abnormalities were observed during follow-up.

**Conclusion:**

The patients included in the Spanish AD upadacitinib compassionate use program had an important baseline severity. They had a clinical history of multiple treatment failures, including dupilumab in more than 90% of them. In our series, upadacitinib significantly and rapidly improved the signs and symptoms of AD, as well as QoL, which were sustained along the time. In fact, despite the initial severity, the results in real practice are superior to those reported in clinical trials. The treatment was well-tolerated, with no severe adverse events.
Abstract N°: 6113

Long-Term Safety of Upadacitinib in Atopic Dermatitis Stratified by Age

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Introduction & Objectives: The safety and efficacy of upadacitinib (UPA) was well documented in previous clinical studies in patients with atopic dermatitis (AD); however, long-term safety stratified by age group is less well known. The objective of this integrated analysis of three ongoing UPA clinical studies in AD was to evaluate long-term safety for up to 4 years of UPA 15 and 30 mg by age group in the overall long-term global and US populations.

Materials & Methods: Data from three ongoing randomized, double-blinded, placebo-controlled, phase 3 trials were included (Measure Up 1, Measure Up 2, and AD Up). All 3 studies enrolled adults and adolescents with moderate-to-severe AD who were randomly assigned (1:1:1) to UPA (15 or 30 mg) or placebo once daily as monotherapy (Measure Up 1, Measure Up 2) or in combination with topical corticosteroids (AD Up). At week 16, patients receiving UPA 15 or 30 mg during the double-blinded period continued their assigned treatment in the long-term blinded extension (BE) period, whereas patients receiving placebo were re-randomized 1:1 to receive either UPA 15 or 30 mg in the BE period. Treatment-emergent adverse events (AEs) and adverse events of special interest (AESI) were evaluated as exposure-adjusted rates per 100 patient-years (PY) for the entire treatment period (up to 4 years).

Results: A total of 2693 (6286.3 PY) adults and adolescents (UPA 15 mg, n=1340 [3055.3 PY]; UPA 30 mg, n=1353 [3231.0 PY]) who received at least 1 dose of UPA were included in the integrated analysis. Approximately half of patients were between ≥18 and 39 years old. Median exposure was approximately 2.7 years for each treatment group. The rates of overall AEs, including severe AEs, serious AEs, and AESI leading to discontinuation of study drug were generally similar across age groups among patients <65 years old; higher rates were observed among patients ≥65 years old with both UPA doses. Rates of AESI were low and generally similar for UPA 15 and 30 mg groups, including malignancy excluding non-melanoma skin cancer (NMSC; 0.4/100 PY and 0.3/100 PY), NMSC (0.4/100 PY and 0.3/100 PY), adjudicated major adverse cardiovascular event (<0.1/100 PY and <0.1/100 PY), and venous thromboembolism (<0.1/100 PY and <0.1/100 PY). No dose-relationship was observed for NMSC and malignancy excluding NMSC. A dose-dependent increase in herpes zoster was observed across age groups among patients <65 years old. Overall, <5% of patients in each treatment group had prior shingles vaccines (UPA 15 mg, 3.8%; UPA 30 mg, 4.9%). Compared with other age groups, AESI rates were generally higher among patients ≥65
years old (Table 1). In the US population, rates of AESI were generally consistent with the overall global population. No herpes zoster cases were reported in the US adolescent population (Table 2).

**Conclusion:** Based on the integrated analysis of long-term safety data for up to 4 years, rates of AESI were low for UPA 15 and 30 mg in patients with moderate-to-severe AD. Rates were generally consistent across age groups among patients <65 years old. Patients ≥65 years old, and particularly those taking UPA 30 mg, had higher rates of any AESI, severe AESI, AEs leading to drug discontinuation, and several AESI, suggesting that using a lower dose and closer monitoring of patients in this age group are warranted. Overall, these results continue to support the safety of UPA for the long-term treatment of adults and adolescents with moderate-to-severe AD.

### Table 1. Overview of Treatment-Emergent AESI in Exposure-Adjusted Rate per 100 PY by Age Group for the Global Population

<table>
<thead>
<tr>
<th>AESI</th>
<th>15 mg</th>
<th>30 mg</th>
<th>18-36 years</th>
<th>&gt;65 years</th>
<th>18-36 years</th>
<th>&gt;65 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>1340</td>
<td>1353</td>
<td>267</td>
<td>172</td>
<td>588</td>
<td>700</td>
</tr>
<tr>
<td>Exposure (PY)</td>
<td>2055.3</td>
<td>2323.0</td>
<td>567.1</td>
<td>686.3</td>
<td>1509.4</td>
<td>1957.4</td>
</tr>
<tr>
<td>Serious infections</td>
<td>2.2</td>
<td>2.8</td>
<td>2.5</td>
<td>1.5</td>
<td>2.1</td>
<td>2.6</td>
</tr>
<tr>
<td>Opportunistic infection (excl. TB/herpes zoster)</td>
<td>1.8</td>
<td>2.4</td>
<td>1.8</td>
<td>0.7</td>
<td>2.1</td>
<td>3.4</td>
</tr>
<tr>
<td>Active TB</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>0</td>
<td>0</td>
<td>&lt;0.1</td>
<td>0</td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>3.1</td>
<td>5.6</td>
<td>1.6</td>
<td>3.0</td>
<td>3.8</td>
<td>6.2</td>
</tr>
<tr>
<td>Malignancy excl. NMSC*</td>
<td>0.4</td>
<td>0.3</td>
<td>0.2</td>
<td>0.1</td>
<td>&lt;0.1</td>
<td>0.6</td>
</tr>
<tr>
<td>MACE*</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>0</td>
<td>0</td>
<td>&lt;0.1</td>
<td>0.1</td>
</tr>
<tr>
<td>VTE*</td>
<td>&lt;0.1</td>
<td>&lt;0.1</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Gastric perforation</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>AEs leading to death</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

*AESI, adverse events of special interest; E, event; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PY, patient years; TB, tuberculosis; VTE, venous thromboembolism.*

### Table 2. Overview of Treatment-Emergent AESI in Exposure-Adjusted Rate per 100 PY by Adolescent/Adult for Patients in the United States

<table>
<thead>
<tr>
<th>AESI</th>
<th>All Patients</th>
<th>Adolescents (12-17 years)</th>
<th>Adults (≥18 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>342</td>
<td>15 mg 327 30 mg 76 84</td>
<td>15 mg 265 30 mg 243</td>
</tr>
<tr>
<td>Exposure (PY)</td>
<td>727.4</td>
<td>721.1 139.0 165.2</td>
<td>598.4 535.9</td>
</tr>
<tr>
<td>Serious infections</td>
<td>2.3</td>
<td>2.6 2.9 0 2.2 3.5</td>
<td></td>
</tr>
<tr>
<td>Opportunistic infection (excl. TB/herpes zoster)</td>
<td>1.4</td>
<td>0.8 2.2 1.1 1.2 0.7</td>
<td></td>
</tr>
<tr>
<td>Active TB</td>
<td>0</td>
<td>0 0 0 0</td>
<td></td>
</tr>
<tr>
<td>Herpes zoster</td>
<td>0.6</td>
<td>0 0 0 0 0 0</td>
<td></td>
</tr>
<tr>
<td>Malignancy excl. NMSC*</td>
<td>0.3</td>
<td>0.3 0 0 0.3 0.6</td>
<td></td>
</tr>
<tr>
<td>NMSC*</td>
<td>0.4</td>
<td>0.4 0 0 0.5 0.8</td>
<td></td>
</tr>
<tr>
<td>MACE*</td>
<td>0.3</td>
<td>0.3 0 0 0.3 0.2</td>
<td></td>
</tr>
<tr>
<td>VTE*</td>
<td>0.3</td>
<td>0.3 0 0 0.3 0.4</td>
<td></td>
</tr>
<tr>
<td>Gastric perforation</td>
<td>0</td>
<td>0 0 0 0 0</td>
<td></td>
</tr>
<tr>
<td>AEs leading to death</td>
<td>0</td>
<td>0 0 0 0 0</td>
<td></td>
</tr>
</tbody>
</table>

*AESI, adverse events of special interest; E, event; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PY, patient years; TB, tuberculosis; VTE, venous thromboembolism.*

* Rates shown are n/100 PY=number of patients with at least one event per 100 PY.
Abstract N°: 6191

A Phase 2b, Randomized, Double-blind, Placebo-controlled, Multi-center, Global Study to Evaluate the Efficacy and Safety of ANB032 in the Treatment of Subjects with Moderate to Severe Atopic Dermatitis

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Introduction & Objectives:

BTLA is a key checkpoint receptor that is expressed across a range of activated immune cells, such as T-cells, B-cells and dendritic cells (DC), that drive inflammatory diseases. ANB032, a BTLA agonist antibody, has the potential to modulate all phases of the pathogenic inflammatory response with broad applicability to inflammatory diseases where the BTLA pathway is dysregulated, such as in dermatology, rheumatology, gastroenterology, etc. In preclinical studies, ANB032 inhibited activated T cell proliferation, reduced inflammatory cytokine secretion (Th1, Th2, Th17, and Th22) and modulated DC function, including inducing T regs. In a Phase 1 first-in-human healthy volunteer study, ANB032 was well-tolerated, had a favorable PK profile, demonstrated robust target engagement and a partial reduction in BTLA expression, consistent with observations in animal models of dermatitis and inflammation. The robust pre-clinical data and Phase 1 trial results, support the rationale for advancing the clinical development of ANB032 in a Phase 2 study in atopic dermatitis (AD), a systemic and heterogeneous inflammatory disease driven by the involvement of broad T-cell lineages including Th1, Th2, Th17, and Th22 cells, along with DCs.

Materials & Methods:

This global Phase 2b study is a randomized, double-blind, placebo-controlled, parallel-group, multi-center trial to evaluate the safety, tolerability, and efficacy of ANB032 in subjects with moderate-to-severe AD. Eligible subjects will be 18–65 years of age and have a clinical diagnosis of moderate-to-severe AD affecting at least 10% of their total body surface area, an Eczema Area and Severity Index (EASI) score > 16, and a validated Investigator Global Assessment (IGA) for Atopic Dermatitis score > 3. Importantly, subjects who are either dupilumab/IL-13 blocker-naive or -experienced are eligible for enrolment. The treatment period is 14 weeks (wks) with an additional 12-wks of follow up. Subjects will be randomized in a 1:1:1:1: ratio in 4 equal treatment groups, evaluating 3 SC doses and schedules of ANB032 and placebo. Dosing schedules are every 2 wks or every 4 wks. The primary endpoint is mean change from baseline in EASI at week 14. Secondary endpoints include EASI75, IGA 0/1, PNRS, DLQI, SCORAD50, and safety. Tape strips and/or tissue biopsies will be collected to assess biomarkers, such as Th1/Th2/Th17, as exploratory endpoints.

Results:

The study has initiated in May 2023. Top-line data are expected by year end 2024.

Conclusion:

Current treatment options in AD do not target all of the diverse immune cells and cytokines that contribute to the pathogenesis of this disease. This Phase 2b study of ANB032 will add to the evolving treatment landscape of AD and further the understanding of the biology of this heterogenous disease.
Abstract N°: 6218

A Phase 2b, Randomized, Double-Blinded, Parallel-Group, Placebo-Controlled Study to Evaluate the Efficacy and Safety of Rezpegaldesleukin in Adults with Moderate-to-Severe Atopic Dermatitis

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Introduction:

Atopic dermatitis (AD) is a chronic, relapsing inflammatory skin disorder. Dysfunction of regulatory T cells (Treg) may play a role in AD immunopathogenesis.1 Rezpegaldesleukin (REZPEG: NKTR-358, LY3471851) is a polyethylene glycol (PEG)-conjugated recombinant human interleukin 2 (rhIL-2) with the ability to selectively promote the activation and up-to 12-fold expansion of Tregs, while having relatively minimal effect on conventional T cells (Tcons).2 It represents a potential novel therapeutic approach for patients with moderate-to-severe AD. A Phase 1b study of REZPEG for patients with moderate-to-severe AD demonstrated a rapid time to response (2-4 weeks) during induction therapy and a prolonged durability of response, i.e., throughout the 36-week follow-up after cessation of therapy.3 These results support further development of REZPEG for patients with AD.

Materials & Methods:

We are conducting a Phase 2b, randomized, double-blinded, placebo-controlled, international, multicenter study of REZPEG vs placebo for biologic-naïve patients with moderate-to-severe AD. Eligible requires adult patients (aged 18-70 years) with moderate-to-severe AD with the following inclusion criteria: baseline Eczema Area and Severity Index (EASI) score ≥ 16, Investigator’s Global Assessment (IGA) AD score ≥ 3, total body surface area (BSA) affected ≥ 10%, and chronic AD for at least 1 year and for whom topical treatment was inadequate or inadvisable. Patients will be randomly assigned in a 2:2:2:1 ratio to 3 different REZPEG dosing regimens vs. placebo, administered subcutaneously, during the induction period (Figure 1). Patients on the REZPEG arms with an at-least EASI50 response following induction will be re-randomized to a maintenance REZPEG administration every 4 or 12 weeks. Re-randomized patients with acute exacerbation defined as <EASI25 and patients that do not achieve an EASI50 at end of induction will be placed in an open-label escape arm and administered REZPEG. The primary endpoint for this study is the least-square mean percent reduction in EASI from baseline at end of induction. Key secondary/exploratory endpoints include the following: proportions with IGA 0/1 with at-least 2 point reduction, EASI75, EASI90, EASI50, proportions with Itch Numerical Rating Scale [NRS] improvement of ≥ 4 pts, improvement in % BSA involvement, safety/tolerability, various patient reported outcomes (PROs), pharmacokinetics, and pharmacodynamics.

Conclusion:
REZPEG is a novel regulatory T cell stimulating therapy that may confer prolonged therapeutic benefit for patients with moderate-to-severe AD. This phase 2b trial is evaluating the efficacy and safety of multiple induction and maintenance dosing regimens of REZPEG in biologic naïve patients with moderate-to-severe atopic dermatitis.

References:


Keywords: Rezpegaldesleukin, NKTR-358, LY3471851, trial in progress, IL-2, Treg, atopic dermatitis, biologic naïve

Figure 1:
Rapid and Effective Response to Upadacitinib in Treatment-Resistant Moderate-to-Severe Atopic Dermatitis: A 26-Week Observational Study

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Introduction & Objectives:

Atopic dermatitis (AD) treatment landscape has improved drastically in the last years. The recent advancements in understanding of Atopic Dermatitis (AD) pathogenesis have led to the development of safer and more effective therapies. Novel therapeutic strategies include biologics and Janus Kinase (JAK) inhibitors, such as upadacitinib. Upadacitinib is a novel JAK-1 inhibitor with promising results both in clinical trials and real-life studies.

Materials & Methods:

We conducted a 26-week prospective observational study at a GA2LEN ADCARE AD referral center in order to assess the effectiveness and safety of upadacitinib in AD patients with moderate-to-severe disease who failed previously to respond to at least one classic systemic therapy, dupilumab and baricitinib. Baseline demographic data and several measures were captured at weeks 0/6/16/26. The number of patients analyzed at each time-point varied depending on follow-up or dropout rates.

Results:

The cohort (n=5), all from male sex, had a mean age of 29.4 years (20-48) and had AD since first childhood. Within just 6 weeks, significant improvements were observed in all subjective and objective scores. There was a mean reduction of 81.1% in Eczema Area and Severity Index (EASI) and 84.5% in Dermatology Life Quality Index (DLQI). The findings from weeks 16 and 26 were also favorable, with all patients achieving an EASI-50 response at these timepoints. Throughout this period, no patients discontinued upadacitinib, though there was a reported case of increased LDL cholesterol.

Conclusion:

In conclusion, this study demonstrates the remarkable and rapid effectiveness of upadacitinib in treating severe AD patients who previously did not respond to conventional immunosuppressants, biologics, and even other JAK inhibitors. We also highlight the rapid response in both patients reported outcome and objective measures. Furthermore, the results underscore the safety profile of upadacitinib in this difficult to treat population.
Abstract N°: 6363

Lebrikizumab reduces the extent of involvement and severity of AD signs across different body regions including the head and neck

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Introduction & Objectives:
Specific body regions in atopic dermatitis (AD) can respond differently to topical or even systemic therapy. The aim of this study was to assess the efficacy of lebrikizumab (LEB), a high-affinity monoclonal antibody targeting interleukin (IL)-13 (a central mediator in AD), in each anatomical region measured by the Eczema Area and Severity Index (EASI) in patients with moderate-to-severe AD. Pooled data from two Phase 3 clinical trials ADvocate1 (NCT04146363) and ADvocate 2 (NCT04178967A) (ADvocate1&2) that evaluated induction and maintenance treatment with LEB monotherapy were analysed. Additionally, data from the Phase 3 clinical trial ADjoin (NCT04392154) that evaluated the long-term extension of patients that completed the phase 3 clinical trial ADhere (NCT04250337) were analysed. ADhere clinical trial assessed induction treatment with LEB plus topical corticosteroids (TCS).

Materials & Methods:
In ADvocate1&2, patients responding to LEB 250 mg every two weeks (LEB Q2W) at Week 16 were re-randomized 2:2:1 to receive LEB Q2W, every 4 weeks (LEB Q4W) or placebo (LEB withdrawal) for 36 additional weeks. Patients were considered responders if they achieved a 75% reduction in the EASI from baseline (EASI 75) or an Investigator Global Assessment (IGA) 0/1 with a ≥ 2-point improvement from baseline at Week 16, without rescue medication use. In ADjoin, ADhere responder patients were re-randomized 2:1 to receive LEB Q2W or LEB Q4W for 100 weeks. Mean percentage change from baseline (% CFB) at Week 52 in ADvocate 1&2 and at Week 56 in ADjoin (ADhere 16-weeks + ADjoin 40-weeks) was calculated for each anatomical region. The mixed-effects model of repeated measures (MMRM) was used to evaluate EASI CFB by anatomical regions. Results were converted to % CFB by dividing EASI least squares mean CFB by EASI total baseline mean for each anatomical region subscore. Data after rescue medication use or treatment discontinuation were considered missing.

Results:
In ADvocate 1&2, the mean % CFB at Week 52 (LEB withdrawal, LEB Q2W and LEB Q4W) in head and neck was 74.04, -79.28 and 81.60; lower extremities 68.34, 82.30 and -82.51; upper extremities 62.52, 78.47 and -79.43, and trunk -72.01, -84.82 and -86.30, respectively. In ADjoin, the mean % CFB at Week 56 (ADhere 16-weeks + ADjoin 40-weeks) (LEB Q2W and LEB Q4W) in head and neck was -91.26 and 92.76; lower extremities 90.81 and -84.16; upper extremities -98.36 and -92.06; and trunk -92.22 and 89.73, respectively.

Conclusion:
LEB as monotherapy and in combination with TCS reduced the extent of involvement and severity of AD across all body regions including the head and neck region, a burdensome and difficult to treat area.
Abstract N°: 6476

Tapinarof Cream 1% Once Daily: Significant Efficacy in the Treatment of Moderate to Severe Atopic Dermatitis in Two Pivotal Phase 3 Trials in Adults and Children Down to 2 Years of Age

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Introduction & Objectives: Tapinarof cream 1% once daily (QD) demonstrated efficacy versus vehicle and was well tolerated in adults and adolescents with moderate to severe atopic dermatitis (AD) in a previously reported phase 2 trial. Here, we report pivotal phase 3 efficacy and safety results for tapinarof cream 1% QD in the treatment of adults and children down to 2 years of age with moderate to severe AD.

Materials & Methods: ADORING 1 and 2 were two identical phase 3, randomized, double-blind, vehicle-controlled trials. Eligibility criteria included a Validated Investigator Global Assessment for Atopic DermatitisTM (vIGA-ADTM) score of ≥3, Eczema Area and Severity Index (EASI) score of ≥6, and body surface area (BSA) involvement of 5–35%. Patients were randomized 2:1 to receive tapinarof cream 1% or vehicle cream QD for 8 weeks. The primary efficacy endpoint was vIGA-ADTM response, defined as a score of clear (0) or almost clear (1) and ≥2-grade improvement from baseline at Week 8. Secondary efficacy endpoints included ≥75% improvement in EASI score (EASI75) and proportion of patients (aged ≥12 years) with a baseline Peak Pruritus-Numerical Rating Scale (PP-NRS) score of ≥4 who achieved a ≥4-point reduction at Week 8. Adverse events (AEs) included rates of AEs of special interest (AESIs): contact dermatitis, follicular event, and headache.

Results: 407 and 406 patients aged 2–81 years were randomized in ADORING 1 and 2, respectively. At baseline, 84.0–89.9% of patients had a vIGA-ADTM score of 3 (moderate), mean EASI score of 12.5–13.3, and mean BSA affected of 16.7–16.9% across trials. At Week 8, both the primary and all secondary efficacy endpoints were met with statistical significance in the tapinarof groups versus vehicle: vIGA-ADTM response rates were 45.4% vs 13.9% and 46.4% vs 18.0% (both P<0.0001); EASI75 response rates were 55.8% vs 22.9% and 59.1% vs 21.2% (both P<0.0001); and a ≥4-point reduction in PP-NRS was achieved by 55.8% vs 34.2% (P=0.0366) and 52.8% vs 24.1% (P=0.0015), in ADORING 1 and 2, respectively. AEs were mostly mild or moderate; the most frequent (≥5% in any group) were folliculitis, headache, and nasopharyngitis. Trial discontinuation rates due to AEs were lower with tapinarof versus vehicle (ADORING 1: 1.9% vs 3.6%; ADORING 2: 1.5% vs 3.0%, respectively). Rates of AESIs with tapinarof versus vehicle were: contact dermatitis 1.5% vs 2.2% and 1.1% vs 1.5%; follicular events 10.0% vs 0.7% and 8.9% vs 1.5%; and headache 7.0% vs 2.2% and 1.5% vs 0%, in each trial, respectively.

Conclusion: Tapinarof cream 1% QD demonstrated statistically significant efficacy compared with vehicle for primary and secondary efficacy endpoints in adults and children down to 2 years of age with moderate to severe AD. Tapinarof was well tolerated, with no new safety or tolerability signals. AEs were mostly mild to moderate and led to low rates of trial discontinuation, demonstrating the predictable safety profile of tapinarof cream 1% QD.
Abstract N°: 6542

**Chronic hand eczema shares a common molecular signature regardless of atopic dermatitis status**

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**Introduction & Objectives:**

Chronic hand eczema (CHE) is a common heterogeneous inflammatory skin condition characterized by multiple morphologic and etiologic subtypes, including 40-50% of patients presenting concomitant atopic dermatitis (AD). The pathogenesis of CHE remains elusive, precluding the development of efficacious, targeted therapies.

**Materials & Methods:**

We aimed to elucidate the molecular skin profile of CHE, studying 95 subjects with CHE and 20 matched healthy controls. 45 of the 95 CHE patients also had AD. Lesional (LS), non-lesional (NL), and normal (N) skin samples were collected via tape-strips and analyzed by RNA-seq. Differentially expressed genes/DEGs (defined as fold change/FCH>1.5 and false discovery rate/FDR<0.05) were evaluated across the entire CHE cohort. Biomarkers were correlated with clinical severity scores (HECSI, mTLSS, DLQI, etc.)

**Results:**

The global CHE transcriptome showed 8902 (5466 Up, 3436 Down) DEGs in LSvsN skin, 3193 (1574 Up, 1619 Down) in LSvsNL and 6782 (4043 Up, 2739 Down) in NLvsN. These included upregulation of several immune pathways and genes, such as Th1 (OASL, IL12B, STAT1), Th2 (IL7R, CCL22, CCL24, OX40), and Th17/Th22 (CXCL3, IL23A). We also observed downregulations in negative regulators (IL34), epidermal terminal differentiation (FLG, LOR), and lipid metabolism (FA2H, GAL) genes. We did not find significant differences in the lesional CHE signature between patients with and without AD. However, the NL skin of CHE patients with AD showed a significantly higher inflammatory tone compared to that of CHE patients without AD across the Th2 (OX40) and Th17/Th22 (IL23A) axes, with a parallel greater barrier dysregulation (LOR, FLG). Significant positive correlations were detected between CHE clinical severity measures (mTLSS and HECSI) and Th1/Th2/Th17 immune markers (i.e. CCR4, STAT3, IL2RB, PDE4B) in CHE patients without AD, and negative correlations with barrier and negative regulator markers (i.e. ELOVL3, LOR, FLG, IL34), while CHE with AD positively correlated with CCL17, and negatively with IL34 (all |r|>0.4; P<0.05).

**Conclusion:**

Tape-strips capture the molecular fingerprint of CHE, showing broadly shared immune and barrier dysregulations in patients with and without AD, suggesting that common therapeutic targeting may be effective in CHE regardless of atopic status. The higher inflammation in NL skin of CHE with AD may also suggest a higher systemic disease burden, similar to “classic” AD.
Rapid and Early Onset of Itch Relief with Tapinarof Cream 1% Once Daily in Two Pivotal Phase 3 Trials in Adults and Children Down to Two Years of Age with Moderate to Severe Atopic Dermatitis

Eric Simpson*, Jonathan Silverberg2, Robert Bissonnette3, Linda Stein Gold4, April W. Armstrong5, Adelaide Hebert6, Rocco Serra7, Jeannette Jakus8, Philip M Brown9, David Rubenstein9, Stephen Piscitelli9, Anna Tallman9, Lawrence Eichenfield10

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Introduction & Objectives: Itch is the most bothersome symptom for patients with atopic dermatitis (AD), with a significant negative impact on health-related quality of life. Rapid onset of pruritus relief with sustained efficacy is a key outcome for AD therapies. In a phase 2 trial in adults and adolescents with moderate to severe AD, tapinarof cream 1% once daily (QD) demonstrated efficacy versus vehicle and was well tolerated. Here, we evaluate time to onset of itch relief in the pivotal phase 3 trials with tapinarof cream 1% QD in the treatment of adults and children down to 2 years of age with moderate to severe AD.

Materials & Methods: In ADORING 1 and 2, two identical, double-blind, vehicle-controlled trials, patients were randomized 2:1 to tapinarof cream 1% or vehicle QD for 8 weeks. Patients with a Validated Investigator Global Assessment for Atopic DermatitisTM score of ≥3, an Eczema Area and Severity Index score of ≥6, and body surface area involvement of 5–35% were included. Efficacy endpoints that evaluated itch relief were mean changes in Peak Pruritus-Numerical Rating Scale (PP-NRS) score (daily and by visit [Weeks 1, 2, 4, and 8]) from baseline through Week 8. The PP-NRS considers a person’s worst itch over the past 24 hours, assessed on an 11-point scale (0 indicates “no itch” and 10 is “worst imaginable itch”). Daily PP-NRS scores were recorded in diaries. Patients aged ≥12 years self-completed the PP-NRS, while caregivers completed it for children aged <12 years.

Results: 407 and 406 patients were randomized in ADORING 1 and 2. At baseline, mean (standard deviation [SD]) PP-NRS scores were 6.7 (2.4) and 6.8 (2.3) in both trials, respectively. For daily evaluations of itch from baseline, greater reductions in PP-NRS scores (mean [SD]) for tapinarof versus vehicle were observed as early as Day 1, 24 hours after initial application, in ADORING 1 (–1.2 [2.2] vs –0.9 [2.0]) and Day 2 in ADORING 2 (–1.6 [2.4] vs –1.4 [2.1]). Improvements in daily PP-NRS scores (mean [SD]) with tapinarof versus vehicle continued through the first 2 weeks (Day 14; –3.0 [2.8] vs –2.0 [2.4] and –2.9 [2.7] vs –1.8 [2.6]), and through Week 8 of both trials. There were statistically significant and clinically meaningful reductions in mean weekly PP-NRS scores as early as Week 1, the first assessment, for patients treated with tapinarof compared with vehicle (–2.0 vs –1.2 [P<0.0001]) and (–2.0 vs –1.3 [P=0.0010]), in ADORING 1 and 2, respectively. Significantly greater reductions in mean PP-NRS scores with tapinarof versus vehicle were seen for all visits through Week 8 (–4.1 vs –2.6 and –4.1 vs –2.4 [both P<0.0001]), for both trials.

Conclusion: Tapinarof cream 1% QD demonstrated rapid, clinically meaningful, and significant onset of pruritus relief as early as 24 hours after initial application compared with vehicle. Improvements in itch with tapinarof cream increased through Week 8 in both trials in adults and children down to 2 years with moderate to severe AD.
Nemolizumab improves skin lesions, itch and sleep disturbance in patients with moderate-to-severe atopic dermatitis: Results from two identical phase 3 multinational studies (ARCADIA 1 and ARCADIA 2)

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Introduction & Objectives: Atopic dermatitis (AD) is a chronic inflammatory skin disease characterised by intense itch and eczematous lesions. Previously, nemolizumab, a first-in-class interleukin-31 receptor alpha antagonist, demonstrated rapid and significant improvements in skin lesions and itch with a favourable safety profile in phase 2 studies in adults with AD. Two identically designed global phase 3 studies evaluated efficacy and safety of nemolizumab after a 16-week treatment period in patients with moderate-to-severe AD inadequately controlled with topical treatments.

Materials & Methods: We conducted two 48-week randomized, placebo-controlled double-blind, phase 3 studies, ARCADIA 1 (NCT03985943) (N=941) and ARCADIA 2 (NCT03989349) (N=787), with a 16-week initial treatment period followed by a 32-week maintenance period. Eligible patients (≥12 years old) with moderate-to-severe AD and associated pruritus were assigned (2:1) to either nemolizumab 30 mg (60 mg at baseline [BL]) or placebo administered subcutaneously every 4 weeks (Q4W) with concomitant background topical corticosteroids (TCS) or topical calcineurin inhibitors (TCI) of medium/low potency. The co-primary endpoints were Investigator’s Global Assessment (IGA) success (IGA score of 0/1 [clear/almost clear skin] with a reduction of ≥2 points from BL) at Week (W) 16 and 75% improvement in the Eczema Area and Severity Index (EASI-75) at W16. Key secondary endpoints included evaluation of itch response (≥4-point improvement in peak pruritus numeric rating scale [PP NRS] score at W16 and earlier timepoints) and improvement in sleep disturbance (≥4-point improvement in sleep disturbance numeric rating scale score [SD NRS]) at W16. Safety was assessed throughout the study.

Results: Both studies met the co-primary, and key secondary endpoints with the outcomes being** consistent between studies. At W16, a significantly greater proportion of nemolizumab- vs placebo-treated patients achieved clinically meaningful improvements in skin lesions (IGA success: 35.6% vs 24.6% [p<0.0006] in ARCADIA 1 and 37.7% vs 26.0% [p=0.001] in ARCADIA 2, and EASI-75: 43.5% vs 29.0% [p<0.0001] in ARCADIA 1 and 42.1% vs 30.2% [p=0.0011] in ARCADIA 2). A significantly higher proportion of nemolizumab- vs placebo-treated patients showed early and sustained improvement in itch (PP NRS response: 27.4% vs 6.5% [p<0.0001] in ARCADIA 1 and 26.1% vs 5.3% [p<0.0001] in ARCADIA 2 at W4; and 42.7% vs 17.8% in ARCADIA 1* [p<0.0001] and 41.0% vs 18.1% in ARCADIA 2 [p<0.0001] at W16). PP NRS percent change from BL was -17.8% vs -7.2% in ARCADIA 1 (p<0.0001) and -18.7% vs -6.1% in ARCADIA 2 (p<0.0001) at W1 which increased through W16 (ARCADIA 1: -56.1% vs -30.6%; p<0.0001 and ARCADIA 2: -55.6% vs 30.3%; p<0.0001 at W16). Improvement in sleep disturbance was observed in a significantly higher proportion of patients in the nemolizumab vs placebo group at W16: 37.9% vs 19.9%; p<0.0001 in ARCADIA 1 and 33.5% vs 16.2%; p<0.0001 in ARCADIA 2. The safety profile was consistent between nemolizumab- and placebo-treated arms, most treatment-emergent adverse events were non serious, and mild or moderate in severity.
Conclusion: Nemolizumab Q4W with background TCS or TCI was well tolerated and led to clinically meaningful and statistically significant improvements in core signs and symptoms of AD in adults and adolescents with moderate-to-severe disease. Resolution of itch and sleep disturbance was rapid and sustained through W16.
**Efficacy and Safety of Single Agent Rezpegaldesleukin, a Selective Regulatory T-Cell-Inducing Interleukin-2 Conjugate, in the Treatment of Atopic Dermatitis: Final Results from a Randomized Phase 1b Study**

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**Introduction & Objectives:**

Decreases in regulatory T-cell (Treg) number or function contribute to the pathogenesis of multiple autoimmune and inflammatory diseases including atopic dermatitis (AD). Rezpegaldesleukin (NKTR-358, REZPEG, LY3471851) is a polyethylene glycol conjugate of recombinant human interleukin-2 that selectively stimulates Treg expansion and regulatory function. Here, we report updated (final) results from a randomized, double-blind, placebo (PBO)-controlled, Phase 1b study of rezpegaldesleukin in patients (pts) with AD (NCT04081350).

**Materials & Methods:**

Pts with moderate-to-severe AD (≥10% body surface area [BSA], Validated Investigator Global Assessment [vIGA] ≥3, and Eczema Area and Severity Index [EASI] ≥16) were randomized to 12 µg/kg rezpegaldesleukin (n=16), 24 µg/kg rezpegaldesleukin (n=17), or PBO (n=10), given by subcutaneous injection every 2 weeks up to Week 12. Pts were followed until Week 19 and those with ≥EASI50 response at Week 19 (10, 9, and 3 pts in the 24 µg/kg, 12 µg/kg, and PBO groups) were followed until Week 48 or until EASI25 response criteria were no longer met. Assessments included efficacy (EASI, vIGA, BSA), pt-reported outcomes (Itch Numerical Rating Scale [NRS], Dermatology Life Quality Index [DLQI], Patient-Oriented Eczema Measure [POEM]), safety and pharmacodynamics (PD; evaluated through Week 14 by flow cytometry).

**Results:**

Baseline characteristics are shown in Table 1. Treatment with rezpegaldesleukin resulted in dose-dependent decreases in the mean percent change in EASI (Fig. 1), vIGA, BSA, and Itch NRS during the treatment period vs PBO, which were maintained at week 48. At the end of the 12-week induction, EASI LS mean reduction from baseline was 83%, 65%, and 47% in the 24 µg/kg, 12 µg/kg, and PBO groups, respectively. Durability of response was shown by EASI75 responder rates (Table 2); e.g., in the 24 µg/kg group, 41% (7/17), 53% (9/17), and 50.0% (5/10) attained EASI75 response at Weeks 12, 19, and 48, respectively. BSA LS mean reduction at week 12 from baseline was 72%, 55%, and 36% in the 24 µg/kg, 12 µg/kg, and PBO groups, respectively. DLQI and POEM scores also showed dose-dependent improvements with rezpegaldesleukin versus PBO during treatment, which were sustained through the 36-week follow-up. A ≥4-point reduction in itch NRS, DLQI and POEM at weeks 12, 19, and 48 are summarized in Table 3. Adverse events (AEs) were reported in 13 (76.5%), 10 (62.5%), and 8 (80.0%) pts in the 24 µg/kg, 12 µg/kg, and PBO groups, respectively. No pts in the rezpegaldesleukin groups had severe or serious AEs and there were no fatal AEs. Compared with PBO, there were sustained increases in absolute numbers...
of circulating total (FoxP3+CD25+) and CD25bright Tregs in the rezageladesleukin groups. The peak increase in CD25bright Treg number was 10-fold above baseline after the first (Week 1) and second (Week 3) doses in the 24 µg/kg group.

**Conclusion:**

In pts with moderate-to-severe AD, treatment with rezageladesleukin showed dose-dependent improvements in physician-assessed disease activity and pt-reported outcomes over 12 weeks of treatment, with post-treatment sustained efficacy over an additional 36 weeks. This durability highlights rezageladesleukin’s disease remittive potential. Treg increases were in line with prior studies and confirm the desired drug action. Together with the observed safety profile, these results support further development of rezageladesleukin at both tested dose levels for AD treatment.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>PBO (n=10)</th>
<th>12 µg/kg rezageladesleukin (n=16)</th>
<th>24 µg/kg rezageladesleukin (n=17)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years (SD)</td>
<td>42.5 (19.8)</td>
<td>47.9 (17.5)</td>
<td>37.5 (16.4)</td>
</tr>
<tr>
<td>Sex, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>6 (60.0)</td>
<td>11 (68.8)</td>
<td>7 (41.2)</td>
</tr>
<tr>
<td>Male</td>
<td>4 (40.0)</td>
<td>5 (31.3)</td>
<td>10 (58.8)</td>
</tr>
<tr>
<td>Race, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>6 (60.0)</td>
<td>11 (68.8)</td>
<td>14 (82.4)</td>
</tr>
<tr>
<td>Black or African American</td>
<td>3 (30.0)</td>
<td>3 (18.8)</td>
<td>3 (17.6)</td>
</tr>
<tr>
<td>Asian</td>
<td>1 (10.0)</td>
<td>2 (12.5)</td>
<td>0</td>
</tr>
<tr>
<td>Ethnicity, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic or Latino</td>
<td>0</td>
<td>3 (18.8)</td>
<td>7 (41.2)</td>
</tr>
<tr>
<td>Not Hispanic or Latino</td>
<td>10 (100)</td>
<td>13 (81.3)</td>
<td>10 (58.8)</td>
</tr>
<tr>
<td>Mean EASI score (SD)</td>
<td>23.7 (7.1)</td>
<td>23.5 (11.2)</td>
<td>21.9 (5.1)</td>
</tr>
<tr>
<td>Mean BSA score (SD)</td>
<td>39.0 (21.6)</td>
<td>33.8 (20.1)</td>
<td>33.5 (15.8)</td>
</tr>
<tr>
<td>vIGA score, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 (moderate)</td>
<td>5 (50.0)</td>
<td>9 (56.3)</td>
<td>11 (64.7)</td>
</tr>
<tr>
<td>4 (severe)</td>
<td>5 (50.0)</td>
<td>7 (43.8)</td>
<td>6 (35.3)</td>
</tr>
<tr>
<td>Mean Itch NRS score (SD)</td>
<td>8.5 (1.3)</td>
<td>7.8 (2.1)</td>
<td>7.4 (2.5)</td>
</tr>
<tr>
<td>Mean DLQI score (SD)</td>
<td>13.0 (5.9)</td>
<td>12.4 (6.7)</td>
<td>11.3 (7.2)</td>
</tr>
<tr>
<td>Mean POEM score (SD)</td>
<td>21.2 (5.7)</td>
<td>20.0 (5.2)</td>
<td>19.6 (7.0)</td>
</tr>
</tbody>
</table>

SD, standard deviation.

**Table 2. EASI75 response rates at Weeks 12, 19, and 48 (NRI)**

<table>
<thead>
<tr>
<th></th>
<th>EASI75 response, % (n/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Week 12</td>
</tr>
<tr>
<td>PBO</td>
<td>20.0% (2/10)</td>
</tr>
<tr>
<td>12 µg/kg rezageladesleukin</td>
<td>25.0% (4/16)</td>
</tr>
<tr>
<td>24 µg/kg rezageladesleukin</td>
<td>41.2% (7/17)</td>
</tr>
</tbody>
</table>

NRI = non-responder imputation for missing data; *Only EASI-50 responders were followed after week 19.

**Table 3. PRO responses at Weeks 12, 19, and 48 (NRI)**

<table>
<thead>
<tr>
<th>Itch NRS</th>
<th>24-point Reduction in PROs, % (n/N*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Wk 12</td>
</tr>
<tr>
<td>PBO</td>
<td>40.0% (4/10)</td>
</tr>
<tr>
<td>12 µg/kg rezageladesleukin</td>
<td>53.3% (8/15)</td>
</tr>
<tr>
<td>24 µg/kg rezageladesleukin</td>
<td>46.7% (7/15)</td>
</tr>
</tbody>
</table>

NRI = non-responder imputation for missing data; *N = number of pts with baseline respective PRO value of ≥24; Only EASI-50 responders were followed after week 19.
Fig. 1. Mean (standard error; SE) percentage change in EASI score from baseline. The table shows the number of pts that had a measurement at each timepoint. The sample sizes were 10, 16, and 17 for the PBO, 12 µg/kg, and 24 µg/kg cohorts, respectively. Two patients in the PBO group and one in the 24 µg/kg group were dosed but had no assessments during the treatment period. The number of patients that began the Weeks 19–48 follow-up period were 3, 9, and 10 for the PBO, 12 µg/kg, and 24 µg/kg groups, respectively.

| Weeks | 0 | 2 | 4 | 8 | 10 | 12 | 14 | 16 | 18 | 20 | 22 | 24 | 26 | 28 | 30 | 32 | 34 | 36 | 38 | 40 | 42 | 44 | 46 | 48 |
|-------|---|---|---|---|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| PBO, n | 10 | 8 | 5 | 5 | 8 | 7 | 5 | 5 | 5 | 5 | 2 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| 12 µg/kg rezepelide | 16 | 16 | 16 | 16 | 14 | 12 | 12 | 12 | 12 | 7 | 5 | 5 | 5 | 5 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 | 4 |
| 24 µg/kg rezepelide | 17 | 16 | 15 | 15 | 14 | 13 | 13 | 13 | 13 | 8 | 9 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 | 7 |

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Abstract N°: 6703

**Topline results from TREK-AD: a randomized, double-blind, placebo-controlled, Phase 2b study of eblasakimab in adult patients with moderate-to-severe atopic dermatitis**

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**Introduction & Objectives:** Atopic dermatitis (AD) is a common, chronic, multifactorial skin disease with a predominant immune signature of T-helper 2 cells. Cytokines interleukin (IL)-4 and IL-13 have been postulated as key drivers of AD. Both signal through a shared type-2 receptor, a heterodimer comprised of IL-4Rα and IL-13Rα1. Eblasakimab is a potential first-in-class, monoclonal antibody that binds IL-13Rα1 with high affinity and blocks the signaling of IL-4 and IL-13 through the type-2 receptor, while sparing the type-1 receptor. TREK-AD (TRials with Eblasakimab in Atopic Dermatitis), a randomized, double-blind, placebo-controlled, Phase 2b dose-ranging dose study [NCT05158023] evaluated the efficacy and safety of eblasakimab as monotherapy in adult patients with moderate-to-severe AD who are candidates for systemic therapy.

**Materials & Methods:** 289 patients were randomized (1:1:1:1:1) to receive one of four doses of subcutaneous injections of eblasakimab once-monthly [Q4W] at 400mg [n=59] or 600mg [n=59], or once every two weeks [Q2W] at 300mg [n=58] or 400mg [n=56]), or placebo Q2W [n=57] for 16 weeks, following 2–3 loading doses of 600mg or placebo for Q2W or Q4W groups, respectively. Patients had chronic AD present for ≥1 year and at screening and baseline had eczema area and severity index (EASI) ≥16; validated Investigator’s Global Assessment of AD (vIGA-AD) score ≥3 (scale of 0 to 4); ≥10% body surface area of AD involvement. Primary and key secondary endpoints at week 16 included EASI percent change from baseline (%CFBL), the proportions of patients with at least a 75% or 95% improvement in EASI (%CFBL), and EASI75, EASI90, and vIGA-AD score of 0/1.

**Results:** The primary endpoint, EASI %CFBL to week 16, was met for eblasakimab doses 600mg Q4W, 300mg Q2W, and 400mg Q2W vs placebo (73.0% [P<0.001], 69.8% [P<0.005], and 65.8% [P<0.029] vs 51.1%), respectively. %CFBL was significant from Week 4. Eblasakimab at 600mg Q4W also achieved significantly greater EASI75 vs placebo at week 16 (52.0% vs 24.4% P=0.004). Other efficacy outcomes for this treatment arm vs placebo at week 16 included: EASI90 (27.6% vs 7.9%, P=0.008), vIGA-AD (31.2% vs 15.1%, P=0.050). The Q2W regimens were also significantly better vs placebo for EASI75, EASI90, and vIGA 0/1 with eblasakimab 400mg Q2W (43.6%, P=0.036; 25.3%, P=0.018; and 32.6%, P=0.038) and eblasakimab 300mg Q2W (51.2%, P=0.005; 30.8%, P=0.003; and 33.1%, P=0.033). Discontinuation rates were comparable between active arms and higher for placebo. Eblasakimab was safe and well-tolerated. 5.2% of patients experienced conjunctivitis (placebo: 1.8%); 4.7% experienced injection site reactions (placebo: 1.8%); otherwise the frequency of adverse events was comparable between active and placebo arms.
Conclusion: In moderate-to-severe AD, eblasakimab demonstrated a competitive efficacy and safety profile, with monthly dosing from initiation comparable to dosing every two weeks, supporting advancement to a Phase 3 clinical program.
Nemolizumab monotherapy improves itch and skin lesions in patients with moderate-to-severe prurigo nodularis: Results from a global phase 3 trial (OLYMPIA 1)

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Introduction & Objectives: Prurigo nodularis (PN) is a chronic and debilitating skin condition, characterized by itch with multiple nodular skin lesions. Nemolizumab, a first-in-class interleukin-31 receptor alpha antagonist, demonstrated clinically and statistically significant improvements in itch and skin nodules in adult patients with moderate-to-severe PN in a phase 3 study OLYMPIA 2 (NCT04501679). Here we report results from another phase 3 study OLYMPIA 1 (NCT04501666), which aimed to assess the efficacy and safety of nemolizumab compared with placebo in adult patients with moderate-to-severe PN after a 16-week treatment period.

Materials & Methods: We conducted a phase 3, multicentre, double-blind study in adults with PN presenting ≥20 nodules, Investigator’s Global Assessment (IGA) score ≥3 (range 0-4) and Peak Pruritus Numerical Rating Scale (PP-NRS) score ≥7.0 (range 0-10). The study consisted of screening (up to 4 weeks), a 24-week treatment and an 8-week follow-up periods. Eligible patients were assigned (2:1) to either nemolizumab (N=190) or matching placebo (N=96). Following an initial 60 mg subcutaneous dose, patients received 30 mg or 60 mg (depending on a baseline weight below or ≥90 kg, respectively) every 4 weeks. Topical calcineurin inhibitors (TCI) and topical corticosteroids (TCS) were not allowed during study treatment unless required as a rescue medication. The primary endpoints evaluated were itch response (proportion of patients with a ≥4-point improvement in PP-NRS score) and IGA success (proportion of patients with IGA score of 0/1 [clear/almost clear skin] with a reduction of at least 2 points from baseline) at Week 16. We also assessed itch response at Week 4, which was a key secondary endpoint. Prurigo Activity Score (PAS), a secondary endpoint, was evaluated throughout the study. Safety was also assessed all through the study.

Results: All primary and key secondary endpoints were met. At Week 16, a significantly greater proportion of patients receiving nemolizumab vs placebo achieved a ≥4-point improvement in PP-NRS (58.4% vs 16.7%; P<0.0001). This ≥4-point improvement in PP-NRS was already achieved as early as Week 4 (41.1% vs 6.3%; P<0.0001). A significantly greater proportion of patients receiving nemolizumab vs placebo achieved significant improvements in skin lesions at Week 16, including IGA success (i.e., IGA 0/1): 26.3% vs 7.3% (P<0.0001) and ≥75% healed lesions (PAS item 5b): 41.1% vs 11.5% (P<0.0001). Improvements in itch and skin lesions were observed up to Week 24. Treatment-emergent adverse events (TEAEs) were reported in 71.7% of nemolizumab- and 65.3% of placebo-treated patients, while serious TEAEs were reported in 8.6% of nemolizumab- and 10.5% of placebo-treated patients. Most of these TEAEs were mild-to-moderate in severity.

Conclusion: Nemolizumab monotherapy administered every 4 weeks without background TCS or TCI was well...
tolerated and led to clinically meaningful and statistically significant improvements in core symptoms (itch) and signs (skin lesions) of PN. These results confirm those of the OLYMPIA 2 study, previously reported.
Abstract N°: 6744

**Efficacy and safety of amlitelimab (an anti-OX40 ligand antibody) in patients with moderate-to-severe atopic dermatitis: 24-week results from a Phase 2b trial (STREAM-AD)**

Stephan Weidinger1, Andrew Blauvelt2, Kim Papp3,4, Adam Reich5, Chih-Hung Lee6, Margitta Worm7, Charles Lynde8, Yoko Kataoka9, Peter Foley10, Christine Weber11, Wanling Wong12, Natalie Rynkiewicz13, Karl Yen14, John T. O’malley15, Charlotte Bernigaud11

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**Introduction & Objectives:**

Targeting and binding OX40Ligand (OX40L) expressed on antigen-presenting cells may inhibit the persistent immune response that drives atopic dermatitis (AD) pathophysiology. Amlitelimab (SAR445229; KY1005) is a potential first-in-class, fully human, non-depleting anti-OX40L monoclonal antibody that blocks OX40L-OX40 interactions and that has shown efficacy and an acceptable safety profile in a Phase 2a trial in adults with moderate-to-severe AD. Here, we present 24-week efficacy and safety results (Part 1) from an ongoing dose-ranging Phase 2b trial. The study remains blinded to individual patient data (Part 2 ongoing).

**Materials & Methods:**

STREAM-AD (NCT05131477) is a 52-week, randomised, double-blinded, placebo-controlled Phase 2b monotherapy trial. This study is designed with 2 parts (double-blind throughout): a 24-week treatment period (Part 1, completed and presented here) and a 36-week maintenance/withdrawal period (Part 2, ongoing). Adults (18 to <75 years; n=390) with moderate-to-severe AD were randomised 1:1:1:1:1 to receive subcutaneous amlitelimab Q4W (250 mg with 500 mg loading dose [LD], n=77; 250 mg without LD, n=78; 125 mg without LD, n=77; or 62.5 mg without LD, n=79) or placebo Q4W (n=79). The primary endpoint was percentage change in Eczema Area and Severity Index (EASI) from baseline at Week 16. Key secondary endpoints included percentage changes in EASI at Week 24 and results at Weeks 16 and 24 for percentages of patients with at least 75% reduction from baseline in EASI (EASI-75), percentages of patients with Investigator Global Assessment response of 0 (clear) or 1 (almost clear) and a reduction from baseline of ≥2 points (IGA 0/1), and proportions of patients with a weekly average reduction of Peak Pruritus Numerical Rating Scale (PP-NRS) ≥4 points from baseline. The primary efficacy analysis included all randomised patients who completed Week 24 or discontinued treatment or study prior to Week 24 visit (n=390), whereas the safety analysis included all treated patients (n=388).

**Results:**

Treatment with amlitelimab resulted in statistically significant improvements in percentage change in EASI from baseline to Week 16 compared to placebo for all four doses studied. The 250 mg with LD group had the numerically highest response versus placebo at Week 16, with a least-squares mean change from baseline of –
32.1% (95% CI: –43.9, –20.3; \( P<0.0001 \)); the remaining groups without LD had the following responses versus placebo: 250 mg, –27.3 (–39.1, –15.6; \( P<0.0001 \)); 125 mg, –22.2 (–34.0, –10.4; \( P=0.0002 \)); and 62.5 mg, –30.2 (–41.9, –18.5; \( P<0.0001 \)). There were also clinically meaningful improvements in all key secondary efficacy outcome measures, with all amlitelimab dose groups demonstrating nominally significant (\( P<0.05 \)) efficacy versus placebo for EASI-75, IGA 0/1, and PP-NRS \( \geq 4 \), except 250 mg (no LD) in IGA 0/1 at Week 16. Continued improvements were observed through Week 24 in primary and key secondary efficacy outcomes. Amlitelimab was well-tolerated across all dose groups, with no safety concerns identified.

**Conclusion:**

In this dose-ranging Phase 2b trial of amlitelimab in adults with moderate-to-severe AD, amlitelimab demonstrated clinically meaningful efficacy over 24 weeks with an acceptable safety profile across all four dose groups.
Abstract N°: 6746

A Phase 3 Study of Ruxolitinib Cream in Children Aged 2–<12 Years With Atopic Dermatitis (TRuE-AD3): 8-Week Analysis

Lawrence Eichenfield*, Linda Stein Gold, Eric Simpson, Andrea Zaenglein, April W. Armstrong, Megha Tollefson, Weily Soong, Lara Wine Lee, Alim R. Devani, Seth Forman, Dareen S. Siri, Brett Angel, Howard Kallender, Qian Li, Amy Paller

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Introduction & Objectives:

Ruxolitinib cream, a selective Janus kinase (JAK) 1/JAK2 inhibitor, is approved in the United States for the treatment of atopic dermatitis (AD) in adolescents/adults based on results from 2 phase 3 studies (TRuE-AD1/TRuE-AD2 [NCT03745638/NCT03745651]). In a pediatric pilot pharmacokinetics (PK)/safety study (NCT03257644), ruxolitinib cream was well tolerated in patients ≥2 years old (y/o) with AD; efficacy was consistent with TRuE-AD1/TRuE-AD2 results. This phase 3 pediatric study (TRuE-AD3 [NCT04921969]) evaluated efficacy, safety, and PK of ruxolitinib cream in patients 2–<12 y/o with mild to moderate AD.

Materials & Methods:

Patients 2–<12 y/o with an AD diagnosis for ≥3 months, Investigator’s Global Assessment (IGA) of 2 (mild) or 3 (moderate), 3%-20% affected body surface area (BSA), and (for 6–<12 y/o) mean itch Numerical Rating Scale (NRS) score ≥4 were randomized 2:2:1 to twice-daily 0.75%/1.5% ruxolitinib cream or vehicle for 8 weeks of double-blind treatment; rescue therapy was not permitted. The primary endpoint was percentage of patients achieving IGA treatment success (IGA 0/1 with ≥2-grade improvement from baseline) at Week 8. Secondary endpoints included percentage achieving ≥75% improvement in Eczema Area and Severity Index (EASI75) at Week 8, ≥4-point improvement in itch NRS score (NRS4) at Week 8 in patients 6–<12 y/o, time to achieve NRS4, and safety; PK was an exploratory endpoint.

Results:

Of 330 randomized patients, 288 (87.3%) completed the 8-week vehicle-controlled period; all 330 were included in the efficacy population (vehicle, n=65; 0.75%/1.5% ruxolitinib cream, n=134/n=131). Median (range) age was 6 (2–11) years; 54.2% were female; 54.5% White; 32.1% Black; 6.4% Asian. Mean (SD) affected BSA was 10.5% (5.40%); EASI was 8.6 (5.40); 76.4% of patients had IGA 3; 67.3% had AD therapy in the prior 12 months. A clinical effect was observed in patients applying 0.75%/1.5% ruxolitinib cream vs vehicle at Week 2, increasing through Week 8 for IGA-TS (36.6%/56.5% vs 10.8%; P≤0.0001 for both) and EASI75 (51.5%/67.2% vs 15.4%; P<0.0001 for both). In patients 6–<12 y/o, NRS4 at Week 8 was achieved by 37.5%/43.4% vs 29.7%; median time to NRS4 was
11.0/13.0 days vs 23.0 days (hazard ratio, 1.74/1.77; \( P < 0.05 \) for both). Treatment-related adverse events (AEs) during the vehicle-controlled period were reported in 5.3% of patients applying ruxolitinib cream (combined; 2.7% reported application site pain) vs 3.1% of patients applying vehicle (0% reported application site pain). No AEs suggestive of systemic JAK inhibition, serious AEs, or deaths were reported. No substantial changes in mean hematology values were observed. Mean (SD) steady-state plasma concentrations (Css) of ruxolitinib at Week 8 for 0.75%/1.5% ruxolitinib cream were 15.8 (30.4)/28.4 (59.2) nM, well below that required to inhibit thrombopoietin phosphorylation of STAT3 (half-maximal inhibitory concentration, 281 nM).

**Conclusion:**

In patients 2–<12 y/o with mild to moderate AD, ruxolitinib cream achieved significant efficacy at Week 8 vs vehicle for IGA-TS and EASI75. Patients 6–<12 y/o had improved itch in NRS4 at Week 8 and reduced time to NRS4 vs vehicle. Ruxolitinib cream was well tolerated. Low mean ruxolitinib plasma Css and a safety profile similar to vehicle suggest physiologically meaningful systemic JAK inhibition is highly unlikely. These results were similar to the phase 3 results in adolescents/adults.