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Abstract N°: 15

Pharmacokinetics, Efficacy and Safety after Multiple Switches from Reference Adalimumab to Adalimumab Biosimilar (CT-P17) in comparison with the Maintenance Group (Reference Adalimumab) in Patients with Moderate-to-Severe Plaque Psoriasis: Week 27 Results from the Phase III Interchangeability Study

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Introduction & Objectives:

CT-P17 is a biosimilar to the reference adalimumab (ADA) and this study was conducted to demonstrate interchangeability of CT-P17 with ADA.** The primary objective of the study was to demonstrate the pharmacokinetics (PK) similarity between patients receiving ADA continuously and those who alternate between ADA and CT-P17 in terms of area under the concentration-time curve over the dosing interval of Week 25-27 (AUCtau, 25-27) and maximum serum concentration during the dosing interval of Week 25-27 (Cmax, 25-27).

Materials & Methods:

Patients with moderate to severe plaque psoriasis received initial dose of ADA (80 mg) and ADA (40 mg) every other week starting one week after the initial dose. Prior to dosing at Week 13, patients were randomized a 1:1 ratio to Switching group which underwent repeated switches between ADA and CT-P17 (receiving CT-P17 at Weeks 13 and 15, ADA at Weeks 17 and 19 and CT-P17 at Weeks 21, 23 and 25) or ADA maintenance group (received ADA until Week 25). The randomization to treatment assignment was stratified by disease activity by PASI score at Week 13 (pre-dose); responder (≥PASI75) vs. non-responder (<PASI75).

Results:

A total of 367 patients were enrolled in this study and 346 patients (Switching: 172, ADA: 174) were randomized at Week 13. Baseline demographic and disease characteristics including stratification factors were well balanced between Switching and ADA maintenance groups. Switching between ADA and CT-P17 and ADA maintenance were bioequivalent, as measured by primary pharmacokinetics (PK) endpoints (AUCtau, 25-27 and Cmax, 25-27). The 90% confidence intervals of percent ratios of least square means for the parameters were entirely contained within the boundary of 80% to 125% (94.11, 105.08 for AUCtau, 25-27 and 95.03, 106.17 for Cmax, 25-27) and the criterions were also well satisfied in t-value (Table 1). All secondary PK parameters (Tmax, 25-27 and Ctrough) were also comparable between the groups. The median (minimum, maximum) Tmax, 25-27 for the Switching and ADA maintenance groups were similar (71.83 [19.800, 240.250] and 72.00 [21.417, 335.300] hours, respectively for Switching and ADA maintenance groups). Overall, the serum concentrations of adalimumab were generally similar for Switching and ADA maintenance groups (Figure 1). Mean improvement in PASI score from baseline at Week

13 was 88.17%, 87.70% and 92.34%, 91.27% at Week 27 in the Switching and ADA maintenance groups, respectively. The proportion of PASI 50/75/90/100 responders and the proportion of patients with an sPGA score of 0 or 1 up to Week 27 was also similar between the groups (Table 2). Overall, a total of 261 TEAEs were reported in 74 (43.0%) and 76 (43.9%) patients in the Switching and ADA maintenance groups, respectively (Table 3). Switching between ADA and CT-P17 was well tolerated and the safety profile including immunogenicity was similar between the groups. In addition, no notable safety issue or increase in immunogenicity was observed following switching between ADA and CT-P17 up to Week 27.

Conclusion:

The equivalent PK and similar efficacy and safety profile support the interchangeability of CT-P17 and ADA.

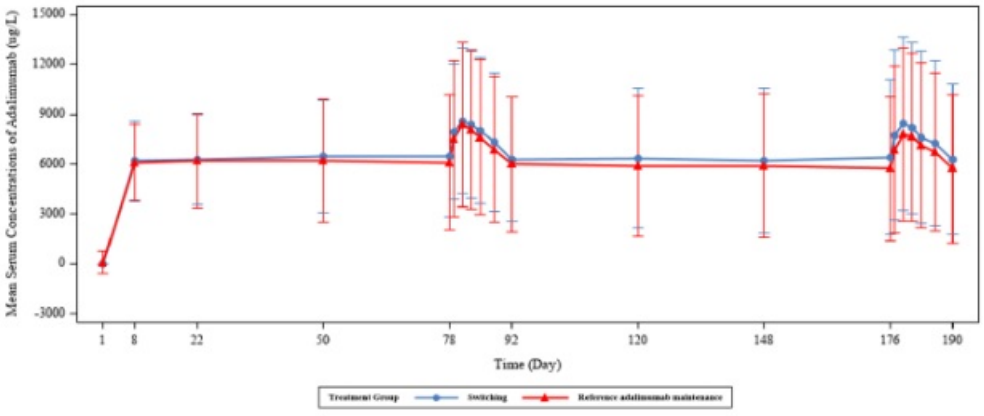
Table 1. Statistical Analysis of Primary PK Parameters ($AUC_{tau,\ 25\text{-}27}$ and $C_{max,\ 25\text{-}27}$) of Adalimumab (ANCOVA): PK set

Parameter	Treatment	n	LS Mean	Ratio (%) of LS Means [1]	90% CI [1]	Criterion [2]
$AUC_{tau,\ 25\text{-}27}$ (h*ng/mL)	Switching	151	2477520.08	99.45	(94.11, 105.08)	42.96
	Reference adalimumab maintenance	158	2491344.67			
$C_{max,\ 25\text{-}27}$ (ng/mL)	Switching	157	8696.02	100.45	(95.03, 106.17)	42.41
	Reference adalimumab maintenance	163	8657.03			

Abbreviations: ANCOVA, analysis of covariate; $AUC_{tau,\ 11\text{-}13}$, area under the concentration-time curve over the dosing interval of Week 11-13; $AUC_{tau,\ 25\text{-}27}$, area under the concentration-time curve over the dosing interval of Week 25-27; CI, confidence interval; $C_{max,\ 11\text{-}13}$, maximum serum concentration during the dosing interval of Week 11-13; $C_{max,\ 25\text{-}27}$, maximum serum concentration during the dosing interval of Week 25-27; LS, least squares; n, the number of patients with non-missing PK parameter values; PASI, psoriasis area and severity index; PK, pharmacokinetic.
An ANCOVA was performed with the PK parameter as the dependent variable, treatment as a fixed effect, and body weight at Week 13, natural logarithm of PASI score ratio between Week 13 and PASI score at Baseline, and $AUC_{tau,\ 11\text{-}13}$ or $C_{max,\ 11\text{-}13}$ for the corresponding primary endpoint as covariates. Primary PK parameters were multiplied by (protein content of the CT-P17) / (protein content of dose received at Week 25 for each patient) in the summary for the purpose of correcting PK parameters for protein content.

1. The ratio of LS means and 90% CIs for the ratio (Switching group / Reference adalimumab maintenance group) were calculated according to Fieller's theorem.
2. The criterion was compared to $t_{0.95,304} = 1.65$ for $AUC_{tau,\ 25\text{-}27}$ and $t_{0.95,315}=1.65$ for $C_{max,\ 25\text{-}27}$.

Figure 1. Mean (±SD) Serum Concentrations of Adalimumab (Linear Scale): PK set



Note: Below lower limit of quantification (BLQ) prior to the first study drug administration (Day 1) is treated as zero (0), and all other BLQ values are set to Lower Limit of Quantification.

Table 2. Secondary Efficacy Endpoints: Safety set

	Switching (N=172)	Reference adalimumab maintenance (N=173)
Week 13		
Percent improvement from baseline in PASI score		
n	172	173
Mean (SD)	88.17 (17.56)	87.70 (15.60)
Patients achieving PASI response, n (%)		
PASI 50	165 (95.9)	166 (96.0)
PASI 75	149 (86.6)	148 (85.5)
PASI 90	105 (61.0)	102 (59.0)
PASI 100	55 (32.0)	51 (29.5)
Patients with sPGA score of 0 or 1, n (%)	148 (86.0)	148 (85.5)
Week 27		
Percent improvement from baseline in PASI score		
n	162	166
Mean (SD)	92.34 (19.24)	91.27 (15.33)
Patients achieving PASI response, n (%)		
PASI 50	158 (91.9)	159 (91.9)
PASI 75	150 (87.2)	153 (88.4)
PASI 90	128 (74.4)	120 (69.4)
PASI 100	82 (47.7)	72 (41.6)
Patients with sPGA score of 0 or 1, n (%)	146 (84.9)	144 (83.2)

Abbreviations: PASI, Psoriasis Area and Severity Index; PASI 50/75/90/100, 50/75/90/100% improvement in Psoriasis Area and Severity Index from baseline; SD, standard deviation; sPGA, static Physician's Global Assessment.

Table 3. Summary of Treatment-Emergent Adverse Events (Switching Period): Safety Set

	Switching (N=172)	Reference adalimumab maintenance (N=173)
Total number of TEAEs	117	144
Patients with ≥1 TEAE, n (%)	74 (43.0)	76 (43.9)
Study drug-related	16 (9.3)	23 (13.3)
Grade ≥3 in intensity	10 (5.8)	7 (4.0)
Total number of TESAEs	2	4
Patients with ≥1 TESAE, n (%)	2 (1.2)	4 (2.3)
Study drug-related	0	2 (1.2)
Total number of TEAEs leading to study drug discontinuation	1	0
Patients with ≥1 TEAE leading to study drug discontinuation, n (%)	1 (0.6)	0
Study drug-related	1 (0.6)	0
Total number of TEAEs classified as ISR	8	12
Patients with ≥1 TEAE classified as ISR, n (%)	3 (1.7)	6 (3.5)
Study drug-related	3 (1.7)	6 (3.5)
Total number of TEAEs classified as infection	32	37
Patients with ≥1 TEAE classified as infection, n (%)	27 (15.7)	28 (16.2)
Study drug-related	4 (2.3)	8 (4.6)
Total number of TEAEs classified as hypersensitivity (including anaphylaxis)	0	0
Total number of TEAEs classified as malignancy	0	0
Total number of TEAEs classified as demyelinating disease	0	0
Total number of TEAEs classified as heart failure	0	0
Total number of TEAEs classified as lupus-like syndrome	0	0
Total number of TEAEs leading to death	0	0

Abbreviations: ISR, injection site reaction; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

Note: Switching Period is defined as from Week 13 dose to Week 27. The total number of TEAEs count included events for all patients in the safety population. At each level of summarization, patients were counted once if they reported one or more events. Only the most severe event was counted. The event was considered to be related if the relationship was defined as 'possible', 'probable' or 'definite'.

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Abstract N°: 178

effect of rituximab on clinical and serological profile of all cases of pemphigus: a prospective observational study

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Introduction & Objectives:

Pemphigus vulgaris (PV), characterized by autoantibodies targeting desmoglein (DSG) 3 and 1, presents a therapeutic challenge. Rituximab, in combination with corticosteroids, is a primary treatment option. This prospective observational study investigates the impact of Rituximab on the clinical and serological profiles of Pemphigus patients.

Materials & Methods:

Primary Objective: Assess the efficacy of Rituximab (RTX) in Pemphigus patients.

Secondary Objective: Evaluate the safety profile of RTX in Pemphigus patients.

Patients with Pemphigus, regardless of Pemphigus Disease Area Index (PDAI) scores, were enrolled with informed consent. Efficacy was evaluated through PDAI scores, clinical responses, Visual Analogue Scale (VAS) assessments for itching and pain, Physician Global Assessment (PGA), Dermatology Life Quality Index (DLQI), and monitoring of adverse events (AEs) at baseline, 3, 6, and 12 months post-RTX infusion. Serum levels of anti-desmoglein (Dsg) 1 and Dsg 3 were measured at similar intervals.

Results:

Twenty-five Pemphigus patients were treated with RTX, with a mean age of 38.58 ± 11.77 years and a mean follow-up of 16.22 ± 3.45 months. Significant reductions in PDAI scores, anti-Dsg 1 and Dsg 3 levels, pain severity, and prednisolone dosages were observed within 1 to 3 months. Median time to achieve complete remission (CR) was 3-4 months, with a median CR duration and relapse time of 9 and 12 months, respectively. Newly diagnosed patients (NDPs) exhibited higher CR rates, longer remission durations, and lower relapse risks compared to previously treated patients (PTPs). No infusion reactions occurred, but four patients reported side effects like facial palsy, dental abscess, scabies, and myiasis.

Conclusion: Rituximab administration in Pemphigus patients showed favorable efficacy and safety profiles for both NDPs and PTPs. Complete remission was typically achieved within 3-4 months. These findings underscore the potential of RTX as a promising treatment option for Pemphigus, with implications for disease monitoring and management.

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Abstract N°: 229

Real-world baseline characteristics of patients with psoriasis from Europe, the Middle East and Africa who were treated with guselkumab or interleukin-17 inhibitors in the Psoriasis Longitudinal Assessment and Registry (PSOLAR)

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Introduction & Objectives:

The Psoriasis Longitudinal Assessment and Registry (PSOLAR; NCT00508547) is a large, international, longitudinal, disease-based registry that prospectively enrolled patients with psoriasis (PsO) who were receiving or were candidates for systemic therapy. The aims of PSOLAR are to assess the long-term safety and improve understanding of real-world biologic use in PsO. PSOLAR was initiated in 2007 and was expanded in 2018 to include patients receiving guselkumab (GUS), an interleukin (IL)-23p19 subunit inhibitor, or IL-17 inhibitors (IL-17i).

Materials & Methods:

Baseline demographic, disease and treatment characteristics are described for patients with PsO treated with GUS and IL-17i from Europe, the Middle East and Africa (EMEA) enrolled in PSOLAR.

Results:

As of 12 July 2023, PSOLAR included 1019 patients from EMEA who initiated GUS (n=665) or IL-17i (n=354) prior to or at enrolment.

Baseline characteristics were similar between groups (Table 1). Median (interquartile range [IQR]) age was 49.0 (39.0–60.0) and 50.0 (39.0–60.0) years in the GUS and IL-17i groups, respectively; both had a slightly higher proportion of male patients (GUS: 59.8%; IL-17i: 61.4%). A high proportion of patients had body mass index values indicating overweight (GUS: 38.3%; IL-17i: 37.9%) or obese (GUS: 35.5%; IL-17i: 37.3%) status; approximately two-fifths of patients in both groups had a history of cardiovascular disease.

Most patients had longstanding plaque PsO, with a median (IQR) time since diagnosis of 18.5 (9.1–29.5) years in the GUS group and 17.5 (9.6–28.1) years in the IL-17i group (Table 2). Median (IQR) PASI score was slightly higher in the GUS group (GUS: 3.6 [0.6–11.2]; IL-17i: 2.7 [0.0–10.6]); approximately one-third of patients in both groups had a PASI score >10. Most patients had prior biologic use (GUS group: 79.4%; IL-17i group: 85.3%). In the GUS group, 40.5% and 38.9% of patients had used 1 or ≥2 prior biologics, respectively. Similarly, in the IL-17i group, 48.6% and 36.7% had used 1 or ≥2 prior biologics. Most patients had prior non-biologic systemic immunomodulator use (GUS group: 70.8%; IL-17i group: 78.2%), most commonly methotrexate and ciclosporin.

The proportion of patients self-reporting psoriatic arthritis was higher in the IL-17i group (GUS: 20.5%; IL-17i:

25.9%). Psoriasis Epidemiology Screening Tool (PEST) score distribution was similar between groups; approximately two-thirds of patients had a score <3. Median 12-domain Psoriatic Arthritis Impact of Disease (PsAID-12) score was low in both groups, indicating an acceptable symptom state.

Conclusion:

Baseline demographic, disease and treatment characteristics of patients enrolled in PSOLAR were largely similar for those receiving GUS or IL-17i, and were representative of a moderate-to-severe PsO population. These descriptive analyses may help physicians better understand the characteristics of patients with PsO prescribed GUS or IL-17i in a real-world setting in EMEA.

Table 1. Baseline demographics, patient characteristics, and family and medical history

Characteristic	GUS (n=665)	IL-17i (n=354)
Enrolment by country, n (%)		
Italy	151 (22.7)	68 (19.2)
Czech Republic	89 (13.4)	64 (18.1)
Greece	51 (7.7)	63 (17.8)
Slovakia	108 (16.2)	1 (0.3)
Portugal	54 (8.1)	42 (11.9)
Belgium	53 (8.0)	26 (7.3)
Netherlands	25 (3.8)	50 (14.1)
Spain	43 (6.5)	17 (4.8)
Austria	39 (5.9)	1 (0.3)
Israel	33 (5.0)	9 (2.5)
Sweden	19 (2.9)	13 (3.7)
Age, n	662	352
Median age, years (IQR)	49.0 (39.0–60.0)	50.0 (39.0–60.0)
Age category, n (%)	662	352
18–24 years	38 (5.7)	13 (3.7)
25–34 years	74 (11.2)	46 (13.1)
35–44 years	141 (21.3)	70 (19.9)
45–54 years	159 (24.0)	91 (25.9)
55–64 years	144 (21.8)	73 (20.7)
≥65 years	106 (16.0)	59 (16.8)
Gender, n	662	352
Male, n (%)	396 (59.8)	216 (61.4)
Race, n (%)	650	317
White	632 (97.2)	306 (96.5)
Black/African American	2 (0.3)	1 (0.3)
Asian	3 (0.5)	2 (0.6)
Hispanic/Latino	4 (0.6)	4 (1.3)
Other	9 (1.4)	4 (1.3)
BMI, n	639	322
Median BMI, kg/m² (IQR)	27.7 (24.8–31.4)	28.1 (25.0–31.6)
Weight class, n (%)	639	322
Underweight (BMI <18.5 kg/m²)	9 (1.4)	6 (1.9)
Normal (18.5–24.9 kg/m²)	158 (24.7)	74 (23.0)
Overweight (25.0–29.9 kg/m²)	245 (38.3)	122 (37.9)
Obesity class I (30.0–34.9 kg/m²)	155 (24.3)	77 (23.9)
Obesity class II (35.0–39.9 kg/m²)	45 (7.0)	29 (9.0)
Obesity class III (≥40.0 kg/m²)	27 (4.2)	14 (4.3)
Patients reporting alcohol use, n	657	345
Never used, n (%)	226 (34.4)	102 (29.6)
Current use, n (%)	385 (58.6)	214 (62.0)
Have used and stopped, n (%)	46 (7.0)	29 (8.4)
Patients reporting smoking, n	658	346
Never smoked, n (%)	304 (46.2)	134 (38.7)
Current smoker, n (%)	212 (32.2)	115 (33.2)
Prior smoker but stopped, n (%)	142 (21.6)	97 (28.0)
Patients with family history, n	657	351
Psoriasis, n (%)	253 (38.5)	154 (43.9)
PsA, n (%)	28 (4.3)	29 (8.3)
Patients with medical history, n	662	352
Cardiovascular disease, n (%)	256 (38.7)	140 (39.8)
Pulmonary disease, n (%)	43 (6.5)	29 (8.2)
Psychiatric illness, n (%)	70 (10.6)	51 (14.5)
Hepatic disease, n (%)	39 (5.9)	24 (6.8)
Skin cancer, n (%)	9 (1.4)	6 (1.7)
Other types of cancer, n (%)	22 (3.3)	6 (1.7)
Endocrine disorder, n (%)	108 (16.3)	58 (16.5)
IBD, n (%)	11 (1.7)	0 (0.0)
Demyelinating disease, n (%)	1 (0.2)	0 (0.0)
Lupus, n (%)	2 (0.3)	1 (0.3)
Environmental allergy, n (%)	17 (2.6)	12 (3.4)
Drug allergy, n (%)	43 (6.5)	27 (7.7)

BMI, body mass index; GUS, guselkumab; IBD, inflammatory bowel disease; IL-17i, interleukin-17 inhibitor; IQR, interquartile range; PsA, psoriatic arthritis.

Table 2. Disease characteristics

Characteristic	GUS (n=665)	IL-17i (n=354)
Psoriasis type, n (%)	662	353
Plaque	636 (95.6)	346 (97.7)
Other	81 (12.2)	33 (9.3)
Time since psoriasis diagnosis, years, n	653	345
Median (IQR)	18.5 (9.1–29.5)	17.5 (9.6–28.1)
Time since psoriasis diagnosis distribution, n (%)	653	345
<2 years	39 (6.0)	19 (5.5)
≥2 and <5 years	50 (7.7)	26 (7.5)
≥5 and <10 years	89 (13.6)	45 (13.0)
≥10 and <15 years	81 (12.4)	64 (18.6)
≥15 and <20 years	101 (15.5)	48 (13.9)
≥20 years	293 (44.9)	143 (41.4)
BSA score by palm method, n	624	317
Median (IQR)	6.0 (1.0–16.0)	5.0 (0.2–18.0)
Peak historical BSA score by palm method, n	276	170
Median (IQR)	22.0 (14.0–35.0)	24.5 (13.5–40.0)
BSA score distribution, n (%)	624	317
BSA <3	221 (35.4)	139 (43.8)
BSA 3–10	190 (30.4)	71 (22.4)
BSA >10	213 (34.1)	107 (33.8)
PGA, n	636	312
Median score (IQR)	2.0 (1.0–3.0)	2.0 (1.0–3.0)
Peak historical PGA score, n	283	154
Median (IQR)	3.0 (3.0–4.0)	3.0 (3.0–4.0)
PGA score distribution, n (%)	636	312
0 – Clear	140 (22.0)	77 (24.7)
1 – Minimal	114 (17.9)	56 (17.9)
2 – Mild	101 (15.9)	50 (16.0)
3 – Moderate	188 (29.6)	86 (27.6)
4 – Marked	88 (13.8)	38 (12.2)
5 – Severe	5 (0.8)	5 (1.6)
PASI, n	635	316
Median PASI score (IQR)	3.6 (0.6–11.2)	2.7 (0.0–10.6)
PASI score distribution, n (%)	635	316
PASI <3	294 (46.3)	163 (51.6)
PASI 3–10	153 (24.1)	66 (20.9)
PASI >10	188 (29.6)	87 (27.5)
PsA (self-reported), n (%)	136 (20.5)	91 (25.9)
PEST score, n	528	274
Median PEST score (IQR)	1.0 (0.0–3.0)	1.0 (0.0–3.0)
PEST score distribution, n	528	274
<3 (no referral)	369 (69.9)	186 (67.9)
≥3 (referral to rheumatologist recommended)	159 (30.1)	88 (32.1)
PsAID-12 score, n	360	188
Median PsAID-12 score (IQR)	1.5 (0.0–4.2)	1.2 (0.1–3.6)
Prior biologic therapies, n (%)	665	354
0	137 (20.6)	52 (14.7)
1	269 (40.5)	172 (48.6)
≥2	259 (38.9)	130 (36.7)
Prior non-biologic systemic immunomodulatory therapies, n (%)*	665	354
Any	471 (70.8)	277 (78.2)
Methotrexate	358 (53.8)	202 (57.1)
Ciclosporin	303 (45.6)	161 (45.5)
Other immunomodulator(s)	27 (4.1)	27 (7.6)

*Patients may have reported prior use of >1 immunomodulatory therapy.
BSA, body surface area; GUS, guselkumab; IL-17i, interleukin-17 inhibitor; IQR, interquartile range; PASI, Psoriasis Area and Severity Index; PEST, Psoriasis Epidemiology Screening Tool; PGA, Physician's Global Assessment; PsA, psoriatic arthritis; PsAID-12, 12-domain Psoriatic Arthritis Impact of Disease.

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Abstract N°: 253

A case report of alopecia universalis effectively treated with oral Upadacitinib

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A case report of alopecia universalis effectively treated with oral Upadacitinib

Introduction & Objectives:

Alopecia universalis is the most severe form of alopecia areata, an autoimmune condition attacking hair follicles causing nonscarring hair loss. Blocking of Janus kinase pathways involved in the disease pathogenesis may help hair regrowth. We present a case of a 29-year-old man with alopecia universalis successfully treated with the second-generation Janus kinase 1 inhibitor Upadacitinib. The latest literature concerning Upadacitinib for treating alopecia universalis is also reviewed.

Materials & Methods:

A 29-year-old man presented with alopecia universalis for 10 years refractory to intralesional steroids. Physical examination showed complete scalp hair loss (Severity of Alopecia Tool score 100%), no eyelashes, sparse eyebrows, and hairless limbs. He had no history of atopy or systemic conditions, and was a nonsmoker and non-drinker. Blood tests for complete blood count, renal function, liver function, lipid profile, hepatitis and tuberculosis screening were unremarkable. Oral Upadacitinib 15mg daily was started, with a view to increase the dose if no response was seen after 2 weeks. Follow-up visits were arranged every 2 weeks. We also summarised the demographics and the Upadacitinib response of alopecia universalis in our patient and in the five previous case reports (Table 1).

Results:

Table 1 shows both genders of different races were affected. The mean age was 27.8 years. All but two had comorbidities. The mean disease duration was 2.8 years. All had failed previous topical and/or systemic therapies. One was also treated with Adalimumab then Ustekinumab for Crohn's disease. The Upadacitinib daily dose used in children was 15mg and in adults was 30mg, except in our patient and the 67-year-old who were given 15mg. The mean first clinical sign of hair regrowth was 6 weeks, and the mean complete hair regrowth was 15 weeks. All reported hair regrowth in the scalp, eyebrows, and eyelashes. Three including our patient also had beard regrowth, and only one reported limb hair regrowth after 28 weeks of treatment. Two maintained full hair regrowth after treatment cessation for 2 months and 6 months respectively. There were no adverse events except one adolescent with transient mild leukopenia. Our patient achieved first clinical signs of hair regrowth on the scalp after 2 weeks. This was followed by eyebrow, eyelash, beard, and lastly pubic hair regrowth. The same daily dose of 15mg was used throughout his treatment period. After 10 weeks, he had complete hair regrowth of all areas (Severity of Alopecia Tool score 0%), except partial regrowth of beard and pubic area and no limb hair regrowth. No side effects were noted. He stopped the medication after 20 weeks due to significant hair regrowth.

Conclusion:

Upadacitinib at a lower dose of 15 mg resulted in a rapid and effective response for alopecia universalis in our patient. Further studies are needed to evaluate the most appropriate dose, treatment duration and long-term safety of Upadacitinib for adults with alopecia universalis.

Table 1: Summary of case reports of the treatment of alopecia universalis with oral Upadacitinib (UPA)
Authors
Youssef et al.
Johnston et al.
Gori et al.
Yu et al.
Kolz et al.
Present case

Table 1: Summary of case reports of the treatment of alopecia universalis with oral Upadacitinib (UPA)

Authors	Age (years), sex, race	Comorbidities	Disease duration	UPA daily dose(mg)	First clinical sign of hair regrowth (weeks)	Complete hair regrowth) (weeks)
Youssef et al.	67 M, Caucasian	Cardiovascular disease	6 months	15	8	16
Johnston et al.	23 M, Caucasian	Crohn's disease	3 years	30	16	28
Gori et al.	25 M, Not stated	None	4 years	30	4	12
Yu et al.	9 F, Asian	Atopic dermatitis	7 years	15	2	12
Kolz et al.	14 F, Caucasian	Atopic dermatitis	16 months	15	4	12
Present case	29 M, Asian	None	10 years	15	2	10

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AMSTERDAM 25-28 SEPTEMBER 2024
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Abstract N°: 353

Weight Gain Secondary to the Use of Systemic Janus Kinase Inhibitors in Various Indications: A Systematic Review and Meta-analysis

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Introduction & Objectives:

Recently, oral Janus kinase inhibitors (JAKi) and Tyrosine kinase-2 inhibitors have become increasingly popular for the treatment of various inflammatory and hematological conditions. These include, but are not limited to alopecia areata, psoriasis, atopic dermatitis, rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, inflammatory bowel disease, myelofibrosis, polycythemia vera, and graft-versus-host disease. Several adverse effects have been documented with the use of JAKi such as acne, nausea, dyslipidemia, and herpes zoster, among others. Interestingly, there are a growing number of reports linking the usage of oral JAKi with weight gain. In this study, we conducted a systematic review and meta-analysis to review this possible association. The study objectives were to examine the incidence rate, and to describe the characteristics of weight gain secondary to use of various JAKi for all indications.

Materials & Methods:

Searches were conducted in April 2024 on Ovid MEDLINE, Embase, Web of science, Clinicaltrials.gov, and preprint databases. 953 studies were screened by two independent reviewers according to a predetermined criteria of which 57 eligible studies were identified. This process was repeated for 127 RCT protocols, which yielded 33 eligible trials. Inter-rater reliability was strong with a rounded Cohen's kappa of 0.8. Data from 16,000 patients (4774 male, 10486 female, and 740 of unreported sex) across 90 articles was extracted. The weighted mean age of patients was 54.8 (range: 16-92). Random-effects meta-analysis was performed on RStudio, stratified by study type with 95% confidence intervals.

Results:

Across all included studies, weight gain was reported in 5.9% (947/16000) of patients. Weight gain events were recorded at 73.9 weeks after JAKi initiation on average. Among the 90 studies examined, 29 reported the magnitude of weight gain showing an average of 8.6kg gain from a baseline mean weight of 63.4kg, recorded at an average of 74.3 weeks into treatment.

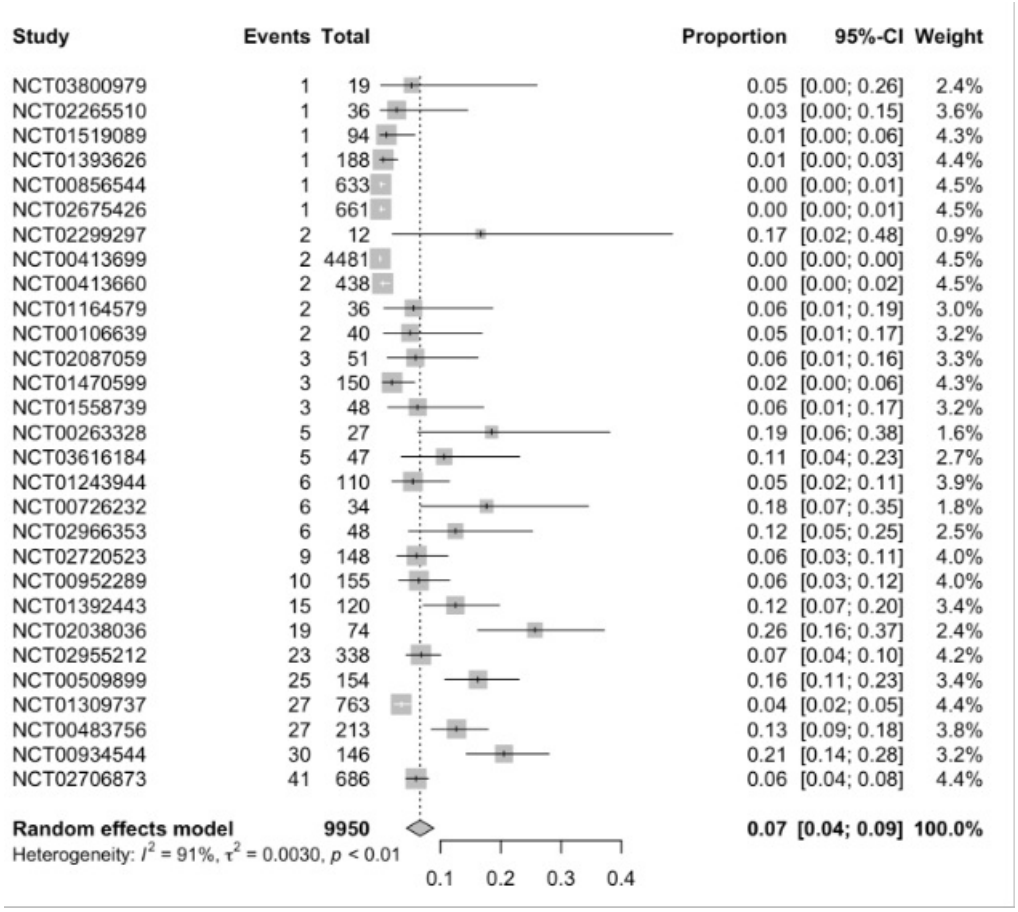
In RCTs, weight gain secondary to JAKi usage across all indications was observed in 7% (95% CI: 0.04; 0.09) of patients (Figure 1). Further subgroup analysis of RCTs found ruxolitinib to have the highest rate of weight gain at 12% (95% CI: 0.08; 0.16) followed by upadacitinib [5% (95% CI: 0.01; 0.08)] and tofacitinib [3% (95% CI: 0.01; 0.05)]. Notably, dermatologic indications had lower rates of weight gain at 4% (95% CI: 0.01; 0.06) compared to 7% (95% CI: 0.04; 0.09) for non-dermatologic indications (Figure 2).

Pooled results for observational and non-randomized studies showed substantially larger rates of weight gain, at 26% (95% CI: 0.11; 0.41) and 39% (95% CI: 0.15; 0.64), respectively (Figure 3 and 4). The larger effect sizes can be explained by confounding variables and discrepancies between definitions of weight gain in these study designs, compared to RCTs.

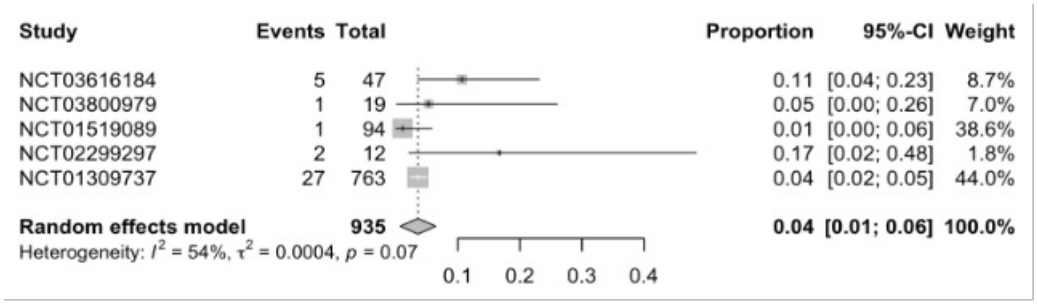
Conclusion:

Use of JAKi is associated with weight changes, particularly weight gain, which may be crucial for patient counselling. This study's limitations include heterogeneity between included studies and publication bias due to underreporting of smaller effect sizes. Further investigation is necessary, and researchers are encouraged to include weight changes in future study protocols to reduce publication bias and identify true effect sizes.

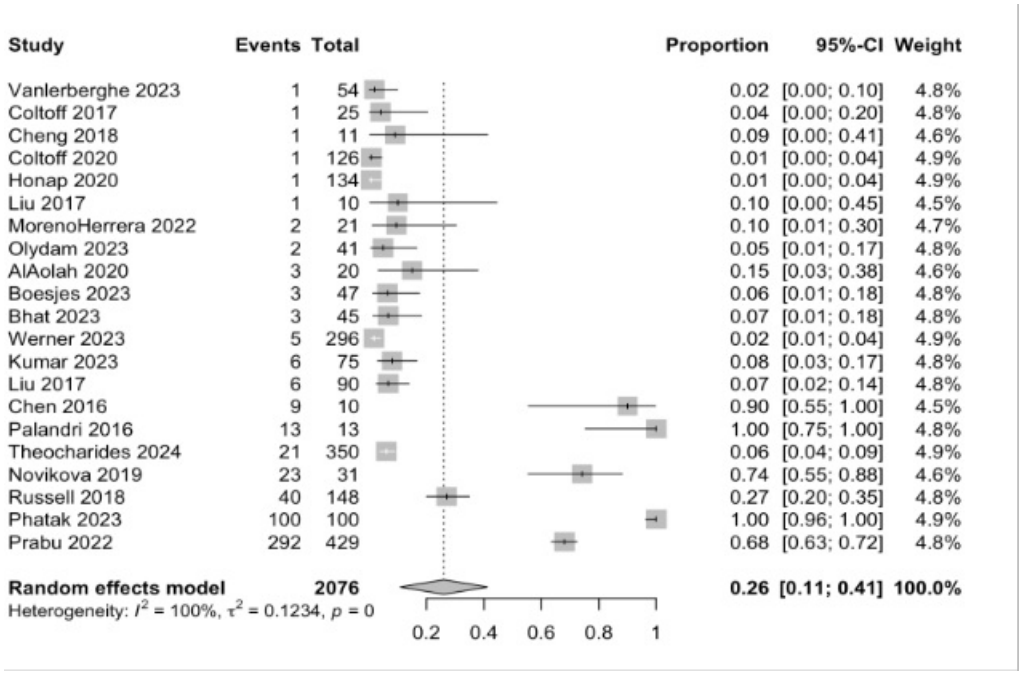
Appendix 1: Forest Plot of Included RCTs – Weight Gain



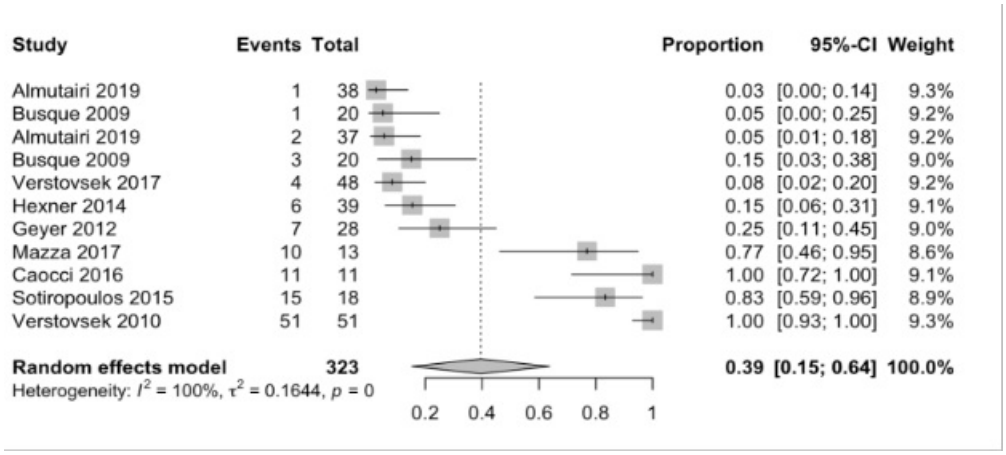
Appendix 2: Forest Plot of Included RCTs – Weight Gain in Dermatology Indications



Appendix 3: Forest Plot of Included Observational Studies – Weight Gain



Appendix 4: Forest Plot of Included Non-interventional Studies – Weight Gain



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Abstract N°: 514

Improvements in Clinical and Patient-Reported Outcomes in Patients With Active Psoriatic Arthritis With and Without Radiographic Progression at 1 Year: A Post Hoc Analysis From KEEPsAKE 1

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Introduction & Objectives:

The modified Total Sharp Score (mTSS) is a validated instrument that measures radiographic progression and is a clinically important measure of joint outcomes in clinical studies of rheumatoid arthritis and psoriatic arthritis (PsA). However, the magnitude of change in mTSS that would be associated with a clinically relevant impact in patient symptoms and function remains unclear. To better understand risankizumab's clinical outcomes in PsA, we evaluated clinical and patient-reported improvements and their relationship to radiographic change. In this post hoc analysis, data from the KEEPsAKE1 trial were assessed.

Materials & Methods:

KEEPsAKE 1 (NCT03675308) is an ongoing, global, phase 3, placebo-controlled study of risankizumab 150 mg for treatment of active PsA. Patients included in this post hoc analysis were initially randomized to receive risankizumab and treated for 52 weeks. Radiographic progressors and non-progressors were defined as having a change from baseline to week 52 in mTSS > 0 and ≤ 0, respectively (mTSS range: 0–528). Clinical outcomes were percent change from baseline to week 52 in tender joint count (TJC), swollen joint count (SJC), and Physician's Global Assessment (PhGA) of disease activity (100-mm visual analog scale [VAS]). Patient-reported outcomes (PROs) were percent change from baseline to week 52 in the Patient's Global Assessment (PtGA), Health Assessment Questionnaire-Disability Index (HAQ-DI), pain (100-mm VAS), and the physical and mental components of the 36-Item Short Form Health Survey (SF-36). A mixed-model repeated measures was used to minimize potential bias related to data with high variability or missing at random, including patients with ≥ 1 change from baseline value and no missing data for factors and covariates in the model (subgroup [progressors vs non-progressors], visit, subgroup × visit interaction, current use of csDMARD [0 vs ≥1], baseline dactylitis [yes vs no], enthesitis [yes vs no], and psoriasis [≥ 3% or < 3% body surface area]. This post hoc analysis is descriptive and formal hypothesis testing was not conducted.

Results:

A total of 430 risankizumab-treated patients were included in this analysis. At week 52, few patients showed radiographic progression (progressors, n = 35 [8.1%]; non-progressors, n = 395 [91.9%]). Progressors had greater clinical disease activity at baseline compared with non-progressors, as demonstrated by relatively higher TJC and SJC (**Table**). However, the percent improvements with risankizumab in clinical outcomes (TJC, SJC, and PhGA) and PROs (PtGA, HAQ-DI, pain, SF-36 [physical], and SF-36 [mental]) at week 52 were similar between the progressor and non-progressor cohorts (**Figure**).

Conclusion:

Irrespective of progression status, risankizumab-treated patients with PsA experienced similar improvements in

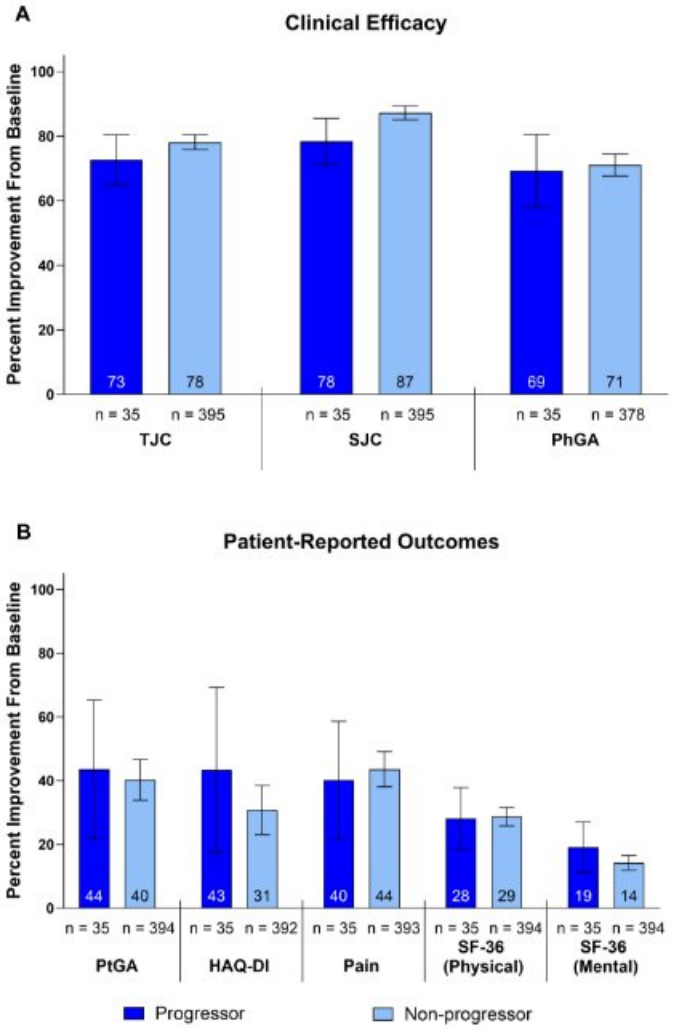
clinical outcomes and PROs at week 52. Change in mTSS over time is a useful measure of joint outcomes and disease progression, but these results suggest that mTSS changes may not reflect observed clinically meaningful short-term improvement in clinical outcomes or PROs. Future research would be required to determine if progression status over longer time periods could result in differences with regard to clinical outcomes or PROs.

Table. Baseline Characteristics for Patients Who Were Radiographic Progressors (Change From Baseline mTSS > 0) or Non-Progressors (Change From Baseline mTSS of ≤ 0) at Week 52

Characteristic	Progressor (n = 35)	Non-progressor (n = 395)	Total (N = 430)
Duration of PsA, years			
n	35	393	428
Mean (SD)	6.6 (5.6)	7.4 (7.1)	7.3 (7.0)
Median (range)	4.3 (0.4–19.8)	4.9 (0.4–35.1)	4.9 (0.4–35.1)
TJC			
Mean (SD)	27.7 (16.9)	20.2 (13.8)	20.9 (14.2)
Median (range)	26 (5–61)	16 (5–68)	17 (5–68)
SJC			
Mean (SD)	15.1 (8.5)	12.0 (7.8)	12.2 (7.9)
Median (range)	13 (5–36)	9 (5–50)	9 (5–50)

PsA, psoriatic arthritis; SJC, swollen joint count; TJC, tender joint count.
All patients were randomized to receive risankizumab 150 mg. Percentages calculated on non-missing values.

Figure. LS Mean (95% CI) Percent Change From Baseline to Week 52 in Radiographic Progressors (Change From Baseline mTSS > 0) and Non-Progressors (Change From Baseline mTSS of ≤ 0) in Measures of Clinical Outcomes (A) and PROs (B).



csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire-Disability Index; MMRM, Mixed Effect Model Repeated Measures; mTSS, modified Total Sharp Score; PGA, Physician's Global Assessment; PsA, psoriatic arthritis; PtGA, Patient's Global Assessment; SF-36, 36-Item Short Form Health Survey; SJC, swollen joint count; TJC, tender joint count.

MMRM analysis included subgroup (non-progressor vs progressor), visit, subgroup-by-visit interaction, use of csDMARD (0 vs ≥ 1), dactylitis (yes vs no), enthesitis (yes vs no), psoriasis body surface area (≥ 3% vs < 3%), and patient's discontinuation status.

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Abstract N°: 538

Successful treatment of lichen planus of the skin with upadacitinib

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Introduction & Objectives:

Lichen planus is a very common inflammatory immune dermatosis that can affect the skin, mucous membranes and skin appendages. Cutaneous lichen planus (CLP) typically presents clinically with purple, raised, polygonal, slightly scaly and very itchy flat papules. Many different variants of CLP have been described, including CLP exanthematicus and CLP verrucosus. The pathogenesis of CLP has not yet been fully clarified. Among other things, it is assumed that the accumulation of T cells in the dermis, both CD4+ and CD8+, leads to the release of various cytokines, which leads to apoptosis of the basal cells of the epidermis.

CLP can be treated with both topical corticosteroids and systemic therapies, including systemic retinoids. Phototherapy can also be helpful. In some cases, CLP is refractory to approved systemic therapies. It has been shown that various previously unapproved therapies can be used successfully in refractory CLP, including interleukin (IL)-17 inhibitors and Janus kinase inhibitors (JAKIs).

Upadacitinib is a JAKI that can be used to treat several chronic inflammatory diseases, including rheumatoid arthritis, psoriatic arthritis, atopic dermatitis and alopecia areata. JAKIs activate the signal transducers and activators of transcription that modulate gene expression and cell function. In contrast to most biologics, JAKIs interrupt the signaling effect of several ILs that are important for the pathophysiology of the above-mentioned diseases.

We report on a 55-year-old patient with refractory CLP who showed no significant improvement despite treatment with systemic retinoids and secukinumab. In this case, treatment with upadacitinib 30 mg p.o. once daily led to a rapid improvement of the skin condition and significant relief of itching. With this case, our working group was able to show that upadacitinib can be successfully used as a possible therapy outside the approval for refractory CLP.

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Abstract N°: 547

Effectiveness of abrocitinib for the treatment of moderate-to-severe atopic dermatitis in patients switched from dupilumab and/or tralokinumab: a real-world retrospective study

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Introduction & Objectives:

Dupilumab and tralokinumab are biologic therapies approved for the treatment of moderate-to-severe atopic dermatitis (MtS-AD). However, many patients in real-world settings either do not respond adequately to these treatments or encounter adverse events (AEs). Abrocitinib, a Janus kinase (JAK) 1-selective inhibitor, has demonstrated superior efficacy compared to both dupilumab and tralokinumab. Despite this, there is limited evidence regarding the outcomes of real-world patients who have switched to abrocitinib following prior therapy with either dupilumab or tralokinumab. Our objective is to describe the outcomes of such patients.

Materials & Methods:

We conducted a retrospective single-institution study of 25 adult patients with MtS-AD treated with abrocitinib 100 mg or 200 mg following treatment with dupilumab or tralokinumab for at least 16 weeks. The patients' baseline demographic and clinical characteristics were recorded before treatment with biologic agents (**Table 1**). Clinical outcomes at week 16 were assessed with Physician Global Assessment (PGA) and Peak Pruritus Numerical Rating Scale (PP-NRS), as well as the achievement of ≥ 75% improvement in the Eczema Area and Severity Index (EASI-75).

Results:

EASI-75 was achieved by 76% of all patients, with a higher proportion of patients receiving abrocitinib 200 mg achieving EASI 75 (88%) compared to patients receiving abrocitinib 100 mg (56%) (**Table 2**). While 65% of patients achieved a PGA score of 0-1 at week 16, PGA 0 was only attained by patients who received abrocitinib 200 mg. Almost all patients receiving abrocitinib 200 mg achieved PP-NRS <4 (94%). Treatment-related AEs were uncommon, occurring in 28% of patients throughout the 16-week period. This included acne and/or folliculitis (8%), nausea (8%), oro-facial herpes (4%), weight gain (8%), fatigue (4%) and tremor (4%).

Conclusion:

Similar findings were observed in previous studies on patients who switched from dupliumab to abrocitinib. However, our study is the first to evaluate outcomes in patients who switched to abrocitinib from tralokinumab. Our findings demonstrate that abrocitinib is an effective treatment option for patients with MtS-AD who either fail to respond to, cannot tolerate, or experience AEs with biologic therapy.

Table 1: Clinical and demographic characteristics of patients at baseline before starting biologic agents.
EASI: Eczema Area and Severity Index, NBUVB: Narrowband Ultraviolet B, PGA: Physician Global Assessment, PP-NRS: Peak Pruritus Numerical Rating Scale, SD: Standard Deviation

Demographic or clinical characteristics	n, (%)
Age (years) mean ± SD	31.16 ± 10.82
Female gender	15 (60)
Fitzpatrick skin type	
• 1	3 (12)
• 2	8 (32)
• 3	7 (28)
• 4	4 16)
• 5	2 (8)
• 6	1 (4)
Atopic dermatitis onset	
• Childhood	19 (76)
• Adult	5 (20)
• Unspecified	1 (4)
Other atopic diathesis	
• Asthma	7 (28)
• Allergic rhinitis	6 (24)
Previous non-biologic treatment	
• Phototherapy (NBUVB)	6 (24)
• Oral methotrexate	11 (44)
• Cyclosporine	3 (12)
Previous biologic treatment	
• Dupilumab only	19 (76)
• Tralokinumab only	5 (20)
• Dupilumab and tralokinumab	1 (4)
Baseline EASI, mean (range)	20.35 (16-32)
Baseline PGA	
• PGA 3	11 (44)
• PGA 4	14 (56)
Baseline PP-NRS, mean (range)	7.36 (5-10)

Table 2: Efficacy outcomes after 16 weeks of abrocitinib. EASI 75: ≥ 75% improvement in Eczema Area and Severity Index, PGA: Physician Global Assessment, PP-NRS: Peak Pruritus Numerical Rating Scale

Outcome	Total patients (N = 25) n (%)	Abrocitinib 200 mg (n = 16) n (%)	Abrocitinib 100 mg (n = 9) n (%)
Patients achieving EASI 75	19 (76)	14 (88)	5 (56)
Patients achieving PGA 0-1	16 (64)	14 (88)	2 (22)
Patients achieving PGA 0	8 (32)	8 (50)	0 (0)
Patients achieving PP-NRS <4	19 (76)	15 (94)	4 (44)
Patients achieving PP-NRS 0-1	8 (32)	7 (44)	1 (11)

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Abstract N°: 577

Omalizumab and dupilumab – successful use in a refractory case of bullous pemphigoid secondary to nivolumab

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Omalizumab and dupilumab – successful use in a refractory case of bullous pemphigoid secondary to nivolumab

Introduction & Objectives:

Bullous pemphigoid secondary to immunotherapy has presented a new cohort of patients with many unique therapeutic challenges. Greater understanding of the pathophysiology of bullous pemphigoid has led to the off licence use of newer targeted biologic therapies. Dupilumab and omalizumab are emerging as potential safe and effective targeted treatment options particularly in cases recalcitrant to standard treatments.

Materials & Methods:

We present the case of a 43 year old female patient, with a background history of Hodgkin's lymphoma was referred to the dermatology department with a two-week history of a pruritic blistering rash. She had completed 14 cycles of nivolumab.

Three months following the course of nivolumab she developed a pruritic, urticated and eczematous rash predominantly affecting her trunk and proximal limbs. This rapidly evolved to become a widespread bullous eruption with tense intact bullae and erosions affecting her upper thighs, back and arms.

A skin biopsy taken at this time demonstrated subepidermal bullous formation with abundant eosinophils. Direct immunofluorescence showed linear IgG and C3 along dermal-epidermal junction. ELISA tests demonstrated positive serum antibodies against BP-180 with an antibody titer of 193 U/ml and BP-230 with an antibody titer of 90 U/ml. These findings were consistent with a diagnosis bullous pemphigoid.

The patient was initially treated with oral prednisolone 0.5mg/kg, doxycycline 100mg twice daily and topical clobetasol propionate. Mycophenolate mofetil 1g twice daily was added as a steroid sparing agent. Her skin continued to blister despite treatment necessitating admission for inpatient intensive skin care and further medical treatment. At this point the bullae and erosions involved over 70% of her body surface area with painful crusted erosions on her back, sacrum and breasts. Despite treatment with oral prednisolone, mycophenolate mofetil, IVIg and rituximab her condition continued to progress. She was transferred to a tertiary care centre for treatment with six cycles of plasma exchange, which resulted in significant reduction of blistering activity.

Omalizumab 300mg alternate weeks was added at this point due to further blistering and an elevated IgE. This resulted in significant clinical improvement noted within two weeks of commencing treatment. Unfortunately, over the following month the patient was readmitted to hospital because of worsening blistering, pain and itch. Dupilumab 300mg alternate weeks was added in combination with omalizumab. A decrease in itch was noted within days of commencing dupilumab, and the patient reported feeling much more comfortable with less pain.

Results:

While the patient was on this treatment with combination omalizumab and dupilumab, she remained blister free while allowing a continued tapering of oral prednisolone to 5mg. Interestingly a recent attempt to stop omalizumab resulted in a pre-bullous eruption on her forearms and abdomen which subsequently resolved upon its reintroduction.

Conclusion:

Given the many inherent risks and complications associated with immunosuppression in this patient group, targeted therapies such as dupilumab and omalizumab may provide a safe and efficacious option, either as single agents or in severe refractory cases such as this one, as combination therapy.

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Abstract N°: 762

Bullous pemphigoid secondary to dipepitidyl peptidase-4 inhibitors complicated by reactive perforating dermatosis with response to dupilumab

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Introduction & Objectives: Bullous pemphigoid (BP) is an autoimmune blistering disease of unknown etiology. Cases secondary to dipeptidyl peptidase-4 inhibitors (DPP4i), used for the management of diabetes mellitus (DM), have been described. The association of BP with reactive perforating dermatosis (RPD) unrelated to DPP4i has been previously reported in sporadic cases.

Case report: We present the case of an 81-year-old woman with a history of type II DM treated with linagliptin. She initially presented with intense pruritus and erosions on the trunk and limbs. Histopathological examination revealed a lymphocytic infiltrate with eosinophils in the dermis. Direct immunofluorescence showed a linear deposit of IgG at the basement membrane. ELISA testing revealed a concentration of anti-BP180 antibodies of 43 U/mL. With all this, the diagnosis of DPP4i-induced BP with a partial response to topical clobetasol propionate was established. During follow-up, the patient developed new lesions on the trunk and limbs that looked like umbilicated papules with a keratotic center. A biopsy of one lesion showed transepidermal elimination of altered collagen and elastic fibers, compatible with RPD. After failure of treatment with topical and systemic corticoids, topical retinoids, and UVB phototherapy, treatment with dupilumab was initiated with a significant improvement after 6 doses.

Discussion: RPD lesions represent a cutaneous reaction to trauma due to itching. Cases of RPD associated with DPP4i-induced BP have been described, most of them preceding the onset of BP. Dupilumab is a monoclonal antibody against IL-4 and IL-13 that has emerged as a safe and effective treatment in moderate-to-severe forms of BP. RPD lesions show a Th2 dermal infiltrate. For this reason, it has been proposed as an effective alternative in the management of refractory RPD.

Conclusion: In conclusion, we present the case of a woman with DPP4i-induced BP with secondary RPD with a good response to dupilumab.

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Abstract N°: 826

Chronic prurigo treated with dupilumab. A case series

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Introduction & Objectives:

Chronic prurigo is a neuroinflamatory dermatosis characterized by chronic pruritus (pruritus for at least 6 weeks), scratch-associated pruriginous skin lesions and history of repeated scratching.

Dupilumab is a monoclonal human IgG antibody that inhibits the alpha subunit of the interleukin 4 receptor. It has been used with satisfactory results in the treatment of patients with chronic prurigo.

Our objective is to review our patients with chronic prurigo treated with dupilumab in order to study its effectiveness and safety.

Materials & Methods:

We conducted a retrospective single-center case series of six patients treated with dupilumab for chronic prurigo.

Results:

Six patients were included in this study, with ages ranging from 38 to 81 years old with a median age of 59,6 years old. 50% were female. 50% had atopic dermatitis. 33,3% had psychiatric comorbidities.

The dose of dupilumab used was 300mg every 2 weeks with a starting dose of 600mg.

5 patients received dupilumad for at least 6 months with improvement of their skin lesions and pruritus within the first three months.

One patient received dupilumab for eight weeks and then was switched to baricitinib due to lack of efficacy.

Before treatment with dupilumab, all patients had used topical corticosteroids and oral antihistamines. 50% had been treated with narrowband ultraviolet B. 2 patients had used topical calcineurin inhibitors. 2 patients had been treated with cyclosporine. 1 patient had been treated with oral corticosteroids and methotrexate.

4 patients achieved a complete (2 patients) or nearly complete (2 patients with only a single prurigo lesion) response of their prurigo lesions. 1 patient had a partial response with less prurigo lesions but persistence of pruritus. 1 patient did not respond to dupilumab and was switched to baricitinib with partial response.

Concomitant treatments were used in 5 patients; topical corticosteroids in 4 patients, topical calcineurin inhibitors in 2 patients, narrowband ultraviolet B in 1 patient.

None of the patients experienced any side effect during the treatment with dupilumab.

Conclusion:

Dupilumab is an effective and safety treatment for chronic prurigo, with a rapid improvement of the pruritus and prurigo lesions in the majority of patients and complete or nearly complete response in more than 65% of patients

in our case series.

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Abstract N°: 994

Dupilumab Induced Hair Repigmentation

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Dupilumab Induced Hair Repigmentation

Introduction & Objectives:

Antibody-based therapies that inhibit proinflammatory cytokine signaling are commonly used in dermatology. Paradoxically, these medications may induce or exacerbate other inflammatory conditions. Dupilumab is a humanized monoclonal antibody that targets IL-4 and IL-13. In some studies, dupilumab has been shown to trigger hair growth in patients with atopic dermatitis, in which specific mechanism has not been fully explained. Herein, a patient hair repigmentation after treatment of with dupilumab will be presented.

Materials & Methods:

A 79-year-old male with the diagnoses of Atopic Dermatitis for 5 years admitted our clinic. His past medical hyistory revealed hypertension, cholestasis and sleep disorders and medications Telmisartan for 3 years, Ursodeoxycholic acid for 1 year and Venlafaxine for 1.5 years. For dermatologic lesions topical calcineurin inhibitors, 10% topical urea, and bilastine was used for about 6 months. On dermatologic examination there were nodular, chronic eczematous lesions and fewer lichenified plaques on the back and flexural extremities.

Results:

Dupilumab was started with the initial dose 600 mg, then 300 mg every 2 weeks. Two months after the start of dupilumab treatment, he noticed repigmentation of the scalp hair in the frontoparietal and temporal regions with increased hair dansity.

Conclusion:

Very few cases regarding the effects of dupilumab on hair repigmentation has been reported. Melanocytes connects with numerous keratinocytes and transfer melanosomes Melanin is synthesized in the cytoplasm of melanocytes. Substances such as ET1, nerve growth factor (NGF), α-MSH, ACTH, prostaglandin E2 (PGE2) and β endorphins from keratinocytes play a role in melanocyte dendritization. Human skin and hair colour variations is regulated by α-MSH. It decreases the production of proinflammatory and immunomodulatory cytokines such as IL-1, IL-6, TNF-α, IL-2, IFN-γ, IL-4, IL-13 and the expression of costimulatory molecules such as CD68, CD40, ICAM-1 in antigen-presenting dendritic cells. Dupilumab is thought to increase the effect of α-MSH by inhibiting IL-4 and IL-13 cytokines.

Although the relationship between Dupilumab and α-MSH has not been fully explained, it may have a common effect on cytokines. In addition, a repigmentation effect may occur with Th1 suppression and IL-4 and IL-13 decrease. Further studies are required to differentiate the effect of cytokine or dupilumab.

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Abstract N°: 1058

Imsidolimab, an IL-36 Receptor Antagonist, was Effective and Well Tolerated for Treatment and Prevention of Flares in Patients with Generalized Pustular Psoriasis: Results from the Phase 3 Trials, GEMINI-1 and GEMINI-2

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Introduction & Objectives: Generalized pustular psoriasis (GPP) is a rare, severe disease characterized by debilitating flares of non-infectious pustular and erythematous skin lesions, with systemic impacts that can be life-threatening. Recurrent flares are common. The pathogenesis of GPP can be mainly attributed to excessive activity of IL-36 pathway. Imsidolimab, an investigational IgG4 antibody, binds the IL-36 receptor and antagonizes IL-36 signaling. In the Phase 2 GALLOP trial, imsidolimab showed rapid and sustained improvements in symptoms and pustular eruptions with an acceptable safety profile. Reported here are results from the Phase 3 trials, GEMINI-1 (NCT05352893) and GEMINI-2 (NCT05366855).

Materials & Methods: In GEMINI-1, a randomized, double-blind, placebo (PBO)-controlled, global trial,** 45 patients with GPP received a single IV dose of imsidolimab 750mg, imsidolimab 300mg, or PBO. The primary efficacy endpoint at Wk 4 was achievement of GPP Physician Global Assessment (GPPPGA) score of clear/almost clear (0/1) collectively across all GPP disease attributes (pustulation, erythema, scaling), a stringent and comprehensive characterization of disease severity. Patients who were GPPPGA responders, partial responders, or needed rescue therapy (RT) could enroll in GEMINI-2, a follow-on trial of imsidolimab 200mg SC given every 4 wks with evaluation of safety, maintenance of response and prevention of GPP flares. Responders in GEMINI-1 were re-randomized to blinded imsidolimab or PBO, while all partial responders received imsidolimab. Patients in the GEMINI-1 PBO group who needed RT crossed into GEMINI-2 and received imsidolimab 750mg IV followed by 200mg SC every 4 wks.

Results: *GEMINI-1:*** GPPPGA 0/1 was achieved in 53.3% of patients in the imsidolimab 750mg group, 53.4% in the imsidolimab 300mg group, vs 13.3% of patients on PBO. Among PBO patients that exited GEMINI-1 to receive RT in GEMINI-2, 55.6% attained GPPPGA of 0/1 at Wk 4. *GEMINI-2:* None of the responders re-randomized to imsidolimab maintenance dosing had a GPP flare, and all maintained a GPPPGA score of 0/1, while in the PBO group, 62.5% flared (GPPPGA ≥ 3), and 75.0% lost GPPPGA 0/1 response. None of the PBO cross-over patients had a flare, and all maintained GPPPGA 0/1. *Safety:* In GEMINI-1, imsidolimab 300mg and 750mg doses were well tolerated. All adverse events (AEs) in imsidolimab-treated patients were mild or moderate and balanced across imsidolimab- and PBO-treated patients. No treatment-related SAEs or severe AEs were reported. In GEMINI-2, imsidolimab 200mg SC was well tolerated. There were no SAEs leading to discontinuation, and no treatment-related SAEs. Across the trials, there was a low incidence and no elevation of infections vs PBO. There were no reported cases of Drug Reaction with Eosinophilia and Systemic Symptoms or Guillain-Barre syndrome. No infusion reactions were reported. Overall, detection of anti-drug antibodies was uncommon, and none were

neutralizing.

Conclusion: Single IV doses of imsidolimab 300mg and 750mg demonstrated clinically meaningful results and were well tolerated in patients with GPP flares. Maintenance dosing with monthly SC imsidolimab for at least 24 wks was also well tolerated, maintained GPPPGA 0/1 responses and prevented GPP flares. Targeting IL-36 signaling with imisdolimab represents a promising therapeutic option for GPP patients.

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Abstract N°: 1165

Real-world effectiveness of risankizumab in the multi-country post-marketing VALUE study: 148-week interim analysis

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EADV 2024 Encore Abstract - Real-world effectiveness of risankizumab in the multi-country post-marketing VALUE study: 148-week interim analysis – (IFPA 2024)

Encore (IFPA 2024)

Introduction & Objectives:

Risankizumab is an optimized IL-23 inhibitor approved for treatment of moderate-to-severe plaque psoriasis, psoriatic arthritis, and Crohn's disease. VALUE is an ongoing 3-year study evaluating the long-term durability of risankizumab compared to other approved biologics(OtherBios) in patients with psoriasis in real world practice. At 100-week interim analysis, a higher proportion of patients maintained ≥ 90% improvement in psoriasis area and severity index (PASI 90) compared to patients in OtherBios group. This is an updated 148-week analysis. The objective of this study is to characterize the durability of response of risankizumab compared to OtherBios in real world practice.

Materials & Methods: VALUE is a multi-country, prospective post-marketing observational study that enrolled patients (≥18 years) with moderate-to-severe psoriasis who the treating physician decided to treat with risankizumab or OtherBios, independent of this study and per local label, in a 2:1 ratio. Effectiveness endpoints included absolute PASI, Dermatology Life Quality Index (DLQI), and proportions of patients achieving PASI 90 and PASI 100, treatment Satisfaction Questionnaire for Medication (TSQM) score, and changes to treatment. Results (database lock: 7 December 2023) are reported by modified non-responder imputation (mNRI) where patients who switched or discontinued initiated biologic due to ineffectiveness or intolerability were judged as treatment failures for subsequent visits. Propensity score match (PSM) with 1:1 ratio using greedy algorithm and exact match for bio-naive/bio-experienced status was employed to account for imbalance between treatment groups. Nominal p values are presented.

Results: Baseline demographics and characteristics were mostly comparable among 1765 (risankizumab) and 874 (OtherBios) patients enrolled in this study with a few exceptions. The risankizumab group had patients with a higher baseline PASI (15.0 vs 13.9; p=0.004), history of psoriatic arthritis (259 [14.7%] vs 233 [26.7%]; p<0.0001) and were bio-experienced (870 [49.3%] vs 324 [37.1%]; p<0.0001). Most differences were balanced in the PSM set and results from PSM set are shown below. The proportion of patients who achieved PASI 90 at week 16 and maintained the response up to week 148 was significantly higher in the risankizumab group compared to the OtherBios group (45.4% vs 29.6%; p=0.0002). Significantly fewer patients in the risankizumab group changed treatment compared to the OtherBios group (10.9% vs 24.2%; p<0.0001). At week 148, patients in the

risankizumab group achieved significantly lower absolute PASI (1.4 vs 3.6; p<0.0001) compared to OtherBios (Table). A significantly higher proportion of patients achieved PASI 90 (67.2% vs 45.3%; p<0.0001) and PASI 100 (55.2% vs 34.6%; p<0.0001) in the risankizumab group compared to OtherBios. DLQI in the risankizumab group was significantly lower than the OtherBios group (2.5 vs 5.2; p<0.0001). Significantly higher TSQM global satisfaction scores were reported for patients in the risankizumab group compared to the OtherBios group (86.1 vs 75.5; p<0.0001). Safety for risankizumab was consistent with previous studies.

Conclusion: This updated analysis from VALUE study demonstrates that patients treated with risankizumab achieve higher durable clinical responses in real-world practice compared to OtherBios. This study is ongoing and not all patients have reached week 148.

Table. Patient outcomes in 148-week VALUE update

Responses	Week 52		Week 100		Week 148	
	RZB	OtherBios	RZB	OtherBios	RZB	OtherBios
Absolute mean PASI						
mNRI mean (95% CI) n	1.2 (1.1, 1.4)*** 1355	2.3 (1.9, 2.6) 659	1.3 (1.2, 1.5)*** 1084	2.6 (2.2, 3.0) 519	1.8 (1.5, 2.1)*** 582	3.7 (3.1, 4.4) 314
PSM mean (95% CI) n	1.2 (1.0, 1.5)*** 614	2.3 (1.9, 2.6) 587	1.1 (0.9, 1.4)*** 489	2.5 (2.1, 2.9) 478	1.4 (1.1, 1.8)*** 260	3.6 (3.0, 4.3) 288
PASI 90						
mNRI % n/N	74.6 (72.2, 76.9)*** 1007/1350	58.6 (54.7, 62.4)) 385/657	70.9 (68.1, 73.6)*** 770/1086	51.5 (47.1, 55.9) 267/518	66.0 (62.0, 69.8)*** 386/585	42.1 (36.6, 47.7) 133/316
PSM % n/N	74.5 (70.9, 77.9)*** 456/612	59.6 (55.5, 63.5) 355/596	71.2 (66.9, 75.1)*** 348/489	54.3 (49.7, 58.8) 259/477	67.2 (61.1, 72.9)*** 174/259	45.3 (39.5, 51.3) 131/289
PASI 100						
mNRI % n/N	54.6 (52.0, 57.3)*** 741/1356	39.8 (36.1, 43.7) 263/660	53.5 (50.5, 56.5)*** 583/1089	38.3 (34.1, 42.6) 200/522	51.5 (47.4, 55.7)*** 302/586	32.3 (27.2, 37.7) 102/316
PSM % n/N	54.4 (50.4, 58.4)*** 334/614	40.3 (36.3, 44.4) 241/598	56.6 (52.1, 61.1)*** 277/489	40.2 (35.8, 44.7) 193/480	55.2 (48.9, 61.4)*** 143/259	34.6 (29.1, 40.4) 100/289
DLQI						
mNRI mean (95% CI) n	2.0 (1.8, 2.2)*** 1322	3.3 (2.9, 3.7) 646	1.8 (1.6, 2.0)*** 1046	3.7 (3.2, 4.2) 501	2.4 (2.1, 2.8)*** 531	5.3 (4.5, 6.1) 296
PSM mean (95% CI) n	2.2 (1.9, 2.5)*** 605	3.4 (2.9, 3.8) 583	1.9 (1.6, 2.3)*** 465	3.6 (3.1, 4.1) 461	2.5 (1.9, 3.0)*** 233	5.2 (4.4, 6.0) 272
TSQM (Global)						
mNRI mean (95% CI) n	84.6 (83.5, 85.6)*** 1291	77.5 (75.7, 79.4) 626	86.0 (84.9, 87.2)*** 1010	78.8 (76.7, 80.8) 470	84.7 (83.0, 86.5)*** 483	74.6 (71.3, 77.8) 259
PSM mean (95% CI) n	85.0 (83.5, 86.4)*** 582	77.8 (75.9, 79.7) 566	86.0 (84.4, 87.7)*** 443	79.4 (77.4, 81.5) 436	86.1 (83.6, 88.7)*** 210	75.5 (72.2, 78.9) 240

PASI, Psoriasis Area and Severity Index; DLQI, Dermatology Life Quality Index; TSQM, Treatment Satisfaction Questionnaire for Medication; n, number; CI, confidence interval; mNRI, modified non responder imputation; PSM, Propensity Score Matched; *p≤0.05; **p≤0.01;***p≤0.0001

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Abstract N°: 1201

Efficacy and safety of secukinumab in psoriasis: Five-year real life experience

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Introduction & Objectives: The aim of this study was to evaluate the efficacy and safety of secukinumab in plaque psoriasis.

Materials & Methods: Data of 101 plaque psoriasis patients who received at least 16 weeks of secukinumab treatment between June-2018 and June 2023 were retrospectively analyzed.

Results: Fifty-three (53%) of the patients were bionaive. PASI 75, 90, 100 response rates were 72%, 50%, 30% respectively at week 16 in all patients. PASI 75 and 90 responses were higher in naive patients at weeks 16 and 28 ($p<0.001$, $p<0.001$, $p<0.01$, $p=0.01$, respectively). The percentage of the all patients with PASI ≤ 1, ≤ 3, ≤ 5 were in 50%, 77%, 92%, respectively at week 16. They were higher in naive group than nonnaive group at weeks 16 and 28 ($p=0.02$, $p<0.01$, $p=0.05$, $p=.0.07$, $p<0.01$, $p=0.03$, respectively). In our study, 56 (56%) of the patients were smoking. At 52 weeks, PASI 75, 90, 100 responses were statistically significantly lower in patient with smoking ($p=0.04$, $p=0.03$, $p<0.01$, respectively). Mean duration of secukinumab treatment was 19.80±12.76 months. Secukinumab was discontinued 14 (26.4%) of naive patients and 28 (58.3%) of nonnaive patients at one time of treatment ($p<0.001$) The most common adverse events in patients was mucocutaneous candida infection (8%). Twenty (20%) of the patients were received prophylaxis for inactive hepatitis B virus infection Fourty-eight (48%) of the patients received isoniazid prophylaxis for latent tuberculosis. No hepatitis B or C reactivation and no active tuberculosis or reactivation was observed in any of the patients during the follow-up period.

Conclusion: Secukinumab seems to be effective in plaque psoriasis particularly in bionaive and non smokers. Moreover it is safe in patients with inactive hepatitis and tuberculosis.

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Abstract N°: 1495

Off-label oral roflumilast in dermatology: A case series

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Introduction & Objectives:

In recent decades, biologic therapies have revolutionized the treatment of inflammatory dermatoses such as psoriasis and eczema. One limitation of these therapies is their high cost.

Apremilast is an oral inhibitor of the enzyme phosphodiesterase-4 (PDE4), with an immunomodulatory effect, approved by the European Medicines Agency (EMA) for psoriasis, psoriatic arthritis and Behcet's disease. Roflumilast is another PDE4 inhibitor, approved by the EMA to reduce the risk of exacerbations in chronic obstructive pulmonary disease (COPD) and chronic bronchitis phenotype. Topical roflumilast 0.3% was approved by the Food and Drug Administration (FDA) in 2022 in the treatment of plaque psoriasis and in 2023 in seborrheic dermatitis.

Due to its safety profile, simple dosing and low cost, roflumilast has been used orally off-label in inflammatory dermatoses such as plaque psoriasis, hidradenitis suppurativa, nummular eczema and lichen planus. Herein, we present our experience with roflumilast off-label in a total of 9 patients with cutaneous inflammatory diseases.

Materials & Methods:

We collected data on the 9 patients treated with oral roflumilast off-label in our department, with the aim of assessing the safety and effectiveness of this drug in dermatological pathologies.

Results:

We collected a total of 9 patients treated with oral roflumilast 500mg per day, with a mean age of 57 years, 4 patients with eczema and 5 patients with psoriasis. All patients had received multiple topical treatments prior to the initiation of oral roflumilast, and half of them had also undergone treatment with other systemic drugs. Seventy-eight percent of the patients presented partial improvement of the skin lesions, with two patients presenting complete resolution. Seven of the nine patients had to discontinue treatment due to adverse effects, five due to gastrointestinal intolerance (feeling of fullness, diarrhea), one due to insomnia and one due to agitation. 1 patient abandoned treatment due to lack of improvement. 1 patient maintains treatment at present with no adverse effects.

Conclusion:

In our series, oral roflumilast was partially effective in 78% of patients with inflammatory dermatoses. However, the vast majority of these patients had to discontinue treatment due to adverse effects, the most frequent being gastrointestinal alterations.

New studies with a larger sample of patients are needed to evaluate the effectiveness and safety of this drug in dermatology.

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Abstract N°: 1619

Systemic Targeted Therapies in Patients with Relapsed/Refractory Advanced Stage Cutaneous T-cell Lymphoma: A Real-World Single-Centre Case Series

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Introduction & Objectives:

Cutaneous T-cell lymphomas (CTCLs), including mycosis fungoides (MF) and Sézary syndrome (SS), are rare skin-homing T-cell cancers with variable prognoses depending on subtype and disease stage. Systemic treatments targeting surface proteins on malignant T-cells, such as Mogamulizumab, Brentuximab Vedotin (BV), and Alemtuzumab, have shown varying efficacy in advanced relapsed/refractory (R/R) CTCLs. This retrospective study evaluates the effectiveness of these treatments in a real-world clinical setting.

Materials & Methods:

A retrospective cohort case series evaluated real-world outcomes of patients with R/R cutaneous T-cell lymphomas treated with intravenous systemic targeted therapies. This single-center retrospective cohort study analyzed adult patients with histopathologically confirmed CTCLs treated with Mogamulizumab, BV, or Alemtuzumab from 2013 to 2023. Patients were classified according to WHO-EORTC criteria, and treatment decisions were made in multidisciplinary team conferences. Clinico-pathologic data were extracted from electronic medical records. Treatment response, time to progression (TTP), and overall survival (OS) were assessed.

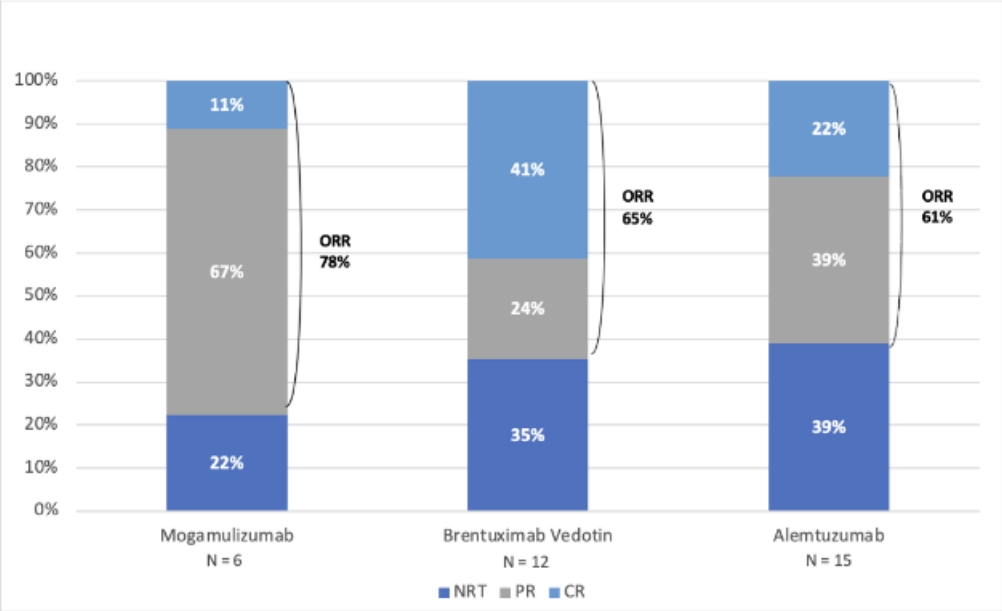
Results:

Twenty-seven patients were included, with 20 males and a median age of 72 years. Mogamulizumab (n=6) achieved an overall response rate (ORR) of 78%, with 33% sustaining complete remission (CR). BV (n=12) demonstrated an ORR of 65%, with 12% sustaining CR. Alemtuzumab (n=15) showed an ORR of 61%, with 22% sustaining CR. Median TTP varied: 2.5 months for Mogamulizumab, 4 months for BV, and 11 months for Alemtuzumab.

Conclusion:

Mogamulizumab, BV, and Alemtuzumab show efficacy in advanced CTCLs, with variable response rates and TTP. This study highlights the importance of real-world data in guiding therapeutic strategies for CTCL patients. Further research is needed to optimize treatment regimens and improve outcomes in this challenging disease. Our study demonstrates the effectiveness of the therapies described, with emphasis on the promising results observed with Alemtuzumab administered in a low-dose protocol. Particularly noteworthy is the unique perspective this paper offers on the complexities of clinical practice when managing advanced-stage R/R CTCL cases. Understanding these challenges is crucial for tailoring treatment approaches to individual patients, considering factors such as disease stage, surface marker profile of the cutaneous T-cell lymphoma and the malignant T-cell clone.

Table 2. Overall response rate according to systemic targeted treatment



NRT: No response to therapy; PR: partial remission; CR: complete remission; ORR: overall response rate.

TABLE 1.

	Mogamulizumab	Brentuximab Vedotin	Alemtuzumab
No. of patients	6	12	15
Age at targeted treatment start (years) [a]	64,5 (59-74)	73 (59-84)	73 (59-82)
Sex			
Male	3 (50)	9 (75)	10 (83)
Female	3 (50)	3 (25)	5 (17)
CTCL subtype			
Mycosis Fungoides			
Patch/plaque	1	8	5
Folliculotropic variant	-	2	2
pcALCL	-	1	-
Sezary's syndrome	5	1	7
Sezary phenotype with B1	-	-	1
Stage			
IIB	1	4	5
IIIA	4-	4	3
IIIB	-	-	1
IVA	3	2	1
IVB	2	2	2
Time from diagnosis to targeted treatment (years) [a]	1 (0-3)	3 (0-20)	1 (0-18)
Comorbidities			
Cardiac/vascular disease	2	8	8
Diabetes	-	2	-
Secondary hematologic malignancy	1	3	5
Secondary non-hematologic malignancy	-	4	4
Other	2	4	2
Previous systemic treatment regimens [a]	2 (1-4)	3 (0-6)	2 (1-6)
Involvement			
Skin only	1	8	2
Extracutaneous disease (blood, lymph nodes, bone marrow, viscera)	5	4	13
Blood involvement			
B0	1	10	4
B1	-	1	4
B2	5	1	7
Treatment duration (months)[a]	6,5 (2-72)	-	-
No. of treatment series [a]	-	1 (1-3)	1 (1-2)
No. of responses	9	17	18
Complete response	1	7	4
Partial response	6	4	7
No response to therapy	2	6	7
Overall response rate	7 (78)	11 (65)	11 (61)
No progression	3 (33)	2 (12)	4 (22)
Time to progression[a] (months)	2.5 (0-8)	4 (0-96)	11 (0-48)
MAR	3 (50)	-	-
PN	-	3 (25)	-

Abbreviations: a, median. **MAR,** Mogamulizumab associated rash. **PN,** Peripheral neuropathy.

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Abstract N°: 1647

Super response to an inconsistent administration of tildrakizumab in a biologic-naïve obese patient: A case report

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Introduction & Objectives:

Commonly acknowledged as a chronic inflammatory skin disease, psoriasis can be associated with multisystemic disorders. Obesity is a frequently occurring coexisting condition in patients with psoriasis, where adipokines are also involved. Adiponectin, with its anti-inflammatory role, is decreased in obese patients, while leptin and resistin, on the other hand, stimulate the production of pro-inflammatory cytokines (IL-6, IL-12, TNF-alpha).

Biologics are now the effective treatment for moderate-to-severe psoriasis and among these, the latest additions are Il-23 inhibitors (tildrakizumab, risankizumab, guselkumab) and IL-17 inhibitors (secukinumab, ixekizumab, bimekizumab, brodalumab). The extended interval between doses after the first month in tildrakizumab's treatment regimen represents an important asset within the IL-23 inhibitors class.

However, even though the treatment is based on general guidelines and standard dosing regimens, the aspect of dose customization dependent on the patient should be taken into consideration. Research has shown that the safely decrease of the dosing interval of older generations of biologics such as adalimumab, etanercept and ustekinumab in patients with low disease activity could have considerable potential. Therefore, a new question mark has emerged regarding the dose reduction of IL-23 and IL-17 inhibitors.

Materials & Methods:

We present a 34-year-old Caucasian male who sought medical guidance at our clinic for multiple cutaneous plaques which were erythematous, symmetrically and generally distributed, with sharply defined margins and silvery scale on the surface, ranging from 0.5 to more than 11 cm in diameter. The onset of psoriasis was in 2018, with histopathological confirmation being made in 2022.

The PASI score of 18.7 and DLQI of 25 indicate that the patient's psoriasis is classified as severe. The personal history includes grade 1 obesity and voluntary weight loss of approximately 8 kg over the past 3 months. Also, the patient has never undergone treatment with biologic therapy.

After undergoing narrowband UVB phototherapy and systemic treatment involving methotrexate with unsatisfactory results, it was decided to initiate tildrakizumab therapy in September 2022.

Results:

Following the administration of only two doses during the initiation period (at weeks 0 and 4), the patient did not revisit the clinic for six months. However, the PASI score recorded was 4.8 and DLQI stood at 2 in March 2023. After this episode, due to personal reasons, the patient came back again in February 2024 after a break of more than 11 months once again. The new PASI score detected was 1, and the DLQI was 0.

Conclusion:

Considering the excellent response of the patient following inconsistent administration at significantly extended

intervals compared to the prospectus, the administration frequency of IL-23 inhibitors should be studied thoroughly. Moreover, tildrakizumab could potentially have a significant effect on lowering adipokine levels (resistin and leptin) in patients affected by psoriasis and obesity. Therefore, the selection of the optimal treatment based on various characteristics of patients with a particular condition should be personalized, rather than based solely on the disease itself.

EA DV CONGRESS
AMSTERDAM 25-28 SEPTEMBER 2024
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Abstract N°: 1756

New-onset cutaneous vasculitis after Covid-19 vaccination: a systemic review

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Introduction & Objectives:

Several vaccines have been utilized during COVID-19 pandemic. These vaccines had a wide spectrum of side-effects. A systemic review was done to ascertain the development of new-onset cutaneous vasculitis after post covid-19 vaccination.

Objective:To ascertain the types of cutaneous vasculitis developing after post covid-19 vaccination, their association with different vaccines, associated systemic features, and outcome of cutaneous illness

Materials & Methods:

PROSPERO Identifier: CRD42022340901

All studies published between January 2021 to May 2022 which reported

vasculitis after covid-19 vaccination were screened. Out of these, the studies

which reported new onset cutaneous vasculitis were included.

Analysis was done for type of vaccine, time of appearance of cutaneous

vasculitis, clinical-histopathologic type, treatment given, and outcome.

Results:

822 were screened, out of which 92 studies reported vasculitis after post-covid 19 vaccination. Finally, 42 studies (82 patients) reporting new-onset cutaneous vasculitis were included in the analysis.

Out of 82 patients, 49 were females.

There were 8 different groups of vasculitis observed amongst which most common vasculitis new-onset vessel vasculitis(51/82-62.2%) followed by IgA vasculitis(18/82-21.9%).

The BNT162b2 (Pfizer mRNA) vaccine was most commonly associated with new-onset cutaneous vasculitis (31/82 patients) followed by Astrazaneca (26 /82patients). Most cases occurred after 1st dose of vaccine (54 patients)

Systemic involvement in the form of arthralgia, fever and abdominal pain was observed in 21/82 (26%) patients but it couldn't be ascertained as whether these symptoms were due to vasculitis or due to vaccination.

Recovery rate was very good. All cases recovered with either topical or short course of oral steroids, NSAIDS and antihistamines, and none of the cases progressed to systemic vasculitis.

Conclusion:

New-onset cutaneous vasculitis after post-covid vaccination is not infrequent. It is benign as all the cases recovered with a short course of steroids and symptomatic treatment. Cutaneous vascultis after covid vaccination usually doesn’t progress to systemic vasculitis.

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Abstract N°: 1855

Successful treatment of recalcitrant pityriasis rubra pilaris and hidradenitis suppurativa with brodalumab (anti-IL-17) - a case report

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Introduction: IL-17 is a proinflammatory cytokine involved in the pathophysiology of multiple inflammatory skin conditions, such as pityriasis rubra pilaris (PRP) and hidradenitis suppurativa (HS), among others. For that reason, anti-IL-17 therapies are now approved for the treatment of HS; however, they are not yet approved for PRP. Brodalumab is a monoclonal antibody that blocks the A subunit of the IL-17 receptor; its use has already been described in patients with refractory PRP and HS.

Case report: We present a case of a 43-year-old man with a history of chronic hepatitis B infection and depression, who was referred to our center with generalized erythematous confluent plaques with scaling in more than 90% of his body surface area. He claimed his lesions had a fluctuating course since his childhood. After histological confirmation, a diagnosis of PRP (type III) was made. It partially responded to acitretin and systemic prednisolone at first, but multiple flares occurred over time, with periods of erythroderma. He concomitantly suffered from HS since he was 36 years old - lesions were located on both axillas, groins and gluteal regions, and these were classified as Hurley 3, HS-PGA 3, IHS4 10, DLQI 13. Multiple antibiotic regimens failed to adequately control the disease. He was first treated with infliximab, but this had to be discontinued after a period of 10 months due to lack of response. Brodalumab was then commenced, starting with a loading dose of 210 mg at weeks 0, 1 and 2 followed by a 210 mg administration every two weeks. A clear response of both diseases was noticed after 12 weeks of treatment, which is maintained after a one year follow-up: IHS4 0, HS-PGA 0, regarding his PRP he currently presents with only mild scaling, no erythema, DLQI 7. He subsequently underwent a wide excision of his HS lesions of both axillary regions, one of the procedures while being treated with brodalumab, both with no complications reported.

Discussion: We report the case of a patient with PRP and HS who was successfully treated with brodalumab. Studies have demonstrated quick and meaningful clinical responses of PRP (within 8 and 10 weeks) and HS (at 12 and 24 weeks) to brodalumab. Likewise, considerable improvement of both skin conditions in our patient was achieved after 12 weeks of treatment and maintained after one year. A weekly administration of brodalumab in cases of HS has proved very efficient - disease control has been achieved sooner compared to the standard psoriasis regimen; still, differences were neglectible at week 24. We demonstrate an early response with the standard psoriasis administration interval. We also report no adverse events, which is in accordance with the favorable safety profile found in the literature.

A comprehensive understanding of the pathophysiology behind each inflammatory disease is mandatory in order to implement effective and safe therapies.

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Abstract N°: 1863

Insights into the Therapeutic Potential of CCR4 therapies targeting in T-Cell Malignancies: a glance of the current state.

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Introduction & Objectives:

This work provides a brief overview of the therapeutic landscape surrounding CCR4 targeting in T-cell malignancies. We aimed to report therapies already validated, in development, currently being tested, or about to be tested around CCR4, which appears to be a fundamental signalling pathway for the development and malignancy of cutaneous lymphomas (CTCLs).

Materials & Methods:

We have gathered data from the literature through the main medical database, including monoclonal antibodies, small molecule inhibitors, and chimeric antigen receptor (CAR) T-cell therapy.

Results:

Except for the well-known mogamolizumab, for which real-life data remain solid and promising, there are few CCR4-targeted therapies with at least promising clinical trials.

A series of small soluble inhibitory molecules capable of binding effectively to the receptor are emerging, but in most cases, they do not go beyond pre-clinical studies. However, CAR-T therapy with engineered CCR4 holds significant promise, offering a beacon of hope in the treatment of T-cell malignancies. The potential of chloroquine towards this receptor seems exclusively theoretical. Finally, some real-life data on mogamolizumab associated with checkpoint inhibitors are reported, but it remains a currently controversial therapy.

Conclusion:

As of now, the only therapy with a solid basis for CCR4-based oncological treatment remains mogamolizumab. CAR-T therapy, with its promising potential, is on the horizon. However, in the short term, we do not expect the release of therapies based on soluble antagonists.

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Abstract N°: 2013

Cost and Access Changes Noted with TNFa Inhibitor Biosimilars Entering the Market

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Introduction & Objectives:

Biologics, including adalimumab, are some of the most expensive medications in the US. This study set out to predict the changes in pricing and access to adalimumab after losing patent exclusivity by investigating other biosimilars that have lost exclusivity.

Materials & Methods:

Center for Medicare Services (CMS) Medicare spending data from 2017 to 2021 was utilized to investigate market trends for several branded biologics and their biosimilars. Changes in cost per unit, total beneficiaries on the brand and change in total beneficiaries on brand or biosimilar were analyzed.

Results:

Over this time frame with no competitor, branded adalimumab had a 72% cost per unit increase and 23% increase in total beneficiaries. Branded infliximab with competitors had a 53% cost reduction, 26% reduction of beneficiaries on the branded medication and a 1% decrease in beneficiaries on any form of infliximab branded or biosimilar.

Other medications that lost exclusivity saw changes as follows:

Branded bevacizumab: 11% cost decrease per unit, 30% decrease in brand beneficiaries, 19% drop in overall bevacizumab patients.

Branded pegfilgrastim: 11% cost increase per unit, 50% decrease in brand beneficiaries, 0.4% increase in overall patients.

Branded filgrastim: 8% cost increase per unit, 69% decrease in brand beneficiaries, 19% increase in overall patients.

Branded epoetin alfa: 7% cost increase per unit, 34% decrease in brand beneficiaries, 10% increase in overall patients.

Branded rituximab: 6% cost decrease per unit, 48% decrease in brand beneficiaries, 5% decrease in overall patients.

Branded trastuzumab: 13% cost decrease per unit, 90% decrease in brand beneficiaries, 20% increase in overall patients.

Conclusion:

The trends seen here indicate that biologics losing exclusivity, such as adalimumab, lead to a cost decrease with a loss in market share as expected. However, it is unknown if accessibility and affordability of these medications is

changing as a corresponding increase in total beneficiaries on any form of the medication is not seen as might be expected with lower cost alternatives entering the market.

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Abstract N°: 2099

Skin-Targeted PD-1 Agonists for Localized Immunosuppression in Atopic Dermatitis

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Introduction & Objectives:

T cells, particularly CD4 T helper cells, have a central role in the pathogenesis of atopic dermatitis (AD). They respond to allergens in an environment created by a compromised skin barrier and orchestrate the atopic inflammatory response. A range of immunosuppressive and immunomodulatory drugs are currently used to treat moderate to severe AD, but all are systemically active and are associated with significant adverse effects, some severe. The PD-1 receptor is a key immune checkpoint that primarily restrains T cell responses. PD-1 inhibitory signals regulate the threshold for T cell activation to limit effector T cell responses, facilitate resolution of inflammation and establish T cell tolerance. Recent data has highlighted the importance of the PD-1 pathway in regulating skin immunity.

We have published proof of concept studies demonstrating the ability of cell-tethered PD-1 agonist bispecifics to mimic the natural ligand, PD-L1, by facilitating the co-localization and clustering of PD-1 with the TCR complex at the target cell: T cell interface. This leads to the inhibition of TCR signaling and suppression of T cell responses. Non-tethered PD-1 agonist bispecifics are inactive, therefore this approach could deliver localized T cell inhibition while avoiding systemic effects.

Materials & Methods:

We now describe the development of skin - targeted PD-1 agonist bispecifics as a novel strategy to treat inflammatory skin diseases. We have engineered PD-1 agonist antibodies that are non-competitive with the ligands PD-L1 and PD-L2. These are fused to a high affinity targeting domain against an abundant target found on skin antigen presenting cells (APCs) and a silenced Fc domain for half-life extension.

Results:

Target engagement studies in human skin explants demonstrate specific binding of a fluorescently labelled, skin-targeted PD-1 agonist bispecific to skin APCs in healthy and AD skin. We show that skin-directed PD-1 agonist bispecifics, when bound to APCs, potently inhibit TCR activation in a Jurkat PD-1 reporter line and cytokine release in primary human CD4 T cells, whilst untethered bipecifics are inactive. In a model using primary monocyte-derived Langerhan's (MoLCs) cells, the bispecifics bind to the MoLCs and potently inhibit MoLC-stimulated T cell activation. The PD-1 agonist bispecifics act additively with PD-L1 and PD-L2, that are endogenously expressed on moLCs, to provide enhanced T cell suppression. Furthermore, chronic stimulation of CD4 T cells with SEB-loaded APCs in the presence of skin-targeted PD-1 agonist bispecific, followed by washout and restimulation in the absence of bispecific, leads to enhanced CD4 T cell exhaustion.

Conclusion:

These studies show the potential for skin-targeted PD-1 agonist bispecifics to provide localized and prolonged inhibition of inflammatory T cells in the skin, whilst avoiding systemic immunosuppression.

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Abstract N°: 2101

ALPHA-STAR, a Phase 1b/2 Clinical Trial of Single and Multiple Doses of STAR-0215 in Patients with Hereditary Angioedema: Initial Safety and Efficacy Outcomes

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Introduction & Objectives: Hereditary Angioedema (HAE) is a rare, inherited disease that causes recurrent edema of cutaneous surfaces and mucosa of the upper airway and gastrointestinal tract, which impinge on quality of life, and can be life-threatening when affecting the upper airway. STAR-0215 is an investigational humanized immunoglobulin G1 monoclonal antibody inhibitor of plasma kallikrein with long-lasting activity enabled by a YTE-modified Fc domain. ALPHA-STAR (NCT05695248) is an ongoing Phase 1b/2 clinical trial in patients with HAE, evaluating the safety, tolerability (primary endpoints), efficacy, pharmacokinetics, pharmacodynamics, and immunogenicity (secondary endpoints) after subcutaneous administration of single and multiple doses of STAR-0215.

Materials & Methods: Adults (n=16) with HAE Type 1 and 2, reporting ≥ 2 HAE attacks during the 8-week run-in period, were sequentially assigned to receive STAR-0215 subcutaneously. Participants were recruited into 3 dose cohorts, Cohort 1: 450 mg (day 1); Cohort 2: 600 mg (day 1), 300 mg (day 84); Cohort 3: 600 mg (day 1), 600 mg (day 28) and followed for 6 months after the last injection. Results reported here are from an initial analysis (data cut-off 13-Mar-2024).

Results: The mean age (SD) of study participants across all three cohorts was 46 (20) years, 56% were female, and 88% had Type 1 HAE. Safety and efficacy outcomes are based on 6.5 patient years (PY) of accumulated follow-up (individual follow-up at the time of data cut-off is shown in Figure 1). Treatment-emergent adverse events (TEAEs) occurred in 13 (81%) participants and related TEAEs occurred in 2 (13%) participants who received STAR-0215. No serious TEAEs and no treatment discontinuations were reported (Table 1). In Cohort 1 (n=4), mean/median baseline attack rate per month was 2.7/2.9 and decreased to 0.22/0.18 post treatment, the mean (median) percent reduction from baseline was 84% (94%). In Cohort 2 (n=6), mean/median baseline attack rates decreased from 2.3/1.9 to 0.13/0.0, the mean (median) percent reduction from baseline was 93% (100%). In Cohort 3 (n=6), mean/median baseline attack rate was 1.8/1.7 which decreased to 0.16/0.0 post STAR-0215 treatment, the mean (median) percent reduction from baseline was 90% (100%). For the first 3 months, 50%, 67%, and 50% of participants with available follow-up were HAE attack-free in Cohorts 1-3, respectively. There were no severe HAE attacks during the treatment phase (Figure 1).

Conclusion: This initial analysis of the ongoing ALPHA-STAR clinical trial demonstrated that STAR-0215 has a favorable safety profile with reductions in HAE attack frequency and severity. STAR-0215, a monoclonal antibody inhibitor of plasma kallikrein, has the potential to offer effective long-acting prevention of HAE attacks sustained for up to 6 months, supporting progression into Phase 3 to evaluate effectiveness of every 3- and 6-month administration.

Figure 1. HAE attacks for each ALPHA-STAR participant (initial analysis)

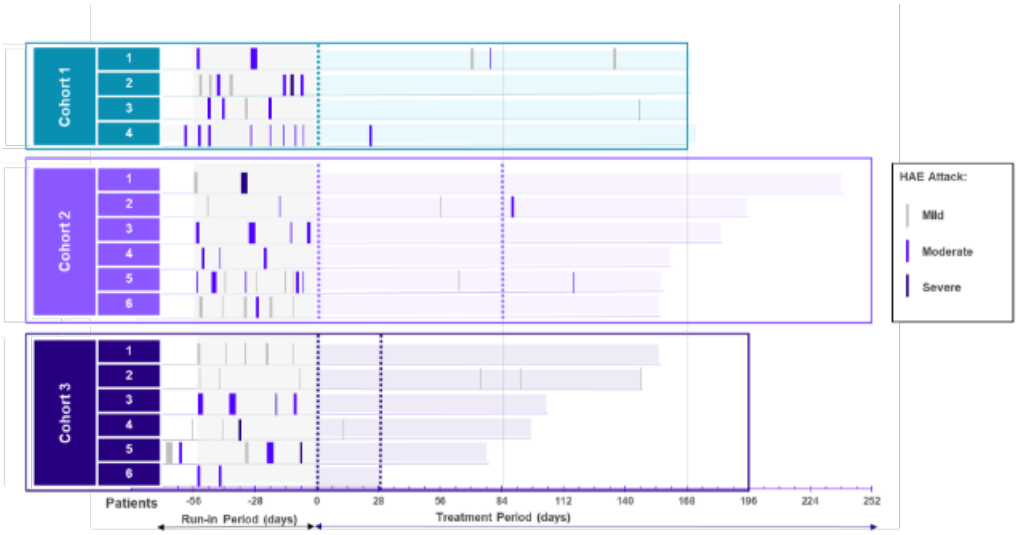

Figure Legend:

Solid boxes around each Cohort indicate 6-month period after the last injection, dashed lines indicate STAR-0215 administration in** Cohort 1: 450 mg (day 1); Cohort 2: 600 mg (day 1), 300 mg (day 84); Cohort 3: 600 mg (day 1), 600 mg (day 28). Vertical lines indicate efficacy analyses at Day 84 (3 months) and Day 168 (6 months). Thickness of vertical bars indicate various duration of discrete HAE attacks.

Table 1. Cumulative safety in ALPHA-STAR participant (6.5 PY as of March 13, 2024)

System Organ Class Preferred term*	ALPHA-STAR participants			
	COHORT 1 (N=4)	COHORT 2 (N=6)	COHORT 3 (N=6)	ALL (N=16)
Number of subjects with at least 1 TEAE, n (%)	4 (100)	3 (50)	6 (100)	13 (81)
Subjects with a related TEAE n (%)	0	1 (16.6)	1 (16.6)	2 (12.5)
Subjects with a serious TEAE n (%)	0	0	0	0
Number of TEAEs	20	3	9	32
Number of related TEAEs	0	1	1	2
Number of serious TEAEs	0	0	0	0
Number of TEAEs leading to study discontinuation	0	0	0	0
TEAEs occurring in 2 or more participants				
Nasopharyngitis n (%)	1 (25)	1 (16.6)	1 (16.6)	3 (18.75)
Contusion n (%)	2 (50)	0	0	2 (12.5)
Headache n (%)	2 (50)	0	0	2 (12.5)

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Abstract N°: 2269

Treatment with Tildrakizumab in a patient with psoriasis and silicosis

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Introduction & Objectives:

Silicosis is an occupational lung disease caused by inhalation of free crystalline silica, and can lead to progressive massive fibrosis. There is no specific treatment, and the associated morbidity and mortality are high.

There are several therapies indicated for psoriasis, and patients' comorbidities should be considered to choose the most adequate alternative.

Materials & Methods:

We present the case of a patient with psoriasis and history of chronic severe silicosis that has received treatment with Tildrakizumab, with good response and no worsening of silicosis.

Results:

A 60-year-old man was referred to the Dermatology department with a 3-month history of generalized erythematous and descamative plaques. His medical history was remarkable for silicosis in constant care by Pneumology.

Physical examination revealed psoriasis plaques on the trunk, upper and lower limbs, as well as in the scalp. Treatment with dimethylfumarate was initiated and the patient maintained a good response for one year without adverse effects. However, during follow-up he presented with new lesions that did not respond to added topical treatment. As a consequence of loss of efficacy, treatment was changed to a biologic therapy, and Tildrakizumab was started after Pneumology approval.

The patient had worked for 22 years as sandblaster with silica sand, with diagnosis of silicosis in 2008. Radiology images showed progressive massive fibrosis, with calcified mediastinal adenopathies and biapical silicotic conglomerates. In addition, he suffered from frequent bacterial superinfections and required antibiotic treatment.

After 8 months of treatment with Tildrakizumab the patient presented complete clearance of psoriasis plaques and silicosis remained stable, without increment on fibrosis or bacterial infections.

Conclusion:

Psoriasis is a systemic inflammatory disease, and currently there are several treatment alternatives. For this reason, it is important to take into account the characteristics and comorbidities of each patient while choosing a treatment.

To our knowledge, this is the first case reported of treatment with Tildrakizumab in a patient with silicosis. It has been described the development of accelerated silicosis in a patient whilst on TNF-inhibitor therapy, so treatment with IL23 inhibitors were preferred in our patient. Treatment has been maintained for 8 months now with close monitoring, with good clinical response and without worsening of his previous disease.

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Abstract N°: 2292

Severe epidermal growth factor receptor inhibitors- induced papulo-pustular eruption with good response to low-dose isotretinoin and low-dose systemic corticotherapy

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Introduction & Objectives:

Epidermal growth factor receptor inhibitors (EGFRi) are approved for treating non-small-cell lung cancer, head and neck squamous-cell carcinoma, pancreatic cancer, colorectal cancer, cancers of the large bowel, stomach cancer, ovarian cancer, and breast cancer. Since EGFR signaling is essential for the normal growth and regeneration of the skin, blocking EGFR has been noted to disrupt the skin's balance and structure, causing a decline in its outer layer strength and ultimately leading to dryness and the emergence of cutaneous fissures. The release of cytokines and activation of inflammatory cells further exacerbate the skin's susceptibility when EGFRi are used.

Results:

We report the case of a 71 years old male patient, known with advanced colorectal cancer (extension to the upper bladder wall, multiple associated loco-regional adenopathies, multiple liver metastases), under treatment with panitumumab, a humanized monoclonal antibody that inhibits EGFR. The patient presented to our department with a generalized papulo-pustular eruption, developed after 3 weeks of oncologic therapy with panitumumab. The patient reported itch, a burning sensation, and sensory disturbance, clearly impacting his activities of daily living.

The physical examination revealed folliculocentric erythematous pustules and papules affecting >30% of the body surface area (face, scalp, thorax, and extremities), notably lacking the presence of comedones or purulent cysts, generalized xerosis and cutaneous erythema, painful erosions of the nasal and oral mucosa, paronychia, and trichomegaly. Laboratory tests revealed an inflammatory biological syndrome.

He was diagnosed with grade 3 papulopustular eruption secondary to epidermal growth factor receptor inhibitors treatments and recommended oral antibiotherapy with doxycycline 200 mg daily, topical low-potency corticosteroids along with general measures like avoidance of frequent washing with hot water using hard soaps, detergents, solvents, or disinfectants, limitation of sun exposure, usage of broad-spectrum sunscreen and emollients twice daily.

During the three months of treatment, the patient showed poor therapeutic response with recurrences every 7-10 days after the administration of panitumumab, with grade 2/3 papulopustular eruptions. Therefore, under the close surveillance of the liver tests and of the lipidogram, and with the oncologist's approval, we have decided to initiate isotretinoin 10mg/day and low-dose systemic corticotherapy (prednisone 5 mg/day). After one month, the

patient showed very good therapeutic control of the panitumumab cutaneous toxicity, allowing the continuation of oncological treatment without dose adjustment. There were no dynamic pathologic changes in the laboratory tests.

Conclusion:

The papulo-pustular rash triggered by EGFRi treatment has a prognostic role, its severity being linked with enhanced overall survival and progression-free survival among colorectal cancer patients. On the other side, severe eruptions may be difficult to manage and lead to interrupting, reducing, or discontinuing oncologic therapy, limiting the therapeutic options in patients with advanced neoplasms. The approach with low-dose isotretinoin and low-dose systemic corticotherapy may prove effective in the management of severe cases when standard measures fail.

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Abstract N°: 2375

First-in-human study to evaluate the safety, tolerability, and pharmacokinetics of NBL-012, a novel anti-IL-23p19 monoclonal antibody, in healthy subjects

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Introduction & Objectives:

NBL-012 is a novel, fully human monoclonal antibody that selectively targets the p19 subunit of interleukin-23 (IL-23), a key cytokine implicated in the pathogenesis of psoriasis and other chronic inflammatory diseases. Preclinical studies demonstrated that NBL-012 exhibits high binding affinity to human IL-23 (KD: 45.1 vs 96.9 pM for guselkumab) and potently inhibits IL-23-induced STAT3 signaling (IC50: 157.4 vs 72.5 pM for guselkumab). Furthermore, NBL-012 showed an excellent safety profile with a No Observed Adverse Effect Level (NOAEL) of 150 mg/kg and minimal immunogenicity in cynomolgus monkeys. The fully human IgG4 NBL-012 may confer advantages in safety, half-life, and exposure compared to existing therapies. Thus, NBL-012 represents a promising treatment option for challenging inflammatory conditions, including inflammatory bowel disease. This first-in-human study aimed to assess the safety, tolerability, and pharmacokinetics of single ascending doses of NBL-012 in healthy Chinese subjects.

Materials & Methods:

In this phase I, randomized, placebo-controlled study, healthy subjects aged 18-45 years with a body mass index of 18-26 kg/m2 were enrolled. Following a starting dose of 20 mg in two subjects and safety assessment, cohorts of 10 subjects each were sequentially assigned to receive single subcutaneous dose of NBL-012 at 50, 100, 200, 300, or 400 mg, or matching placebo, in a 4:1 ratio. Safety, tolerability, and pharmacokinetics were evaluated at predefined timepoints post-dose.

Results:

Fifty-two healthy subjects were enrolled, with 49 completing the study. Three subjects withdrew (two in the 200 mg group due to consent withdrawal and pregnancy, one in the 400 mg group due to loss to follow-up). Treatment-emergent adverse events (TEAEs) occurred in 70.7% (29/41) of NBL-012-treated subjects and 70.0% (7/10) of placebo recipients, mostly grade 1 in severity and self-limiting. Grade 2 TEAEs included leukopenia, elevated creatine kinase, and insomnia (n=1 each). The most frequent treatment-related TEAEs in NBL-012 vs. placebo group were injection site erythema (29.3% vs. 0%), elevated direct bilirubin (12.2% vs. 10%), hyperuricemia (12.2% vs. 60%), and leukocyturia (7.3% vs. 20%). No nasopharyngitis or severe/≥grade 3 TEAEs were reported. Following single subcutaneous administration of NBL-012 20-400 mg, median time to maximum concentration (Tmax) ranged from 5.5-10.5 days, and mean elimination half-life (t1/2) was 30.6-36.0 days. Mean maximum concentration (Cmax) and area under the concentration-time curve from time zero to last measurable concentration (AUC0-t) increased dose-proportionally from 2.86±0.24 to 61.0±19.8 μg/mL and 139±0.84 to 2540±636 μg·day/mL, respectively, demonstrating linear pharmacokinetics over the tested dose range.

Conclusion:

Single doses of NBL-012 up to 400 mg exhibited a favorable safety and tolerability profile in healthy Chinese subjects. NBL-012 displayed linear pharmacokinetics, a prolonged half-life supporting once-quarterly dosing, and superior exposure which may be advantageous for certain inflammatory indications requiring higher doses. These

results support further clinical development of NBL-012. Exploration to develop NBL-012 as a 6-monthly dosing formulation is ongoing.

Clinical Trial Registration ClinicalTrials.gov NCT05259189

Figure 1. Mean (SD) serum NBL-012 concentration over time profiles following single subcutaneous administrations of NBL-012 to healthy subjects. a. Linear and b. Log scale. SD standard deviation.

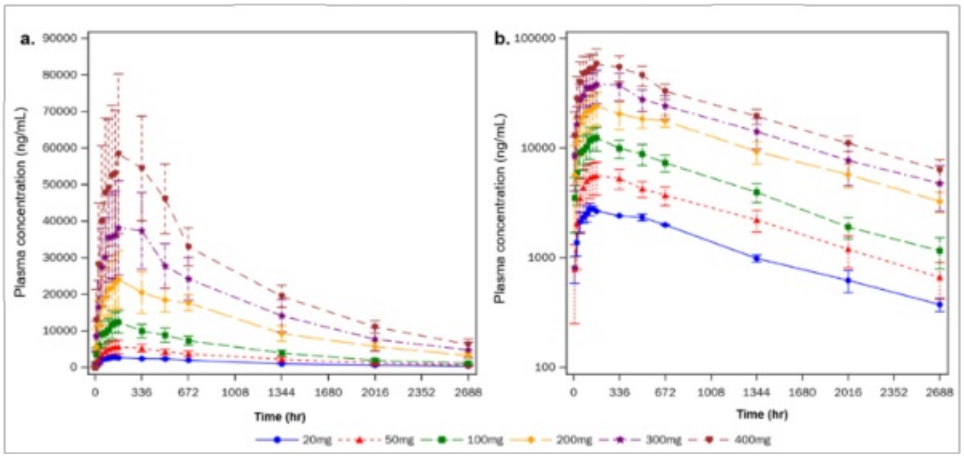

Table 1. Pharmacokinetic parameters of NBL-012 after a single subcutaneous dose of NBL-012 50, 100, 200, 300, or 400 mg

	NBL-012					
PK Parameter	20 mg (n=2)	50 mg (n=8)	100 mg (n=8)	200 mg (n=7)	300 mg (n=8)	400 mg (n=8)
T_{max} (day)* Median (min, max)	5.50(5.00 ~ 5.99)	10.50(4.99 ~ 28.02)	6.00(5.00 ~ 7.00)	6.01(5.00 ~ 7.00)	6.50(4.00 ~ 28.02)	7.00(5.00 ~ 21.08)
C_{max} (μg/mL)	2.86±0.24	5.91±1.53	13.2±2.90	24.8±7.88	41.3±10.1	61.0±19.8
AUC_{0-t} (day·μg /mL)	139±0.84	280±55.5	532±80.1	1140±454	1850±459	2540±636
$AUC_{0-\infty}$ (day·μg /mL)	157±4.44	312±66.7	589±80.3	1460±264	2100±589	2990±595
$t_{1/2}$ (day)	33.8±5.07	31.4±4.38	30.6±6.52	36.0±3.00	34.2±5.82	34.4±4.14
V_z/F (L)	6.19±0.76	7.50±1.48	7.71±2.59	7.24±1.08	7.35±1.35	6.86±1.53
CL/F (L/day)	0.127±0.004	0.168±0.041	0.173±0.026	0.140±0.022	0.155±0.052	0.138±0.026
$MRT_{0-\infty}$ (day)	51.52±6.25	49.86±7.23	46.41±9.33	53.49±5.12	50.96±8.03	49.99±5.27

Data are presented as mean ± SD unless otherwise specified.
* T_{max} was described as median (min, max).

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Abstract N°: 2399

Drug-free remission duration after the end of long-term treatment for psoriasis with three different IL-23 inhibitors in pivotal clinical trials: A single center experience

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Drug-free remission duration after the end of long-term treatment for psoriasis with three different IL-23 inhibitors in pivotal clinical trials: A single center experience

Introduction & Objectives:

Knowing the remission duration after biologics discontinuation in patients with psoriasis is important, especially when disease relapse is defined as the restart of systemic agents, because it also reflects the real-world clinical practice when topical treatment alone is not adequate for disease control and a systemic treatment, including biologic, is needed. Biologics are currently indicated for patients with psoriasis who are candidate for systemic treatment.

Materials & Methods:

We included 42 patients who were followed up regularly after the end of risankizumab, guselkumab and mirikizumab trials and investigated the drug-free remission (DFR) and risk factors for relapse by Kaplan-Meier survival analysis and Cox regression model.

Results:

Overall, 38/42 (90.5%) patients experienced relapses after discontinuing trial biologics during the follow-up period at least 96 weeks and up to 227 weeks. In all patients with relapses, the mean/median DFR were 168.8±155/104 days. Kaplan-Meier survival analysis revealed a significant one-year drug-free survival (DFS) difference between risankizumab (Z) and guselkumab (T)+ mirikizumab(M) (p=0.0462). Difference of DFS curves was noted when patients were categorized by disease duration > or ≤2 years (p=0.1577) and maintenance of PASI 90 at the end of trials (p=0.1177). Univariate Cox regression model identified age (HR=1.030(1.000-1.060), p= 0.0467) and disease duration (HR= 1.046(1.009-1.084), p= 0.0134) were significantly associated with relapse risk. A risk model was established according to the coefficient of each variable in multivariate cox regression model. Risk score=0.02481*Age+0.51930*PASI_imp_end (1 for <0.9; 0 for ≥0.9)+0.37233*First_IL23 (1 for ≥T or M; 0 for Z)+0.02599*Duration. When categorizing the patients by the median risk score, low-risk group had a significantly better one-year DFS than the high-risk group (p=0.0297).

Conclusion:

Types of biologics use, disease duration, and PASI 90 improvement at the end of trial affect the one-year DFS and relapses after biologics discontinuation. Further studies consisting a larger patient number and longer follow-up period are needed to verify our findings.

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Abstract N°: 2436

Guselkumab treatment shows rapid onset of effect on components of American College of Rheumatology response criteria: Results of 2 randomised Phase 3 trials

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Introduction & Objectives:

Guselkumab (GUS), an anti-interleukin-23p19-subunit monoclonal antibody, demonstrated efficacy vs placebo (PBO) in achieving American College of Rheumatology 20% improvement (ACR20) response in patients (pts) with active psoriatic arthritis (PsA) in two Phase 3 trials, DISCOVER-1 and -2.1,2 This analysis assessed the differential treatment effects of GUS across individual components of ACR response in pts with PsA in DISCOVER-1 and -2.

Materials & Methods:

In DISCOVER-1 and -2, 1120 pts were randomised and treated with GUS 100 mg every 4 weeks (Q4W; N=373); GUS 100 mg at Week (W)0 and W4, then Q8W (N=375); or matching PBO (N=372). Pts were evaluated by independent joint assessors at study visits. ACR20 response is defined as ≥20% improvement from baseline in both tender joint count (0–68; TJC68) and swollen joint count (0–66; SJC66) and ≥20% improvement from baseline in ≥3 of 5 assessments: Patient Assessment of Pain (Pt Pain), Patient Assessment of Global Disease Activity (arthritis; PtGA), Physician Assessment of Global Disease Activity (PGA), patient assessment of physical function as measured by the Health Assessment Questionnaire Disability Index (HAQ-DI), and C-reactive protein (CRP). For each ACR component, achievement of ≥20% improvement from baseline was assessed over time through W24 for the combined (Q4W+Q8W) GUS groups, and median time to onset of treatment effect was determined with Kaplan–Meier curves by randomised group.

Results:

Median time to response for all components except SJC66 occurred earlier with GUS than PBO. Time to onset of ACR20 treatment effect is shown in Figure 1. CRP data show 56% of GUS-treated pts had diminution of systemic inflammation by W4 (Table 1). Reduction in systemic inflammation was accompanied or rapidly followed by GUS-related improvement in PtGA and PGA (median W4–8). Although SJC66/TJC68 data showed similar patterns, there was also a high PBO response (data not shown). Consistent with early reductions in systemic inflammation, 48–61% of GUS-treated pts had ≥20% improvement in TJC68/SJC66/PGA at W4 (Table 1), and 45–48% had ≥20%

improvement in HAQ-DI/PtGA/Pt Pain by W8. By W24, >80% of GUS-treated pts had ≥20% improvement in SJC66/TJC68/PGA, followed by 63–64% with this improvement in PtGA/CRP/Pt Pain, and 57% for HAQ-DI.

Conclusion:

GUS demonstrated ACR20 improvements with separation from PBO in ACR components as early as W4, which is consistent with reduced inflammation by GUS and prior serological studies.3 At early study time points, pts and physicians were able to discern improvements in signs and symptoms of arthritis that rapidly followed reductions in systemic inflammation (CRP). The predominant drivers of ACR20 response rates at W24 in GUS-treated pts were SJC66/TJC68/PGA.

Previously presented at the EULAR 2021 virtual congress (2–5 June 2021).

References:

\1. Deodhar et al. Lancet 2020;395:1115–25

\2. Mease et al. Lancet 2020;395:1126–36

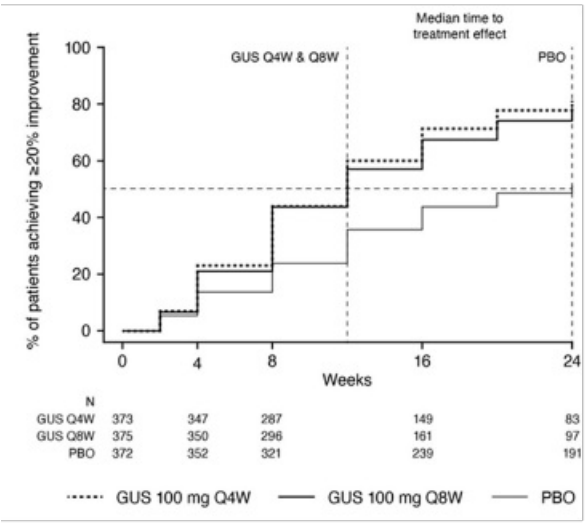
\3. Siebert et al. EULAR 2020. OP0229

Table 1. Proportion of patients (%) achieving ≥20% improvement in endpoints by visit (combined GUS group; N=748)

	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24
ACR20	20	39	50	56	*60*	*61*
HAQ-DI score	36	45	52	54	56	57
SJC66	*61*	*74*	**84**	**86**	**87**	**88**
TJC68	48	*65*	*75*	*79*	**80**	**81**
PGA	50	*67*	*74*	*78*	**81**	**81**
PtGA	35	48	58	59	*62*	*64*
Pt Pain	32	48	55	58	*61*	*63*
CRP	56	*60*	*62*	*63*	*64*	*64*

ACR20, American College of Rheumatology 20% improvement; CRP, C-reactive protein; GUS, guselkumab; HAQ-DI, Health Assessment Questionnaire Disability Index; PGA, Physician Assessment of Global Disease Activity; PtGA, Patient Assessment of Global Disease Activity (arthritis); Pt Pain, Patient Assessment of Pain; SJC66, swollen joint count (0–66); TJC68, tender joint count (0–68).

Figure 1. Median time to ACR20 response



Data shown at W2 were derived solely from DISCOVER-2, as DISCOVER-1 did not include assessments at W2. The intersection of horizontal and vertical dashed lines denotes the time at which 50% of patients in a treatment group achieved ACR20 response.
ACR20, American College of Rheumatology 20% improvement; GUS, guselkumab; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; W, Week.

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Abstract N°: 2454

Omalizumab for the treatment of bullous pemphigoid: a single center experience

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Introduction & Objectives: Bullous pemphigoid is the most common bullous dermatosis seen in

elderly population and accompanied by many comorbidities. Since immunoglobuline-E (Ig-E) antibodies play an important role in the pathogenesis of the disease, omalizumab targeting Ig-E proposes an

effective and safe profile. In this study, we aimed to evaluate the efficacy and safety of omalizumab in bullous pemphigoid patients.

Materials & Methods: Nineteen patients who received omalizumab treatment for at least 3 months with

the diagnosis of bullous pemphigoid were included in the study.

Results: All patients had at least 1 comorbid condition, the most common being hypertension (79.0%) and type 2 diabetes mellitus (68.4%). The mean number of omalizumab treatments was 7.0±2.9. With omalizumab treatment, complete response was achieved in 11 (57.9%) of the patients and partial response was achieved in 8 (42.1%). The initial systemic steroid dose could be reduced in all patients with a complete response. All patients tolerated omalizumab without side-effects.

Conclusion: Omalizumab is an effective and safe treatment option that reduces the need for systemic corticosteroids in patients with older age and multiple comorbidities. Further large-scale and prospective studies are needed to evaluate the efficacy of omalizumab in the treatment of bullous pemphigoid.

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Abstract N°: 2458

Crusted scabies in a atopic dermatitis patient treated with dupilumab: case report

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Introduction & Objectives:

Crusted or Norwegian scabies is a rare contagious variant of scabies caused by hyperinfestation with Sarcoptes scabiei variety hominis. In most cases, it affects immunocompromised patients or institutionalized elderly people. (1) There are few reports showing using immunobiological therapy and Norwegian scabies, as well as masking the initial symptoms of scabies leading to the diagnosis of other dermatoses. We present a case of crusted scabies in a patient using dupilumab for severe atopic dermatitis.

Results: A 24-year-old male with severe atopic dermatitis (AD) since 15 days of age, treated with topical corticosteroids and moisturizers. He began dermatological follow-up with our group in 2021, using non-pharmacological treatment in addition to oral methotrexate (suspended due to nausea) and subcutaneous methotrexate, reaching a maximum dose of 25 mg/week, with a partial response after 1 year of treatment, SCORAD 70. Dupilumab was started 600mg followed by 300mg every 14 days in May 2021 with significant improvement, SCORAD 20. In May 2023, the itching worsened significantly, without changes in treatment or triggers. Papule-crusted lesions appeared in the armpits, chest, wrists, and interdigital region of the hands. Oral ivermectin 15 mg and 5% topical permethrin in an alcoholic vehicle was prescribed by a generalist, but the patient don't tolerate. Family members also presented similar symptoms but don't treated.

There was slight improvement, but worsening after 30 days, when patient returned to our group. Dupilumab was discontinued and oral ivermectin 15 mg per week for 4 doses was started. After 4 weeks, there was partial improvement, and topical permethrin in lotion was started. The patient underwent three cycles of three nights of 5% permethrin, with a one-week interval between applications. The lesions improved and Dupilumab was restarted in August 2023.

Conclusion: Atopic dermatitis is a chronic inflammatory disease characterized by itching, recurrent eczema, disruption of the skin barrier and cutaneous microbiome, as well as immune dysregulation. Patients with AD have an increased risk of serious cutaneous and systemic infections compared to non atopics. (2) Furthermore, immunomodulators used for treat immune-mediated diseases also increase infections risk. Dupilumab, significantly improves AD, with a lower incidence of non-herpetic skin infections compared to other immunomodulators.(3)

However, rare cases of serious skin infections in AD patients using dupilumab have been reported. (4,5). Similar to our case, was reported a case of Norwegian scabies in a patient with AD treated with Dupilumab. In this patient, ivermectin 14mg was used on days 1, 2, 8, 9 and 15 associated with the use of 5% permethrin and 5% salicylic acid cream, with a good response. Recently, researchers have questioned the development of resistance in *S. scabiei* to topical permethrin and oral ivermectin. Although there is still no clear evidence regarding the mechanism, the possibility should be considered in cases that are difficult to treat.

We report the case to draw attention to the care of patients with atopic dermatitis using dupilumab who experience a marked worsening of itching, and the possibility of presenting an associated infectious disease such as crusted scabies.

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Abstract N°: 2463

Low occurrence of predefined safety events across six randomised clinical trials of spesolimab in dermatological conditions

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Introduction & Objectives

The interleukin (IL)-36 pathway plays a central role in the pathogenesis of generalised pustular psoriasis (GPP), and IL-36 signalling has been implicated in other chronic, inflammatory skin diseases. In the randomised, placebo-controlled EFFISAYIL 2 trial, the anti-IL-36 receptor antibody spesolimab demonstrated a favourable safety profile for prevention of flares in patients with GPP when given over 48 weeks. Nevertheless, given its novel mechanistic approach, it is important to characterise events relating to IL-36 receptor inhibition with spesolimab as well as those of potential relevance to an intravenously/subcutaneously administered biologic.

Materials & Methods

In this analysis, rates of such predefined events – severe/serious/opportunistic infections, potential hypersensitivity reactions, peripheral neuropathies, and malignant tumours – were examined using available data from placebo-controlled periods of six randomised trials of spesolimab across GPP and other dermatological conditions.

Results

Events reported in patients receiving spesolimab at various doses and schedules in two trials in GPP, two in palmoplantar pustulosis (PPP), one in atopic dermatitis (AD), and one in hidradenitis suppurativa (HS) were included (total n=342 for spesolimab and n=145 for placebo). Total exposure to spesolimab was 657.8 patient-years (PY): 244.3 PY for GPP, 327.8 PY for PPP, 40.0 PY for AD, and 45.7 PY for HS. Incidences of severe/serious/opportunistic infections were low with spesolimab and were only found in GPP trials (3.2% in one GPP trial; 2.9% in the second GPP trial vs. 0% with placebo). The incidences of potential hypersensitivity reactions were similar for spesolimab (7.7–33.3%) and placebo (5.6–44.4%) across trials. There was one report of peripheral neuropathy with spesolimab in a PPP trial (incidence 0–0.9% across trials) versus two (one GPP, one PPP) with placebo (0–3.3%), and one malignancy with spesolimab in GPP (0–1.1% across trials) versus one with placebo in PPP (0–2.3%).

Conclusion

There were no consistent differences between spesolimab and placebo in the placebo-controlled periods of trials

included. Across all trials, spesolimab demonstrated a consistent and favourable safety profile in multiple dermatological conditions.

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Abstract N°: 2568

Long-term efficacy of stapokibart in adults with moderate-to-severe atopic dermatitis achieving and not achieving optimal responses following short-term treatment

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Introduction & Objectives: Stapokibart is a novel humanized monoclonal antibody targeting interleukin-4 receptor alpha (IL-4Rα). A pivotal phase 3 trial (NCT05265923) has shown favorable efficacy and safety of stapokibart compared with placebo in adults with moderate-to-severe atopic dermatitis (AD) following 16-week treatment and sustained improvements through week 52. However, long-term effects of stapokibart on patients based on different short-term treatment response have not been elucidated. This post-hoc analysis aimed to evaluate the efficacy of stapokibart following 52-week treatment in patients achieving and not achieving optimal response at week 16 in the pivotal phase 3 trial.

Materials & Methods: This analysis included patients who were randomized to receive subcutaneous stapokibart 300 mg (a loading dose of 600 mg) every 2 weeks during the 16-week double-blind period and continued the same dose of stapokibart during the subsequent 36-week maintenance period. Patients were classified as responders and non-responders based on whether they achieved an optimal response at week 16, defined as a

≥75% improvement from baseline in the Eczema Area and Severity Index score (EASI-75) and Investigator's Global Assessment (IGA) 0/1 response (IGA score of 0 or 1 and a ≥2-point improvement from baseline). Post-hoc endpoints, including proportions of patients achieving EASI-75 and IGA 0/1 from week 20 to 52 in responders and non-responders, were analyzed as observed without imputation.

Results: A total of 237 patients were analyzed, including 106 responders and 131 non-responders. Mean age of responders and non-responders was 39.6 (standard deviation [SD], 16.7) and 41.4 (SD, 17.0) years, respectively. Median duration of AD was 7 (interquartile range, 3-13) years in both responders and non-responders. Mean baseline EASI score of responders and non-responders was 22.6 (SD, 6.9) and 26.7 (SD, 9.6), respectively. At baseline, 37.7% (40/106) of the responders and 57.3% (75/131) of the non-responders had severe AD (IGA score of 4). At week 20, 100.0% and 92.2% of the responders achieved EASI-75 and IGA 0/1 response, respectively, and the proportions were maintained high through week 52, reaching 99.0% and 87.0%, respectively. Among the non-responders, 65.4% achieved EASI-75 and only 18.1% achieved IGA 0/1 response at week 20, while the proportions increased to 86.8% and 50.0%, respectively, at week 52 (**Fig 1**).

Conclusion: Long-term stapokibart treatment improves response in patients with moderate-to-severe AD who have not achieved optimal response during short-term treatment and enables the maintenance of response in initial responders.

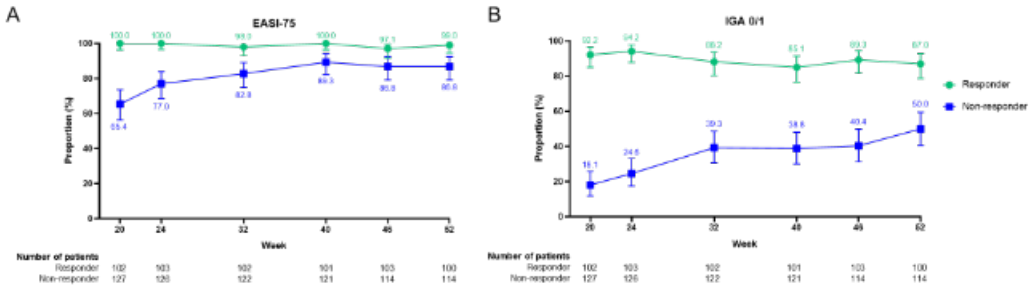

Figure 1. Treatment response during weeks 20-52 in initial responders and non-responders. (A) Proportions of patients achieving ≥75% improvement from baseline in the Eczema Area and Severity Index score (EASI-75). (B) Proportions of patients achieving Investigator's Global Assessment (IGA) 0/1 response (IGA score of 0 or 1 and a ≥2-point improvement from baseline).

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Abstract N°: 2636

Long-term sustained efficacy and safety of bimekizumab across the full spectrum of axial spondyloarthritis: 2-year results from two phase 3 studies

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Introduction & Objectives:

Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has shown efficacy and safety to 1 year (yr) in patients (pts) with active non-radiographic (nr-) and radiographic axial spondyloarthritis (r-axSpA) in phase 3 studies, BE MOBILE 1 and 2.1,2 Here, 2-yr efficacy and safety of BKZ are assessed.

Materials & Methods:

In BE MOBILE 1 (NCT03928704; nr-axSpA) and 2 (NCT03928743; r-axSpA) pts were randomised to subcutaneous BKZ 160 mg every 4 weeks (wks; Q4W) or placebo (PBO); all pts received BKZ 160 mg Q4W from Wk 16. On completion at Wk 52, pts could enter BE MOVING (NCT04436640), an ongoing open-label extension (OLE) study.

Efficacy data are reported for pts from BE MOBILE 1 and 2 and the combined OLE up to 104 wks (N=586). Data are reported for the randomised set using non-responder imputation (NRI; binary outcomes), multiple imputation (MI; continuous outcomes) and observed cases (OC); pts not enrolled in the OLE were imputed as non-responders. Pooled safety data (MedDRA v19.0) are reported up to 2 yrs for all pts who received BKZ (N=574).

Results:

Of the 254 nr-axSpA and 332 r-axSpA randomised pts, 494 pts entered BE MOVING at Wk 52. By July 2023, 189 nr-axSpA and 267 r-axSpA pts completed Wk 104.

Wk 52 efficacy was sustained to Wk 104 in both nr-/r-axSpA populations (**Figure**; **Table**),2 including Assessment of SpondyloArthritis international Society 40% (ASAS40; **nr-axSpA**: 55.9% to 49.2% [NRI]; 60.0 to 58.9 [MI]; 65.1% [142/218] to 66.1% [125/189; OC]; **r-axSpA**: 61.7% to 53.9% [NRI]; 64.3% to 61.0% [MI]; 68.8% [205/298] to 67.0% [179/267; OC]).

At Wk 104, Ankylosing Spondylitis Disease Activity Score (ASDAS) low disease activity (<2.1) was achieved by

61.2% and 63.4% nr-/r-axSpA pts (MI), ASDAS inactive disease (ASDAS <1.3) by 31.6% and 31.3% nr-/r-axSpA pts (MI), and ASAS partial remission by 30.7% and 31.3% nr-/r-axSpA pts (NRI). BKZ treatment led to sustained inflammation suppression, shown by hs-CRP levels.

To Wk 104, 89.5% (514/574) of pts with axSpA had ≥1 treatment-emergent adverse event (TEAE) on BKZ; most common TEAEs by preferred term (exposure-adjusted incidence rate/100 pt-yrs [EAIR/100 PY]) were SARS-CoV-2 infection (13.2), nasopharyngitis (10.2), and upper respiratory tract infection (6.0). Incidence of serious TEAEs was low (5.4); no major adverse cardiovascular events, active tuberculosis cases, serious SARS-CoV-2 infections, anaphylaxis, or deaths occurred. Incidence of suicidal ideation and behaviour was low (0.1). Hepatic events occurred in 72 patients (5.5/100 PY); most had liver function test elevations or transient abnormalities (n=53; no cases of confirmed Hy's law). 122 pts had fungal infections (21.3%; 10.0/100 PY); 76 had Candida infections (13.2%; 5.8). None were serious/systemic – 6 cases led to study discontinuation. Tinea infections (2.8%; 1.1/100 PY) and fungal infections not elsewhere classified, such as oral, skin, and vulvovaginal infections (8.5%; 3.6) were less common. Incidence of IBD (0.6) and uveitis (1.6) was low.

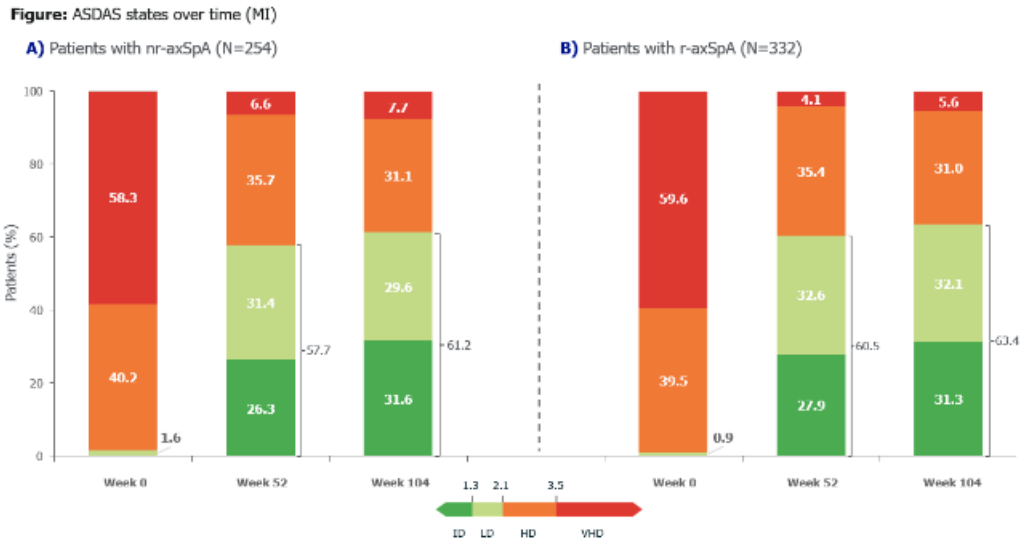
To Wk 104, most EAIRs of the above TEAEs were similar to or lower than reported to Wk 52; no new safety signals were observed.

Conclusion:

Across the full disease spectrum of axSpA, BKZ had sustained efficacy to 2 yrs. No new safety signals were observed.

References: 1. van der Heijde D. Ann Rheum Dis 2023;82:515–26; 2. Baraliakos X. Ann Rheum Dis 2024;83:199-213

Figure: ASDAS states over time (MI)



Pooled randomised set. Patients treated with BKZ 160 mg Q4W; includes patients originally randomised to PBO. ASDAS <2.1 values shown next to bars are manually calculated from ASDAS state response rates. ASDAS: Ankylosing Spondylitis Disease Activity Score; axSpA: axial spondyloarthritis; BKZ: bimekizumab; HD: high disease; ID: inactive disease; LD: low disease; MI: multiple imputation; nr-axSpA: non-radiographic axSpA; PBO: placebo; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis; VHD: very high disease.

Table. Efficacy to 2 years (Wk 104)

	nr-axSpA	r-axSpA
	BKZ 160 mg Q4W N=254	BKZ 160 mg Q4W N=332
ASAS40 [NRI] n (%) [MI] % (95% CI) [OC] n/N (%)	125 (49.2) 58.9 (52.6, 65.2) 125/189 (66.1)	179 (53.9) 61.0 (55.5, 66.5) 179/267 (67.0)
ASAS Partial Remission [NRI] n (%)	78 (30.7)	104 (31.3)
ASDAS [MI]		
Mean at baseline (SE)	3.7 (0.1)	3.7 (0.0)
Mean at Wk 104 (SE)	1.9 (0.1)	1.9 (0.1)
Mean CfB at Wk 104 (SE)	−1.8 (0.1)	−1.9 (0.1)
BASDAI [MI]		
Mean at baseline (SE)	6.8 (0.1)	6.5 (0.1)
Mean at Wk 104 (SE)	2.9 (0.1)	2.6 (0.1)
Mean CfB at Wk 104 (SE)	−4.0 (0.1)	−3.9 (0.1)
Total resolution of enthesitis[a] [NRI] n (%)	78 (41.9)[b]	106 (53.3)[c]
hs-CRP, mg/L [MI]		
Median at baseline	6.3	7.4
Median at Wk 104	2.1	2.3

Pooled randomised set. [a] MASES=0 in pts with MASES >0 at baseline; [b] n=186; [c] n=199. ASAS: Assessment of SpondyloArthritis international Society; ASAS40: ASAS 40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BKZ: bimekizumab; CfB: change from baseline; CI: confidence interval; hs-CRP: high-sensitivity C-reactive protein; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; MI: multiple imputation; nr-axSpA: non-radiographic axial spondyloarthritis; NRI: non-responder imputation; Q4W: every 4 weeks; r-axSpA: radiographic axial spondyloarthritis; SE: standard error; Wk: Week.

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Abstract N°: 2786

Real-world efficacy and safety of abrocitinib in Chinese patients with moderate to severe atopic dermatitis: a single-centre prospective study

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Introduction & Objectives:

Abrocitinib is a selective Janus kinase 1 inhibitor approved for the treatment of moderate-to-severe atopic dermatitis (AD). The efficacy and safety of abrocitinib have been reported in phase 3 clinical trials; whereas the real-world data after its post-marketing is scarce.This study aims to explore the efficacy and safety of abrocitinib for AD in a real-world Chinese single-centre prospective cohort.

Materials & Methods:

A total of 103 moderate-to-severe AD patients were enrolled, who received oral 100 mg abrocitinib once daily for 12 weeks. The patients were evaluated at baseline, 2, 4, 8, and 12 weeks after first abrocitinib administration for multiple physician- and patient-reported outcome measures. Peripheral blood eosinophil counts, total serum IgE, and serum levels of 24 cytokines/chemokines were assayed from specimens obtained at study visit.

Results:

Abrocitinib treatment resulted in a fast and sustained improvement in disease severity during a follow-up period of 12 weeks. Sixty one (71.8%) AD patients achieved an improvement of ≥75% in the Eczema Area and Severity Index from baseline at week 12, and 45 (52.9%) AD patients reached EASI90. Fifty seven (67.1%) patients achieved the Investigator's Global Assessment 0/1 (or a reduction of ≥2 points from baseline). Post hoc analysis revealed that the onset time for efficacy of abrocitinib was faster than that of dupilumab. A larger proportion of patients treated with abrocitinib achieved early itch relief at week 2 compared to dupilumab, and the proportion of patients reaching EASI 75 at week 8 was also higher in the abrocitinib-treated group. Adverse events were reported by 43.7% patients, and gastrointestinal symptoms (17.5%) and acne (14.6%) were the most commonly seen. After 12 weeks' treatment, eosinophils counts were reduced significantly compared to the value at baseline; whereas the levels of total serum IgE were not changed. Serologic analysis revealed that the levels of Th2, Th1, and Treg cytokines/chemokines were significantly decreased after 12 weeks' abrocitinib treatment. Body mass index (BMI) <24 (OR, 3.46; 95%CI, 1.17-10.30) and no previously treatment with dupilumab (OR, 3.49 ;95%CI, 1.05-11.63) were identified as potential predictive factors of good response. Low levels of TSLP at baseline were predictors for good outcome of abrocitinib treatment.

Conclusion:

Abrocitinib demonstrated promising efficacy with a well-tolerated safety profile in Chinese patients with moderate-to-severe AD in daily practice, which also facilitated the normalization of inflammatory cytokines in the serum.

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Abstract N°: 2858

Interleukin-17 inhibitors for the management of severe rosacea

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Introduction & Objectives:

Rosacea is a chronic inflammatory skin condition with unknown aetiology. It involves dysregulation in the immune system, vascular and nervous systems, as well as skin barrier function impairment. Rosacea has a significant impact on the patients' psychological, social, and occupational status. Challenges linked to treating rosacea include the risk of relapse after discontinuation and a limited range of options for severe and treatment-resistant cases.

Materials & Methods:

We report two cases of severe rosacea managed with an interleukin 17 (IL-17) inhibitors.

Results:

A 72-year-old female with psoriasis and severe papulopustular rosacea was commenced on brodalumab for treatment of her moderate to severe plaque psoriasis. At three-month review, there was marked improvement in her psoriasis, and incidentally her rosacea had cleared. Due to the unavailability of brodalumab, she was commenced on secukinumab 300mg SC weekly injections as a loading dose then every 4 weeks. Her rosacea remained clear with an ongoing reduced dose of secukinumab of 150 mg every 4 weeks.

A 42-year-old female presented with long-term severe erythematotelangiectatic rosacea including facial erythema and swelling. Based on our previous case and subsequent published study, she was commenced on a compassionate supply of secukinumab 300mg SC weekly injections for four weeks as a loading dose then 300mg SC every four weeks . The patient had marked improvement in her symptoms with only occasional flushing after 12 weeks of treatment. She remained on secukinumab 300mg SC every five weeks with good control of her rosacea.

Conclusion:

Recent literature has suggested that IL-17 plays a crucial in the pathogenesis of rosacea. A recent small study, assessing the efficacy of secukinumab in moderate-to-severe papulopustular rosacea, has shown that secukinumab could potentially have activity in rosacea. These two case reports contribute to the growing evidence that IL-17 inhibitors could play a role in managing rosacea. We advocate for larger randomised clinical trials to confirm these findings.

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Abstract N°: 2908

Alcohol-induced facial erythema in patients treated with Dupilumab: A case series and systematic review.

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Introduction & Objectives:

Dupilumab is approved for the treatment of atopic dermatitis (AD), prurigo nodularis, asthma, eosinophilic esophagitis, and chronic rhinosinusitis with nasal polyposis. A regional or localized persistent dermatitis on the face, periauricular region, and/or neck is a well-known adverse event documented only in patients with AD. Face and neck erythema appearing shortly after alcohol ingestion has also been described by patients treated with dupilumab on social media and in a few case reports. We recently encountered similar cases. The objective of this study is to characterize this phenomenon.

Materials & Methods:

A systematic review of alcohol-induced facial erythema on dupilumab. The review included a PubMed search for publications on alcohol-induced facial erythema on dupilumab regardless of age or indication, with no limitation on study design. Publications describing an eruption with no temporal association to alcohol consumption were excluded. Abstracts were reviewed followed by a full-text review of candidate studies. A case series of patients from our center was added to the review. The data was summarized using descriptive statistics and a narrative review. This study was exempt from institutional review board review.

Results:

The search yielded 126 studies, with 4 remaining after exclusion. Overall, 11 cases were described, of them 4 females, at a mean age of 27 years. All were adults treated for AD using the approved dosage. One patient used concomitant topical calcineurin inhibitors. The time from initiation of dupilumab to the first alcohol-induced facial erythema was mostly within 4-6 months (range 3 weeks-3 years). The interval between alcohol ingestion and flushing was minutes, with resolution within an hour. The rash appeared after all types of alcohol, worse after hard liquor in some patients. No patients stopped dupilumab.

Conclusion:

Alcohol-induced facial erythema in patients treated with dupilumab is a newly emerging phenomenon, characterized by facial flushing shortly after alcohol ingestion of any kind and even in small amounts, and rapid spontaneous resolution. The acute onset and fast resolution differentiate this eruption from dupilumab-induced or atopic head and neck dermatitis. The association with dupilumab cannot be determined due to the small number of cases, lag period from dupilumab initiation, and the use of topical calcineurin inhibitors in some cases, which can cause a similar eruption. Judging from the limited publications, alcohol-induced facial erythema on dupilumab is very uncommon. However, the abundance of reports on social media and online patient forums suggest that it may be under-reported, and perhaps patients are reluctant to share this complaint with their doctors. Future studies are needed to evaluate the association of alcohol-induced erythema with dupilumab treatment and whether it is unique to AD, the underlying mechanisms, and potential treatments.

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Abstract N°: 2909

Clinical and serology effects of upadacitinib in atopic dermatitis with chronic spontaneous urticaria

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Introduction & Objectives:

Atopic dermatitis (AD) is a type 2 immunity (T2) - driven disorder characterized by relapsing eczema, intense pruritus and the accompaniment with other chronic inflammatory diseases including chronic spontaneous urticaria (CSU). Conventional therapies such as glucocorticoids and immunosuppressants are associated with potential side effects or limited efficacy. Upadacitinib, a small-molecule Janus kinase -1 (JAK-1) inhibitor (JAKinib) has been approved for the treatment of AD. However, data on its efficacy in CSU patients are lacking. Our study reports the clinical and serology effects of upadacitinib in AD overlapped with CSU.

Materials & Methods:

A retrospective study was conducted, and 26 patients with AD accompanied with CSU were included. These patients were all treated with oral upadacitinib (15mg every day) for 16 weeks. Clinical indicators, including eczema area and severity index (EASI), numerical rating scale (NRS), dermatology life quality index (DLQI) and weekly urticaria score (UAS7) were assessed at weeks 0, 4, 12, and 16. Related laboratory including total serum immunoglobulin E (IgE) levels, eosinophil counts, IL-4, IL-13, TNF-α, and IFN-γ were recorded.

Results:

At 16 weeks of treatment, the mean EASI score significantly decreased by 70.38%, DLQI score decreased by 93.81%, NRS score decreased by 76.78%, and UAS7 score decreased by 71.40%, with wheal score decreased by 68.67% compared with the corresponding scores before treatment ($p < 0.05$). The expression levels of IL-4 and IL-13 in serum significantly decreased from 8.70 ± 7.04 pg/ml and 115.07 ± 79.51 pg/ml to 3.19 ± 3.30 pg/ml and 60.26 ± 49.68 pg/ml after treatment, without any significant TNF-α or IFN-γ relievement. Out of 26 patients, 16 (61.64%) responded to upadacitinib treatment, while 10 (38.46%) showed poor response. Statistical analysis suggested that patients with higher wheal scores and eosinophils at baseline had a better response rate.

Conclusion:

Upadacitinib exhibited a marked efficacy in the treatment of AD with CSU, and achieved significant decreases in type 2 inflammatory factors.

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Abstract N°: 2925

Successful treatment of hand and foot eczema with tralokinumab: a case series

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Title: Successful treatment of hand and foot eczema with tralokinumab: a case series

Introduction & Objectives:

Hand and foot eczema is** considered to be a part of the spectrum of atopic dermatitis. It can be debilitating as it affects the quality of life hugely despite the limited body surface area involved Treatment mirrors the traditional treatment of atopic dermatitis. Recently various case reports have shown the efficacy of dupilumab in the treatment of hand and foot eczema. Our case series of 5 patients highlights the successful use of tralokinumab in treating hand and foot eczema.

Materials & Methods:

A retrospective chart review of patient records from 1st January 2023 to 31st March 2024 identified 5 patients of hand and foot eczema who were receiving tralokinumab. The results are presented.

Results:

All 5 patients responded to tralokinumab with a significant decrease in their SCORAD and EASI scores. Four out of the 5 patients started noticing improvement after the loading dose and 1 patient observed remission after the first 2 doses. All 5 patients are still receiving tralokinumab although 2 patients are not regular on their treatment due to frequent travel. All the patients have been advised to use topical steroids such as mometasone furoate and clobetasol propionate ointments in case of a flare of their hand and foot eczema. Three patients have used them on 2-3 occasions since starting tralokinumab compared to more frequent use prior to staring tralokinumab. Two out of the 5 patients developed injection site reactions after the first few injections of tralokiumab which did not recur subsequently. There were no other side effects reported.

Conclusion:

This case series of 5 patients highlights the off-label use of tralokinumab in hand and foot eczema.Tralokinumab had a rapid onset of action with decreased EASI scores and SCORAD within a month of initiating treatment leading to improvement in the patients' quality of life. Tralokinumab was found to be safe in these patients with 2 out of 5 reporting injection site recations and no other side effects. Newer indications of the use of tralokinumab have been reported recently and include prurigo nodularis and nummular eczema. Our case series provides new hope for patients of chronic hand and foot eczema for whom the quality of life can be improved significantly with the use of tralokinumab. Larger studies are required for the use of tralokinumab in indications other than atopic dermatitis such as hand eczema.

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Abstract N°: 2934

Successful Treatment of Refractory Pyoderma Gangrenosum with Guselkumab: a Case Series

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Successful Treatment of Refractory Pyoderma Gangrenosum with Guselkumab: a Case Series

Introduction & Objectives:

Pyoderma gangrenosum (PG) is a rare neutrophilic dermatosis characterized by rapidly evolving, extremely painful, ulcerations with undermined erythematous-violaceous borders. Therapy of PG remains a major multidisciplinary challenge. Due to diagnostic delays, patients often present at a late clinical stage with large ulcerations and the focus is placed on systemic therapies to gain rapid control of the disease. Corticosteroids and/or cyclosporine remain the systemic therapeutics of choice for most patients. However, PG is often refractory to standard therapies. In recent years, an increasing number of studies have shown the positive effects of biologic therapies including inhibitors of interleukin-23. As IL-23 is implicated in the pathogenesis of PG and associated inflammatory comorbidities, newer IL-23 inhibitors targeting the p19 subunit are now starting to be used in the treatment of PG. To the best of our knowledge there are only two reported cases in the literature of PG successfully treated with Risankizumab and one case of PG successfully treated with Guselkumab.

Materials & Methods:

We present a case series of two patients with refractory PG associated ulcers who showed significant clinical improvement with Guselkumab therapy.

Results:

1. A 60-year-old female with a 5-year history of PG was referred to our center for multiple large skin ulcers on the lower and upper extremities recalcitrant to treatment with advanced wound care, systemic corticosteroids, cyclosporine and TNF-alpha inhibitors. The ulcers were complicated by recurrent bacterial superinfections, often involving multidrug-resistant organisms, and disabling pain necessitating frequent cycles of potent analgesic therapies.
2. A 64-year-old male with a 7-year history of PG presented with progressive non-healing ulcers on the lower extremities despite previous treatments with advanced wound care, corticosteroids, cyclosporine and TNF-alpha inhibitors. The patient's clinical course was complicated by ulcers' superinfections leading to osteomyelitis in the left tibia along with an associated sepsis due to *Streptococcus pneumoniae* necessitating intensive care unit admission and aggressive antibacterial therapy.

After a thorough discussion our team decided to initiate therapy with Guselkumab 100 mg subcutaneous injections every 6 weeks. In both cases nearly complete healing of the ulcers occurred within 16 weeks. Follow-up assessments revealed systemic inflammatory markers normalization and sustained response to the therapy with remarkable improvement in the patient's overall quality of life.

Conclusion:

These cases highlight the challenging management of PG which is often refractory to standard therapies and can be burdened by severe complications. Systemic therapy with corticosteroids and/or cyclosporine remains the treatment of choice for most patients with PG. Although, new data supports the efficacy of biologics targeting IL-23 p19 subunit as an alternative in treating refractory cases of PG or as first-line therapy in patients with associated inflammatory comorbidities. The successful use of Guselkumab in these cases shows its potential as a promising therapeutic option in such recalcitrant cases.

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Abstract N°: 2944

Digital sequential imaging of eruptive naevi induced by Encorafenib and Cetuximab for Colorectal Carcinoma

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Introduction & Objectives:

Materials & Methods:

Results:

BRAF inhibitors such as Encorafenib are designed to selectively target and inhibit mutated BRAF kinase, thereby disrupting the mitogen-activated protein kinase (MAPK) signalling pathway. These inhibitors are utilised in the treatment of an increasing range of malignancies, including malignant melanoma, colorectal carcinoma (as a second-line therapy), non-small cell lung cancer, and anaplastic thyroid carcinoma. Notably, the administration of BRAF inhibitors, has been associated with the development of eruptive melanocytic naevi, a phenomenon predominantly documented in patients requiring treatment for melanoma. This occurrence is thought to arise from a paradoxical activation of MEK/ERK signalling in BRAF wild-type cells, which in turn prompts melanocytic proliferation.

In this context, we present the case of a 49-year-old male diagnosed with stage IV metastatic caecal BRAF positive colorectal adenocarcinoma, marked by extensive lymph-node dissemination. The patient was under pre-existing follow up with digital sequential imaging (DSI) due to multiple atypical melanocytic naevi. Following second-line treatment with Encorafenib and Cetuximab the patient developed eruptive and evolving naevi which were monitored using DSI. Given the scarcity of literature on the dermatological impact of Encorafenib in colorectal cancer patients, this case adds valuable insight into the spectrum of cutaneous adverse events associated with BRAF inhibitors. It highlights the benefit of careful dermatological surveillance with digital sequential imaging (DSI) for managing melanocytic lesions in patients treated with BRAF inhibitors, enabling precise identification and removal of high-risk naevi while reducing unnecessary excisions, thus streamlining patient care.

Conclusion:

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Abstract N°: 3002

Generalized cutaneous lichen planus induced by atezolizumab treatment for small cell lung cancer

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Introduction & Objectives:

Immune checkpoint inhibitors targeting programmed cell death protein-1 (PD-1) and programmed death ligand-1 (PD-L1) are being increasingly used in the treatment of multiple neoplasms (melanoma, non-small cell lung cancer, small cell lung cancer, liver cancer, alveolar soft part sarcoma, hematologic malignancies). They prevent the suppression of cytotoxic T lymphocytes, thereby augmenting the immune response against tumors. Unfortunately, they also increase the risk of autoimmunity and various immune-related adverse events, among which, cutaneous toxicities represent the most common. Reported dermatologic toxicities include various eruptions (maculopapular, lichenoid, psoriasiform, vesiculo-bullous), vitiligo, prurigo, and others. Several scientific reports underline the important predictive value of these cutaneous eruptions and their subtypes regarding cancer survival.

Results:

We report the case of a 59 years female patient, with a medical history of stage IVA (T4N2M1a) small cell lung cancer, affecting the inferior lobe of the right lung associated with carcinomatous lymphangitis, pleural and pericardial effusion and supradiaphragmatic adenopathies, with disease progression under chemotherapy and radiotherapy, currently under treatment with atezolizumab, an anti- PD-L1 immune checkpoint inhibitor. The patient presented to our department with a generalized pruritic eruption of shiny purpuric, polygonal papules, with sizes ranging from 4-5 milimeters to one centimeter, merging into plaques, mainly affecting the trunk, the upper and lower limbs, without response to high-potency topical corticosteroids. Laboratory tests revealed leukopenia. No systemic viral infections were detected. No other drugs that could induce the lichenoid rash were identified.

Histopathological examination revealed moderate focal orthokeratosis, hypergranulosis and moderate acanthosis. At the level of the basal epithelial portion, rare apoptotic keratinocytes (Civatte bodies) were found, in association with a moderate band-like lymphocytic inflammatory infiltrate, arranged at the dermo-epidermal interface and basal epithelial vacuolar degeneration.

The patient was diagnosed with generalized lichen planus induced by atezolizumab for advanced small cell lung cancer. With the oncologist's approval, based on the severe extension of the disease and the high impact on the patient's quality of life, we decided to initiate low-dose isotretinoin (10mg/day) for 3 months and topical high-potency corticosteroids.

Following one month on the previously mentioned therapy, her cutaneous lesions showed regression, with good tolerance (clinical, blood chemistry), enabling uninterrupted continuation of atezolizumab therapy.

Conclusion:

Prompt identification, correct diagnosis, and early management of immunotherapy-induced dermatologic adverse effects are essential to mitigate the potential risk of disrupting cancer treatment regimens due to cutaneous toxicity. This may be difficult in the case of rare adverse events such as generalized lichen planus to atezolizumab. Therefore, an interdisciplinary collaboration among dermatologists specialized in cutaneous adverse reactions to oncologic therapy, dermatopathologists, and oncologists is imperative for their prompt recognition and management.

EADV CONGRESS
AMSTERDAM 25-28 SEPTEMBER 2024
EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

Abstract N°: 3077

Risk factors for the efficacy of biologics in psoriatic arthritis: A cohort study

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Introduction & Objectives:

Targeted biological immunotherapies have been shown to be more effective than traditional disease-modifying antirheumatic drugs in treating psoriatic arthritis (PsA) in recent years. However, while they are highly effective in controlling psoriatic skin lesions, fewer than 60% of PsA patients achieve an American College of Rheumatology (ACR)20 response. Additionally, significant differences exist in biological treatment response among PsA patients. This study aims to identify risk factors of biological efficacy in PsA patients, offering clinicians valuable guidance in biologic therapy selection.

Materials & Methods:

This prospective cohort study enrolled PsA patients receiving biological treatments (IL-17 inhibitors and TNF inhibitors) between March 2020 and October 2022. Before initiating treatment, detailed baseline information (48 variables), including demographic data, disease history, previous treatments, comorbidities, evaluations of skin lesions and arthritis, nail involvement, and Health Assessment Questionnaires (HAQ), was collected. Patients were followed for one year, at week 52 their ACR20/50/70 responses, Psoriatic Arthritis Response Criteria (PsARC), and Minimal Disease Activity (MDA) response were calculated. Initially, single-factor logistic regression was performed to obtain *p*-values for each variable, using ACR20/50/70, PsARC, and MDA responses as the dependent variables. Then, variables with a *p*-value < 0.2 were selected for inclusion in the multifactor logistic regression model, which was constructed using a stepwise variable screening method.

Results:

There were 116 patients included in this study. Age, pain VAS, HAQ, and family history of PsA were included in the final multifactor logistic regression model. Among these variables, age emerged as the most stable factor, consistently demonstrating significant contributions across all models for the five outcome indicators (ACR20: OR 0.92, 95% CI 0.88-0.97; ACR50: OR 0.92, 95% CI 0.87-0.96; ACR70: OR 0.93, 95% CI 0.89-0.97; PsARC: OR 0.91, 95% CI 0.87-0.96; MDA: OR 0.95, 95% CI 0.91-0.99). Similarly, HAQ and family history of PsA also emerged as risk factors for biological efficacy, with high HAQ scores and a positive PsA family history predicting poor biological efficacy. Interestingly, our results indicated that the pain VAS score is a strong protective factor for biological efficacy in the ACR20/50/70 and PsARC models, but not in the MDA model. This discrepancy may be attributed to the calculation methods of ACR20/50/70 and PsARC, which are based on the percentage of joints restored, while pain VAS scores are related with more severe arthritis. Therefore, we speculated that patients with severe PsA are more likely to achieve a certain percentage remission rate, but may not be more likely to achieve MDA.

Conclusion:

Our study suggests that younger patients with well-functioning joints and those without a family history of PsA are more likely to benefit from biologic therapy and achieve favorable outcomes. However, PsA patients with higher joint severity may achieve a certain percentage of remission more readily with biologics, but may not achieve MDA as easily.

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Abstract N°: 3186

Biologic use and treatment outcomes in patients with psoriasis in real-world settings among the Japanese population

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Introduction & Objectives:

The IL-17 inhibitors (IL-17i) and IL-23 inhibitors (IL-23i) have been approved for treatment of plaque psoriasis (Pso) in Japan since 2015 and 2018, respectively. Pso requires chronic treatment, but biologic efficacy may decline over time. In real-world studies, biologic persistence is a surrogate measure of long-term treatment response. However, biologic discontinuation without further Pso treatment may indicate disease remission. This study provides real-world evidence (RWE) on biologic use and treatment outcomes in patients with Pso in Japan.

Materials & Methods:

This is a retrospective cohort study using the Japanese Medical Data Vision database, which contains hospital-based claims data on 46 million patients in Japan. Patients diagnosed with Pso and newly initiated on IL-17i [secukinumab (SEC), ixekizumab (IXE), brodalumab (BRO)] or IL-23i [guselkumab (GUS), risankizumab (RIS), tildrakizumab (TIL)] therapy between Jan 1, 2015 and Dec 31, 2022 were included. Persistence of biologic use was measured from the date of the first identified biologic prescription, and ended at the time of discontinuation, switch, loss to follow-up or study end (Dec 31, 2022), whichever came first. Discontinuation was defined as a treatment gap of at least twice the maintenance dosing interval (16 weeks for GUS, 24 weeks for RIS and TIL, 8 weeks for SEC and IXE, 4 weeks for BRO). Median [IQR] duration of persistent biologic use was described for each group. Biologic persistence rates (percentages with 95%CI) at 3, 6, 12, and 24 months post biologic initiation were reported, with the number of patients still enrolled at each time point as the denominator. Use of Pso-related treatments following discontinuation was assessed among those who received biotherapy for ≧ 6 months. The proportions of patients who were completely treatment-free (i.e., never used any Pso-related treatment), systemic treatment-free (i.e., used no treatments except for topical drugs) and who restarted biotherapy were reported with 95%CI. Patients followed for less than 6 months after discontinuation were excluded.

Results:

In total 1,751 and 1,721 patients were identified as new IL-17i and IL-23i users for the treatment of Pso, with a median duration of follow-up of 2.7 and 1.4 years respectively. In the IL-17i and IL-23i groups, median age was 55 and 58 years, with males accounting for 67.7% and 64.1% of patients, respectively. In the IL-17i group, median duration of persistent biologic use was 9.9 (3.9-22.5) months, and persistence rates at months 3, 6, 12, and 24 were 85.5% (84.7-87.1%), 72.1% (69.8-74.3%), 55.8% (52.2-58.4%) and 38.7% (35.8-41.6%), respectively. In the IL-23i group, median duration of persistent biologic use was 12.0 (6.0-21.7) months, and persistence rates at months 3, 6, 12, and 24 months were 95.8% (94.7-96.7%), 90.1% (88.5-91.5%), 77.3% (74.7-79.7%) and 60.0% (56.1-63.8%), respectively (Fig. 1). Among patients who discontinued biologic use after at least 6 months of persistent biotherapy, 2.3% of IL-17i and 6.7% of IL-23i patients were completely treatment-free; 10.4% and 23.6% were systemic treatment-free; and 82.6% and 60.7% restarted biotherapy, respectively (Table 1).

Conclusion:

Higher biologic persistence and treatment-free rates were observed for Japanese patients who received IL-23i for Pso compared to those who used IL-17i. These findings are similar to those from previous studies using US claims data, supporting the conclusions of this study.

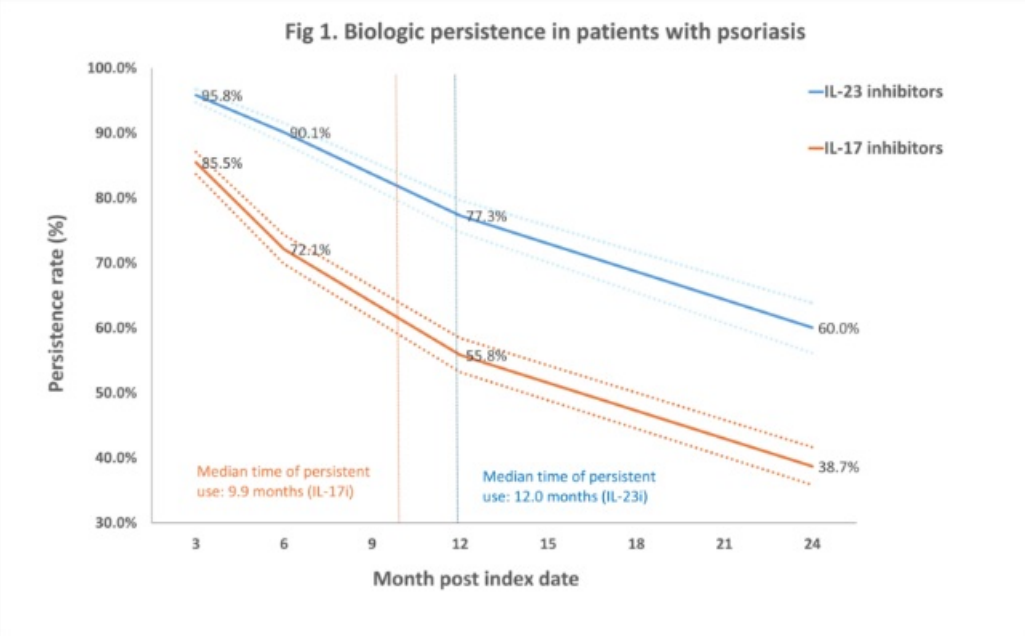

Table 1. Psoriasis-related treatments after bio-discontinuation

	IL-17i		IL-23i	
Total number, n	1751		1721	
Patients with bio-discontinuation, n	802		324	
Long-term biologic users (>=6 months) with bio-discontinuation, n	445		220	
Long-term bio users (>=6 months) with bio-discontinuation, and >= 6 months follow-up after bio-discontinuation, n	386		178	
Complete treatment free, n (%)	9	2.3%	12	6.7%
Systemic treatment free, n (%)	40	10.4%	42	23.6%
Bio-restart rate, n (%)	319	82.6%	108	60.7%
Time to bio-restart				
Median, months	1.8		4.5	
IQR, months	1.1-3.9		2.6-7.7	

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Abstract N°: 3245

Use of bimekizumab in treatment of moderate-to-severe psoriasis vulgaris: A real-world retrospective study of 24 patients

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Introduction & Objectives:

Bimekizumab is a humanized monoclonal IgG1 antibody which selectively inhibits IL-17A and IL-17F, two cytokines that play a critical role in the pathogenesis of psoriasis vulgaris (PSO). Randomized clinical trials (BE VIVID, BE READY, BE SURE, BE BRIGHT) demonstrated high percentages of PASI 90 responses among patients treated with bimekizumab compared to placebo and other injectable biologics, leading to its approval by the United States Federal Drug Administration for moderate-to-severe plaque PSO. Due to strict inclusion criteria utilized in clinical trials, patient outcomes in real practice may differ, making real-world studies important and necessary. Herein, we describe treatment of moderate-to-severe PSO with bimekizumab in an outpatient dermatology clinic in the USA.

Materials & Methods:

Charts of patients prescribed bimekizumab for moderate-to-severe PSO between 10/2023 – 4/2024 at an outpatient clinic were retrospectively retrieved. For inclusion, a body surface area (BSA) affected by PSO of at least 10% at time of bimekizumab start and one follow-up visit within 2-4 months of treatment initiation was necessary. Patient demographics, comorbidities, previously attempted systemic agents, response to treatment, and adverse events (AEs) were analyzed.

Results:

Of the 24 patients prescribed bimekizumab, 83.3%, had diagnoses of PSO and psoriatic arthritis; the remaining 16.7% had PSO only. The average age, body mass index, and number of previously unsuccessful systemic therapies at bimekizumab initiation was 54.6 years, 28.2 kg/m2, and 4.5 therapies, respectively. The most common comorbidities were hypertension (25.0%), type 2 diabetes mellitus (16.7%), and hyperlipidemia (16.7%). Mean BSA at baseline versus 2-4 months after initiating treatment (exact duration varied per patient) was 13.9% versus 4.0%, respectively. Overall, 79.2% of patients experienced a decrease in BSA after initiating bimekizumab, with 41.7% of these patients obtaining a BSA of 0% (skin clear). In contrast, 20.8% of patients experienced no change in disease. Three patients experienced AEs, two resulting in discontinuation of bimekizumab (gastrointestinal symptoms, injection site reaction).

Conclusion:

Aligning with clinical trials, this study reinforces that bimekizumab is a useful therapeutic option for moderate-to-severe psoriasis vulgaris. Herein, bimekizumab successfully and rapidly reduced BSA, even among patients with disease refractory to multiple systemic therapies. Interestingly, several AEs commonly reported in clinical trials (nasopharyngitis and candidiasis) were not observed here, which may be due to limited follow-up. Future real-world studies would benefit from increased size/longer duration. Despite its limitations, this study corroborates evidence demonstrated in clinical trials, supporting bimekizumab as an appropriate option for treatment of moderate-to-severe psoriasis vulgaris among patients in real clinical practice.

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Abstract N°: 3300

Safe application of Ustekinumab in a psoriasis patient combined with coronary heart disease after percutaneous coronary intervention for acute myocardial infarction

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Introduction & Objectives:

Recent research indicated psoriasis not only lead to increase of inflammatory cytokine level in skin lesion, but also cause systemic inflammation, furtherly induce several comorbidities such as cardiovascular disease□arthritis□ metabolic syndrome□inflammatory bowel disease and so on. For patients combined with acute myocardial infarction (MI) need to be treated by percutaneous coronary intervention (PCI), there is a lack of evidence indicating how to select a safe biologic after PCI.

Materials & Methods:

Here we report a long disease duration psoriasis patient underwent PCI and then treated with Ustekinumab without relapse of acute MI for half one year, maybe can bring some experience for the treatment of similar situation.

A 32 years old male severe plaque psoriasis □PASI 21.8; BSA 35%; sPGA 3□came to our department at March 2022. The first syndrome of plaque psoriasis appeared 21 years ago and he was treated by topical therapy then with several times of relapse of skin lesion until 2017. Then he was successively treated with methotrexate combination with folic acid and oral splenic peptide with limited efficacy of skin lesion clearance. He was diagnosed as coronary heart disease with 50% stenosis of right coronary artery and circumflex branch shown by coronary angiography and then treated with oral aspirin irregularly without periodical reexamination.

Results:

At March 2022, he was treated with Ustekinumab with recommended dosage (subcutaneous 45 mg at week 0□4 and then every 12 week) in our department after routine screenings of blood test and chest CT before biologic treatment. He achieved 85% percentage improvement of skin lesion after 16-week treatment and significantly improvement of life quality and then continuously treated with Ustekinumab for one year with stable skin lesion clearance and no adverse event occurred. Routine test of blood pressure and blood fat didn't appear to be abnormal. But at May 2023 the patient experienced a burst of acute MI and treated with PCI. According to suggestion provided by multiple disciplinary team, for the treatment of psoriasis, he restarted maintenance dose of subcutaneous Ustekinumab 45 mg every 12 week after PCI and reexamined regularly at cardiology and dermatology department. After 6 months follow up, the patient didn't appear any abnormality of examination for cardiovascular disease. Also the skin lesion of psoriasis was controlled well without relapse or exacerbation. No safety issues appeared during the follow up too.

Conclusion:

We firstly report a long-term plaque psoriasis case combined with coronary heart disease treated with Ustekinumab, and underwent PCI for acute MI during maintenance treatment period, then continued treated with Ustekinumab after PCI. Application of Ustekinumab after PCI was proved to be safe and maintain stable skin lesion clearance efficacy.

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Abstract N°: 3346

generalized lichen planus pigmentosus and a new management approach

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Introduction & Objectives:

Materials & Methods:

Results: Lichen Planus Pigmentosus (LPP) is an uncommon form of lichen planus, which presents with annular violaceous to brown lesions.Skin lesions are distributed over the sun-exposed areas, including the face and neck.In this study, we are reporting the first case of generalized LPP accompanied by palmar involvement that experienced notable improvement with tofacitinib (Janus Kinase inhibitor) after two months. **

A 50-year-old female patient was referred to our dermatology clinic with widespread skin lesions that had been gradually developing over the past 14 years , initially in the groin region. She also had mild pruritus. She had Hashimoto hypothyroidism, which was managed with levothyroxine. No other medical or drug histories were disclosed. In her examination,the lesions were distributed over 90% of her body particularly her face, and other sun-exposed areas with no mucosal involvement. The lesions were mostly violaceous and brown with fine scale, especially on the borders. Exfoliation in the lesions was detected on the palmar regions of her both hands. Furthermore, telangiectasia was observed at the center of the lesions mainly on the face. She had undergone two skin biopsies, both of which indicated atypical findings of Lichen Planus pigmentosus and she was prescribed oral prednisolone (20mg daily); but no significant improvements were detected in her lesions after six months. Thus, a subsequent skin biopsy was conducted with differential diagnoses such as Subacute Cutaneous Lupus (SCLE), mixed connective tissue disease, dermatomyositis, systemic lupus erythematosus, Lichen planus (LP) pigmentosus, lichen planus atrophicus, ashy dermatosis, and Mycosis Fungoides (MF). The microscopic examination indicated acanthosis , mild superficial perivascular inflammation, lichenoid interface reaction and some Civatte bodies in the basal layer.Melanin incontinence and vascular ectasia are also noted. PAS staining revealed mild thickening of the basement membrane. No mucin deposition has been observed by Alcian blue staining. The Direct immunofluorescence (DIF) showed multiple globular deposits of immunoglobulin (Ig) G and M at the epidermis and dermoepidermal junction. Routine laboratory findings was normal . Collagen vascular tests were all negative.A chest Computed Tomography (CT) was performed to rule out interstitial lung disease.

We diagnosed lichen planus pigmentosus with telangiectasia for her due to the clinical and histopathological features and Tofacitinib (15 mg daily) was started for her. In the next month’s follow-up, her lesions improved significantly .

As a result, the medication was continued until the disease was completely resolved.In this study, we are reporting a case of generalized LPP with skin lesions over the palmar regions.Diffuse form of the disease is a rare variant in which nails and palmoplantar area are often spared; however, palmar involvement has been observed in a few cases similar to our patient.

The signaling of interferon-g through the Janus kinase (JAK) - signal transducer and activator of the transcription pathway can induce inflammation and destruction of keratinocytes .Hence JAK inhibitors are

promising therapeutic candidates for LPP. There is a lack of research on the impact of tofacitinib on the more widespread form of LPP. To our knowledge, this is the first report in which tofacitinib dramatically improves the generalized LPP with palmar involvement.

Conclusion:

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Abstract N°: 3426

experience with spesolimab in the treatment of generalized pustular psoriasis

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Introduction & Objectives:

Generalized pustular psoriasis is a condition characterized by the appearance of visible pustules at a macroscopic level, sterile, throughout the body except on the palms and soles. Unlike plaque psoriasis, this condition shows an alteration of IL36 (both by overexpression of the agonist and by loss of function of the antagonist), leading to the proliferation of keratinocytes, elevation of proinflammatory cytokines and acute-phase reactants, and migration of neutrophils to the epidermis, resulting in the characteristic lesions of this disease.

Materials & Methods:

Presentation of two cases of generalized pustular psoriasis treated with Spesolimab. Patient 1: An 87-year-old woman, with multiple comorbidities, with generalized pustular psoriasis (GPP) of more than 10 years of evolution who had been treated with multiple classical systemic drugs and biologics. After lowering the dose of acitretin, she presented a flare with a GPPASI of 18 and a BSA of 30%. Patient 2: A 71-year-old woman with GPP of 3 years of evolution on treatment with acitretin. For the past two months, she has had a flare with a GPPASI of 3.1 and BSA of 12% that was not controlled with systemic corticosteroids and methotrexate. Both cases were flares of GPP that were not controlled with the usual systemic drugs, so administration of Spesolimab was requested.

Results

After Spesolimab infusion, the patients showed significant improvement with almost complete clearance at 4 weeks (GPPASI 1), which has been maintained for over 12 weeks of follow-up.

Discussion and Conclusions

Spesolimab is a monoclonal antibody that blocks the binding of the different isoforms of IL36 (IL36α, IL36β, IL36γ) to the receptor (IL36R), attenuating the inflammatory response mediated by this pathway.

We present our experience with this drug in the treatment of two patients with GPP at the Basurto University Hospital.

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Abstract N°: 3531

Successful Treatment Of Recalcitrant Bullous Pemphigoid In A 73 Year Old Female With Subcutaneous Dupilumab

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Introduction & Objectives:

Bullous pemphigoid (BP) is a chronic autoimmune subepidermal blistering disorder with several clinical variants, primarily affecting the elderly population. BP poses a therapeutic challenge due to its chronic nature and significant impact on patients' quality of life. This autoimmune disorder primarily affects the elderly, presenting with blistering, erythematous patches, and intense pruritis. Current management involves a stepwise approach, ranging from topical corticosteroids to systemic immunomodulators.

Materials & Methods:

We present a 73-year-old lady with a background of type 2 diabetes, hypertension, hyperlipidaemia presented with intractable night time pruritis and xerosis. Dermatology review revealed excoriations and discrete ulcerated lesions on the arms, legs and back. Emollients and a course of UVB phototherapy provided limited benefit. She re-presented several months later with a worsening of her symptoms. A skin biopsy was performed at this stage which confirmed a diagnosis of bullous pemphigoid.

Despite initial control of symptom burden with oral prednisolone, her disease flared upon dose reduction. Screening for alternative therapies revealed contraindications or intolerances to various agents. We successfully obtained funding for the use of Dupilumab, a monoclonal antibody inhibiting IL-4 and IL-13 for the next line of treatment. She was started on 600mg followed by 300mg every two weeks. Pre-treatment DLQI was 6 with widespread skin involvement predominantly affecting the back. After three weeks her pruritis symptoms had significantly improved and she was asymptomatic after 17 weeks with no adverse effects with a DLQI of 1 and was sustained at 39 weeks.

Results:

Dupilumab led to rapid and sustained improvement in symptoms, achieving complete resolution of pruritis and blistering within weeks. There have been emerging studies documenting the safety and efficacy of dupilumab in BP. The largest study to date was a retrospective multi centre cohort study evaluated the use of dupilumab in biopsy proven BP in 146 patients with a primary outcome of disease control including resolution of pruritus within 4 weeks. Patients are currently being recruited for a large multicentre randomised double-blind, placebo-controlled trial to evaluate the safety and efficacy of dupilumab in adult patients in the USA. This study will be pivotal in delivering high quality validated data to support the use and licencing of dupilumab in BP patients.

Conclusion:

We present a case of a 73-year-old lady who had significant symptom burden secondary to BP for over two years refractory to systemic therapy who had complete resolution of pruritis and blistering with dupilumab. There is growing evidence base to suggest safe and efficacious use of this novel therapy for BP patients with significant symptom burden who are unsuitable for common systemic agents.

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Abstract N°: 3650

A randomised, double-blind trial to compare the efficacy, safety, and immunogenicity of the proposed biosimilar ustekinumab (FYB202) with reference ustekinumab in patients with moderate-to-severe plaque psoriasis

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Introduction & Objectives:

Biosimilars can allow more patients to access affordable treatment options and help reduce the cost burden on healthcare systems. Ustekinumab is an interleukin (IL)-12 and IL-23 antagonist approved for the treatment of moderate-to-severe plaque psoriasis, active psoriatic arthritis, and active inflammatory bowel disorders, i.e., Crohn's disease and ulcerative colitis. This multicentre, randomised trial compared the efficacy, safety, and immunogenicity of the proposed biosimilar ustekinumab FYB202 with reference ustekinumab.

Materials & Methods:

Eligible patients were ≥18 years old with body weight ≤100 kg and stable moderate-to-severe plaque psoriasis for ≥6 months with a Psoriasis Area and Severity Index (PASI) score of ≥12, plaque psoriasis affecting ≥10% of body surface area, a Physician's Global Assessment score of ≥3, and inadequate treatment response to or intolerance of ≥1 previous systemic treatment for psoriasis. Patients were randomised (1:1) to double-blind treatment with proposed biosimilar ustekinumab (FYB202) or EU-approved reference ustekinumab (both 45 mg at Weeks 0, 4, and 16); patients in the reference group who achieved PASI 75 at Week 28 were re-randomised to receive FYB202 or reference product at weeks 28 and 40, while responders in the FYB202 group continued the same treatment. The primary efficacy endpoint was percent improvement in PASI score from baseline to Week 12. Therapeutic equivalence was demonstrated if, depending on the regulatory requirement with respect to the significance level, the two-sided 95% and 90% confidence intervals (CIs) were within the pre-defined equivalence intervals of ±11% and ±10%, respectively. Secondary efficacy endpoints, safety and immunogenicity were also assessed.

Results:

A total of 392 patients were randomised to receive FYB202 (n=197) or reference ustekinumab (n=195); at Week 28, 189 patients in the FYB202 group continued treatment and 186 in the reference group were re-randomised (89 switched to FYB202 and 97 continued with reference ustekinumab). Baseline demographics and clinical characteristics were well-balanced between treatment groups; overall, 40% of patients were female, mean age was 42 years, and mean PASI score was 24.4. For the primary endpoint, the estimated mean percent improvement in PASI score from baseline to Week 12 was equivalent between FYB202 and reference ustekinumab with an estimated least-squares mean treatment difference of 3.27% and the two-sided 95% (−0.90%, 7.44%) and 90% (−0.22%, 6.77%) CIs fully contained within the pre-defined equivalence margins. All secondary efficacy endpoints were also similar between treatment groups and efficacy was maintained over the whole 52-week study period. The safety profiles were comparable between groups, with 39.6% of patients in the FYB202 group and 41.0% in the reference group reporting adverse events. Prevalence of anti-drug antibodies (ADAs) was generally lower in the FYB202 group; ADA titres were low and comparable in both treatment groups at all timepoints and proportions of patients with neutralising antibodies were similar between groups. Switching from reference

product to FYB202 had no clinically relevant effect on efficacy, safety, or immunogenicity.

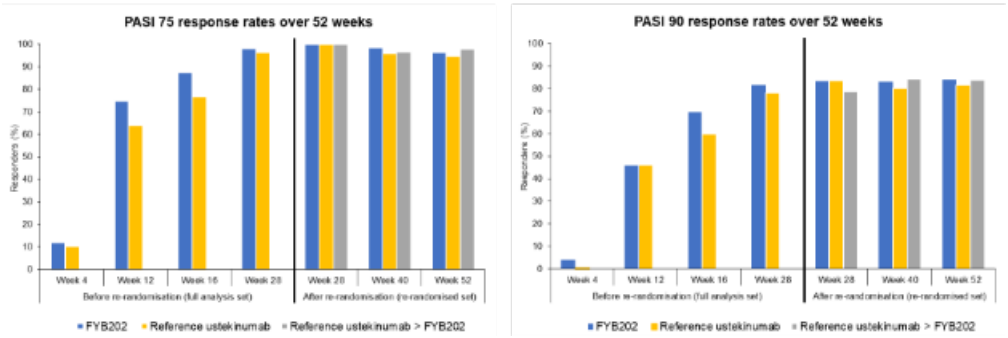
Conclusion:

Proposed biosimilar ustekinumab (FYB202) demonstrated therapeutic equivalence to reference ustekinumab in patients with moderate-to-severe plaque psoriasis, with comparable safety and immunogenicity profiles.

Primary endpoint analysis: comparison of percentage improvement in PASI score from baseline to Week 12 in the full analysis set

			Mixed model repeated measures least squares estimation			
	N	n*	LS mean change† ± SE, (95% CI), %	LS means treatment difference ± SE (FYB202 – reference ustekinumab), %	2-sided 95% CI	2-sided 90% CI
FYB202	197	195	79.51 ± 2.48 (74.64; 84.38)	3.27 ± 2.12	(-0.90; 7.44)	(-0.22; 6.77)
Reference ustekinumab	195	195	76.24 ± 2.44 (71.45; 81.02)			
Equivalence‡					2-sided 95% CI contained within (-11%; 11%)	2-sided 90% CI contained within (-10%; 10%)

*Patients with missing assessments at all post-baseline visits until Week 28 were not included in the calculation of LS means (FYB202 group, missing n=2).
†Estimates were adjusted for baseline PASI score, baseline body weight, time since onset of psoriasis, and prior inadequate response or intolerance to a systemic biological treatment.
‡Therapeutic equivalence was established if 2-sided CIs were contained within the prespecified equivalence intervals. Equivalence intervals were agreed with regulatory authorities: EU, 2-sided 95% CI contained within (-11%; 11%); US, 2-sided 90% CI contained within (-10%; 10%). CI, confidence interval; LS, least squares; PASI, Psoriasis Area and Severity Index; SE, standard error.



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Abstract N°: 3673

The views of dermatology patients concerning the environmental impact of their biologic medication

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Introduction & Objectives:

The pharmaceutical industry produces 0.5% of global greenhouse gas (GHG) emissions1. The European Commission's Draft Packaging Regulation states that medical packaging is exempt from recyclability targets until 20342. Dermatology patients have previously demonstrated positive recycling practices regarding topical agents3. There is no data examining the views of dermatology patients regarding the environmental impact of biologic medications.

Materials & Methods:

We conducted a single centre prospective study distributing an anonymous 19-point questionnaire to dermatology patients on biologic medication examining attitudes to recycling, practices regarding disposal of their drug delivery device and knowledge regarding the environmental

impact of biologic medication.

Results:

Sixty-seven patients responded (median age 46.3years) of whom 58% were male and 60% were taking Adalimumab. Although 96% felt that recycling was worthwhile, only 22% were aware of the circular economy; 53% stated that their injection came with too much packaging and 66% recycled this packaging; 53% believed the used injection device was incinerated while 13.6% thought they were recycled. The remaining 33.4% did not know or thought it was disposed of in a landfill. On the environment, 47% were concerned about the adverse impact of their medication production; 83% would prefer a biologic with a recyclable dispensing device. Factors influencing their choice of drug included a partly recyclable device in 44%; a drug requiring less frequent administration in 30% and by both in 11%. The remainder of patients asked about influencing choice of drug would not be influenced by either factor. When asked about energy used to produce their medication 33% believed the majority went in manufacturing of the dispensing device whereas 18% felt it was the active drug and 49% did not know. The most important factor for the patient when choosing treatment was complete clearance of skin for 66% followed by long term treatment effectiveness for 24% while none rated the environmental impact of medication.

Conclusion:

In conclusion our results reveal a favourable view of recycling and recycling practices amongst patients using biologic agents, but the majority are unaware of disposal practices of their device, energy us used in drug manufacturing and do not rate the environmental impact of their medication as an important consideration when choosing treatment.

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AMSTERDAM 25-28 SEPTEMBER 2024
EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

Abstract N°: 3720

Safety and Pharmacokinetics of a Highly Selective Oral TYK2 Inhibitor (ICP-488): A Phase I, Randomized, Double-Blind, Placebo-Controlled, Dose-Escalation Study

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Introduction & Objectives:

ICP-488 is a potent, highly selective, allosteric, small-molecule inhibitor of tyrosine kinase 2 (TYK2) that acts through a novel mode of binding to the JH2 pseudokinase domain and inhibits TYK2-dependent receptor signaling pathways. The objectives of this first-in-human study (ICP-CL-01001) were to assess the safety, tolerability, and pharmacokinetics (PK) of ICP-488 in healthy subjects and the preliminary efficacy and safety in psoriasis patients.

Materials & Methods:

This phase I study was designed as a randomized, double-blind, placebo-controlled study and comprised three parts: part 1, single-ascending dose (SAD) and food effect (FE) in healthy subjects; part 2, multiple-ascending dose (MAD) in healthy subjects; and part 3, multiple dosing in patients with plaque psoriasis. The primary endpoint was to evaluate the safety and tolerability of ICP-488.

The healthy subjects were randomly assigned to receive either ICP-488 or placebo in a ratio of 3:1 for each dose cohort. They were administered a single oral study drug dose at 1, 3, 6, 12, 24, or 36 mg during the SAD period or 3, 6, or 12 mg once daily (QD) for 14 days during the MAD period. Eight additional subjects enrolled in the FE cohort, and all received ICP-488 6 mg. Twenty-one patients with moderate-to-severe psoriasis were randomly assigned to receive ICP-488 6 mg QD or placebo in a ratio of 2:1 for 28 days (Figure 1).

Results:

A total of 92 healthy subjects enrolled in the study. ICP-488 was safe and well tolerated in the evaluated doses (up to a single dose of 36 mg and up to multiple doses of 12 mg QD). All treatment emergent adverse events (TEAEs) were mild or moderate. There were no deaths, severe TEAEs, or serious TEAEs.

In healthy subjects, ICP-488 was rapidly absorbed and exhibited an apparent mean terminal elimination half-life (t1/2) of 4.99-16.1 hrs following single dosing and 7.17-11.2 hrs after multiple dosing. ICP-488 demonstrated PK linearity in the dose range of 6 mg-36 mg. No clinically significant differences in ICP-488 PK were observed following administration of ICP-488 with a standard high-fat, high-calorie meal. A similar PK profile was seen in patients with moderate-to-severe plaque psoriasis.

In the psoriasis patient cohort, all TEAEs were mild or moderate, and the overall frequency of TEAEs (71.4%) and treatment related adverse events (TRAEs) (57.1%) were same in the ICP-488 6 mg QD and placebo groups. The preliminary data of percentage change from baseline in Psoriasis Area and Severity Index (PASI) score showed a preliminary significant difference between the ICP-488 6 mg QD group and placebo group at week 4 (38% vs 14%, p=0.0870, two sided alpha = 0.1) (Table 1).

Conclusion:

ICP-488 was safe and well tolerated with favorable PK profiles. ICP-488 showed preliminary efficacy in psoriasis patients within 4 weeks of treatment.. Further clinical development in psoriasis is warranted. 2** / 2**

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Abstract N°: 3876

Successful treatment of chronic actinic dermatitis with abrocitinib: a case series and review of the literature

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Introduction & Objectives:

A proportion of patients with resistant CAD experienced no or limited response to conventional management options or had side effects. Previous reports have demonstrated that some patients with severe CAD have achieved satisfactory clinical outcomes with Janus kinase (JAK) inhibitors when conventional therapies have failed. More evidence is needed to confirming the effectiveness of this novel therapy in clinical settings.

Materials & Methods:

We reviewed the literature published in the last 10 years on CAD treatment with JAK inhibitors available in the online PubMed database. Additionally, we assessed the efficacy and safety of an oral JAK-1 inhibitor, abrocitinib (100 mg once daily) in three patients who failed to respond to the conventional therapies.

Results:

All three patients responded successfully to abrocitinib therapy in a short period of time, and no relapse has been detected after follow-up. To our best knowledge, five studies have reported the treatment of patients with CAD with JAK inhibitor, as shown in **Table 1.** All patients had failed to respond sufficiently to at least one line of previous therapy and after receiving the treatment of JAK inhibitor combined with other treatments, these patients all experienced significant improvement.

Conclusion:

Our study suggests that patients who were previously unresponsive to conventional therapies experienced successful resolution following treatment with JAK inhibitors.

Table 1. Clinical Data on JAK inhibitor for the Treatment of Seven Patients with CAD, Including Our Case Series.
Age (Years) / Sex
68/M
63/M
45/M
65/M
55/M
58/M
60s/M
69/M
75/M
58/M

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Abstract N°: 3955

Guselkumab real-world efficacy and impact on quality of life and sexual life in moderate to severe psoriasis patients with genital involvement: data from the CASSIOPEE study

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Introduction & Objectives:

Genital psoriasis (G-PsO) results in significant impairment of quality of life (QoL) and is considered a difficult-to-treat area. Guselkumab (GUS), a p19 subunit-targeted anti–IL-23 monoclonal antibody, is approved for the treatment of moderate to severe psoriasis (PsO). The CASSIOPEE study assessed the impact of GUS on overall and sexual QoL of patients with moderate to severe PsO in real life practice. This sub-analysis aims to evaluate the impact of GUS on G-PsO.

Materials & Methods:

CASSIOPEE is a prospective, multicenter, non-interventional study on 207 psoriatic patients followed up for 6 months after GUS initiation in France. This analysis focused on the 65 patients (31.4%) having G-PsO at baseline (Genital area specific PGA, as-PGA ≥ 1), with 2 subgroups based on G-PsO severity. At M0, M3, and M6 as-PGA and PGA were evaluated by investigators, and DLQI and RSS (Relationship & Sexuality Scale, ranging from 10 to 46 points) were completed by patients.

Results:

At baseline, the mean PGA, as-PGA and DLQI scores for G-PsO patients were respectively 3±0.8 (95%CI: 2.8-3.2), 2.2±1 (95%CI: 2-2.5) and 12.3±6.6 (95%CI: 10.6-14.1). Patient characteristics are summarized in Table 1. PsO severity at M0 was mild (PGA 2), moderate (PGA 3) and severe (PGA 4) in 29.2%, 43.1% and 27.7% of patients respectively. Moreover, 60% of patients with G-PsO had an as-PGA score of 1 or 2 (milder group) and 40% had an as-PGA of 3 or 4 (more severe group). The mean DLQI score was 12.3±6.6 (95%CI: 10.6-14.1), 11±6.3 (95%CI: 8.8 - 13.2) and 14.3±6.7 (95%CI: 11.4-17.2) in overall, milder and more severe G-PsO groups, respectively. Before GUS initiation, 87.1% of patients had received a conventional systemic treatment and 24.2% had at least one previous biologic.

At M3 and M6, respectively 93.6% and 96.3% of patients achieved an as-PGA ≤ 1, 72.3% and 79.6% achieved complete clearance of their G-PsO (as-PGA 0). The mean as-PGA score in the G-PsO population decreased on average by 1.9±1.2 at M3 and 1.9±1.1 at M6, from 2.2±1 at M0. Improvements in genital lesions were observed regardless of severity (Figure 1).

At M6, 79.5% of overall G-PsO patients achieved a ≥5-point reduction in DLQI score. Interestingly, 74.1% of patients in the milder group vs up to 88.2% for the more severe group achieved ≥5 points reduction in DLQI score.

Mean total RSS score at M0 was 28.9±5.8 (95%CI: 27.3-30.4), 28.6±6.1 (95%CI: 26.5-30.8) and 29.2±5.5 (95%CI: 26.7-31.7) in the overall, milder and more severe G-PsO groups respectively; at M6, total RSS scores improved by 4.5±6.1 (95%CI: 2.5-6.4), 3.1±5.1 (95%CI: 0.9-5.2) and 6.6±7 (95%CI: 2.8-10.3), respectively.

Regarding specific RSS items, whereas only 26.4% of G-PsO patients reported that they “never experienced fear of sexual intercourse” at M0, 54.2% reported never fearing sexual intercourse at M6. Similarly, at M0, only 1.8% of patients with G-PsO reported being “very much satisfied with their intercourse” vs 8.5% of patients at M6 (Fig.2).

Conclusion:

This analysis shows that for patients with G-PsO receiving GUS in a real-life setting, substantial clinical benefit was observed with 79.6% of patients reaching complete clearance of their genital lesions and clear improvement in their quality of life and sexual life. Interestingly, these outcomes showed greater improvements in patients with more severe G-PsO at baseline.

Table 1: Baseline characteristics of G-PsO patients

		as-PGA 1/2 (N=39)	as-PGA 3/4 (N=26)	as-PGA≥1 (N=65)
Age (years)	Mean (±SD)	43.5 (± 11.7)	41.2 (± 12)	42.6 (± 11.8)
Gender	Male	26 (66.7%)	13 (50.0%)	39 (60.0%)
	Female	13 (33.3%)	13 (50.0%)	26 (40.0%)
BMI (kg/m²)	Mean (±SD)	28 (± 5.5)	27.1 (± 5.9)	27.7 (± 5.6)
Time since first PsO symptoms (years)	Mean (±SD)	21.2 (± 13.8)	18.4 (± 11.9)	20.1 (± 13.1)
PsO severity psoriasis at baseline (PGA)	2: Mild	13 (33.3%)	6 (23.1%)	19 (29.2%)
	3: Moderate	15 (38.5%)	13 (50.0%)	28 (43.1%)
	4: Severe	11 (28.2%)	7 (26.9%)	18 (27.7%)
G-PsO severity at baseline (As-PGA)	1: Almost Clear	18 (46.2%)	0 (0.0%)	18 (27.7%)
	2: Mild	21 (53.8%)	0 (0.0%)	21 (32.3%)
	3: Moderate	0 (0.0%)	20 (76.9%)	20 (30.8%)
	4: Severe	0 (0.0%)	6 (23.1%)	6 (9.2%)
DLQI score at baseline	Mean (±SD)	11 (±6.3)	14.3 (±6.7)	12.3 (±6.6)
At least one previous treatment within the 5 years	Conventional systemic treatment	33 (89.2%)	21 (84.0%)	54 (87.1%)
	Previous biologic therapy	8 (21.6%)	7 (28.0%)	15 (24.2%)

Figure 1. Evolution of mean as-PGA score in G-PsO patients’ groups

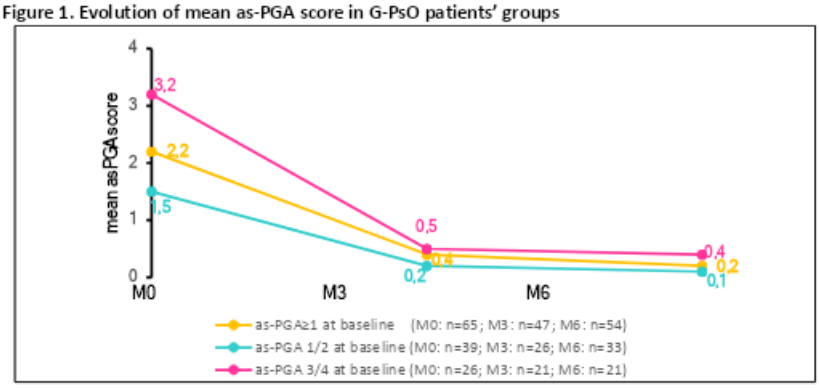
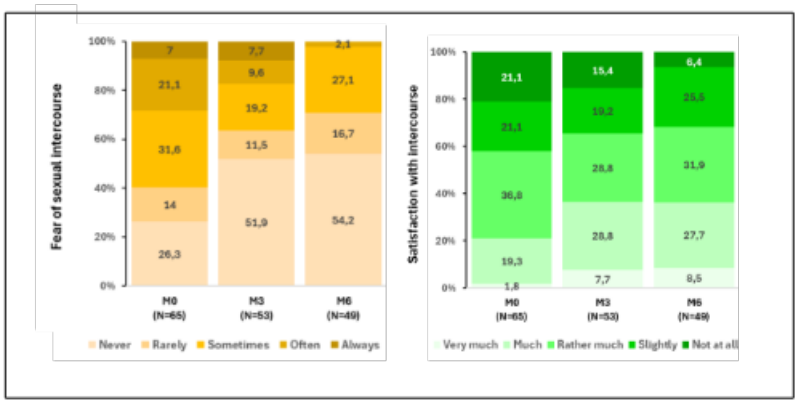


Figure 2. Evaluation of the impact of the disease on 2 aspects (out of 10) evaluated by the *Relationships and Sexual Scale* (RSS) over the first 6 months of GUS therapy in G-PsO patients



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Abstract N°: 3998

Experience with multiple non-medical switches between originator and biosimilars of adalimumab in patients with psoriasis

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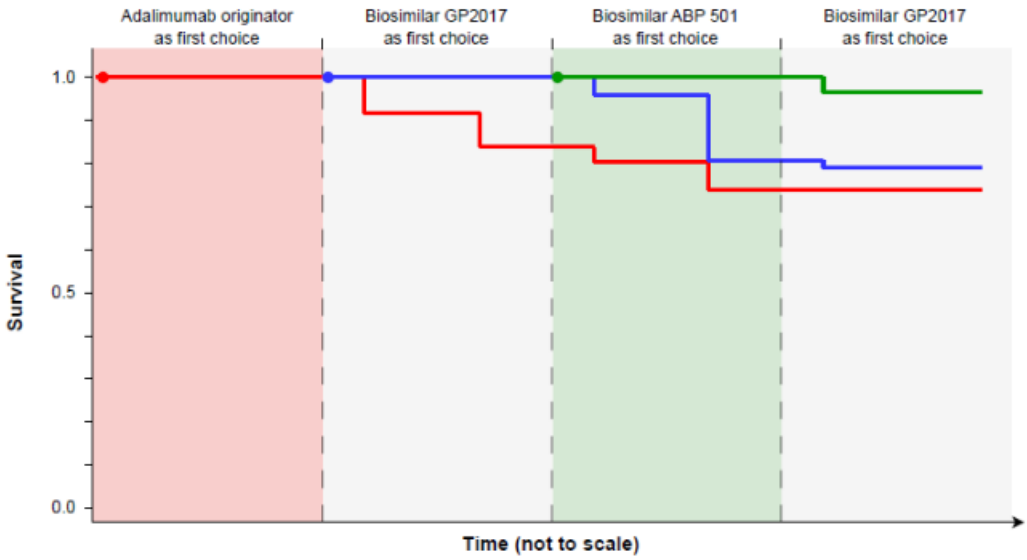
Introduction & Objectives: As of October 2018, the patent of the adalimumab originator expired in the EU and, currently, there are ten adalimumab biosimilars that are approved for treatment of psoriasis. A biosimilar is highly similar to the original biologic, but not identical. Prior to approval, biosimilars undergo extensive analytical studies and must, in a clinical trial, demonstrate efficacy and safety that is comparable to that of the originator. In the EU, biologics and biosimilars can be used interchangeably which may result in patients with psoriasis undergoing multiple non-medical switches to reduce costs. Data on multiple switches between originator and biosimilars of adalimumab are lacking and studies assessing the impact of drug adherence are needed.

Materials & Methods: We included all adult patients with psoriasis from our hospital department who had been treated for at least six months with an adalimumab product (originator or biosimilar) before undergoing a mandatory non-medical switch. At our department, there have been three mandatory non-medical switches: from the originator to GP2017 to ABP 501 to GP2017. Patients were assigned to different subcohorts based on the initial adalimumab product administered: the originator cohort, the GP2017 cohort, and the ABP 501 cohort. This implies that patients in the originator cohort may experience up to three switches, those in the GP2017 cohort up to two switches, and all in the ABP 501 cohort one switch. The outcome was discontinuation of therapy within the first six months following the non-medical switch allowing for the discontinuation to be attributable to the switch. Due to the limited number of patients in each subcohort, the data are presented descriptively.

Results: We included a total of 182 patients: 61 in the originator cohort, 67 in the GP2017 cohort, and 54 in the ABP 501 cohort. In the originator cohort, 5/61 patients discontinued therapy within the first six months after the first non-medical switch (Figure 1). Of these five patients, two discontinued therapy due to side effects, two discontinued therapy due to loss of effectiveness, although a flare was present prior to the switch, and the last patient was lost to follow-up. At the second and third switch in the originator cohort, 2/51 and 0/45 patients discontinued therapy, respectively. In the GP2017 cohort, 3/67 and 1/54 patients discontinued therapy within the first six months following the first and second non-medical switch, respectively. In the ABP 501 cohort, 2/54 discontinued therapy after the non-medical switch. Of all the patients who discontinued therapy within the first six months, only one stopped due to loss of effectiveness.

Conclusion: The findings indicate that multiple non-medical switches between originator and biosimilar adalimumab are safe and without loss of effectiveness among patients with psoriasis.

FIGURE 1. Survival plot visualising the number of patients within each subcohort at different time points.



Number undergoing mandatory non-medical switch (number discontinuing therapy within six months after switch)

Originator cohort	61 (5)	51 (2)	45 (0)
GP2017 cohort		67 (3)	54 (1)
ABP 501 cohort			54 (2)

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Abstract N°: 4019

Type I cryoglobulinemic vasculitis successfully treated with bortezomib plus dexamethasone therapy.

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Introduction & Objectives:

Cryoglobulins are a type of immunoglobulins that precipitate at temperatures below 37ºC, resulting sometimes in vessel occlusion and vasculitis. Type I cryoglobulins are monoclonal immunoglobulins often associated with hematological malignancies, especially B cell proliferative diseases (multiple myeloma, monoclonal gammopathy of undetermined significance, chronic lymphocytic leukemia). Treatment of symptomatic cases is directed to the underlying neoplastic process. Bortezomib is a proteasome inhibitor used as a first-line treatment for multiple myeloma which has also shown positive results in refractory cryoglobulinemic vasculitis and other autoimmune vasculitis.

Materials & Methods:

A 42-year-old woman presented with painful ulcers on the lower extremities. She also experienced recent-onset Raynaud's phenomenon affecting the fingers. A biopsy of the skin ulcers revealed small vessel vasculitis with a significant thrombotic component. Laboratory tests detected type I cryoglobulins associated with IgG lambda monoclonal gammopathy. Cryocrit was 25%. A bone marrow biopsy showed 7.8% atypical plasma cells, M component was 0,44 gr/dL. There were no renal nor peripheral nerve involvement. The final diagnosis was type I cryoglobulinemic vasculitis (CV) secondary to monoclonal gammopathy of unknown significance (MGUS). Initial treatment consisted in prednisolone and azathioprine achieving poor control. Treatment was switched to bortezomib plus dexamethasone with excellent clinical and analytical response after the 2nd cycle. At the 7th cycle therapy was ceased. She referred mild paresthesia as an adverse effect. Currently, 7 months after finishing treatment, she is lesions free (M component 0,15 gr/dL and cryocrit 6%).

Results:

The skin is the most commonly affected organ in type I CV. Livedo reticularis, Raynaud's phenomenon, acrocyanosis, ulcers and digital gangrene are typically observed. Renal and peripheral nerve involvement may be present. The therapeutic approach is unclear due to its low prevalence. Initial treatment usually involves systemic glucocorticoids. Rituximab and other alkylating agents are alternative options. Bortezomib is a first-line therapy in CV associated with multiple myeloma due to its ability to reduce immunoglobulin production. In our case, the patient received azathioprine and glucocorticoids with limited effectiveness. Second-line therapy with bortezomib plus dexamethasone led to a rapid improvement of ulcers and reduction of the monoclonal component. To date, we have found 7 similar cases of MGUS related type I CV with cutaneous involvement, successfully managed with bortezomib.

Conclusion:

CV is an infrequent disorder with high morbidity. Bortezomib has proven to be a fast and effective option in type I CV secondary to MGUS as it targets the underlying monoclonal gammopathy responsible for the disease. Thus, it

is expected to be positioned as the first therapeutic regimen in future.

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Abstract N°: 4087

Treatment with dupilumab during pregnancy is associated with decreased risk for adverse pregnancy outcomes: A large-scale, propensity-matched retrospective cohort study

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Introduction & Objectives: There's s a high prevalence of atopic diseases in the cohort of reproductive-aged women. Dupilumab, a monoclonal antibody inhibiting IL-4 and IL-23 signaling, is approved for moderate to severe atopic dermatitis, severe bronchial asthma with type 2 reaction, severe chronic rhinosinusitis with nasal polyps, prurigo nodularis, and eosinophilic esophagitis. Official approval for dupilumab treatment during pregnancy is lacking. Limited case reports and series suggest no increased risk of pregnancy complications with its use. However, larger controlled studies are lacking. Thus, the aim of this study was to assess the risk of adverse pregnancy outcomes (APOs) associated with dupilumab treatment in a substantial cohort.

Materials & Methods: Retrospective propensity-matched cohort study using electronic health records of the US Collaborative Network of TriNetX. Women aged 12-55 were identified, and baseline criteria were established by initial coding of diagnoses indicating pregnancy. Patients receiving dupilumab for any condition it is approved, either on the day of or up to nine months after the initial coding of a pregnancy were included. Controls were individuals without dupilumab or other relevant systemic treatments. Propensity-matched cohort studies were conducted to evaluate the risk of preterm labor, gestational hypertension, pre-eclampsia, HELLP syndrome, spontaneous abortion, gestational diabetes, and any analyzed APO. Survival analyses were performed using the Kaplan-Meier method, and differences in outcome distribution were assessed using the log-rank test. Hazard ratios (HR) were obtained using the Cox regression model, with patients censored at death or last follow-up.

Results: After matching, each group consisted of 702 participants. The mean age was 31.9 ± 9.22 years in the dupilumab group and 31.7 ± 9.29 years in the control group.

There were no significant differences in demographic variables or the prevalence of smoking, obesity, diabetes mellitus, hypertension, chronic kidney disease, atopic dermatitis, asthma bronchiale, nasal polyps, prurigo nodularis, or eosinophilic esophagitis between the two groups.

Compared to the dupilumab group, the control group had a higher risk of preterm labor (HR:3.89, 95% CI:1.60-9.41, p=0.001), gestational hypertension without significant proteinuria (HR:2.42, CI:1.32-4.45, p=0.003), pre-eclampsia (HR:2.36, CI:1.28-4.35, p=0.005), gestational diabetes (HR:3.2, CI:1.53-6.70, p=0.001), and any analyzed APO (HR:2.76, CI:1.81-4.19, p <0.0001).

There were no significant differences in the risk for HELLP syndrome (HR:2.27, CI:0.44-11.71, p=0.31) or spontaneous abortion (HR:2.01, CI:0.88-4.62, p=0.09) between the two groups. Limitations include the retrospective nature of the study and the potential impact of unmeasured confounders.

Conclusion: In conclusion, this study represents the first larger study with a control group assessing the risk of APOs associated with dupilumab treatment during pregnancy. Consistent with previous reports, no increased risk

of APOs was observed with dupilumab. Furthermore, this study suggests a potential decreased risk for preterm labor, gestational hypertension, pre-eclampsia and gestational diabetes compared to the control group. To validate these findings and establish a potential causal relationship, further prospective randomized clinical trials and meta-analyses of observational cohorts are warranted.

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Abstract N°: 4100

A Case of Retropharyngeal Abscess and Mediastinitis Occurred During Ixekizumab Treatment

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Introduction & Objectives: Ixekizumab is a biologic agent used in the treatment of psoriasis by acting as an IL-17A inhibitor. However, adverse effects and rare complications associated with the use of this agent require careful clinical follow-up. In this case report, we present a case of retropharyngeal abscess and mediastinitis that occurred during ixekizumab treatment in a male patient with psoriasis vulgaris.

Case: A 61-year-old man was diagnosed with psoriasis vulgaris for 30 years and previously treated with acitretin and methotrexate. His only comorbidity was benign prostate hyperplasia. After developing joint pain, the patient was evaluated as psoriatic arthritis by rheumatology and was planned to be switched to ixekizumab treatment. The patient, who was administered with induction doses of week 0, 2, 4 and 6, presented to the emergency department with chest and throat pain 3 days after the week 6 dose. The patient had complaints of dysphagia and chest pain while breathing. There was no history of trauma, foreign body ingestion or instrumental procedure. The chest X-ray of the patient showed poor definition of the margins of the superior mediastinum. Neck and thorax CT revealed air densities in the retropharyngeal area and mediastinum. A collection with a thickness of 5mm starting from the level of the C2 vertebra and increased density in mediastinum was observed. Intravenous antibiotics were initiated and the patient underwent surgery following the diagnosis of retropharyngeal abscess and mediastinitis secondary to deep neck infection. Abscess drainage was performed and loculated material was aspired in the paratracheal area. There was no growth in the culture of the tracheal aspirate. Klebsiella pneumoniae was isolated from the culture obtained from mediastinal fluid. Ixekizumab treatment was discontinued and the patient was discharged with oral antibiotics. Follow-up CT scans, performed one and a half months post-operation, revealed regression of deep neck infection and mediastinitis. After consultation with thoracic surgeons and otolaryngologist, the patient was considered at high risk to continue ixekizumab treatment due to recurrent mediastinitis.

Conclusion: Ixekizumab, an IL-17A inhibitor used in the treatment of psoriasis and psoriatic arthritis. Ixekizumab demonstrated a low incidence of severe infection in phase 3 studies, with no cases of retropharyngeal abscess and mediastinitis reported, although rare instances of septic shock and severe candida infections have been documented. Mediastinitis due to retropharyngeal abscess may occur as a result of progression of deep neck infections and diagnosed with CT. Treatment usually requires intravenous antibiotics and surgical drainage. A reported case in the literature involves retropharyngeal abscess complicated by mediastinitis in a patient receiving abatacept. Regular follow-up for retropharyngeal abscesses in patients using biologic agents is advised to monitor for complications. In our case, retropharyngeal abscess and mediastinitis developed after the 6th week of the ixekizumab treatment. Following surgical drainage and antibiotic treatment, both clinical and radiological improvements were achieved. We would like to emphasize that patients who develop infections while treated with biological agents should be closely monitored for potentially life-threatening complications as in our case.

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Abstract N°: 4169

Comparison of clinical and demographic characteristics of patients with psoriasis receiving a single biologic agent and those receiving at least two different biologic agents: A retrospective study

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Introduction & Objectives:

Psoriasis is a chronic inflammatory systemic disease that primarily affects the skin but can also involve the joints. A new era has opened in psoriasis with the use of biological drugs. Some patients can now achieve disease-free skin with a single medication. However, some patients require switching due to primary or secondary unresponsiveness. The reasons for this different response among patients are still unknown.

This study aims to compare the clinical and demographic characteristics of patients receiving a single biologic agent with those receiving multiple biologic agents. The study also aims to investigate factors influencing switching and determine independent risk factors in patients receiving multiple biological agents.

Materials & Methods:

The medical records of patients were retrospectively reviewed. The patients were divided into two groups: those receiving a single biologic agent and those receiving multiple biologic agents. Statistical analysis was performed using SPSS 22.0 (Statistical Packages of Social Sciences).

Results:

A total of 314 patients diagnosed with psoriasis and receiving biologic therapy were included in the study. Among them, 185 patients (58.9%) received a single biologic agent, while 129 patients (41.1%) received multiple biologic agents.

In the group receiving multiple biological drugs, compared to another group statistically significant differences were found in the baseline PASI score, frequency of erythroderma, nail involvement, psoriatic arthritis, dactylitis, earlier onset of skin involvement before joint involvement, diabetes mellitus, obesity, dyslipidemia, hepatosteatosis, and use of conventional treatment alongside the first biological drug.

Univariate logistic regression analysis revealed that disease duration, follow-up duration, baseline PASI score, nail involvement, history of erythroderma, psoriatic arthritis, dactylitis, cardiovascular/metabolic comorbidity, obesity, diabetes mellitus, dyslipidemia, and hepatosteatosis were positively associated with the likelihood of switching biologic medication, while the age of psoriasis onset showed a negative association.

In the multivariate reduction model, the significant independent differentiating factors associated with switching of biologic drug were early age of onset of psoriasis, psoriatic arthritis, history of erythroderma, at least one cardiovascular and/or metabolic comorbidity, and receiving additional conventional treatment with the first biological drug.

In the multivariate logistic regression analysis using the Forward LR method, erythroderma was identified as the independent factor with the highest predictive power for switching.

Conclusion:

This retrospective study provides insights into the clinical and demographic characteristics of patients receiving a single biologic agent versus multiple biologic agents for psoriasis treatment. Younger age of onset of psoriasis, presence of psoriatic arthritis, history of erythroderma, at least one cardiovascular and/or metabolic comorbidity, and receiving additional conventional therapy with the first biologic were identified as independent risk factors for drug switching. Therefore, to act prudently as a dermatologist, we recommended to screen each patient for cardiovascular and/or metabolic comorbidities, control modifiable risk factors, and assess psoriatic arthritis at baseline and periodically thereafter.

EADV CONGRESS
AMSTERDAM 25-28 SEPTEMBER 2024
EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

Abstract N°: 4171

Sneddon Wilkinson disease treated with spesolimab: a case report

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Introduction & Objectives:

Sneddon-Wilkinson Disease (SDW) is a rare, chronic, and recurrent pustular eruption of unknown etiology characterized by subcorneal pustules on histology. It can be very difficult to distinguish from generalized pustular psoriasis and acute generalized exanthematous pustulosis. They appear to be closely related disorders. Spesolimab is a humanized IgG1 monoclonal antibody that blocks human IL36 receptor (IL36R) signaling. It is the first drug indicated for outbreaks in adult patients with generalized pustular psoriasis.

Materials & Methods:

We present the case of an 81-year-old male with a medical history of hypertension, dyslipidemia, diabetes, and IgA kappa monoclonal gammopathy of uncertain significance with recurrent episodes of a pustular eruption for the past 5 years, histologically confirmed as subcorneal pustulosis. Previously, the patient had been treated with sulfone, with excellent response initially but poor tolerance, ultimately leading to discontinuation. Other therapies attempted included various cycles of corticosteroids, narrowband UVB, methotrexate, and adalimumab, none of which resulted in a satisfactory response or were poorly tolerated. Given persistently elevated triglyceride levels above 700 mg/dl, treatment with acitretin was contraindicated. Following a generalized flare of extensive pustulosis accompanied by intense itching, compassionate use of spesolimab was requested.

Results:

The patient received a single IV infusion of 900 mg of spesolimab, in conjunction with a tapering dose of corticosteroids. One week post-infusion, most lesions cleared, and itching notably improved. This improvement persisted for several weeks, after which a recurrence occurred, albeit with localized lesions that could be controlled temporarily with topical sulfone.

Conclusion:

Spesolimab, a selective inhibitor of the IL-36 receptor, a key cytokine involved in pustular psoriasis pathogenesis, has been approved by the European Medicines Agency for the treatment and prevention of pustular psoriasis flares based on the results of the Effisayil 1 and 2 trials. Given the clinical and histological resemblance between pustular psoriasis and SWD, and the ongoing debate regarding their potential representation as a clinical spectrum, spesolimab was considered for symptomatic control in this patient, yielding excellent results. However, further studies are warranted to substantiate its use in this condition, as its chronic nature necessitates medications capable of providing long-term control. Spesolimab may potentially serve as an alternative therapy for preventing and controlling disease flare-ups in SWD. Our case highlights a patient with SWD who achieved successful management of an extensive outbreak of pruritic lesions with a single infusion of spesolimab, resulting in rapid clearance of the lesions within 1-week post-infusion.

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Abstract N°: 4320

Comparison of Chronic Spontaneous Urticaria (CSU) Patients Receiving Standard Dose and High Dose Omalizumab

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Introduction & Objectives: This study aimed to compare patients diagnosed with CSU who received 300mg omalizumab (OMA) treatment every four weeks with treatment-resistant patients receiving high doses (450/600mg) OMA.

Materials & Methods: The files of patients diagnosed with CSU in our outpatient clinic who were unresponsive to antihistamine dose up to 4 times second-generation antihistamine treatment and who were started on OMA treatment were retrospectively analyzed. Patients receiving 300mg, 450mg and 600mg OMA every four weeks,demographic features, disease duration, body mass index (BMI), presence of angioedema(AE), CRP, anti-TPO, D-Dimer, Total IgE, absolute number of basophils, neutrophil/lymphocyte ratio (NLR), urticaria activity score (UAS) were recorded. Two groups were compared: patients receiving standard dose 300mg/4 weeks and high dose (450-600mg/4 weeks) OMA.Pearson chi-square, Fisher Freeman Halton test, Fisher exact chi-square tests were used to examine the relationships between qualitative variables. The compatibility of quantitative variables with normal distribution was evaluated by Kolmogorov Smirnov test. Student t test was used for mean comparison of two independent groups, Mann Whitney U test was used for median comparison of two independent groups.

Results: Of all 171 patients, 80(46.8%) were female and 91 (53.2%) were male. A total of 171 CSU patients were included in the study, 143 (83.6%) patients receiving 300mg OMA and 28 (16.4%) patients receiving high dose OMA. Of the 143 patients who received a dose of 300mg in four weeks, 63 (44.1%) were women and 80(55.9%) were men. Of the 28 patients who received high doses, 17 (60.7%) were women and 11 (39.3%) were men. The mean age (47) and BMI (28.9) of those in the high dose group were significantly higher than the mean age (41.6) and BMI (25.58) of those given low doses ($p=0.040$; $p=0.050$). No dose-related side effects were observed in any patient. 85% of patients on high dose were in the overweight group, while 15% were not overweight. We found that BMI was significantly higher in the group using high dose OMA ($p<0.001$). The rate of being overweight was significantly higher in those on high dose group ($p=0.01$). The presence of AE, mean disease duration, CRP, Anti-TPO, D-Dimer and Total IgE elevation were seen as a higher percentage in the high dose group. No statistically significant difference was observed between the standard and high dose drug groups in terms of gender, presence of angioedema, NLR, basophil absolute number, UAS7, CRP, Anti-TPO, D-Dimer, Total IgE elevation and disease duration averages ($p>0.05$). In the 300mg dose group, the mean of UAS7 was 28.4, while it it was higher in the high dose group, with an average of 32. No statistically significant difference was observed between the drug groups in terms of mean UAS7 ($p=0.091$).

Conclusion: In the study, it was observed that patients with higher BMI and older age needed higher doses of omalizumab. Although there was a difference in proportion in other parameters, no statistically significant difference was found. This result may be due to the small sample size of the high dose group.

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Abstract N°: 4403

Would ustekinumab biosimilars bring positive changes to patient access to PsO and PsA treatment in Sweden?

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Introduction & Objectives:

The Swedish reimbursement guidelines recommend ustekinumab as a second or third-line biologic treatment for psoriasis (PsO) and psoriatic arthritis (PsA), only after patients have used TNF, interleukin, and JAK inhibitors. Following the reassessment of reimbursement guidelines by the Dental and Pharmaceutical Benefits Agency (Tandvårds- och läkemedelsförmånsverket, TLV) in 2022, ustekinumab coverage in PsO and PsA is limited to patients who were already receiving Stelara before 2022. The TLV justifies this policy by noting that the cost of Stelara exceeds what it considers reasonable for reimbursement in the treatment of PsO and PsA. Meanwhile, ustekinumab biosimilars are expected to launch in the second half of this year and are anticipated to significantly improve patient accessibility due to their affordability compared to the original ustekinumab. The primary purpose of this budget impact model (BIM) is to investigate the potential additional patients who could receive treatment with the biosimilar ustekinumab CT-P43 and to evaluate the overall cost savings from the Swedish healthcare perspective.

Materials & Methods:

A prevalence-based budget impact model was developed using epidemiological data along with specific drug patient shares in the Swedish PsO and PsA market. This analysis compares two scenarios: a current scenario without ustekinumab biosimilars and a revised scenario with ustekinumab biosimilars. The model incorporates the drug acquisition costs of IL-17, IL-23, IL-12/23, JAK and TNF inhibitors. It assumes that biosimilar ustekinumab will be offered at 50% to 80% of the originator Stelara's price.

Results:

The results of the base case analysis of the BIM estimated that in Year 1, of the Swedish population with PsO and PsA (n=275,000), 12,250 patients will be treated with biological treatments. Among them, 884 (7.2%) patients will receive the ustekinumab biosimilar in the 'world with' scenario. Considering the proportion of PsO and PsA patients expected to receive CT-P43, the total budget savings resulting from its introduction to the Swedish healthcare system are projected to range from €1.9 million to €6.4 million in Year 1 and from €14.8 million to a maximum of €45.6 million over a five-year period. Such savings may enable an additional 140 to 750 patients to be treated during the first year, with a total of 1,500 to 7,340 patients over five years.

Conclusion:

Ustekinumab reimbursement is currently limited due to the high cost of treatment. However, once the biosimilar is launched in Sweden, patient access to ustekinumab is expected to improve dramatically. In addition to budget savings, patients will benefit from the long-acting agent, which requires only 4 injections in a year. The model, based on the assumption that the analysed molecules have similar efficacy, suggests that treatment with CT-P43 would be cost-effective while also improving patient convenience for many additional patients.

Figure 1. Potential Additional Patients & Budget Impact Results – biosimilar ustekinumab priced at 50% of

the originator

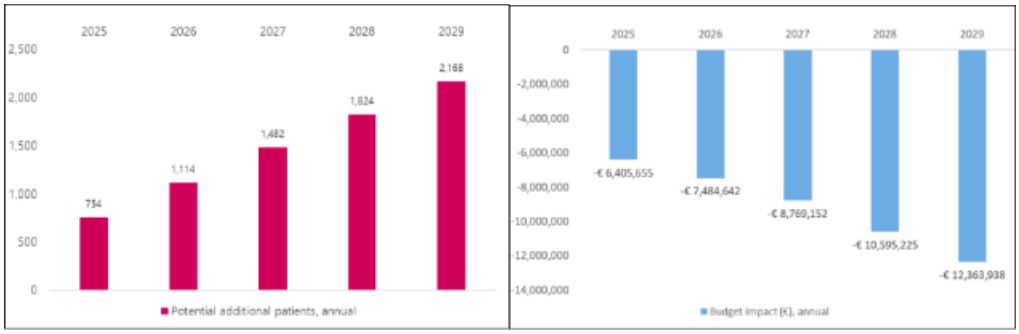
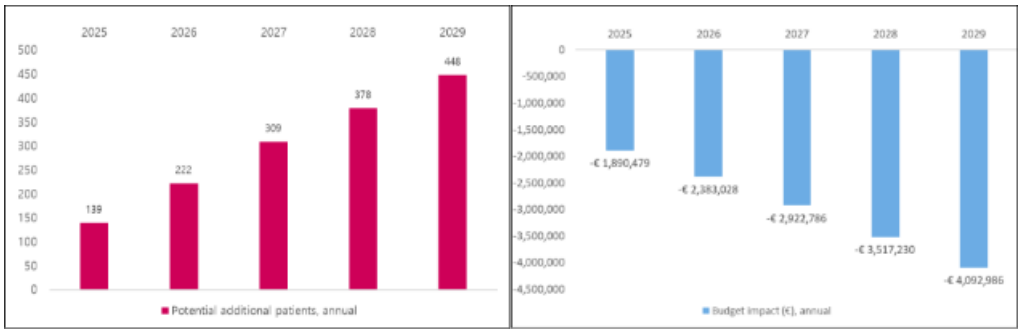


Figure 2. Budget Impact results – biosimilar ustekinumab priced at 80% of the originator



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Abstract N°: 4426

Real-world safety of spesolimab in generalised pustular psoriasis: Evidence from expanded access programmes in Japan, China and Argentina

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Introduction & Objectives:

Generalised pustular psoriasis (GPP) is a heterogeneous, neutrophilic inflammatory disease, characterised by chronic skin symptoms and potentially life-threatening flares. The first-in-class monoclonal antibody spesolimab, targeting the interleukin-36 receptor, is approved in several countries for the treatment of GPP flares.1 Here, we present real-world safety data from three expanded access programmes (EAPs) in Japan, China and Argentina, where patients (pts) not eligible for clinical trials and with no other treatment options were provided early access to spesolimab.

Materials & Methods:

Pts (18–75 years old) received a 900 mg dose of intravenous spesolimab for treatment of a GPP flare, with an optional second dose after 1 week for persistent flare symptoms. Treatment-emergent adverse events (TEAEs), serious AEs (SAEs) and AEs of special interest (AESIs) were recorded for up to 16 weeks after the last spesolimab infusion.

Results:

Fifty-six pts received spesolimab (Japan: n=11, China: n=39, Argentina: n=6*; female: n=35 [62.5%]). Mean

(±standard deviation [SD]) follow-up was 3.8 (0.4) months. Fifty-five pts (98%) had 1 flare and 1 pt (2%) had 2 flares during follow-up. Time since GPP diagnosis was ≤1 year (n=12), >1 and ≤5 years (n=13), >5 and ≤10 years (n=8), >10 years (n=22) and missing (n=1). Mean (±SD) pt age was 42.6 (14.6) years (range: 18–68 years); mean (±SD) body mass index was 24.2 (5.0) kg/m2. At baseline, most pts (n=50; 89%) had ≥1 comorbidity, the most common (>10% of pts) being plaque psoriasis (n=17; 30%), pyrexia and hypertension (n=10; 18% for each), and psoriatic arthropathy and anaemia (n=6; 11% each). Eighteen pts (32%) had baseline infections or infestations (folliculitis and tuberculosis [n=3 each; 5.4%] were the most common). Most pts (n=52; 93%) reported the use of ≥1 concomitant medication (immunosuppressants, corticosteroids, topicals, biological therapies and others). Twenty-seven pts (48%) were receiving treatment for ongoing chronic plaque psoriasis.

Forty pts (71%) experienced TEAEs, which were mostly mild (n=21; 38%) or moderate (n=15; 27%). The most frequently reported AE categories (MedDRA System Organ Class level) were infections and infestations (n=21; 38%), skin and subcutaneous tissue disorders (n=15; 27%), general disorders and administration site conditions (n=10; 18%), investigations (n=8; 14%), and metabolism and nutrition disorders (n=6; 11%). At the MedDRA preferred term level, the most frequently reported TEAEs (>10% of pts) were COVID-19 (n=10; 18%) and pyrexia (n=6; 11%). Hypersensitivity events were non-serious and mild or moderate. Two pts (3.6%) had AESIs (pneumonia [n=2], COVID-19), and 3 pts (5.4%) had SAEs (pneumonia, 2 pts [3.6%]; COVID-19, respiratory failure and pustular psoriasis, 1 pt each [1.8%]). Fifteen pts (27%) had investigator-defined drug-related AEs. No AEs led to discontinuation/death.

Conclusion:

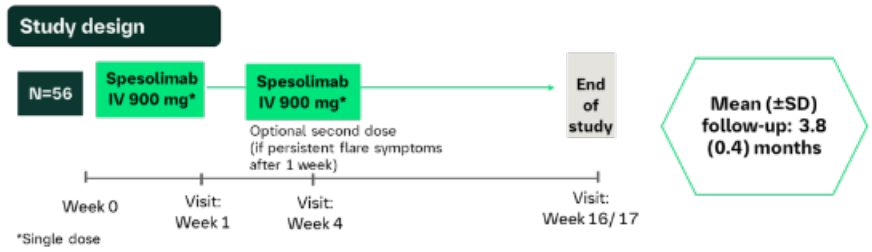
Spesolimab demonstrated a favourable benefit−risk profile in a real-world population of pts with GPP, including pts with comorbidities and those taking other medications. Findings were consistent with a previous clinical trial in pts with GPP flares (EFFISAYIL 1)2,3 and the healthcare context of the COVID-19 pandemic in which the EAPs were conducted.

*Data cutoff was 28 Dec 2023; the trial was still ongoing.

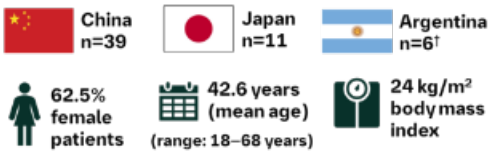
References:

1. Kaplon H et al. *MAbs* 2023;15:2153410.
2. Bachelez H et al. *N Engl J Med* 2021;385:2431-40.
3. Morita A et al. *J Dermatol* 2023;50:183-94.

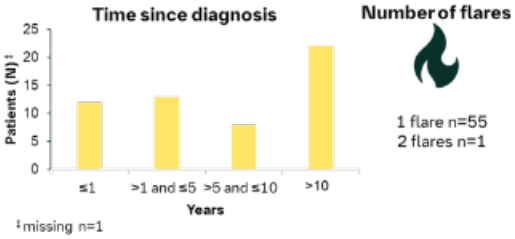
Figure. Summary of findings



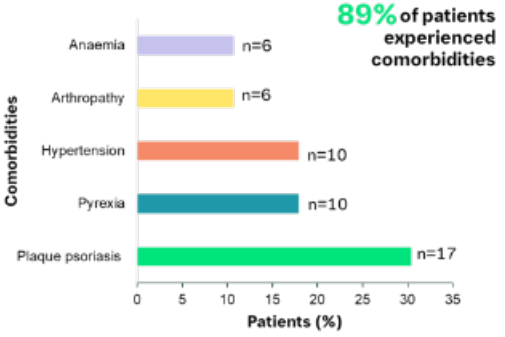
Demographics and baseline characteristics



†The data cutoff was 28 December 2023, during which the trial was still ongoing.



‡missing n=1



Safety

Most common AE (>10% of patients)	
Infections and infestations	38%
COVID-19	18%
Upper respiratory tract infection	7%
Skin and subcutaneous tissue disorders	27%
Pruritus	9%
Pustular psoriasis	5%
Rash	5%
General disorders and administration site conditions	18%
Pyrexia	11%
Investigations§	14%
Metabolism and nutrition disorders	11%
Hypoproteinaemia	7%
Hyperuricaemia	5%
Hypokalaemia	5%

§No AE was reported in >1 patient

AE, adverse event; COVID-19, Coronavirus disease 2019; IV, intravenous; SD, standard deviation.

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Abstract N°: 4429

Proactive Therapeutic Drug Monitoring Versus Routine Care with the Novel Biologics in Psoriasis: a Pragmatic, Multicentric, Randomised, Controlled Study – the HELIOS Study.

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[1]Ghent University Hospital, Dermatology, [2]Ghent University

Introduction & Objectives:

Psoriasis is a chronic immune-mediated inflammatory skin disease for which treatment with biologics is highly effective. In general, these drugs are prescribed according to a 'one-dose-fits-all' principle, which might lead to under- and overdosing, causing suboptimal response and unnecessary high drug exposure, respectively. A tool that may support rational use of biologics is therapeutic drug monitoring (TDM). TDM is the measurement of blood drug concentrations in order to individualize dosing regimens to achieve maximal clinical efficacy and minimize adverse events. The primary objective of this trial is to assess if proactive TDM of IL-17 and/or IL-23 inhibitors is non-inferior compared to standard of care (SOC) with respect to sustained disease control in patients with moderate-to-severe psoriasis.

Materials & Methods:

This is a pragmatic, multicentric, individually randomised, controlled non-inferiority trial. A total of 210 patients using secukinumab, ixekizumab or guselkumab for at least 6 months according to the standard dosing scheme, will be randomised (1:1) to TDM or SOC. In the TDM group, dosing intervals will be prolonged or shortened in a stepwise manner. This will happen based on the blood drug concentrations of the biologic, measured every 3 months and in accordance with the decision tree pictured in figure 1. Disease activity and quality of life will be monitored every 3 months by PASI, IGA, BSA, DLQI-R and SF-36. The primary endpoint is sustained disease control, defined as an absolute PASI $\leq$ 2 or a delta PASI from baseline $\geq$ 50% during at least 80% of all 3-monthly study visits over a period of 18 months. Secondary outcomes include course of PASI and DLQI, serious adverse events, health related quality of life, cost-effectiveness and treatment satisfaction. Outcomes of TDM will be compared to SOC.

Secukinumab	
Normal dose	300 mg/4 weeks
Dose escalation In case < 39.1 µg/ml [35.2-43.0]	
First step dose escalation	300 mg/3 weeks
Second step dose escalation	300 mg/2 weeks
Further step dose escalation	Stepwise reduction of 1 week
Dose de-escalation In case > 39.1 µg/ml [35.2-43.0]	
First step dose de-escalation	300 mg/6 weeks
Second step dose de-escalation	300 mg/8 weeks
Further step dose de-escalation	Stepwise increase with 1 week

Ixekizumab	
Normal dose	80 mg/4 weeks
Dose escalation In case < 3.4 µg/ml [3.1-3.7]	
First step dose escalation	80 mg/3 weeks
Second step dose escalation	80 mg/2 weeks
Further step dose escalation	Stepwise reduction of 1 week
Dose de-escalation In case > 3.4 µg/ml [3.1-3.7]	
First step dose de-escalation	80 mg/6 weeks
Second step dose de-escalation	80 mg/8 weeks
Further step dose de-escalation	Stepwise increase with 1 week

Guselkumab	
Normal dose	100 mg/8 weeks
Dose escalation In case < 1.6 µg/ml [1.4-1.8]	
First step dose escalation	100 mg/6 weeks
Second step dose escalation	100 mg/4 weeks
Further step dose escalation	Stepwise reduction of 1 week
Dose de-escalation In case > 1.6 µg/ml [1.4-1.8]	
First step dose de-escalation	100 mg/12 weeks
Second step dose de-escalation	100 mg/16 weeks
Further step dose de-escalation	Stepwise increase with 1 week

Figure 1. HELIOS trial decision tree for proactive treatment modifications of secukinumab, ixekizumab and guselkumab based on blood drug concentrations of these biologics in psoriasis patients.

Results:

Inclusion is planned to start in August 2024. First preliminary results will be presented at the European Academy of Dermatology and Venereology Congress 2026.

Conclusion:

With this study, we aim to assess whether proactive TDM of IL-17 and IL-23 inhibiting biologics is feasible, safe and cost-effective. Proactive TDM in psoriasis patients may lead to more efficient and rational use of biologics.

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Abstract N°: 4481

Spesolimab increases the percentage of generalized pustular psoriasis (GPP) patients with clear skin over time as measured by the Physician's Global Assessment for GPP (GPPGA): Results from the EFFISAYIL 2 trial

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[1]Icahn School of Medicine at Mount Sinai, [2]Yale University School of Medicine, [3]UT Southwestern Medical Center, [4]Brigham and Women's Hospital, Harvard Medical School, [5]Bare Dermatology, [6]Boehringer Ingelheim Pharmaceuticals, Inc, [7]Boehringer Ingelheim (China) Investment Co. Ltd, [8]Boehringer Ingelheim International GmbH

Introduction & Objectives: Generalized pustular psoriasis (GPP) is a chronic inflammatory, potentially life-threatening skin disease. Most patients experience chronic skin symptoms between flares which can lead to significant patient burden. Spesolimab, an anti-interleukin-36 receptor monoclonal antibody, is approved in the United States to treat GPP in adults and pediatric patients 12 years of age and older and weighing at least 40 kg. EFFISAYIL 2 (NCT04399837) evaluated the efficacy and safety of subcutaneous (SC) spesolimab in GPP. Here, we report the percentage of patients achieving clear skin (Physician's Global Assessment for GPP [GPPGA]=0)1 over time from patients who were treated with the FDA approved spesolimab dosing regimen (600 mg loading dose, then 300 mg maintenance dose every 4 weeks) in EFFISAYIL 2.

Materials & Methods: Measurements were completed for each subject at 4 timepoints (baseline, Week 4, Week 16, and Week 48). Data collected closest to the given time points were used by including the effect of potential intravenous spesolimab treatment and subsequent open-label SC spesolimab treatment in patients who experienced a flare. The data were analyzed as observed.

Results: Proportion of patients with GPPGA total score of 0 increased over time under spesolimab treatment (10.0% (N=3/30) at baseline, 27.6% (N=8/29) at Week 4, 48.1% (N=13/27) at Week 16, and 52.2% (N=12/23) at Week 48).

Conclusion: Continuous treatment with spesolimab SC improved skin symptoms in GPP, with 50% of patients achieving clear skin at Week 48. These findings suggest a role of spesolimab in complete resolution of GPP skin symptoms.

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EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

Abstract N°: 4520

Spesolimab decreases generalized pustular psoriasis (GPP) body surface area (BSA) over time in patients switching from conventional systemic treatments: Results from the EFFISAYIL 2 trial

Joseph Merola*[1], Bruce Strober[2], Alice B. Gottlieb[3], Arash Mostaghimi[4], Jason Hawkes[5], Jason Guercio[6], Ming Tang[7], Christian Thoma[8], Mark Lebwohl[3]

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Introduction & Objectives: Generalized pustular psoriasis (GPP) is a chronic inflammatory, potentially life-threatening skin disease. Most patients experience chronic skin symptoms between flares which can lead to significant patient burden. Spesolimab, an anti-interleukin-36 receptor monoclonal antibody, is approved in the United States to treat GPP in adults and pediatric patients 12 years of age and older and weighing at least 40 kg. EFFISAYIL2 (NCT04399837) evaluated the efficacy and safety of subcutaneous (SC) spesolimab in GPP. Here, we report the effects on GPP body surface area (BSA) over time in patients switched from a small-molecule systemic therapy at randomization when treated with the FDA approved spesolimab dosing regimen (600 mg loading dose, then 300 mg maintenance dose every 4 weeks) in EFFISAYIL 2.

Materials & Methods: Total BSA was determined based on a weighted average of the extent of involvement over 4 main body regions, with head = 10%, upper extremities = 20%, trunk = 30%, and lower extremities = 40%. Total BSA involvement was calculated for each subject at 4 timepoints (baseline, Week 4, Week 16, and Week 48). Data collected closest to the given time points were used by including the effect of potential intravenous spesolimab treatment and subsequent open-label SC spesolimab treatment in patients who experienced a flare. The data were analyzed as observed.

Results: Within the FDA approved spesolimab regimen group, the average BSA for patients who stopped a systemic medication for GPP (Total N=22; acitretin = 13, cyclosporine = 7, methotrexate = 1, acitretin/methotrexate = 1) was 11.1 at baseline, decreasing to 8.2 at Week 4, 6.4 at Week 16, and then ending at 3.6 at Week 48.

Conclusion: Total BSA involvement decreased over the 48 weeks of the trial in spesolimab-treated patients who stopped an off-label systemic medication for GPP at randomization.

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Abstract N°: 4566

Spesolimab decreases generalized pustular psoriasis (GPP) body surface area (BSA) over time in patients with various lengths of disease history: Results from the EFFISAYIL 2 trial

Arash Mostaghimi[1], Bruce Strober[2], Joseph F. Merola[3], Alice B. Gottlieb[4], Boni Elewski[5], Jason Guercio[6], Ming Tang[7], Christian Thoma[8], Mark Lebwohl[4]

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Introduction & Objectives: Generalized pustular psoriasis (GPP) is a chronic inflammatory, potentially life-threatening skin disease. Most patients experience chronic skin symptoms between flares which can lead to significant patient burden. Spesolimab, an anti-interleukin-36 receptor monoclonal antibody, is approved in the United States to treat GPP in adults and pediatric patients 12 years of age and older and weighing at least 40 kg. EFFISAYIL 2 (NCT04399837) evaluated the efficacy and safety of subcutaneous (SC) spesolimab in GPP. Here, we report the effects on GPP body surface area (BSA) over time in patients diagnosed <5 vs ≥5 years prior to enrollment when treated with the FDA approved spesolimab dosing regimen (600 mg loading dose, then 300 mg maintenance dose every 4 weeks) in EFFISAYIL 2.

Materials & Methods: Total BSA was determined based on a weighted average of the extent of involvement over 4 main body regions, with head = 10%, upper extremities = 20%, trunk = 30%, and lower extremities = 40%. Total BSA involvement was calculated for each subject at 4 timepoints (baseline, Week 4, Week 16, and Week 48). Data collected closest to the given time points were used by including the effect of potential intravenous spesolimab treatment and subsequent open-label SC spesolimab treatment in patients who experienced a flare. The data were analyzed as observed.

Results: Within the FDA approved regimen spesolimab group, average BSA for patients diagnosed with GPP for <5 years (N=13) was 14.7 at baseline, 15.0 at Week 4, then decreasing to 11.7 at Week 16, and then to 5.0 at Week 48. For patients diagnosed with GPP for ≥ 5 years (N=17) the values were 12.3 at baseline, decreasing to 7.0 at Week 4, increasing slightly to 7.6 at Week 16, and decreasing to 4.1 at Week 48.

Conclusion: Total BSA involvement decreased over the 48 weeks of the trial in spesolimab-treated patients regardless of whether they were early (< 5 years) or late (≥ 5 years) in their disease course. This finding demonstrates the efficacy of spesolimab in controlling GPP consistently for patients with various lengths of disease history.

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Abstract N°: 4609

Spesolimab decreases generalized pustular psoriasis (GPP) body surface area (BSA) over time: Results from the EFFISAYIL 2 trial

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Introduction & Objectives: Generalized pustular psoriasis (GPP) is a chronic inflammatory, potentially life-threatening skin disease. Most patients experience chronic skin symptoms between flares which can lead to significant patient burden. Spesolimab, an anti-interleukin-36 receptor monoclonal antibody, is approved in the United States to treat GPP in adults and pediatric patients 12 years of age and older and weighing at least 40 kg. EFFISAYIL 2 (NCT04399837) evaluated the efficacy and safety of subcutaneous (SC) spesolimab in GPP. Here, we report the effects on GPP body surface area (BSA) over time in patients treated with the FDA approved spesolimab dosing regimen (600 mg loading dose, then 300 mg maintenance dose every 4 weeks) in EFFISAYIL 2.

Materials & Methods: Total BSA was determined based on a weighted average of the extent of involvement over 4 main body regions, with head = 10%, upper extremities = 20%, trunk = 30%, and lower extremities = 40%. Total BSA involvement was calculated for each subject at 4 timepoints (baseline, Week 4, Week 16, and Week 48). Data collected closest to the given time points were used by including the effect of potential intravenous spesolimab treatment and subsequent open-label SC spesolimab treatment in patients who experienced a flare. The data were analyzed as observed.

Results: Total BSA improved continuously under spesolimab treatment (13.3% at baseline, 10.6% at Week 4, 9.4% at Week 16, ending at 4.5% at Week 48).

Conclusion: Continuous treatment with spesolimab SC improved BSA from 13% to 5% at the end of the trial. These findings suggest a role of spesolimab in improving area of involvement as measured by BSA.

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Abstract N°: 4649

Reassuring laboratory safety but distinct effects of different biologic classes in real-life psoriasis patients

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Introduction & Objectives:

Biologics targeting the pathogenic TNF/IL23/IL17-pathway were shown to be highly effective and their safety and tolerability appear to be remarkable across the years. However, evidence-based guidelines have still not been clearly defined regarding laboratory monitoring. Here, we collected and analyzed data on laboratory results in psoriasis patients receiving biologics to evaluate the relevance and necessity of regular blood testing.

Materials & Methods:

Retrospective analysis of blood values, measured before treatment initiation, after 3, 6, 12, 18, and 24 months of 400 patients receiving methotrexate (MTX) or representatives of the biological classes anti-TNF (Adalimumab), anti-IL12/23b (Ustekinuma), anti-IL23 (Guselkumab) and (anti-IL17) Secukinumab.

Results:

Our analyses revealed no worrying laboratory values among patients receiving biologics. Abnormal values were mostly self-limiting, and no cases of severe laboratory abnormalities were detected in the biologics group. However, we identified distinct effects of the biologic classes on certain blood parameters. While the other biologics (and MTX) showed a decrease in leucocyte counts, patients receiving adalimumab showed a significant increase in leucocytes. TNF blockade might increase circulating leucocytes via prolonged survival, inhibition of the migration into inflamed tissues, and by promoting type I IFN production. The lymphocyte curve under MTX was significantly lower than under biologics, probably due to bone marrow suppression, which was shown also for low dose MTX.

As IL17 promotes neutrophil granulopoiesis and plays an important role for the survival of neutrophils, it was not surprising that IL17 blockade has been linked to transient neutropenia. However, we did not observe a significantly different overall trend under Secukinumab as compared to the other treatments. These data indicate that additional neutrophil testing in anti-IL17 treated patients is unnecessary and only indicated in cases of unexplained fever.

Unsurprisingly, Methotrexate showed some hepatotoxic effect with increase in liver transaminases ALAT and ASAT. Adalimumab and Secukinumab showed a general trend of decreasing transaminase values suggesting a hepatoprotective effect of TNF and IL17 blockade. Unexpectedly, Ustekinumab and Guselkumab did not show such a declining curve of the more liver-specific ALAT but rather a slightly increased risk for pathological values over time These results might indicate that anti-IL23 and anti-IL12/23 lack such a hepatoprotective effect. However, differences could potentially also be explained by a selection bias, as Ustekinumab and Guselkumab might have been preferentially chosen for patients presenting liver disease or having at-risk alcohol consumption.

Conclusion:

The results of our study are very reassuring regarding the safety profiles of biologics in real-life patients. Our data suggest that reducing frequent laboratory analyses to 12 months intervals are sufficient and would be cost saving in the management of psoriasis patients receiving biologics.** Our study also indicates some distinct organ-

specific effects of the different biologic classes, which might help guiding treatment decisions in the future.

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Abstract N°: 4705

Patient-Reported Outcomes in the Randomized, Double Blind Phase 2 Study of ESK-001, an Oral Allosteric TYK2 Inhibitor, in Adults with Moderate-to-Severe Plaque Psoriasis

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Introduction & Objectives: ESK-001 is an oral, highly selective allosteric TYK2 inhibitor being developed for patients with moderate-to-severe plaque psoriasis. The Phase 2 ESK-001 program consists of a completed randomized, placebo-controlled dose ranging study (STRIDE, NCT05600036), and an ongoing open label extension study (OLE, NCT05739435). Here the patient-reported outcomes (PROs) from these studies are reported.

Materials & Methods: STRIDE was a randomized, double-blinded, placebo-controlled study in psoriasis patients with PASI≥12, sPGA≥3 and BSA≥10%. Patients were randomized (1:1:1:1:1:1) to one of five ESK-001 dose arms (10 mg QD, 20mg QD, 20mg BID, 40mg QD, 40mg BID) compared to placebo. The primary endpoint was PASI-75 at Week 12 and PRO secondary endpoints included achievement of DLQI-0/1 and improvement in pruritus numerical rating scale (NRS). Eligible patients from STRIDE were enrolled in the OLE study (currently ongoing) into one of two dose arms (40mg BID or 40mg QD).

Results: The primary and key secondary endpoints were met ($p<0.0001$, top three doses) with a dose-dependent response. At the highest dose (40 mg BID), 64%, 39% and 15% (placebo = 0%) of patients achieved PASI-75, PASI-90 and PASI-100; 59% and 23% (placebo = 8%, 0%) of patients achieved sPGA-0/1 and sPGA-0 at Week 12, respectively. Concordant with these findings, dose-dependent improvements in DLQI and pruritus were observed at Week 12 (**Table**). At the 40mg BID dose, 64% of patients achieved DLQI-0/1 and median % improvement in pruritus for both on-average and at-worst scores were 88%. Improvements for both DLQI-0/1 and pruritus scores were maintained at Week 16 of the OLE study based on 08 Dec, 2023 data date (**Table**). ESK-001 was generally safe and well tolerated in STRIDE with a similar safety profile in the OLE. TEAE severity was similar across dose arms, with the majority of TEAEs mild-to-moderate and self limited. No deaths, treatment related AEs associated with JAK inhibitor class pharmacology, or clinically significant laboratory or ECG trends were observed.

Table: Dose dependent improvement in DLQI and pruritus PROs in STRIDE at Week 12, with maintenance of response at Week 16 in the OLE

STRIDE, Week 12
Placebo (N=38)
40 mg BID (N=39)
40 mg QD (N=39)
20 mg BID (N=39)
20 mg QD (N=36)
10mg QD (N=36)
Open Label Extension, Week 16
40mg BID (N=82)
40mg QD (N=82)

* based on non-responder imputation (NRI)

* Median % change from Baseline in pruritus NRS (scored 0-10: severity of itch, on average or at worst, within the past 24 hours)

Conclusion: In these Phase 2 moderate-to-severe psoriasis studies ESK-001 demonstrated significant improvements in patient reported quality of life (DLQI) and psoriasis-associated pruritus (NRS), with a clear dose-dependent improvement observed. Improvements in PROs were maintained with ongoing treatment in the OLE study. These PRO outcomes highlight the positive impact on the lives of patients with psoriasis, while receiving ESK-001.

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Abstract N°: 4848

To kill two birds with one stone – a case report on the use of dupilumab in prurigo nodularis and managing anti-PD-1 adverse effects in a melanoma patient

Wiktoria Bajek[1], Daria Podleśna[1], Karina Polak[2], Aleksandra Frątczak[2], Mikołaj Łanocha[2], Beata Bergler-Czop[2]

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Introduction & Objectives:

Dupilumab is used in the treatment of prurigo nodularis - chronic skin disease characterized by extremely pruritic hyperkeratotic nodules. Several articles demonstrate its safety and efficacy in managing skin adverse effects associated with anti-PD-1 drugs. We report an extraordinary case of a patient with melanoma treated with dupilumab due to side effects of nivolumab, anti-PD-1 molecule, including prurigo nodularis.

Materials & Methods:

The patient was referred to the dermatology clinic due to numerous erythematous lesions with nodules, primarily located in the trunk and lower limbs. These lesions were accompanied by severe itching. Six years prior to admission, the patient had been diagnosed with BRAF(-) melanoma involving the small intestine and rectosigmoid junction. The patient underwent two surgeries, a left adrenalectomy due to metastases and a mediastinum metastasectomy followed by radiotherapy.

Initially, the patient received pembrolizumab treatment for a duration of two years. However, due to loss of response, the drug was switched to nivolumab. After two months on nivolumab, erythematous lesions began to appear. Despite attempting standard treatment methods, the disease significantly impacted the patient's quality of life. Consequently, nivolumab immunotherapy was discontinued, and the patient was referred to the dermatology clinic.

At the dermatology clinic, the patient received a comprehensive treatment approach, including intravenous steroids, oral antihistamines, and topical treatments. Initially, the diagnosis was contact dermatitis. However, despite these efforts, the patient's condition continued to worsen over subsequent months. New nodular skin lesions appeared on the lower limbs, and the intensity of itching persisted. Ultimately, the diagnosis was revised to prurigo nodularis.

Given the failure of standard prurigo nodularis treatments, the patient was administered dupilumab. Notably, literature supports the use of dupilumab in patients with nivolumab-induced contact dermatitis, emphasizing its effectiveness in managing such side effects. The patient responded well to the standard regimen of dupilumab, with the lesions resolving and a reduction in itchiness. This case highlights the potential of dupilumab as a valuable therapeutic option for prurigo nodularis.

Results:

The patient was treated with good results.

Conclusion:

Dupilumab is an effective way to treat prurigo nodularis, itchiness and post anti-PD-1 adverse effects. We report an interesting case of a patient with melanoma in which this drug worked for all of those skin problems and

turned out to be an effective and safe way of treatment.

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Abstract N°: 4852

Is Omalizumab a New Potential Standard for Mastocytosis Treatment? - a systematic review

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Introduction & Objectives:

Our objective was to evaluate the most recent sources regarding the safety and efficacy of omalizumab in the treatment of mastocytosis in adult patients.

Materials & Methods:

We conducted a search of the following international electronic databases from inception until April 2024: PUBMED, MEDLINE, EMBASE, Web of Science, The Cochrane Central Register of Controlled Trials, and The Cochrane Database of Systematic Reviews. Our search strategy included the key words: 1. Mastocytosis, 2. Cutaneous mastocytosis OR Urticaria pigmentosa, 3. Systemic mastocytosis, 4. Omalizumab. We applied the following inclusion criteria: original trials, case series and case reports concerning humans published in Polish, English, and French. Congress abstracts were excluded. We also manually searched reference lists to find potentially relevant articles.

Results:

Our search yielded two multi-center retrospective cohort studies, one controlled randomized study, one retrospective cohort study, four case series, and ten case reports. In total, 115 patients were included (18 with cutaneous mastocytosis and 97 with systemic mastocytosis). The average treatment period was 17.5 months. The treatment led to tolerable venom immunotherapy and completely eliminated severe reactions in all patients suffering from anaphylaxis due to honeybee stings. A total of 84% of the patients experienced a complete resolution of idiopathic anaphylaxis episodes. Heart palpitations, gastrointestinal, cutaneous, neuropsychiatric and respiratory symptoms were completely resolved at rates of 43%, 29%, 27%, 11%, and 9% respectively. The treatment's effectiveness was sustained throughout its duration for all responders, except for four. However, 14 patients reported adverse events.

Conclusion:

Omalizumab appears to inhibit certain severe reactions associated with mastocytosis, potentially being an effective treatment for disease-related symptoms. However, the supporting evidence is primarily based on observational, uncontrolled data from a limited number of patients. To gain a deeper understanding of omalizumab's role in mastocytosis treatment, more randomized controlled trials are necessary.

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Abstract N°: 4863

Use of Systemic Janus Kinase Inhibition for Neutrophilic Dermatoses: An Evidence-Based Review

Siddhartha Sood[1], Megan Park[1], Ahmed Bagit[1], Khalad Maliyar[2], Muskaan Sachdeva[2], Abrahim Abduelmula[2], Yuliya Lytvyn[2], Asfandyar Mufti[2, 3], Jensen Yeung*[2, 3, 4, 5]

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Introduction & Objectives:

Neutrophilic dermatoses (NDs) are a heterogeneous group of challenging-to-treat immune-mediated skin conditions. This systematic review summarizes emerging evidence regarding the novel use of systemic Janus kinase inhibitors (JAKi) for NDs.

Materials & Methods:

In adherence with PRISMA guidelines, Embase and MEDLINE databases were searched on December 8th, 2023 using specific keywords. After independent screening by two reviewers, 38 articles encompassing 86 patients were included. The mean age was 45 (range: 1.2-89) years with sex reported in 64 (74.4%) patients (36 [56.3%] males; 28 [43.8%] females). NDs were refractory to non-JAKi systemic therapy in 84.9% (73/86) of reported cases.

Results:

Systemic JAKi were used for the following NDs: pyoderma gangrenosum (33.7%, 29/86), VEXAS syndrome (24.4%, 21/86), CANDLE syndrome (19.8%, 17/86), Behcet's disease (17.4%, 15/86), sweet syndrome (3.5%, 3/86), and acne fulminans (1.2%, 1/86). The systemic JAKi utilized were as follows: tofacitinib (51.2%, 44/86), baricitinib (27.9%, 24/86), ruxolitinib (15.1%, 13/86), upadacitinib (4.7%, 4/86), and filgotinib (1.2%, 1/86).

Complete resolution was most commonly observed for sweet syndrome (100%, 3/3), pyoderma gangrenosum (93.1%, 27/29), Behcet's disease (66.7%, 10/15), and VEXAS syndrome (66.7%, 14/21) with the most frequent JAKi being baricitinib (66.7%, 2/3), tofacitinib (pyoderma gangrenosum: 69%, 20/29; Behcet's disease: 100%, 15/15), and ruxolitinib (52.4%, 11/21) respectively for those conditions. Mean treatment duration was 155.4 days (72.1%, 62/86). There were 61 total treatment-emergent adverse events documented in 26 (30.2%, 26/86) patients, most commonly reflecting upper or lower respiratory tract infections (61.5%, 16/26). Toxicity-related discontinuation occurred in 5 (5.8%) cases (herpes zoster [n=2], colon cancer progression [n=1], pneumonia [n=1], COVID-19 [n=1]). There was 1 (1.2%) sepsis-related death reported during treatment with ruxolitinib and several concomitant immunosuppressants for VEXAS syndrome.

Conclusion:

These results, in combination with existing in-vitro studies demonstrating lesional JAK upregulation in several NDs, indicate systemic JAKi, particularly pan-cytokine inhibition via tofacitinib, may be efficacious and safe for these indications. Our findings demonstrated a favourable resolution rate particularly for pyoderma gangrenosum, Behcet's disease, VEXAS syndrome, and sweet syndrome. Placebo-controlled studies are warranted.

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Abstract N°: 4924

Dupilumab-associated ocular surface disease in pediatric atopic dermatitis patients treated with dupilumab: Results from the BioDay registry

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Introduction & Objectives: Dupilumab-associated ocular surface disease (DAOSD) is the most frequently reported adverse event in clinical trials in pediatric atopic dermatitis (AD) patients treated with dupilumab. However, long-term real-world safety data in pediatric patients are limited. Therefore, this study aimed to investigate the incidence of DAOSD in pediatric AD patients treated with dupilumab (Figure 1).

Materials & Methods: This prospective study included pediatric AD patients (aged 3-17 years) treated with dupilumab between August 2019 and March 2024. All patients participated in the BioDay registry. Ocular symptoms were assessed every 4-12 weeks during dupilumab treatment. DAOSD was considered mild if symptoms were controlled with lubricating eye drops, antihistamine eye drops, and/or tacrolimus skin ointment on the external eyelids (referred to as standard therapy). Patients with persistent ocular symptoms despite standard therapy were referred to an ophthalmologist for ophthalmic examination, and were considered as having moderate-to-severe DAOSD if they required ocular anti-inflammatory therapy.

Results: A total of 104 patients (mean age 11.7 ± 4.0) with a median follow-up of 70.5 weeks (interquartile range (IQR): 46.3-113.0) were included. Overall, 36/104 (34.6%) patients developed DAOSD with 25/36 (69.4%) classified as mild and 11/36 (30.6%) as moderate-to-severe. DAOSD occurred at a median treatment duration of 13.0 weeks (IQR 4.0-27.4). The most frequent reported symptoms in both mild and moderate-to-severe DAOSD were pruritus (64.0% and 100.0%), redness (60.0% and 100.0%), and tearing (52.0% and 72.70%). Ophthalmic examination revealed that tarsal conjunctivitis (100.0%), meibomian gland dysfunction (87.5%), and blepharitis (75.0%) were the most common ocular characteristics in patients with moderate-to-severe DAOSD. In 3/104 (2.9%) patients, dupilumab treatment was discontinued due to DAOSD.

Conclusion: This real-world study shows that 34.6% of dupilumab-treated pediatric AD patients develop DAOSD. These high rates underscore the importance of awareness during dupilumab treatment, especially in (young) pediatric patients, where reporting ocular symptoms can be challenging and may lead to delayed diagnosis.

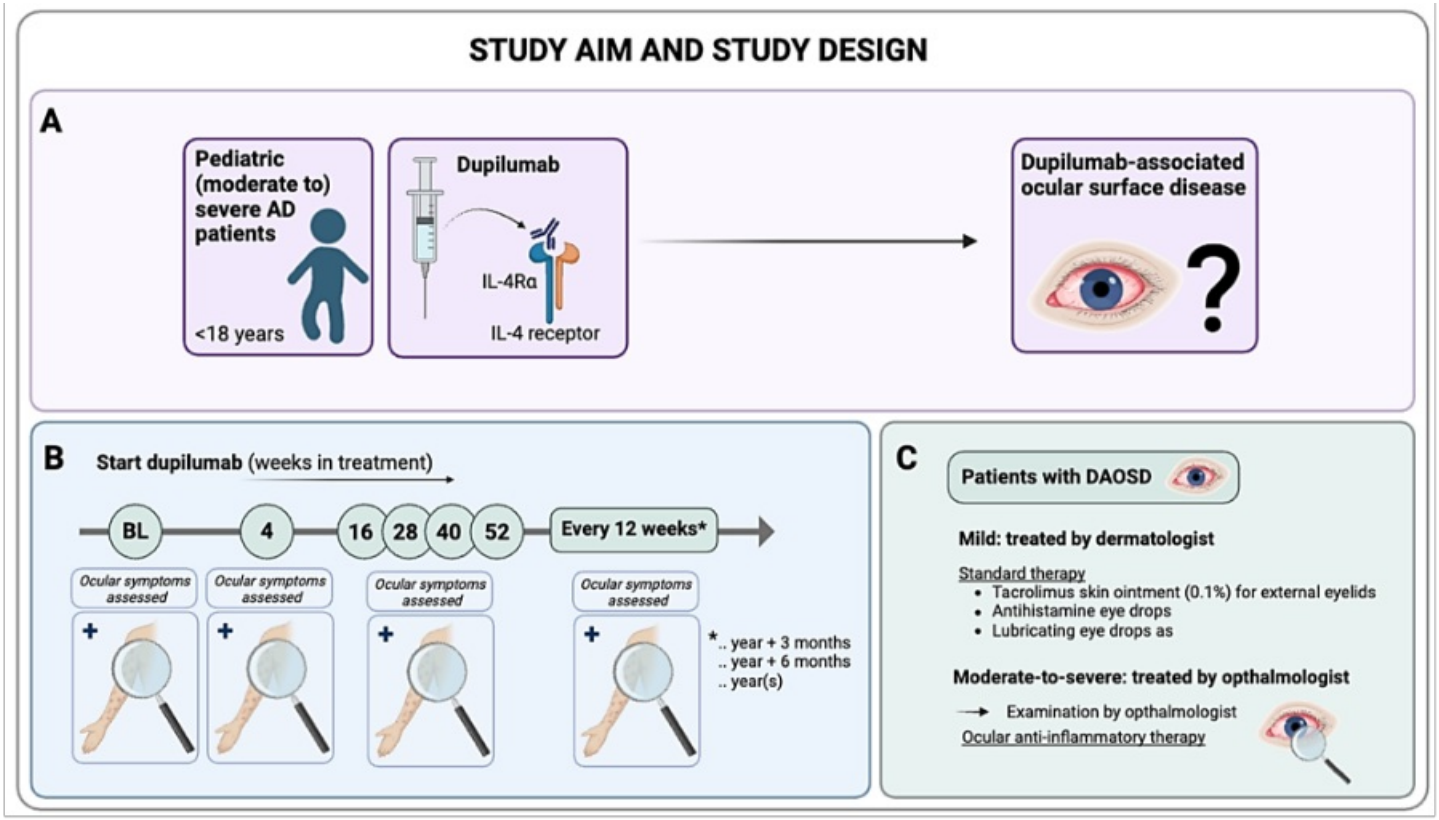

Figure 1. Study aim and study design.

(A) Study aim, (B-C) study design. *Abbreviations*: AD, atopic dermatitis; BL, baseline; DAOSD, dupilumab-associated ocular surface disease.

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Abstract N°: 4937

Bimekizumab efficacy and safety in patients with psoriatic arthritis who had skin and nail psoriasis at baseline: Up to 2-year results from two phase 3 studies

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Introduction & Objectives:

Bimekizumab (BKZ), a humanised monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F in addition to IL-17A, has demonstrated efficacy and tolerability to 1 year in patients with psoriatic arthritis (PsA) and psoriasis.1 Nail psoriasis is associated with increased risk of PsA, as well as more severe disease and decreased quality of life, in patients with psoriasis.2,3 It is therefore clinically important to assess the efficacy and safety of new treatments in patients with PsA, skin involvement and nail psoriasis.

Here, efficacy and safety of BKZ treatment are reported to 2 years in patients with PsA, skin involvement and nail psoriasis who were biologic disease-modifying antirheumatic drug (bDMARD)naïve or had prior inadequate response/intolerance to tumour necrosis factor inhibitors (TNFi-IR).

Materials & Methods:

BE OPTIMAL (NCT03895203; bDMARD-naïve) and BE COMPLETE (NCT03896581; TNFiIR) assessed subcutaneous BKZ 160 mg every 4 weeks (Q4W) in patients with PsA. Placebo (PBO) patients switched to BKZ (PBO/BKZ) at Week 16. BE OPTIMAL included a reference arm (adalimumab [ADA] 40 mg every two weeks [Q2W]); ADA patients switched to BKZ at Week 52 (ADA/BKZ) with no washout between treatments. BE OPTIMAL Week 52 and BE COMPLETE Week 16 completers were eligible to enrol in the openlabel extension, BE VITAL (NCT04009499), in which all patients received BKZ.

Post hoc data are reported for patients with baseline (BL) skin involvement (≥3% body surface area [BSA]) and nail psoriasis (modified Nail Psoriasis Severity Index [mNAPSI] >0). Efficacy outcomes are reported to Week 104 of BE OPTIMAL and Week 100 of BE COMPLETE. Missing data imputed using nonresponder (binary), multiple (continuous) or worst-category (categorical) imputation.

Safety data are reported for all patients treated with BKZ.

Results:

263/852 (30.9%) bDMARD-naïve (133/431 BKZ; 88/281 PBO; 42/140 ADA) and 159/400 (39.8%) TNFi-IR patients

(105/267 BKZ; 54/133 PBO) had BL psoriasis ≥3% BSA and mNAPSI >0. Of those, 230 (87.5%) bDMARD-naïve and 136 (85.5%) TNFi-IR patients completed Week 104/100.

Efficacy responses seen at Week 52 on BKZ were sustained to Week 104/100, with high proportions of bDMARD-naïve and TNFi-IR patients sustaining improvements across joint, skin, nail, physical function and composite outcomes (**Figure**, **Table**).

For bDMARD-naïve and TNFi-IR patients on BKZ, the exposure-adjusted incidence rates per 100 patient-years (EAIR/100 PY) for ≥1 treatment-emergent adverse event (TEAE) were 154.9 and 78.8, respectively. Incidence rates (EAIR/100 PY) of serious TEAEs were 6.6 (bDMARD-naïve) and 5.2 (TNFi-IR). Of reported Candida infections (EAIR/100 PY bDMARD-naïve: 5.9, TNFi-IR: 2.2), none were serious or systemic; 2 infections led to study discontinuation (bDMARD-naïve: 2, TNFi-IR: 0). To 2 years, 2 deaths occurred in bDMARD-naïve patients and 1 death occurred in TNFi-IR patients, deemed unrelated to treatment.

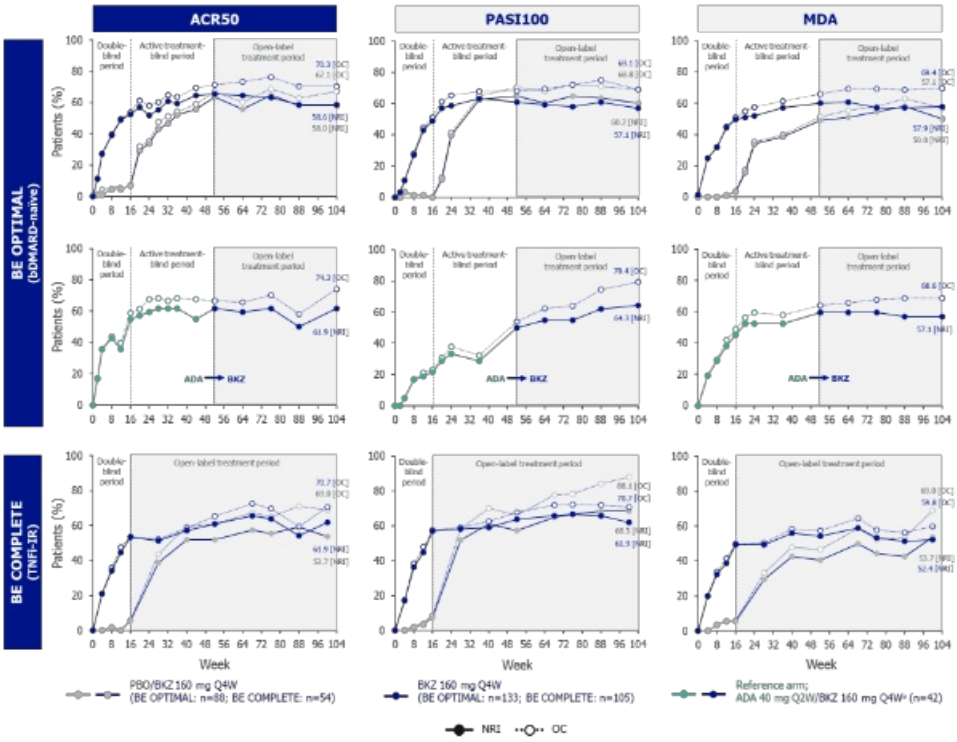
Conclusion:

BKZ treatment resulted in sustained clinical efficacy up to 2 years in patients with PsA, skin involvement and nail psoriasis; improvements were generally similar regardless of prior TNFi treatment. BKZ was well tolerated, with a consistent safety profile to that previously reported.1

References:

1. Coates LC. Ann Rheum Dis 2023;82:346–7; **2.** Zabotti A. Ann Rheum Dis 2023;82:1162–70; **3.** Cengiz G. Int J Rheum Dis 2023;26:43–50.

Figure. Proportion of patients with baseline skin psoriasis (≥3% BSA) and nail psoriasis (mNAPSI >0) achieving ACR50, PASI100 and MDA over time to Week 104/100 (NRI, OC)



Randomised set, in patients with skin psoriasis (≥3% BSA) and nail psoriasis (mNAPSI >0) at baseline. In BE OPTIMAL, patients were randomised 3:2:1 to BKZ 160 mg Q4W:PBO:reference arm (ADA 40 mg Q2W); in BE COMPLETE, patients were randomised 2:1 to BKZ 160 mg Q4W:PBO. In both studies, patients on PBO switched to BKZ 160 mg Q4W at Week 16. In BE OPTIMAL, patients on ADA switched to BKZ 160 mg Q4W at Week 52. [a] Reference arm; study not powered for statistical comparisons of ADA to BKZ or PBO. ACR50: ≥50% improvement in American College of Rheumatology response criteria; ADA: adalimumab; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; BSA: body surface area; MDA: minimal disease activity; mNAPSI: modified Nail Psoriasis Severity Index; NRI: non-responder imputation; OC: observed case; PASI100: 100% improvement in Psoriasis Area and Severity Index; PBO: placebo; Q2W: every two weeks; Q4W: every four weeks; TNFi-IR: prior inadequate response or intolerance to tumour necrosis factor inhibitors.

Table. Additional efficacy outcomes at Week 104/100 for patients with PsA with baseline skin involvement (≥3% BSA) and nail psoriasis (mNAPSI >0) (MI, NRI, WCI)

	BE OPTIMAL (bDMARD-naïve) Week 104			BE COMPLETE (TNFi-IR) Week 100	
Data are NRI unless otherwise stated	PBO→BKZ 160 mg Q4W n=88	BKZ 160 mg Q4W n=133	ADA 40 mg Q2W→ BKZ 160 mg Q4W[a] n=42	PBO→BKZ 160 mg Q4W n=54	BKZ 160 mg Q4W n=105
ACR20 responders, n (%)	62 (70.5)	97 (72.9)	29 (69.0)	40 (74.1)	80 (76.2)
ACR70 responders, n (%)	36 (40.9)	56 (42.1)	19 (45.2)	22 (40.7)	45 (42.9)
PASI90 responders, n (%)	66 (75.0)	92 (69.2)	32 (76.2)	39 (72.2)	79 (75.2)
ACR50 + PASI100 responders, n (%)	37 (42.0)	56 (42.1)	21 (50.0)	25 (46.3)	47 (44.8)
VLDA responders, n (%)	24 (27.3)	47 (35.3)	16 (38.1)	11 (20.4)	31 (29.5)
DAPSA disease state [WCI],[b] n (%)					
LDA+REM	47 (53.4)	74 (55.6)	25 (59.5)	32 (59.3)	61 (58.1)
REM	16 (18.2)	36 (27.1)	15 (35.7)	9 (16.7)	18 (17.1)
TJC=0 (of 68 joints), n (%)	29 (33.0)	50 (37.6)	19 (45.2)	15 (27.8)	35 (33.3)
SJC=0 (of 66 joints), n (%)	60 (68.2)	90 (67.7)	27 (64.3)	35 (64.8)	68 (64.8)
Enthesitis resolution (LEI=0),[c] n/N (%)	18/24 (75.0)	28/43 (65.1)	5/10 (50.0)	7/13 (53.8)	28/39 (71.8)
Dactylitis resolution (LDI=0),[d] n/N (%)	7/7 (100.0)	19/25 (76.0)	4/5 (80.0)	2/5 (40.0)	15/17 (88.2)
Nail psoriasis resolution (mNAPSI=0), n (%)	63 (71.6)	91 (68.4)	32 (76.2)	34 (63.0)	72 (68.6)
HAQ-DI CfB [MI], mean (SE)	−0.40 (0.06)	−0.40 (0.05)	−0.51 (0.11)	−0.51 (0.09)	−0.51 (0.05)
HAQ-DI MCID,[e] n/N (%)	41/70 (58.6)	62/105 (59.0)	22/37 (59.5)	30/47 (63.8)	58/93 (62.4)
PsAID-12 total score MCID,[f] n/N (%)	34/68 (50.0)	50/102 (49.0)	22/35 (62.9)	22/45 (48.9)	52/87 (59.8)
Pain VAS ≥50% improvement,[g] n (%)	53 (60.2)	77 (57.9)	25 (59.5)	31 (57.4)	68 (64.8)

Randomised set, in patients with skin involvement (≥3% BSA) and nail psoriasis (mNAPSI >0) at baseline. In BE OPTIMAL, patients were randomised 3:2:1 to BKZ 160 mg Q4W:PBO:reference arm (ADA 40 mg Q2W); in BE COMPLETE, patients were randomised 2:1 to BKZ 160 mg Q4W:PBO. In both studies, patients on PBO switched to BKZ 160 mg Q4W at Week 16. In BE OPTIMAL, patients on ADA switched to BKZ 160 mg Q4W at Week 52. [a] Reference arm; study not powered for statistical comparisons of ADA to BKZ or PBO; [b] WCI considers patients with missing data or data after study treatment discontinuation to be in the worst category (high disease activity); [c] In patients with baseline enthesitis (LEI >0); [d] In patients with baseline dactylitis (LDI >0); [e] Decrease ≥0.35 from baseline in patients with HAQ-DI ≥0.35 at baseline; [f] Clinically meaningful within-patient improvement referred to here as MCID: decrease ≥3 from baseline in patients with PsAID-12 total score ≥3 at baseline. PsAID-12 MCID data reported to Week 88 for BE COMPLETE as PsAID-12 not collected at Week 100 in BE COMPLETE; [g] Pain VAS assessed using the Patient's Assessment of Arthritis Pain VAS which ranges from 0 to 100, 0 representing 'no pain' and 100 'most severe pain'; pain VAS ≥50% improvement represents a substantial improvement in patient-reported pain. ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology response criteria; ADA: adalimumab; bDMARD: biologic disease-modifying antirheumatic drug; BKZ: bimekizumab; BSA: body surface area; CfB: change from baseline; DAPSA: Disease Activity Index for Psoriatic Arthritis; HAQ-DI: Health Assessment Questionnaire-Disability Index; LDA: low disease activity; LDI: Leeds Dactylitis Index; LEI: Leeds Enthesitis Index; MCID: minimal clinically important difference; MI: multiple imputation; mNAPSI: modified Nail Psoriasis Severity Index; NRI: non-responder imputation; PASI90/100: ≥90/100% improvement in Psoriasis Area and Severity Index; PBO: placebo; PsAID-12: PsA Impact of Disease-12 questionnaire; Q2W: every two weeks; Q4W: every four weeks; REM: remission; SE: standard error; SJC: swollen joint count; TJC: tender joint count; TNFi-IR: prior inadequate response or intolerance to tumour necrosis factor inhibitors; VAS: visual analogue scale; VLDA: very low disease activity; WCI: worst-category imputation.

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Abstract N°: 4950

ATTO-1310: A first-in-class anti-IL31 Attobody® for atopic dermatitis and other pruritic diseases

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Introduction & Objectives:

Chronic inflammatory skin diseases such as atopic dermatitis (AD) and prurigo nodularis (PN) lead to intensely pruritic skin lesions resulting in severe scratching. In patients with moderate-to-severe AD and PN, topical steroids and calcineurin inhibitors are not sufficient to achieve symptom control. Nemolizumab, which binds IL31RA, has shown promising anti-pruritic efficacy in clinical trials, providing validation that targeting the IL31 pathway translates to symptom relief in AD and PN patients. We have discovered a high affinity and potent biparatopic Attobody® to the IL31 ligand, which has the potential to induce fast and prolonged control of pruritis in patients with chronic inflammatory skin disease.

Materials & Methods:

ATTO-1310 consists of biparatopic Attobodies® to IL31 fused to human IgG1-Fc engineered for extended half-life. Each Attobody® is comprised of two VHHs, which on their own bind to distinct epitopes on IL31 with medium to low affinity. Our unique linker technology enables the identification of highly potent biparatopic Attobodies® even in the absence of inhibition by its individual component VHHs. The simultaneous engagement of two distinct epitopes on IL31 by each Attobody® drives the exceptional binding affinity to IL31. ATTO-1310 was assessed for its affinity for IL31 and its ability to suppress receptor dimerization and downstream signaling. Further, we examined the anti-pruritic activity in mice and NHP, as well as the pharmacokinetic (PK) profile in NHP. Finally, the manufacturability and immunogenicity of ATTO-1310 was evaluated.

Results:

Functionally, the high affinity of ATTO-1310 leads to potent suppression of IL31-mediated receptor dimerization and downstream signaling *in vitro*. When administered *in vivo*, ATTO-1310 demonstrates the ability to block IL31-induced pruritus in mice and in NHP, with a clear relationship between dose level, serum drug concentration, and extent of anti-pruritic activity. Importantly, pharmacokinetic (PK) assessment of ATTO-1310 in NHP demonstrates low clearance with a long half-life, clear dose linearity, and >80% bioavailability when administered subcutaneously (SC). PK modeling supports the ability to achieve and maintain therapeutic exposures of ATTO-1310 in humans with SC administration every three months. ATTO-1310 displays excellent manufacturability and developability properties and is produced from CHO cells with high productivity and yield. In *ex vivo* assays, ATTO-1310 has not raised any significant risk of immunogenicity.

Conclusion:

Nonclinical efficacy and PK data to date support advancement of ATTO-1310 to first-in-human clinical studies.

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Abstract N°: 4990

Tofacitinib aids in improving insulin resistance - in patients with psoriasis and diabetes

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Introduction & Objectives:

Tofacitinib is a novel Janus Kinase (JAK) 1 and 3 inhibitor approved by the FDA for the treatment of rheumatoid arthritis (RA), psoriatic arthritis, ulcerative colitis, and polyarticular juvenile idiopathic arthritis.

The drug was originally developed for use in rheumatoid arthritis patients but its action of blocking several cytokine receptors for Interleukin-2,4,7,9, 15, and 21 can modulate several immune and inflammatory mechanisms.

Recently, the JAK-STAT pathway has also been implicated in the pathogenesis of metabolic diseases. Population studies have shown polymorphism in gene JAK3 is linked to increased waist circumference and central adiposity. The activation of the JAK2/STAT1 pathway has been associated with the impairment of pancreatic beta cells, thereby increasing the chances of diabetes mellitus. Recent trials with the use of baricitinib (JAK1 and 2 inhibitors) have demonstrated the preservation of beta cell function in the pancreas.

Aim- To understand the dynamics of blood sugars with the administration of tofacitinib in patients with psoriasis

Materials & Methods:

This is a case of a 67-year-old diabetic male who presented with itchy scaly plaques over the body for 20 years relapsing and remitting. After thorough baseline investigations including a blood panel, Mantoux test, and chest X-ray patient was started on a 5 mg per day dose of tofacitinib which was increased to twice daily after 1 month along with methotrexate 5 mg every week.

The patient was a known case of diabetes and hypertension before starting tofacitinib. He was on glimepiride 0.5 mg and metformin 1000 mg per day with random blood

sugar (RBS) 140 mg/dL and glycated Hb being 6.8% before starting the treatment. After 6 months of tofacitinib the patient started to develop hypoglycemia with blood sugars measuring 60 mg/dL. The dose of oral anti-hyperglycemic tablets were reduced to half dosage which maintained his glycated Hb at approximately 6.5%. After complete clinical resolution of psoriatic lesions after almost 1 year of combination therapy of tofacitinib and methotrexate, both the drugs were tapped slowly. A follow up of 6 months of stopping immunomodulators , patient did not relapse and maintained his blood sugar levels.

Results: This case highlights the adjuvant role of tofacitinib in insulin resistance. While there are reports and studies regarding baricitinib causing hypoglycemia and also providing better control of glycemic index by preserving beta cell function of pancreas, but the reports with tofacitinib are quite rare.

In fact, a study comparing the effects of baricitinib and tofacitinib showed significant improvement in glyco Hb with baricitinib while no significant difference with tofacitinib on glucose levels or insulin resistance.

Conclusion: Tofacitinib can act as an adjuvant therapy for the control of insulin resistance in patients suffering from metabolic disorders along with psoriasis.

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Abstract N°: 5009

Journeying Through Evidence: Scoping the Revival of Anti-TNF Alpha in Psoriasis Treatment and Cardiovascular Risk Reduction

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Introduction & Objectives:

Psoriasis affects 2%-3% of the world's population, imposing significant physical and psychological burdens on patients. Growing evidence suggests a potential resurgence of anti tumor necrosis factor alpha (TNF α) therapy, driven by insights into its efficacy, safety profile, and intriguing cardio-protective properties. This review aims to navigate the existing literature, mapping the landscape of TNF-α treatment and its implications for cardiovascular risk reduction.

Materials & Methods:

A literature search was conducted accross PubMed, ScienceDirect, the Cochrane Library, and Wiley Online Library, limited to English-language publications on biotherapies for psoriasis between 2013 and 2023. Initial screening of titles and abstracts, followed by full-text review, was performed, resulting in the selection of 48 studies.

Results:

TNF-α inhibitors have exhibited a low and stable rate of cardiac events (CEs) over the last decade. Studies from 2013 to 2023, including randomized controlled trials (RCTs) and cohorts involving 254,051 psoriasis patients, affirm the safety of adalimumab, etanercept, infliximab, certolizumab, and golimumab, suggesting their long-term use poses no significant cardiac-related risks. TNF-α inhibitors reduced hazard risks for CEs, major CEs, myocardial infarction, stroke, and angina. While adalimumab lowered cardiovascular biomarkers, a long-term study noted an increased risk of cardiac disorders.

Conclusion:

TNF-α demonstrated superiority over non-biologic and non-systemic medications, evidenced by a reduction in cardiovascular incidence and the possibility of achieving PASI 90. With these benefits, TNF-α could be considered earlier in the treatment algorithm, preceding anti-IL17 or IL23 agents. Further long-term studies are warranted to elucidate their precise cardiovascular effects and optimize treatment strategies in psoriasis management.

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Abstract N°: 5011

Bridging the Gap: Exploring Cardiovascular Risk with Modern Biotherapies in Psoriasis

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Introduction & Objectives:

Psoriasis affects approximately 125 million people worldwide, with 48% experiencing moderate to severe disease and 58% at increased major cardiac events (CEs). Treatment has evolved significantly with the introduction of modern biotherapies; however, concerns have emerged regarding their potential impact on cardiovascular health. This scoping review aims to provide an overview of the current evidence base and to inform clinical practice on cardiovascular risk management for psoriasis patients.

Materials & Methods:

Following PRISMA guidelines. PubMed, ScienceDirect, Cochrane Library, and Wiley Online Library were used to search for publications between 2013 and 2023 in English, focusing on psoriasis patients undergoing biotherapies.

Results:

In the review, 1,380,483 psoriasis patients were studied across 155 publications. Biologic medicines have proven effective in treating psoriasis, with TNF-α inhibitors showing reduced cardiovascular risk biomarkers and lower hazard risks for major CEs, myocardial infarction, stroke, and angina, compared to non-biologic anti-psoriatic medications and even without systemic anti-psoriatic therapy. Anti-IL-17 and Anti-IL-12/23 medications exhibit potential cardioprotective effects against coronary artery disease. However, alternative studies suggest conflicting evidence regarding a potential association between these therapies and an elevated risk of major CEs, necessitating further research to comprehensively elucidate their long-term cardiovascular impact. Anti-IL-23 therapies show no discernible effect on major CEs events or heart failure in short-term studies, warranting further research for a comprehensive understanding.

Conclusion:

TNF-α consistently provide cardiovascular benefits. IL-12/23, IL-17, and IL-23 inhibitors exhibit conflicting findings underscore the complexity of these treatments' effects. These findings underscore the significance of tailored treatment modalities in enhancing the efficacy of psoriasis management strategies, while concurrently prioritizing cardiovascular safety considerations.

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Abstract N°: 5017

Baricitinib: Decrease in Libido as a possible undescribed adverse effect.

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Baricitinib: Decrease in Libido as a possible undescribed adverse effect.

Introduction & Objectives:

Baricitinib a selective JAK 1/2 inhibitor prevents the involvement of different cytokines, suppresses the action of receptor ligands, achieves very good results in patients with moderate to severe atopic dermatitis (AD), decreasing DLQI and SCORAD, improves pruritus at 3 months of therapy. Safety analysis studies have been conducted on baricitinib in which different adverse events have been described with the use of this drug, although it is important to note that there are less prominent effects. Among these is decreased libido, the aim of this abstract is to present a patient with a history of moderate to severe AD, on baricitinib treatment, who experienced decreased libido as a side effect.

Results:

32-year-old male with a history of AD who required management with cyclosporine for 4 months and systemic steroids due to poor response, hospitalisations due to intense pruritus that was difficult to manage, also requiring azathioprine plus irregular phototherapy NB-UVB 80 sessions, with refractory symptoms despite treatment (BSA 25%, SCORAD 55, EASI 20, Pruritus 10/10), treatment was started with Baricitinib 4mg orally daily, with improvement after 6 weeks of treatment (BSA 6%, SCORAD 8, EASI 2, Pruritus 2/10), follow-up documented elevated transaminases, asthenia, extreme myalgias. As a noteworthy effect reported by the patient, there was a significant decrease in libido, which the patient did not associate with other causes.

The information available in the literature on decreased libido secondary to Baricitinib is scarce and the importance of documenting patient-reported adverse effects is highlighted. In a review of the literature on the impact on male fertility, sexual dysfunction and teratogenicity, discontinuation of baricitinib treatment one month prior to conception in men is recommended to prevent major birth defects previously described in animal studies using high doses of the drug. Of note, there have been conflicting results in animal studies regarding baricitinib and its effects on fertility.

Bieber T et al. conducted a study in which they describe the different adverse effects presented by patients, nasopharyngitis, headache, increased blood CK, diarrhoea, herpes simplex, upper respiratory tract infections, acne and major cardiovascular events (MACE), and none appear to have an impact on male sexual activity, but this leads us to hypothesise whether there is any relationship between the increased cardiovascular risk associated with baricitinib therapy and decreased libido.

Conclusion:

Careful and comprehensive assessment when prescribing baricitinib should consider both its therapeutic efficacy and possible side effects, thus emphasising the importance for future researchers to investigate the relationship between baricitinib and the reported adverse effects.

AD is a common pathology in the clinic, which makes it important to know the different types of treatment and their adverse effects, as in this case Baricitinib, to be able to provide the least harmful treatment to our patients.

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Abstract N°: 5044

The Efficacy and Safety of Relatlimab/Nivolumab in Patients with Advanced Melanoma: A Systematic Review

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Introduction & Objectives:

Melanoma, accounting for 1% of skin cancers, is a leading cause of skin cancer-related deaths. While melanoma incidence has increased, mortality rates have decreased due to the effectiveness of immune checkpoint inhibitors (ICIs). ICIs were FDA-approved in 2011 for metastatic melanoma. In March 2022, the FDA approved nivolumab and relatlimab combination (sold under the brand name Opdualag), use for patients over 12 years old with metastatic melanoma or unresectable tumors. This systematic review aims to assess the efficacy and adverse effects of combining nivolumab and relatlimab in advanced melanoma, aiding medical professionals in treatment decisions.

Materials & Methods:

We conducted a search on MEDLINE, EMBASE, and Cochrane Library for studies published in any language up to 29/11/2023. Using Mesh and Emtree words “melanoma”, “relatlimab”, and “nivolumab”, we screened 398 articles and included one single-arm clinical trials (N=1) and two randomized clinical trials (RCTs) (N=2). We excluded case reports, case series, irrelevant clinical trials, preclinical trials, observational studies, review articles, meta-analyses, and conference abstracts.

Results:

After screening databases, 398 articles were initially identified, with 29 full texts meeting inclusion criteria after removing duplicates and irrelevant articles. Three original articles were selected for data extraction. One-year event-free survival rates varied, with Amaria et al reporting 90%, Tawbi et al 47.4%, and Ascietro et al 21.4% (D1) and 16% (D2). One-year overall survival rates were 93% (Amaria et al), 56% (Ascietro et al D1), and 60% (Ascietro et al D2). Among 900 patients, common adverse effects included fatigue (18.33%), pruritus (15.11%), hypothyroidism/thyroiditis (10.88%), and cutaneous rash (8.66%). Grade 3 or 4 treatment-related adverse effects affected 16.44% of patients, with hepatitis (16.98%), diarrhea/colitis (13.5%), and adrenal insufficiency (7.43%) being the most common.

Conclusion:

In conclusion, while relatlimab/nivolumab combination therapy has demonstrated promising results in terms of efficacy in melanoma patients, comparing it to existing treatments necessitates extensive research and longer follow-up periods. Further studies are essential to confirm its long-term effectiveness and safety.

EADV CONGRESS
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Abstract N°: 5090

Experience of usage of sekukinumab in patient with psoriasis and HIV-infection

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Introduction & Objectives: prevalence of psoriasis among HIV-infected patients ranges from 4% to 6%, which is higher than in the general population (2-3%). Clinical trials of monoclonal antibodies for psoriasis treatment excluded patients with HIV and other concomitant diseases as hepatitis, tuberculosis, moreover these diseases are considered as a contraindication for use of monoclonal antibodies. This led to the inability to assess the effectiveness and safety of drugs among groups of patients with concomitant diseases.

Materials & Methods: In November 2023, the Pediatric University Dermatological Clinic admitted a 16-year-old boy with complaints of multiple desquamative rashes, itching, and dry skin. The anamnesis reveals that the child was born to a mother with HIV (+) and was vertically infected the child tested positive for HIV in the first year of life. The patient regularly receives antiretroviral therapy with positive immunological and virological dynamics. His complaints about rashes appeared in 13 years. The child has been under observation at the clinic since 2022. Diagnosis established: psoriasis vulgaris, progressive stage, severe course. Therapy with methotrexate was started 20mg per week. The doctor discharged the patient with recommendations to continue treatment at outpatient polyclinic. However, during a year, according to the patient, he did not receive the drug. Upon re-admission, the medical team objectively observed widespread skin lesions on the patient's scalp, face, neck, and body. They noted multiple edematous papules on the extremities, which merged into plaques and were richly covered with silver-white scales and hemorrhagic crusts (index PASI 67). Because of the severity of the skin process, a decision was made to initiate therapy with secukinumab.

Results: after the first injection (300mg) erythroderma developed, therefore, the administration of the drug was delayed. During 10 days the patient received infusion therapy. After improvement of the condition, sekukinumab was resumed. Already after the second injection, positive dynamics were noted (index PASI 30) and in next 12 weeks all lesions resolved. The patient currently continues to receive secukinumab and antiretroviral therapy, his immunological status is normal.

Conclusion: a clinical example proves the effectiveness and safety of secukinumab for this pathology, which expands the possibilities of providing care to patients with psoriasis with HIV-infection, including pediatric practice.

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Abstract N°: 5096

Clinical effectiveness and safety of tildrakizumab in psoriatic patients with comorbidities: a multicenter real-life study in elderly and frail elderly patients for up to 2 years.

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Introduction & Objectives:

Patients aged ≥65 years represent an increasing percentage of the population with moderate-severe psoriasis. To date, there are no shared guidelines on the therapeutic management of the elderly patient.

The definition of "frail elderly" is not easily framed, generally meaning a patient with unstable homeostasis, vulnerable to external damage, associated with increased hospitalization, institutionalization, falls, death, low income, cognitive function deterioration, and progressive social isolation. To date, there is no study in the literature examining possible differences between frail elderly and non-frail elderly with moderate-severe psoriasis being treated with tildrakizumab.

Materials & Methods:

The present multicentric study evaluated the efficacy and safety for up to 2 years of treatment with tildrakizumab in the elderly population (≥65 years) comparing frail elderly and non-frail elderly patients. Mean PASI and PASI100, 90, and ≤2 at 12-16, 24-28, 48-52, 76-80, and 102-106 weeks, DLQI-derived QoL outcomes at baseline, 48-52 weeks, 76-80 weeks, and 102-106 weeks. Drug survival was also analyzed.

Results:

A total of 217 patients aged ≥65 years were enrolled, of whom 87 (40.1%) were grouped in the frail patient category. In the entire population, 2-year drug survival was ≥80%, and PASI 90 and ≤2 were achieved in 75% and 87.5% of patients, respectively. No difference in effectiveness or safety was found between the frail and non-frail populations. Frail patients were more prone to treatment discontinuation (18% *vs* 8.6%) (p=0.039) and lower drug survival (p=0.042). Adjusting for baseline characteristics at COX regression, frail patients did not show a greater risk of discontinuation (HR 0.51, p=0.091, CI 0.23-1.11). Only 2 patients discontinued treatment due to adverse events.

Conclusion:

Tildrakizumab showed good safety and efficacy at 2 years in the elderly population with or without frailty, confirming it as a potential treatment in comorbid patients. The finding is in line with real-life studies in the general population.

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Abstract N°: 5102

Drug survival and clinical effectiveness of secukinumab, ixekizumab, brodalumab, guselkumab, Risankizumab, tildrakizumab for psoriasis treatment: a retrospective monocentric study

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Introduction & Objectives:

Biologics targeting IL-23, and IL-17A show efficacy and safety in the treatment of moderate-to-severe psoriasis. Achievement of Psoriasis Area Severity Index (PASI) 90 or PASI ≤3 until 16 weeks of treatment, andmajor drug survival (DS).Monocentric real-life experience regarding this topic is still scarce, thus we performed a retrospective indirect comparison between IL-17 and IL-23 inhibitors efficacy and DS for the treatment of moderate-to-severe psoriasis.

Materials & Methods:

We performed a comparative evaluation of the achievement of PASI90 and ≤3 at 16, 28, and 52 weeks along with a DS analysis between IL-17 and IL-23 inhibitors. We then performed a comparison on six cohorts of patients treated with six different biologic molecules: brodalumab, ixekizumab, secukinumab, risankizumab, tildrakizumab, and guselkumab.

Results:

IL-17 inhibitors showed faster achievement of PASI 90 and <3 with significant superiority over IL-23 inhibitors at week 16 ($p<0.001$;56% *vs* 42% and 70% *vs* 59%, respectively).

Of 1057 patients, 203 (19.2%) discontinued therapy of whom 161 (24.8%) on an IL-17 and 42 (10.3%) on anti Il-23. A significant difference was showed in favor of IL-23 inhibitors regarding DS ($p<0.001$), which was 88% at 24 months *vs* 75% for IL-17 inhibitors. At multivariate analysis, IL-23 inhibitors (HR 0.54 CI 0.37-0.78, $p=0.001$), and male sex (HR 0.57 CI 0.42-0.76, $p<0.001$) were all associated with a lower cumulative probability of drug interruption.

Non-homogeneous achievement of PASI 90 was shown between different treatments, with significant differences at each time point ($p<0.001$).

At multivariate analysis, risankizumab (HR 0.42 CI 0.26-0.69, $p=0.001$), guselkumab (HR 0.49 CI 0.24-0.99, $p=0.046$), and male sex (HR 0.57 CI 0.43-0.77, $p<0.001$) showed a lower cumulative probability of drug interruption than secukinumab.

Conclusion:

IL-23 inhibitors showed the best performance on DS. Overall, the most effective class was IL-17 inhibitors considering the short-term efficacy, but long-term efficacy is in favor of anti-IL23 agents.

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Abstract N°: 5200

Efficacy of Bimekizumab in clinical practice. A series of 12 patient cases.

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Introduction & Objectives: To evaluate the efficacy and safety profiles of Bimekizumab in patients with severe psoriasis.

Materials & Methods: Retrospective and descriptive study was conducted including 12 patients with severe psoriasis treated with bimekizumab.

Results: Bimekizumab, a novel humanized monoclonal antibody that selectively targets both IL-17A and IL-17F, was approved for the treatment of moderate to severe plaque psoriasis and it has shown promising results in terms of efficacy with a rapid response. Within our Dermatology Department, 12 patients (8 males and 4 females) are currently receiving bimekizumab. The average PASI score before treatment initiation with bimekizumab was 12. Previous treatments included anti-tumor necrosis factor agents, interleukin (IL)-17 and IL-23 inhibitors.

Data analysis revealed that by week 4, the mean PASI score was 1.9. 93% of patients achieved PASI 75, 60% achieved PASI 90 and 33% achieved PASI 100. These results were sustained at week 12. Only one patient, suffering from palmoplantar psoriasis, did not respond to treatment.

In terms of safety, no serious adverse events were reported. One patient experienced oral candidiasis, successfully treated with topical antifungals.

Conclusion: Bimekizumab is a monoclonal antibody humanized IgG1, which dually and selectively inhibits the A and F isoforms of interleukin-17 (IL-17A and IL-17F) approved for long-term treatment of severe psoriasis. According to the collected data, drug efficacy is early, with visible results in controlling the disease in the early weeks of treatment initiation.

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Abstract N°: 5227

immunotherapy in treatment of genital warts

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Introduction : The Genital warts are common sexually transmitted diseases caused by definite types of human papillomavirus. There are many strategies for the treatment of genital wart and intralesional immunotherapy is considered to be a safe and effective treatment modality. However, there are lack of studies that comparing the clinical effectiveness of intralesional purified protein derivative (PPD) and Candida antigen (CA) in genital wart treatment. **Objectives** :To investigate the effectiveness and safety of PPD and CA in the treatment of genital warts.

Materials & Methods: Eighty patients were enrolled in this study and were randomly divided into 2 groups with 40 patients in each. Each antigen was injected

intralesionally at a dose of 0.1 ml into the largest wart every 2 weeks until complete improvement or for a maximum of four sessions.

Results: Complete clinical response was demonstrated in 65%, 62.5% in PPD and CA groups, respectively. There was no statistically difference between both groups. After the 3-month follow-up period, 72.5%, 85% of patients showed complete clearance in PPD and CA groups respectively. Side effects were mild and insignificant in both groups. Recurrence was observed in only one patient in each group.

Conclusion: Immunotherapy by intralesional PPD and CA injection is considered to be effective and well-tolerated modalities in treatment of genital wart with minimal side effects and recurrence rate compared to other modalities.

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Abstract N°: 5261

Exploring the potential impact of tumour necrosis factor inhibitors compared to conventional therapies on the risk of cardiovascular events in immune-mediated inflammatory diseases

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Introduction & Objectives:

Increased risk of developing cardiovascular (CV) events is associated with immune-mediated inflammatory diseases (IMIDs), like psoriasis (Pso), related psoriatic arthritis (PsA), other inflammatory arthritides as rheumatoid arthritis (RA), or inflammatory bowel diseases (IBD). The excess CV risk may be facilitated by tumour necrosis factor (TNF)-α-mediated immunological pathways involved in the pathomechanisms of both IMIDs and atherosclerosis. Through inhibiting these inflammatory pathways thought to be shared, TNF-α inhibitors (TNFis) can have a superior risk-reducing effect on CV events compared to the conventional systemic non-biological (CSNB) treatments, which do not directly act on TNF-mediated pathways. Our objective was to systematically investigate the effects of TNFis compared to CSNBs in IMIDs on the risk of CV events.

Materials & Methods:

A systematic search was conducted in three databases. Randomised controlled trials, cohort, and case-control studies were eligible through the selection process, investigating the incidence of atherosclerotic CV events in TNFi-treated patients compared to conventional therapies in IMIDs. A random-effect meta-analysis of pooled fully adjusted multivariate hazard ratios (HRs) and incidence rate ratios (IRRs) was performed with major adverse cardiovascular events (MACE), myocardial infarction (MI) and cerebrovascular events (CeVE) as primary outcomes.

Results:

The systematic search resulted in 8724 hits. 56 articles were included in total, of which 29 studies were eligible for the quantitative analyses. In the aggregate analyses including Pso, PsA, RA, and IBD patients, the TNFi group was shown to have a significantly lower risk of MACE compared to the CSNB-treated group (HR= 0.74, 95% confidence interval (CI) 0.58–0.95; IRR= 0.77, 95% CI 0.67–0.88). The clinically and statistically significant benefit of TNFis on MACE reduction was also demonstrated in subgroups of Pso, PsA and RA patients. Furthermore, the superiority of TNFis compared to the CSNB group was also shown for the outcomes of MI and CeVE in IMID-affected patients.

Conclusion:

Prior use of TNFis instead of CSNBs in the therapeutic line can be recommended to decrease the risk of

atherosclerotic-derived CV burden in IMID populations.

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Abstract N°: 5417

Assessing inflammatory bowel disease risk prior to commencing IL-17 inhibitors: a cross sectional analysis of Irish Dermatology and Rheumatology practices.

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Assessing inflammatory bowel disease risk prior to commencing IL-17 inhibitors: a cross sectional analysis of Irish dermatology and rheumatology practices.

Introduction & Objectives:

Interleukin (IL)-17 inhibitors are effective treatments for psoriasis, hidradenitis suppurativa and many arthridities, including psoriatic arthritis and axial spondyloarthritis. However these targeted therapies have been linked to the unmasking of inflammatory bowel disease (IBD) and worsening of existing IBD in some patients.

Materials & Methods:

This study aimed to evaluate Irish Dermatology and Rheumatology practices in assessing IBD risk prior to commencing IL-17 inhibitors. An anonymous survey was disseminated to members of the Irish Association of Dermatologists and the Irish Society of Rheumatology in March 2024.

Results:

Sixty-five doctors at consultant and registrar level responded to the survey (68% dermatology, 32% rheumatology). Most respondents (97%) were aware of an association between IL-17 inhibitors and the unmasking of IBD, but most had no experience of this in their own practice (66%). Faecal calprotectin measurements were used routinely by some clinicians (8%) to screen patients before starting IL-17 inhibitors (all were dermatologists), but if the patient had a positive family history, or gastrointestinal symptoms, a faecal calprotectin measurement would be sought by most (87%). Fifty-seven percent of dermatologists and rheumatologists routinely screen for GI symptoms at follow-up appointments in patients established on IL-17 inhibitors.

Conclusion:

This study highlights the high level of awareness of the risk of unmasking IBD with IL-17 inhibitors, yet there is variation in practice with regards to risk assessment. Faecal calprotectin measurement is a simple test that has high sensitivity and specificity in patients with gastrointestinal symptoms, and a cost of €7-€20 depending on site. Given the profound impact that IBD could have on patients'

health and quality of life, the role of faecal calprotectin screening should be determined, and a screening protocol advised.

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Abstract N°: 5426

Unlocking the Secrets of Psoriasis Treatment: Exploring the Impact of Blood Ratios on Treatment Success with Biological Agents in Psoriasis Vulgaris Patients

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Unlocking the Secrets of Psoriasis Treatment: Exploring the Impact of Blood Ratios on Treatment Success with Biological Agents in Psoriasis Vulgaris Patients

Introduction & Objectives: Psoriasis is a chronic, immune-mediated disorder. The development of psoriasis is attributed to disruptions of the epithelial or immunologic systems, triggered by genetic and environmental factors. Neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR) and mean platelet volume (MPV) were found to be correlated with psoriasis activity which also play an important role in the pathogenesis of psoriasis.Our aim in the study is to examine NLR, PLR and MPV values in psoriasis patients receiving biologic agent therapy and to determine whether biologic therapy has superiority over each other in terms of their effects on these parameters, and whether there is a correlation between clinical responses to treatment at the end of the sixth month and these parameters.

Materials & Methods: In this study, 238 patients who were treated with adalimumab (ADA), etanercept (ETA), infliximab (INF), secukinumab (SEC), and ustekinumab (UST) were evaluated retrospectively.

Results: In patients using ADA, ETA and INF, a decrease in NLR values was found to bestatistically significant at the end of the six months of treatment. The decrease in PLR values a was statistically significant in the groups using ADA and INF. The decrease in MPV was found significant only in the patient group using SEC. Comparison of NLR, PLR and MPV values before biologic agent treatment and at the sixth month of treatment summarized in Table 1.

Conclusion: The new generation patient-physician approach is and should be based on preventive medicine. It may be easier to obtain information about the course of the disease in a busy dermatology clinic with simple blood tests such as MPV, NLR and PLR. A cost-effective approach is taken when both the patients' reintegration into social life and the drug costs are considered. Patients'; quality of life can be increased and disease surveillance can be changed with these easy-to- reach laboratory parameters.

Table 1: Comparison of NLR, PLR and MPV values before biologic agent treatment and at the sixth month of treatment.

		Mean Rank	p value	z value
ADALIMUMAB	NLR 6-NLR 0	Negative ranks	**36,58**	0,00
		Positive ranks	**22,07**	

	PLR 6- PLR 0	Negative ranks	**Mean Rank** 38,10	**p value** 0,00	**z value**
		Positive ranks	19,13	
	MPV 6- MPV 0	Negative ranks	**30,37**	0,27
		Positive ranks	32,37	
ETANERCEPT	NLR 6-NLR 0	Negative ranks	22,43	0,03
		Positive ranks	15,00	
	PLR 6- PLR 0	Negative ranks	23,75	0,13
		Positive ranks	14,78	
	MPV 6- MPV 0	Negative ranks	15,37	0,70
		Positive ranks	21,13	
INFLIKSIMAB	NLR 6-NLR 0	Negative ranks	15,63	0,00
		Positive ranks	10,13	
	PLR 6- PLR 0	Negative ranks	14,42	0,00
		Positive ranks	10,67	
	MPV 6- MPV 0	Negative ranks	10,92	0,25
		Positive ranks	15,71	
SECUKINUMAB	NLR 6-NLR 0	Negative ranks	23,92	0,52
		Positive ranks	21,95	
	PLR 6- PLR 0	Negative ranks	24,82	0,74
		Positive ranks	21,26	
	MPV 6- MPV 0	Negative ranks	24,44	0,043
		Positive ranks	16,15	
USTEKINUMAB	NLR 6-NLR 0	Negative ranks	32,82	0,32
		Positive ranks	29,89	
	PLR 6- PLR 0	Negative	33,17	0,12

	PLR 6- PLR 0	ranks	33,17	0,12
		Positive ranks	29,19	
	MPV 6- MPV 0	Negative ranks	30,79	0,20
		Positive ranks	25,66	

Mean Rank **p value** **z value**

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Abstract N°: 5485

War on warts: Unveiling intralesional Marvels - Vitamin D3 versus Measles, Mumps and Rubella (MMR) vaccine versus Tuberculin purified protein derivative (PPD).

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Introduction & Objectives:

Cutaneous warts are common dermatological conditions caused by human papilloma virus (HPV). Although it is a benign condition, it tends to increase in number, size and cause disfigurement. Various treatment modalities like topical, systemic and ablative are available but immunotherapy is becoming more popular these days due to their less adverse effects, less recurrences, non - destructive action and optimal effectiveness. It modulates the immune system to achieve disease control. Intralesional immunotherapy plays a significant role, as it potentially acts on treated and as well as distant lesions. The aim and objective is to study and compare the efficacy, safety profile and recurrence rates of intralesional immunotherapy modalities in warts [vitamin D3; measles, mumps and rubella (MMR) vaccine and tuberculin purified protein derivative (PPD) injection]

Materials & Methods:

An open-label interventional study of 60 cases of cutaneous viral warts was performed in a tertiary care centre attached to a medical college after obtaining approval from the institutional ethics committee. After receiving written informed consent from participants, they were divided into three groups namely; Group A (vitamin D3: 0.2mL of 15mg/mL), Group B (MMR: 0.5mL), Group C (tuberculin PPD: 0.1mL of 10TU) and were injected slowly into the base of one or two warts. The injections were given 2 weeks apart for a maximum of six sessions. Response was assessed and adverse effects were noted. The patients were followed up 3 months after the last injection.

Results:

A total of 67 patients were enrolled, of which 60 of them have completed the study. The Vitamin D3 group had the maximum patients with complete response (15 of 20, 75%) followed by MMR group (13 of 20, 65%) and tuberculin PPD group (12 of 20, 60%). Adverse effects mainly pain were reported by the majority of patients in the vitamin D3 group (11 of 20, 55%), followed by the tuberculin PPD group (8 of 20, 40%) and MMR group (5 of 20, 25%). One patient in Vitamin D3 group (1 of 20, 5%) had swelling at the site of injection. Recurrence was seen in two patients in tuberculin PPD group (2 of 20, 10%). No major adverse drug reactions were reported in any of the groups.

Conclusion:

Immunotherapy is a simple, well-tolerated, cost- effective modality with better results and patient satisfaction for the treatment of extensive cutaneous warts and difficult to treat sites.

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Abstract N°: 5636

Absence of Clinically Impactful Immunogenicity of Nemolizumab in Long-Term Treatment of Patients with Atopic Dermatitis and Prurigo Nodularis

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Introduction & Objectives:

Nemolizumab, a humanized anti- interleukin-31 receptor A monoclonal antibody, demonstrated clinically and statistically significant improvements in itch and skin lesions in patients with atopic dermatitis (AD) and with prurigo nodularis (PN) in phase 3 studies. As a therapeutic protein, nemolizumab has the potential to induce anti-drug antibodies (ADA) and to stimulate an unwanted immune response. Here, we describe the immunogenicity profile of nemolizumab and its impact on pharmacokinetics (PK), efficacy and safety.

Materials & Methods:

The presence of ADA, their titers, and their neutralizing ability (NAb) following nemolizumab treatment were assessed as part of its clinical development for AD and PN. In addition, the impact of immunogenicity on PK, efficacy and safety was assessed in an integrated analysis of immunogenicity data from pivotal phase 3 and long-term extension (LTE) studies for both indications. ADA were classified according to the definitions of Shankar *et al.* (2014). Treatment-induced ADA were further classified as transient or persistent ADA. The following study assessments were descriptively and graphically compared between patients with and without treatment-emergent ADA:

- PK: The nemolizumab trough serum concentrations over time
- Safety: The proportion of subjects with treatment emergent adverse events (TEAEs), serious adverse events (SAEs), drug related TEAEs, adverse events of special interest (AESIs) and immune mediated disorders
- Efficacy: Primary and selected secondary clinical efficacy endpoints *i.e.*
  - AD indication: IGA success*, EASI-75 responders ** and PP NRS responders***
  - PN indication: IGA success* and PP NRS responders***

* Proportion of patients with IGA of 0 [Clear] or 1 [Almost clear] and a ≥2-point improvement from baseline

** Proportion of patients with ≥75% improvement in EASI from baseline

*** Proportion of patients with improvement of ≥4 from baseline in PP NRS

Results:

Patients with AD: Data were pooled from 1100 patients with AD who received subcutaneous nemolizumab in phase 3 pivotal and LTE studies with a 60 mg loading dose (LD) followed by 30 mg dose given Q4W or Q8W. The median treatment duration was 17 months.

Patients with PN: Data were pooled from 358 patients with PN who received subcutaneous nemolizumab in phase 3 pivotal and LTE studies with a 60 mg LD followed by 30 mg or 60 mg dose given Q4W. The median treatment duration was 14 months.

Consistent results were observed in both indications:

- The overall incidence of treatment-emergent ADA and NAb were 11.2% and 0.5%, respectively, in the AD Phase 3 studies and 12.8 % and 3.4%, respectively, in the PN phase 3 studies.
- ADA positive status, regardless of ADA titer level, had no impact on nemolizumab PK profile.
- There was no apparent relationship between efficacy and ADA status or ADA titers. Overall, efficacy responses were maintained following seroconversion.
- The incidence of TEAEs, SAEs, drug-related TEAEs, and AESIs was similar in patients with treatment-emergent ADA and in those for whom ADAs were not detected. There was no association between ADA positive/negative status and incidence of type I-IV hypersensitivity reactions to nemolizumab.

Conclusion:

There was no discernable impact of immunogenicity (ADA and Nab) on the overall clinical benefit and risk of nemolizumab for AD and PN indications according to the integrated immunogenicity data analysis performed on a robust dataset of 1458 patients from both indications.

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Abstract N°: 5647

Exposure Response To Support Dose Selection Of Nemolizumab In Patients With Prurigo Nodularis

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Introduction & Objectives: Prurigo nodularis (PN) is a chronic and debilitating neuroimmune skin condition, characterized by chronic itch with multiple nodular skin lesions. Nemolizumab, a humanized anti- interleukin-31 (IL-31) receptor A monoclonal antibody, demonstrated clinically and statistically significant improvements in itch and skin nodules in adult patients with PN in phase 3 studies. Here, we describe the use of exposure-response models to support the recommended nemolizumab subcutaneous dose in adult patients with PN.

Materials & Methods:

Exposure-response for efficacy: Data were pooled from 619 adults with PN who received nemolizumab or placebo in phase 2 and phase 3 pivotal studies. Two pharmacokinetic/pharmacodynamic (PK/PD) models were developed from these pooled data to characterize the relationship between nemolizumab exposure and two clinical efficacy assessments for itch and skin nodules: weekly average of peak pruritus numerical rating scale (PP NRS) score and investigator global assessment (IGA).

Simulations: Population PK simulations evidenced that nemolizumab systemic exposure decreases with increasing body weight (BW) when patients receive a flat dose, the subgroup of patients with BW ≥90 kg having on average 1.7 times lower systemic exposure than the subgroup with BW <90 kg. Consequently, the PK/PD models were used to simulate the outcomes of administering 2 flat doses every 4 weeks (Q4W) for 16 weeks in a virtual clinical study (3 arms, 1000 patients per arm).

- Arm 1: Patients with BW <90 kg receiving a 30 mg dose Q4W with 60 mg loading dose (LD)
- Arm 2: Patients with BW ≥90 kg receiving a 30 mg dose Q4W with 60 mg LD
- Arm 3: Patients with BW ≥90 kg receiving a 60 mg dose Q4W

The 60 mg dose adjustment for the subgroup of patients with BW ≥90 kg intended to mitigate the lower systemic exposure in those patients.

Exposure-response for safety: Data were pooled from 556 patients with PN who received nemolizumab or placebo in phase 3 pivotal studies. These pooled data were used to assess potential causal link between nemolizumab exposure and selected adverse events: eczematous reactions (dermatitis atopic, eczema, eczema nummular), headache, asthma, facial and peripheral oedema.

Results:

Simulations results showed similar proportion of PP NRS responders (*i.e.*, subjects with improvement of ≥ 4 points from baseline in PP NRS at Week 16) in the 3 arms, suggesting that the lower systemic exposure of patients with BW ≥ 90 kg had no clinically meaningful impact on pruritus.

Conversely, a lower IGA success rate (*i.e.*, IGA of 0 [Clear] or 1 [Almost clear] and a ≥2-point improvement from baseline at Week 16) was predicted for subjects with BW ≥ 90 kg treated with a non-adjusted dose (arm 2) compared to the 2 other arms. Therefore, the proposed dosing regimens were selected to achieve matching systemic exposure and similar IGA success rate in all patients regardless of their BW.

For safety, the analyses did not show evidence for any increased incidence of the selected adverse events with higher nemolizumab exposure at steady state.

Conclusion:

Exposure-efficacy and exposure-safety analyses provided supportive evidence of the selected Q4W doses in patients with PN, *i.e.* 30 mg (60 mg LD) with a 60 mg dose adjustment based on BW cutoff of 90 kg. The proposed tiered dose adjustment based on BW is adequate to achieve therapeutic exposure and clinical benefit without exposing patients to increased risks.

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Abstract N°: 5668

Biologic therapy and cardiometabolic risk in psoriasis – a retrospective review

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The impact of biologic therapy on cardiometabolic risk parameters

Introduction

Psoriasis is a systemic inflammatory disease that carries an increased cardiometabolic risk including dyslipidaemia and diabetes. The impact of biologic therapy on the cardiometabolic sequale of psoriasis is not clear. This study aimed to assess the effect of biologic therapy on key cardiometabolic risk markers in a cohort of psoriasis patients, who had incurred one year of biologic therapy.

Methods:

A retrospective review was conducted of patients receiving continuous biologic therapy over 1 year for chronic plaque psoriasis in a single dermatology centre at a tertiary hospital in Sydney, Australia. The effect of biologic therapy on psoriasis was assessed using the psoriasis area severity index (PASI). Cardiometabolic risk markers assessed included lipid profile (total cholesterol [TC], low-density lipoprotein [LDL] cholesterol, high-density lipoprotein [HDL] cholesterol and triglycerides [TG]) and Haemoglobin A1c (HbA1c). Measurements at baseline and 1-year were compared using paired *t*-tests for analysis of the parameters which approximated normal distribution (TC, LDL, HDL) and Wilcoxon signed-rank test for analysis of those which did not (TG, HbAlc, PASI). Two-tailed P-values <0.05 were considered significant.

Results:

A total of 200 patients were reviewed, of which n=39 had complete data sets; mean age 51±SD years, 79% male and 67% biologic experienced (BE). The biologic agents used included Risankizumab (33%), Ustekinumab (18%), Secukinumab (18%), Ixekizumab (15%) and Guselkumab (8%). After 12 months, significant skin improvement was seen [PASI reduced from 11.8 (SD 10.0) to 1.1 (SD 2.2), p<0.001]. There was no significant change in lipid profile, including TC (mean difference -0.1 mmol/L, p=0.532), LDL-C (mean difference = -0.1 mmol/L, p = 0.476), HDL (mean difference = -0.1 mmol/L, p=0.125), triglycerides (mean difference = 0.0 mmol/l, p = 0.670) or HbAlc (mean difference 0.3%, p=1.000).

Conclusion:

Key markers of cardiometabolic risk, lipid profile and HbAlc, did not significantly improve after 1 year of biologic therapy despite significant reduction in psoriasis skin severity. The cutaneous benefits of biologic therapy are well proven. Further research in larger cohorts is needed to elucidate potential benefits of biologic therapy on systemic inflammatory sequeale and cardiometabolic risk.

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AMSTERDAM 25-28 SEPTEMBER 2024
EUROPEAN ACADEMY OF DERMATOLOGY & VENEREOLOGY

Abstract N°: 5738

Short-term cardiovascular complications in dermatology patients on JAK-STAT inhibitors: A meta-analysis of randomised controlled trials

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Introduction & Objectives:

Evolving evidence suggests that patients on Janus kinase-signal transducer and activator of transcription (JAK-STAT) inhibitors (JAK-STATi) may be at higher risk of major adverse cardiovascular events (MACE) and venous thromboembolism (VTE). Most existing literature has focused on indications that may confer a higher MACE and VTE risk than that experienced by patients with isolated dermatological indications.

To evaluate risk of MACE, VTE, Serious Adverse Events (SAE) and tolerability of systemic JAK-STATi compared to placebo in those with a dermatologic indication.

Materials & Methods:

A systematic review of the literature was carried out to June 2023, using databases EMBASE, Medline, SCOPUS, Cochrane Library of Registered Trials, and registered Clinical Trials. The analysis was reported in accordance with the PRISMA guidelines. Placebo-controlled randomised trials that compared systemic JAK-STATi with placebo, and investigated the safety in patients with alopecia areata, psoriasis, vitiligo, atopic dermatitis, lichen planus or hidradenitis suppurativa. Crude numbers for MACE, VTE, SAEs and study discontinuation due to treatment emergent adverse events (TEAEs) were pooled and underwent meta-analysis to compare risk ratios (RRs) between cohorts.

Results:

Forty-five RCTs were eligible for inclusion, with 12996 patients receiving active JAK-STATi therapy and 4925 allocated to placebo treatment. Meta-analysis found no significant increase in MACE (I2=0.00%, RR 0.47, 95% CI 0.28–0.80) or VTE (I2 = 0.00%, RR 0.46, 95% CI 0.26-0.80) between placebo and JAK-STATi comparator arms. There was also no significant difference in SAEs (I2 = 12.38%, RR 0.92, 95% CI 0.72-1.20) and discontinuations between JAK-STATi and placebo (I2 = 23.55%, RR 0.94, 95% CI 0.76-1.19).

Conclusion:

This meta-analysis did not identify a significant increase in the risk of MACE and VTE in dermatology patients receiving JAK-STATi for median duration of 16 weeks. The results of this review suggest there is insufficient evidence that JAK-STATi confer an increased risk of cardiovascular complications in dermatological patients, especially when used for short timeframes.

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Abstract N°: 5750

Infection Risk with JAK Inhibitors in Dermatoses:A Meta-Analysis

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Introduction & Objectives:

Evolving evidence suggests Janus Kinase Inhibitors (JAKi) may predispose to certain infections, including tuberculosis and human herpes viruses. The aim of this review was** to evaluate comparative infection risk in patients on a systemic JAKi for a dermatologic indication to placebo.

Materials & Methods: ** A systematic review was carried out to June 2023, using databases EMBASE, Medline, SCOPUS, and Cochrane Library of Registered Trials. Placebo-controlled randomised trials that investigated incidence of infection in patients with a dermatologic indication. Primary outcome measures were incidence of most commonly reported treatment emergent infections reported in studies, including serious and opportunistic infections, upper respiratory tract infections, nasopharyngitis, herpes simplex, varicella zoster, tuberculosis, neutropaenia, and lymphopaenia. Meta-analyses of incidence ratios was carried out to determine odds ratios (OR).

Results:

Meta-analysis found no significant increase in risk of serious (OR 0.92, 95% CI 0.61 – 1.43, p = 0.74) and opportunistic infections (OR 0.65, 95% CI 0.32 – 1.31, p = 0.23). Incidence of varicella zoster infections was significantly higher in the JAKi cohort (OR 1.72, 95% CI 1.08 – 2.72, p = 0.022). From 25 studies, there was no baseline increased risk of herpes simplex infections (OR 1.43, 95% CI 0.93 – 2.23, p = 0.102), but a significantly higher risk in those with AD, compared to AA (OR 1.73, 95% CI 1.13–2.69, p=0.013).

Conclusion:

The results of this analysis do not suggest an increased risk of serious and opportunistic infections in those on JAKi compared to placebo. It does, however, support an increased risk of varicella zoster infections, and a higher risk of herpes simplex infections in those with atopic dermatitis. The results of this report support the short-term safety of these agents, but do signal that vigilance should be practiced in patients at risk for serious or recurrent herpes virus infections.

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Abstract N°: 5805

A unique case of Etanercept-induced juvenile disabling pansclerotic morphea

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Introduction:

Morphea or localized scleroderma is a rare chronic inflammatory connective tissue disorder. Morphea, as a side effect of tumor necrosis factor-α inhibitors, is a rare phenomenon, documented in only a handful of case reports with only one case, ever described of pansclerotic morphea induced by TNFα inhibitors. Here, we present a second case of pansclerotic morphea induced by a TNF-alpha inhibitor, with our case being the first documented occurrence of juvenile pansclerotic morphea induced by etanercept.

Case report:

A 9-year-old boy with a history of polyarticular juvenile idiopathic arthritis evolving over the past 2 years, presented to the dermatology consultation with a history of rapidly progressive “tightening” of the skin, initially involving the four limbs starting in the distal extremities and progressing proximally. Shortly after the onset of the condition, contracture deformities developed in the hands, significantly impairing the patient’s ability to engage in routine daily activities. And within 6 months the sclerosis had already spread to the trunk, neck and face, sparing only the fingertips and toes.

During a thorough patient history review, the mother reported that a novel treatment with etanercept (25mg per week) had been initiated 8 months prior to the onset of symptoms.

On physical examination, confluent hypopigmented and hyperpigmented sclerotic plaques involved his upper and lower extremities, with clawlike contracture deformities of his hands. Closer examination of the trunk showed multiple grouped white shiny macules.

Skin biopsy specimen findings were consistent with pansclerotic morphea with extension through the dermis and panniculus.

Discussion:

Morphea is a rare, chronic inflammatory connective tissue disorder with diverse clinical presentations affecting both adults and children. It is characterized by fibrosis primarily involving the skin and underlying soft tissues.

Adverse events (AEs) resulting from TNFα inhibitors, used for different immune-mediated inflammatory diseases, are frequently documented, with skin involvement being the most prominent. Paradoxical reactions to anti-TNFα medications can induce or exacerbate inflammatory conditions despite their intended suppression of proinflammatory cytokines. While these reactions are not well understood, they have been observed in both adult and pediatric populations, with psoriasiform reactions being the most common.

Morphea, on the other hand, has rarely been described as a side effect of TNF-α inhibitors. To this day, only 9 cases have been reported in the literature, of which only 1 case corresponds to pansclerotic morphea in a 42-year-old woman induced by adalimumab.

Regarding etanercept specifically, according to the available data there have been only 2 reported cases of

morphea induced by this drug, both presenting as plaque forms in adults.

After conducting a thorough search across various databases we conclude that our case is the first documented instance of juvenile pansclerotic morphea induced by etanercept.

Conclusion:

As the scope of indications for anti-TNFα agents expands, it becomes crucial to recognize their potential AE. And given that cutaneous adverse reactions are among the most common AE encountered in patients receiving TNF-alpha inhibitors, as physicians and as dermatologists, we must maintain heightened vigilance

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Abstract N°: 5829

Early treatment with Rituximab is associated with significantly improved cutaneous sclerosis- observations in an Indian cohort

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Introduction & Objectives: Skin fibrosis and internal organ fibrosis in systemic sclerosis cause significant morbidity and mortality. Literature on treatment options for skin fibrosis predominantly stems from rheumatological research, and there is an unmet need for evidence from perspective of skin fibrosis. Rituximab is effective in reducing skin fibrosis, yet there remains insufficient evidence comparing its efficacy to other immunosuppressants. Thus, this study aims to assess rituximab's efficacy against other treatment modalities for SSc, focusing on improvements in modified rodnan skin score (MRSS), factors influencing change in MRSS, and overall survival analysis in both treatment groups.

Materials & Methods: This was a retrospective observational cohort study that was conducted in a tertiary care center in India. Patients of SSc who presented to the dermatology department from January 2016 to December 2023 were included and records were reviewed. Baseline demographic and clinical details were noted for all patients. They were divided into two groups: patients who received rituximab at least once during this period (Rituximab group) and patients who did not receive rituximab at any point of time (Rituximab-naive group). Rituximab was administered to patients having a baseline MRSS of 14 or higher, with or without ILD or baseline MRSS of seven or more along with ILD. Post-treatment MRSS and all-cause mortality (at the time of inclusion into study) was documented.

Results: A total of 98 patients of SSc were included in this study; 37 patients in Rituximab group and 61 in Rituximab-naive group. In Rituximab-naive group, 11 patients received mycophenolate mofetil, 6 received methotrexate, 3 cyclophosphamide, 2 azathioprine and 39 patients did not receive any immunosuppressants. At baseline, the Rituximab group had a lower mean age as compared to Rituximab-naive group (33.9 ± 9.8 vs 39.7 ± 12.4 years, $p=0.012$), higher percentage of patients with diffuse cutaneous SSc (70.3% vs 29.5%, $p<0.001$) and higher mean baseline MRSS (20.1 ± 9.4 vs 11.5 ± 8.0, $p<0.001$). Post-follow-up, mean fall in MRSS in the Rituximab group at a mean follow-up duration of 25.8 ± 31.4 months was 8.9 ± 6.3, which was significantly higher than that of the non-Rituximab group (3.6 ± 4.3) at a mean follow up duration of 22.6 ± 25.9 months [$p<0.001$]. Linear regression analysis was performed to determine the factors influencing the percentage fall of MRSS as compared to baseline. It showed that the presence of digital ulcers was associated with greater percentage fall in MRSS ($p=0.013$). Four deaths (10.8%) were recorded in the Rituximab group, while six were recorded in the non-Rituximab group (9.8%). However, no difference was observed between the survival distribution of both the groups (log rank test, $c2= 0.01$, $p=0.919$). On Cox regression analysis, higher percentage fall of MRSS from baseline ($p=0.025$) and presence of salt and pepper pigmentation ($p=0.022$) were predictive of overall survival. No serious adverse events were observed in either group.

Conclusion: This study highlights the efficacy of rituximab in reducing skin fibrosis in SSc as compared to other modalties of treatment, despite the more severe baseline disease profile of the Rituximab group. Although no significant difference in overall survival was observed between the two groups, reduction in MRSS and salt-pepper pigmentation were predictive factors for overall survival.

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Abstract N°: 5922

Pembrolizumab cutaneous toxicities in 131 patients with metastatic melanoma: Incidence, management, clinical implications and relationship with survival.

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Introduction & Objectives:

Pembrolizumab has revolutionised the treatment of metastatic melanoma. Cutaneous toxicities are a known consequence of pembrolizumab but little is described about their management and impact on patients. We sought to characterise the incidence, management and complications of cutaneous toxicities and their relationship to survival in the New Zealand setting.

Materials & Methods:

A retrospective review was conducted on 131 patients with metastatic melanoma treated with pembrolizumab between March 2016 and August 2020. The occurrence, grade, description, management and patient experience of cutaneous toxicities were recorded. The relationship between the development of rash or vitiligo with progression-free survival (PFS) and overall survival (OS) were estimated using the Kaplan-Meier method.

Results:

Fifty-seven patients (44% of 131 patients) experienced a total of 71 cutaneous toxicities, including 52 cases of rash, 13 cases of vitiligo, three cases of pruritus, two cases of xerostomia and one case of brittle nails. Only two toxicities were above grade 2 and only 20 toxicities (28.2%) resolved. Pruritic rash (34.6%), rash unspecified (23%) and erythematous rash (19.2%) were the most commonly used clinical descriptors. Emollients (34.7%), Hydrocortisone 0.5-1% (30.6%) and antihistamines (20.8%) were the most frequently prescribed treatments. There were three referrals to the Dermatology service, two patients stopped their therapy due to rash and none were hospitalised.

Patients who developed rash (PFS hazard ratio, 0.26; p-value < 0.0001 and OS hazard ratio, 0.21; p-value < 0.0001) or vitiligo (PFS hazard ratio, 0.06; p-value < 0.0001 and OS hazard ratio, 0.04; p-value < 0.0001) had improved PFS and OS relative to those who did not develop rash or vitiligo.

Conclusion:

Cutaneous toxicities are common with pembrolizumab but mostly low-grade and rarely result in Dermatology referral or discontinuation of treatment. At our institution the clinical description of rashes varied from the international standard, there was a preference to use mildly potent topical steroids and the resolution rate was low. Rash and vitiligo were associated with a survival benefit in this cohort.

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Abstract N°: 6034

Vitiligo in patient with metastatic melanoma treated with pembrolizumab

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Introduction & Objectives:

The development of immune checkpoint inhibitors such as anti-cytotoxic T cell lymphocyte antigen-4 (CTLA-4) and anti-programmed cell death 1 (PD-1) represents a therapeutic advance in the management of many cancers. The use of Anti-PD-1 antibody have significantly improved the prognosis of metastatic cancers including advanced melanoma , but it is often associated with adverse skin effects, notably vitiligo lesions.

Materials & Methods:

Here, we report a case of vitiligo in a patient treated with pembrolizumab for metastatic melanoma.

Results:

A 52-year-old woman with a history of acral lentiginous melanoma at the sole of the left foot operated on in January 2021. In 2022, approximately 1 year later, the patient developed subcutaneous nodules on the left leg. A computed tomography (CT) scan was done showing the presence of lung metastases, lymph node and skin metastases in transit.

The patient was treated with anti PD1 (Nivolumab). After 4 cycles of treatment, the evolution was unfavorable with pulmonary and hepatic progression.

After a multidisciplinary consultation meeting, treatment with pembrolizumab was initiated (2 mg/kg, every 3 weeks). Five months after starting treatment with pembrolizumab, the clinical examination of the patient revealed the appearance of a well-limited hypochromic macule on the left knee with leukotrichia. The appearance of this lesion was associated with a complete response in the imaging tests.

Conclusion:

Vitiligo may affect 2% to 9% of patients with melanoma receiving anti CTLA-4 treatment and 7% to 11% of those receiving anti PD-1 treatment. It generally develops between 7 and 65 weeks after the start of anti-PD-1 therapy. It differs from idiopathic vitiligo in its location in photoexposed areas.

The development of vitiligo after anti-PD1 therapy is linked to cross-reactivity between melanoma-associated antigens and melanocytes. The occurrence of vitiligo in these metastatic melanoma patients is often correlated with excellent clinical outcomes. It’s a good prognostic sign in melanoma patients.

Immunological checkpoint inhibitors are revolutionizing the treatment of various cancers. However, cutaneous side effects linked to these treatments can have an impact on patients’ quality of life.

Appropriate diagnosis and management of these skin toxicities are essential for optimal patient care and to avoid the interruption of these cancer therapies.

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Abstract N°: 6036

Sarcoid-like Reaction in Nevi: A Rare Complication of Combined Melanoma Therapy

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Introduction & Objectives:

Combined BRAF and MEK inhibition is one of the first-line treatment strategies for patients with advanced BRAF-mutant melanoma. One of the adverse events following melanoma systemic treatments are sarcoid-like reactions (SLRs), that have been mostly associated with the use of immunotherapy or the BRAF inhibitor, vemurafenib. There have been only few reports of SLRs following combined therapy with BRAF and MEK inhibitors. Herein, we present a peculiar case of SLR observed in nevi of a patient with metastatic melanoma receiving dabrafenib and trametinib.

Materials & Methods: A 52-year-old male underwent surgical excision for a cutaneous melanoma located on the right abdomen (SSM, Breslow thickness 0.62 mm, 1 mitosis/ mm2). One month post-operation, scar excision was performed and histopathological diagnosis yielded no tumor residuals. Subsequently, one year following the surgery, he was diagnosed with metastasis in the right inguinal region. Following lymphadenectomy, adjuvant targeted therapy combining dabrafenib and trametinib was initiated to address the stage III C disease. Patient has been undergoing regular oncologist check-ups. An important aspect of the patient's medical history is a diagnosis of pulmonary sarcoidosis, established at the age of 30; however, it did not require active treatment and has since remained in constant remission.

Results:

Since the melanoma diagnosis, the patient has been undergoing regular dermatological monitoring, including digital dermoscopy. During follow-up examinations, excisions of multiple suspicious lesions, notably one SAMPUS (Superficial Atypical Melanocytic Proliferation of Uncertain Significance) on the lower right back, were performed. All excised lesions shared a peculiar dermatoscopic appearance, characterized by an unclear and blurred pigment network, along with a histopathological finding describing granulomatous inflammation in all lesions. After reviewing the findings, taking into account the previous history of pulmonary sarcoidosis, the patient was referred to a pulmonologist, where chest CT scan and additional tests ruled out active pulmonary sarcoidosis. It was concluded that the condition solely manifests as a cutaneous form of the disease. Aside from evidence of granulomatous inflammation in excised nevoid lesions, no other cutaneous sarcoidosis manifestations were observed in the patient.

Conclusion:

This case report highlights a rare occurrence of sarcoid-like reactions (SLRs) specifically in nevi of a patient undergoing combined targeted therapy with dabrafenib and trametinib for metastatic melanoma. The peculiarity of this case lies in the fact that the mentioned combination therapy for melanoma did not exacerbate pulmonary sarcoidosis, as evidenced by the normal chest CT scan and pulmonary evaluation. Another interesting aspect is that the SLRs were only visible in the patient's nevi, which displayed unusual dermoscopic appereance that could be explained by the underlying granulomatous inflammation. This could mean that the occurrence of such changes in nevi is independent of pulmonary sarcoidosis and corresponds to SLRs associated with combined targeted therapy. Finally, report underscores the importance of comprehensive patient evaluation and management in clinical practice, shedding light on potential dermatological complications in the era of targeted

therapy for advanced melanoma.

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Abstract N°: 6053

Bullous pemphigoid successfully treated with Dupilumab

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Introduction & Objectives:

Bullous pemphigoid (BP), a chronic autoimmune cutaneous blistering disorder affecting predominantly the elderly, is characterized by skin tense bullae formation and pruritus symptoms. At present, the main treatment options are corticosteroids and immunosuppressant drugs, with subsequent adverse events and safety issues. Safer treatment modalities are therefore needed. Dupilumab is a biologic agent used to treat BP in recent years. Here, we describe an elderly patient with recalcitrant BP successfully treated with Dupilumab.

Materials & Methods:

A comprehensive review of the literature was carried out for this case.

Results:

A 89-year-old woman was admitted with a 1-month history of severely itchy erythema, vesicles and blistering on the trunk and extremities. Isolated tense blisters and erosions could be observed on the abdomen and bilateral thighs with sparing of mucosal surfaces. The Nikolsky sign was negative. In addition, the patient had type 2 diabetes mellitus and hypothyroidism for over 20 years. The workup for underlying malignancy and rheumatologic diseases with imaging and laboratory test results proved unremarkable. Skin biopsy demonstrated subepidermal blister formation with eosinophilic infiltrate. Direct immunofluorescence revealed subepidermal separation with continuous linear depositions of IgG and C3 along the basement membrane zone. The clinical picture in combination with the histologic and immunologic findings confirmed the diagnosis of BP. She was started on prednisone 80mg, after 2 flares during tapering of prednisone, we proceeded with Azathioprine 200mg, and Tetracycline 500mg. Attempts to very slowly taper the prednisone doses resulted in disease flare-ups and severe pruritus over three years. Given the patient’s severe disease status, her treatment was transitioned to a therapeutic trial of Dupilumab, with an initial loading dose of 600mg subcutaneous injections followed by weekly 300mg. At the 6-month follow-up, there was a complete resolution of bullae and pruritus after treatment with Dupilumab alone.

Conclusion:

An increasing number of studies revealed that BP is a Th2-dominant disease with subsequent overexpression of Th2-type cytokines such as IL-4, IL-5, and IL-13. Treatment often entails topical/systemic corticosteroids, antibiotics, azathioprine, dapsone, methotrexate, and mycophenolate mofetil. These regimens carry significant adverse effects, and careful consideration is warranted in elderly patients. Treatment of BP can be challenging, especially in refractory cases. However, the role and efficacy of Dupilumab in the treatment of BP is not completely clear yet. Dupilumab is a recently developed monoclonal antibody that blocks signaling of IL-4 and IL-13, both of which are crucial cytokines in the T2 response. For this reason, the hypothesis that the reduction in disease activity obtained in the cases reported so far may be related to the reduction in Th2-type responses induced by the inhibition of IL-4 and IL-13 signal transduction induced by Dupilumab. Certainly, Dupilumab should not be considered the first-choice treatment, but as a rescue therapy for selected patients with recalcitrant BP. While the present case highlights the use of Dupilumab as a novel therapy in the treatment of BP, additional studies are

needed. The mild side effect profile of Dupilumab would make it an ideal option for treating the elderly and patients with comorbidities.

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Abstract N°: 6122

Dupilumab-induced lichen planus in patient with atopic dermatitis: a case report

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Introduction & Objectives:

Biological treatment is currently a widely used therapy for patients with atopic dermatitis. Patients treated with biologics experience a significant improvement in their quality of life and a reduction in the severity of symptoms. Unfortunately, like any therapy, biological treatment also carries a risk of side effects. Recent observational studies and meta-analyses have revealed a potential association between atopic dermatitis and autoimmune disorders such as systematic lupus erythematosus, vitiligo, or alopecia areata.

Materials & Methods:

29-year-old patient with a history of severe atopic dermatitis diagnosed at the age of 2 years, who had been treated with dupilumab for one year, presented to the clinic with an exacerbation of skin lesions.

The patient was treated with UVB phototherapy, oral cyclosporine A, and abrocitinib for many years as part of a clinical trial, without satisfactory therapeutic results. In January 2023, the patient was qualified for treatment with dupilumab at a dose of 300 mg every 2 weeks with good treatment tolerance and an 85% reduction in EASI after 16 weeks of treatment. The patient has asthma, multiple allergies, obesity, and depressive disorders.

In January 2024, the patient presented with an exacerbation of skin lesions. She denied any recent infection or modification of her current medications. The skin lesions were accompanied by pruritus.

Results:

Our dermatological examination revealed flat-topped, shiny and violaceous papules and polygonal plaques on the upper and lower limbs as well as on the trunk. The dermoscopic examination revealed barely seen white lines. Moreover, white streaks and erythema were present on the labia majora, labia minora.

To confirm the diagnosis, we performed a biopsy from the wrist and the histopathological result revealed a skin fragment with a microscopic picture consistent with lichen planus.

The treatment with dupilumab was temporarily suspended and potent topical glucocorticosteroids were introduced. After one month of treatment, a significant improvement in skin lesions was observed, as well as in lesions on the mucous membranes of the intimate areas and residual hyperpigmentary changes. It was decided to try to reintroduce dupilumab with good treatment tolerance and without recurrence of lichen planus lesions.

Conclusion:

Lichen planus is a chronic, inflammatory dermatosis that can affect the skin, scalp, mucous membranes, and nails. It can also be induced by certain medications, such as antimalarials, beta-blockers, and others. In recent years, there have been various reports of an association between the use of biologics, such as TNF-alpha inhibitors, and

the development of lichen planus. Our case involves a patient who developed lichen planus after one year of treatment with dupilumab. In the literature, there is one other case of a patient with lichen planus development after 11 months of dupilumab therapy for atopic dermatitis. Although there is a risk of other autoimmune disease development in patients with atopic dermatitis, it is also important to underline that in some cases treatment-induced complications can involve other disease onset.

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Abstract N°: 6208

Adalimumab – a promising future in livedoid vasculopathy

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Adalimumab – a promising future in livedoid vasculopathy

Introduction & Objectives:

Livedoid vasculopathy (LV) is a rare, chronic thrombo-embolic disorder that specifically targets the dermal blood vessels. The initial symptoms include net-like livid discolouration, followed by painful ulcers in the lower limbs, and ultimately stellate and porcelain-white scars called atrophie blanche. It is debilitating since the course of disease shows spontaneous remissions and exacerbations . This causes a detrimental effect on the patient's overall well-being. The main goal of therapy is to reduce pain, ulceration and the risk of exacerbations. However, its treatment is challenging with resistance to traditional therapy.

We highlight the importance of adalimumab as a treatment modality to speed the resolution of painful ulcers and improve quality of life in these patients.

Objectives: To note the curative efficacy of adalimumab in livedoid vasculopathy for early resolution of ulcer and longer remissions.

Materials & Methods:

3 adults with livedoid vasculopathy were enrolled in the study. Subjects received treatment with injection adalimumab (40 mg), subcutaneously every 2 weeks for total 16 weeks. Photographs were taken before treatment and on every follow up.

Results:

In all 3 subjects, accelerated healing of the ulcer was evident. (Figures) After receiving three doses of adalimumab, an average improvement of over 90% was observed. All patients successfully finished 8 doses of adalimumab and experienced no recurrence in 2-month follow-up. All patients remained free from any adverse events during the treatment.

Conclusion:

Our study found that adalimumab rapidly resolves chronic ulceration and associated pain in LV. As a result, the disease life quality index (DLQI) is enhanced in these patients. Hence, we conclude that adalimumab is an efficacious treatment option for refractory as well as in new cases of livedoid vasculopathy and can be considered as first line agent in severe cases.

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Abstract N°: 6224

Laboratory safety of nemolizumab in prurigo nodularis: Results from two phase 3 trials and one open-label extension study

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Introduction & Objectives: Nemolizumab, an interleukin-31 receptor alpha antagonist, demonstrated efficacy and safety in patients with prurigo nodularis (PN) in two phase 3 pivotal studies (OLYMPIA 1 [NCT04501666] of 24-week treatment period and OLYMPIA 2 [NCT04501679] of 16-week treatment period) and in an interim analysis (up to 52 weeks) of an open-label long-term extension (LTE) study (OLYMPIA LTE [NCT04204616]). Here we sought to further characterise the safety of nemolizumab by evaluating clinical laboratory findings from the OLYMPIA 1 and OLYMPIA 2 phase 3 studies and interim analysis of the OLYMPIA LTE study.

Materials & Methods: Data were pooled from two pivotal studies in which adults with moderate-to-severe PN were randomised (2:1) to receive nemolizumab (initial 60 mg subcutaneous dose, followed by 30 mg/60 mg [depending upon the baseline weight: <90 kg/≥90 kg] every 4 weeks) or matching placebo. Data from interim results of the OLYMPIA LTE study (eligible patients with PN from phase 2 and phase 3 lead-in studies received open-label nemolizumab 30 mg [<90 kg] or 60 mg [≥90 kg] every 4 weeks) were also included. Laboratory data of 556 patients from the pooled analysis and 508 patients from the OLYMPIA LTE study (median treatment duration: 388.5 days) were analysed descriptively.

Results: Baseline laboratory values were similar between the treatment groups and there were no clinically meaningful abnormalities in haematology and clinical chemistry over time. In the pooled pivotal analysis, the mean worst post-baseline eosinophil count (x109/L) was within the normal range and there was no imbalance between nemolizumab- and placebo-treated patients (0.284 [0.34] vs 0.234 [0.28], respectively). There was a slight imbalance in the proportion of patients with a shift from normal to high (>upper limit of normal [ULN]) worst post-baseline eosinophil count (29/370 [7.8%] vs 10/186 [5.4%]). No patient experienced severe eosinophilia (>5×109/L) in any of the studies. With respect to the mean and shift from normal to high worst post-baseline eosinophil count, similar findings were observed in the OLYMPIA LTE study.

The average worst post-baseline creatine kinase (CK) values (U/L) between the nemolizumab- and placebo-

treated groups (146.2 [310.0] and 143.6 [226.6], respectively) were within the normal limits and no imbalance between the treatment groups in the pooled pivotal analysis was observed. No imbalance in the proportion of patients with an adverse event of increased blood CK was noted between the nemolizumab- and placebo-treated patients (2/370 [0.5%] and 4/186 [2.2%], respectively) in the pooled pivotal analysis. Similar findings were observed in the OLYMPIA LTE study in the mean and shift from normal to high worst post-baseline CK levels. The adverse event of increased blood CK was reported in 12/508 (2.4%) patients in the OLMYPIA LTE study, which was similar to the incidence reported in the placebo-treated patients in the pooled pivotal analysis. These events were mild to moderate in severity and did not lead to study discontinuation. No clinically meaningful abnormalities in other haematology and clinical chemistry parameters were observed in any of the studies.

Conclusion: There were no clinically significant changes in haematology and clinical chemistry parameters attributed to nemolizumab in patients with PN. These findings support the use of nemolizumab in PN without laboratory monitoring.

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Abstract N°: 6263

Effective Psoriasis Management with Ixekizumab in a Patient with Preexisting Hepatitis B and C

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Introduction & Objectives:

Psoriasis is a chronic immune-mediated polygenic skin disease with numerous environmental triggering factors (e.g. medication, infections, trauma) that may elicit disease in predisposed individuals. It is acknowledged not solely as a skin disease, but also as a systemic condition.

The introduction of biologics has significantly transformed psoriasis treatment, providing effective and well-tolerated options. Various biologic agents, including Ixekizumab, target key points in immune cell signaling pathways. Ixekizumab, a human monoclonal antibody, specifically inhibits interleukin 17A (IL-17A), a cytokine prevalent in psoriatic lesions. This inhibition holds promise for normalizing downstream inflammatory markers and achieving clinical resolution in psoriasis.
The predominant viral hepatitis infections stem from the hepatitis B virus (HBV) and hepatitis C virus (HCV), each capable of advancing to liver cirrhosis and hepatocellular carcinoma. Psoriasis patients exhibit an increased prevalence of hepatitis C, characterized by a male predilection, later onset of psoriasis (median age 54), with HCV infection commonly preceding psoriasis onset. In contrast, the literature on the association between hepatitis B and psoriasis yields inconsistent data.

Materials & Methods:

We report a case of a 57-year-old male presenting a six months history of widespread, sharply demarcated, erythematous plaques covered in thick silver scales (PASI-53.9). The patient also reported joint involvement, resulting in impaired mobility and intense pain in small joints (hands, feet) as well as knees and elbows. Notably, the patient had no documented medical history or adherence to any prior treatments.

Blood tests, including a complete blood count, liver/kidney function tests, lipid profile, viral hepatitis, and HIV markers, as well as inflammatory markers, were conducted. The results revealed HBsAg negativity, anti-HBs positivity, anti-HBc positivity, and anti-HCV positivity, along with elevated GGT, TGO, TGP, and marked inflammation. The patient was referred to the infectious disease department, where it was confirmed that the patient had active hepatitis C (viral load: 1200x103 IU/ml) and a past resolved infection of hepatitis B. Subsequently, the patient initiated antiviral therapy with glecaprevir/pibrentasvir, leading to undetectable viremia after 3 months.

Top of Form

Bottom of Form

A skin biopsy was performed from a psoriatic plaque on the elbow and histopathologic examination confirmed the diagnosis of vulgar psoriasis.

In this context, we have chosen to administer Ixekizumab (after 3 months of antiviral therapy) for the treatment of both cutaneous and arthropathic psoriasis, following approval from infectious disease doctor.

Results:

Ixekizumab appears to have a favorable safety profile when utilized in patients positive for Anti-HCV and Anti-HBs/Anti-HBc. In our case, after 6 months of treatment, there was no reactivation of hepatitis (with sustained negative viral titers) or progression of hepatic disease. Additionally, employing this treatment resulted in the complete resolution of skin lesions (PASI-0) and notable improvement in joint function.

Conclusion:

In conclusion, we present a case where psoriasis prompted the identification of active hepatitis C and resolved HBV infection, subsequently leading to the successful treatment of both the hepatitis C virus infection and the cutaneous and articular manifestations of psoriasis.

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Abstract N°: 6305

Nemolizumab elicits an early and rapid itch response in prurigo nodularis within 2 days: A post hoc analysis of OLYMPIA 1&2 data

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Introduction & Objectives:

Prurigo nodularis (PN) is a chronic, neuroimmune-mediated skin disease, characterized by debilitating itch and multiple pruriginous lesions. Nemolizumab, an interleukin-31 receptor alpha antagonist, demonstrated efficacy and a positive safety and tolerability profile in two large pivotal Phase 3 studies (OLYMPIA 1 [NCT04501666] and OLYMPIA 2 [NCT04501679]) in patients with PN. Here we present *post hoc* analysis data from early timepoints in these studies evaluating daily itch responses after initial nemolizumab administration.

Materials & Methods:

Data from the two pivotal Phase 3 studies were analyzed *post hoc*; 560 patients with moderate-to-severe PN were randomized (2:1) to receive nemolizumab monotherapy (initial 60 mg subcutaneous dose, followed by 30 mg or 60 mg, depending on baseline [BL] weight: <90 kg and ≥90 kg, respectively) every 4 weeks, or matching placebo. Daily itch scores using the Peak Pruritus Numerical Rating Scale (PP NRS; range 0–10) were recorded, with the BL value defined as the last non-missing daily PP NRS before first dosing.

Results:

Mean daily itch scores rapidly decreased from BL in both OLYMPIA studies after first nemolizumab administration compared with placebo. A notable least squares (LS) mean ± standard error (SE) change from BL was observed at Day 2 in OLYMPIA 1 (−1.8 ± 0.15 nemolizumab vs −0.7 ± 0.20 placebo [P<0.0001]) and OLYMPIA 2 (−1.8 ± 0.14 nemolizumab vs −0.8 ± 0.20 placebo [P<0.0001]). Nemolizumab LS mean daily itch scores continued to substantially decrease through to Day 14 (−3.3 ± 0.19 [OLYMPIA 1]; −3.3 ± 0.20 [OLYMPIA 2]) compared with placebo (−0.9 ± 0.26 [OLYMPIA 1]; −1.2 ± 0.28 [OLYMPIA 2]) (P<0.0001 for both studies).

In both studies, clinically meaningful ≥4-point improvements in PP NRS score (itch response) were observed at Day 2 (nemolizumab-treated patients: 18.4% [N=35/190] and 15.8% [N=29/183] vs placebo: 3.1% [N=3/96] and

4.4% [N=4/91]; OLYMPIA 1&2, respectively; P<0.05 for both). By Day 7 in both OLYMPIA 1&2, the proportion of patients achieving a clinically meaningful itch response was over 30% in the nemolizumab group (30.5% [N=58/190] in OLYMPIA 1 and 32.2% [N=59/183] in OLYMPIA 2; P<0.0001 for both), further increasing to 40.0% and 33.9% of patients, respectively, at Week 2.

Conclusion:

In this *post hoc* analysis from the OLYMPIA 1&2 studies, a rapid onset of nemolizumab action on itch response was observed after the initial loading dose. Substantial improvements in itch were observed between nemolizumab and placebo 2 days after the initial dose, with over a quarter of patients achieving a clinically meaningful response within 1 week.

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Abstract N°: 6341

Rapid joint and skin responses were observed in patients with active psoriatic arthritis treated with bimekizumab: A pooled analysis from two phase 3 studies

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Introduction & Objectives:

Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits IL-17F in addition to IL-17A, has shown superior efficacy at 16 weeks vs placebo (PBO) and tolerability in patients with active PsA who were either biologic disease-modifying antirheumatic drug (bDMARD)-naïve or had prior inadequate response/intolerance to tumour necrosis factor inhibitors (TNFi-IR).1,2 Achieving rapid treatment responses is an important predictor for long-term disease control and improvements in quality of life.3,4

Here, speed of treatment response with BKZ in patients with PsA are reported, using joints, skin and composite outcome data pooled from two trials.

Materials & Methods:

The BE OPTIMAL (NCT03895203; bDMARD-naïve) and BE COMPLETE (NCT03896581; TNFi-IR) phase 3 trials assessed BKZ 160 mg every 4 weeks (Q4W) in patients with active PsA. Both trials were double-blind, PBO-controlled to Week 16. BE OPTIMAL included an adalimumab reference arm (data not reported here).

We present pooled study data to Week 16 for BKZ and PBO treatment arms, plus individual study Kaplan-Meier analyses of American College of Rheumatology response criteria ≥50% improvement (ACR50). Non-responder and multiple imputation (NRI, MI) were used for missing binary and continuous variables.

Results:

Of 1,112 patients randomised to BKZ or PBO, 1,074 (96.6%) completed Week 16 of BE OPTIMAL and BE COMPLETE, including 1 patient not on randomised treatment. Baseline characteristics were generally similar between treatment groups.

Kaplan-Meier analyses showed early separation between BKZ-treated and PBO patients achieving ACR50 for both bDMARD-naïve and TNFi-IR patients (**Figure**). In the pooled analysis, the proportion of patients achieving improvements in the joints was numerically greater on BKZ vs PBO by Week 4 for ACR20 and ACR50 (both nominal $p<0.001$) and for ACR70 (nominal $p=0.001$), and these improvements remained greater at each visit to Week 16 (nominal $p<0.001$; **Table**). Similar results were observed for improvements in tender and swollen joint

count, and improvements in pain.

In patients with substantial skin psoriasis at baseline (≥3% body surface area), a greater proportion of patients achieved stringent thresholds of improvement in the Psoriasis Area and Severity Index (PASI) on BKZ vs PBO by Week 4, including complete skin clearance (PASI100; nominal p<0.001; **Figure**). Achievement of PASI100 remained greater on BKZ vs PBO at each visit to Week 16 (nominal p<0.001). Similarly, the proportion of patients achieving the minimal disease activity composite was greater on BKZ vs PBO by Week 4 and remained greater at each visit to Week 16 (nominal p<0.001).

Conclusion:

Patients treated with BKZ achieved rapid treatment responses, with early differentiation from PBO, across joint, skin and composite outcomes.

References:

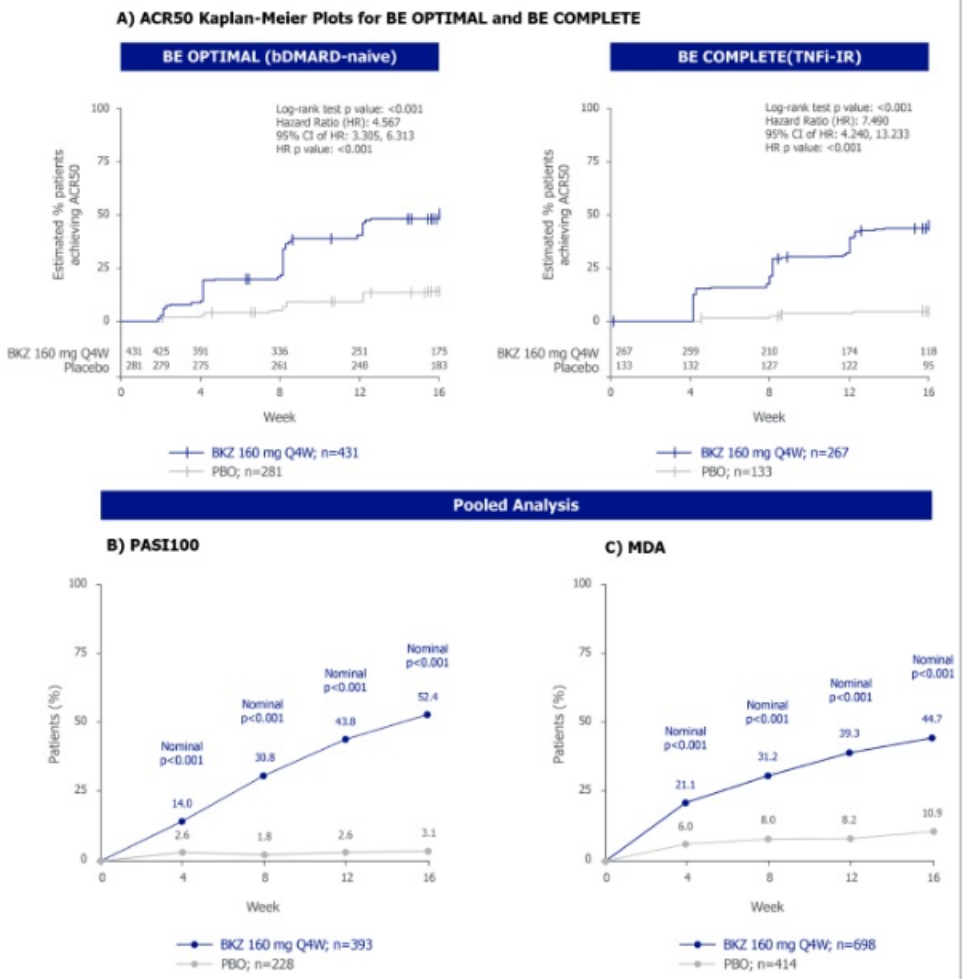
1. McInnes IB. Lancet 2023;401:25–37; **2.** Merola JF. Lancet 2023;401:38–48; **3.** Schoels MM. Rheumatology 2018;57:969–76; **4.** Henkemans SVJS. RMD Open 2022;8:e002706.

Table. Pooled efficacy responses at each visit to Week 16

	Week 4		Week 8		Week 12		Week 16	
Endpoint, n (%) unless otherwise specified	PBO n=414	BKZ 160 mg Q4W n=698	PBO n=414	BKZ 160 mg Q4W n=698	PBO n=414	BKZ 160 mg Q4W n=698	PBO n=414	BKZ 160 mg Q4W n=698
ACR20 [NRI]	46 (11.1)	296 (42.4)	65 (15.7)	399 (57.2)	100 (24.2)	406 (58.2)	88 (21.3)	447 (64.0)
	p<0.001‡		p<0.001‡		p<0.001‡		p<0.001‡	
ACR50* [NRI]	11 (2.7)	119 (17.0)	19 (4.6)	218 (31.2)	22 (5.3)	256 (36.7)	37 (8.9)	305 (43.7)
	p<0.001‡		p<0.001‡		p<0.001‡		p<0.001‡	
ACR70 [NRI]	1 (0.2)	42 (6.0)	3 (0.7)	104 (14.9)	8 (1.9)	145 (20.8)	13 (3.1)	176 (25.2)
	p=0.001‡		p<0.001‡		p<0.001‡		p<0.001‡	
PASI90*,[a] [NRI]	6 (2.6)	90 (22.9)	8 (3.5)	191 (48.6)	8 (3.5)	229 (58.3)	10 (4.4)	254 (64.6)
	p<0.001‡		p<0.001‡		p<0.001‡		p<0.001‡	
TJC CfB [MI], mean (SE)	−2.4 (0.4)	−6.2 (0.4)	−3.4 (0.5)	−8.8 (0.4)	−3.4 (0.5)	−9.5 (0.4)	−2.9 (0.5)	−10.4 (0.4)
	p<0.001‡		p<0.001‡		p<0.001‡		p<0.001‡	
SJC CfB [MI], mean (SE)	−2.0 (0.3)	−4.6 (0.2)	−2.7 (0.3)	−6.0 (0.2)	−3.0 (0.3)	−6.4 (0.3)	−2.7 (0.4)	−6.8 (0.3)
	p<0.001‡		p<0.001‡		p<0.001‡		p<0.001‡	
Pain VAS CfB[b] [MI], mean (SE)	−3.6 (1.0)	−16.0 (0.9)	−6.3 (1.1)	−20.9 (1.0)	−7.3 (1.2)	−22.4 (1.0)	−5.8 (1.2)	−25.1 (1.1)
	p<0.001‡		p<0.001‡		p<0.001‡		p<0.001‡	

Randomised set. *Primary endpoint; †Secondary endpoint; ‡Nominal p values reported for the pooled analysis; not multiplicity-adjusted and should not be used as an indication of statistical significance. [a] In patients with psoriasis affecting ≥3% body surface area at baseline; PBO n=228; BKZ n=393; [b] Pain VAS assessed using Patient's Assessment of Arthritis Pain. ACR20/50/70: ≥20/50/70% improvement in American College of Rheumatology response criteria; BKZ: bimekizumab; CfB: change from baseline; MI: multiple imputation; NRI: non-responder imputation; PASI90: ≥90 improvement in Psoriasis Area and Severity Index; PBO: placebo; Q4W: every 4 weeks; SE: standard error; SJC: swollen joint count; TJC: tender joint count; VAS: visual analogue scale.

Figure. Rapid efficacy responses were observed for A) ACR50 in BE OPTIMAL and BE COMPLETE (OC), B) PASI100 in the pooled analysis set (NRI), and C) MDA in the pooled analysis set (NRI)



Randomised set. ACR50 at Week 16 was the primary endpoint in BE OPTIMAL and BE COMPLETE. Nominal p values reported for the pooled analysis; not multiplicity-adjusted and should not be used as an indication of statistical significance. ACR50: ≥50% improvement in American College of Rheumatology response criteria; bDMARD: biologic disease-modifying antirheumatic drug; CI: confidence interval; HR: hazard ratio; MDA: minimal disease activity; NRI: non-responder imputation; OC: observed case; PASI100: 100% improvement in Psoriasis Area and Severity Index; PBO: placebo; Q4W: every 4 weeks; TNFi-IR: tumour necrosis factor inhibitor inadequate response or intolerance.

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Abstract N°: 6405

Drug survival of secukinumab 2 weekly dosing in psoriasis patients weighing > 90kg: retrospective observational study

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Introduction & Objectives:

Body mass index (BMI) can influence response to biologic treatment, with fewer obese patients achieving clear/ nearly clear skin than non-obese patients. In 2022, secukinumab was granted approval for 2-weekly (Q2W) dosing in patients ³ 90 kg when clinical response was sub-optimal on standard monthly dosing. We published the first real-world prospective observational study assessing efficacy of Q2W dosing. Of 12 patients with suboptimal control (< PASI 90 response) on monthly dosing, 10 (83%) achieved PASI 90 response following 16 weeks of Q2W dosing1. 15 months after completion of the study, we aim to assess the ongoing drug survival of secukinumab in this cohort.

Materials & Methods:

The 10 patients that achieved a PASI 90 response with secukinumab Q2W dosing were re-identified. Data was retrospectively collated from electronic medical notes. New data identified and collected included current biological +/- conventional systemic therapy, any psoriasis flares and length of time to flare, Psoriasis Area Severity Index (PASI) and adverse events. The data was collected via Microsoft Excel which was also used to carry out numerical analysis.

Results:

Of the 10 total patients, 6 (60%) remained on secukinumab Q2W dosing at 15 months. Of these 6 patients, all maintained > PASI 90 response compared to baseline (median absolute PASI 1.6) and 5/6 had a lower absolute PASI compared to week 16 demonstrating ongoing improvement. Of the 4 patients who discontinued secukinumab, 2 retained efficacy (mean PASI 1.6) but discontinued treatment for another reason (flare of psoriatic arthritis and a new diagnosis of endometrial carcinoma deemed not treatment related). Loss of treatment response was observed in only 2 patients (mean PASI 12, mean time to flare post up-titration 9 months). Three patients were switched to a different biologic agent (ixekizumab (n=2) and risankizumab (n=1).

Conclusion:

In our real-world population, 10/12 patients ³ 90 kg with a suboptimal response on monthly secukinumab achieved a PASI 90 response 16 weeks post Q2W up-dosing and 80% of these patients retained a PASI 90 response at > 1 year. This data highlights the benefits of secukinumab up-dosing as an alternative to switching biologic medication in this subgroup. This in itself can reduce the number of biologics needed to control disease and improve patient outcomes.

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Abstract N°: 6449

Paradoxical eccematous reaction in a patient with Crohn's disease resolved after switching to Upadacitinib

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Introduction & Objectives:

Paradoxical reactions can occur with the use of certain biologic drugs by triggering or exacerbating the underlying pathology for which the drug is indicated. Biologics-induced immunophenotypic cross-switching have been described in patients with psoriasis and atopic dermatitis and can also be seen in patients with inflammatory bowel diseases (IBDs).

Materials & Methods:

Case report and literature review.

Results:

We present the case of a 34-year-old male, smoker, with a 15-year history of fistulizing and corticodependent Crohn's disease (CD) complicated by intestinal perforation who required ileocecal resection. His CD was initially managed with corticosteroids and azathioprine and subsequently with adalimumab for ten years, with good control of the disease until 2022, when a rutinary colonoscopy revealed an impassable stenosis of the surgical anastomosis. In addition, the patient started with multiple scaly lesions, psoriasiform in appearance located mainly on hands and thorax. Physical examination revealed also an intense erythema and desquamation on palms and soles. A clinical diagnosis of paradoxical psoriasis due to adalimumab was made and, together with his gastroenterologist, it was then decided to stop treatment with adalimumab and switch to ustekinumab. Furthermore, a topical treatment with clobetasol cream and tacrolimus ointment was prescribed. Despite this, his cutaneous lesions continued worsening and he developed clinical signs of intestinal subocclusion, leading to a new intestinal resection.

At this point, a skin biopsy was performed with a diagnosis of eczematous dermatitis. Given the persistence of skin lesions and the absence of control of his IBD with ustekinumab, a consensus was reached with the Digestive Department to start upadacitinib at 45mg/day, with great improvement of the skin and digestive symptoms, which allowed de-escalation of the dose to 15 mg/day.

Conclusion:

The underlying pathogenic mechanisms of paradoxical reactions in IBDs is still poorly understood and several hypotheses have been proposed. Female sex, CD, personal or familial history of inflammatory skin diseases, smoking, an increased body mass index, and treatment with adalimumab have been identified as independent predictive factors for developing paradoxical reactions.

Regarding the paradoxical eczematous reactions caused by anti-TNF and ustekinumab, their mechanism remains to be established. It is thought that it may be due to a cytokine imbalance by suppressing the Th17/Th1 axis, so Th2 phenotype and the production of IL4 and IL13, among others, would be increased. Th2-related cytokines rely on the JAK pathway to stimulate the production of more cytokines.

The small molecule and oral selective and reversible Janus kinase (JAK) inhibitor upadacitinib, has been approved for the treatment of moderate to severe active CD in adult patients since April 2023 by EMA/FDA. Specifically, it acts on JAK1 or JAK1/3 with functional selectivity on cytokine receptors that transmit signals through JAK2 pairs.

In conclusion, JAK inhibitors are less frequent to over inhibit a certain cytokine leading to immune dysregulation. This confers them the potential for the treatment of paradoxical dermatoses in patients with IBD like ours.

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Abstract N°: 6535

Long-term drug survival of risankizumab in psoriasis: insights from a real-life multicenter study on hard-to-treat areas.

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Introduction & Objectives:

Psoriasis is a chronic inflammatory condition affecting various areas of the body, including challenging sites such as nails, palms/soles, scalp/face, and genitalia. These regions often pose treatment difficulties due to poor responses to topical therapies and limited effectiveness of systemic treatments. The advent of monoclonal antibodies (mAb), such as risankizumab, has significantly improved management, particularly in challenging areas. The aim of the study was to evaluate long-term effectiveness of risankizumab in patients affected by psoriasis in hard-to-treat areas.

Materials & Methods:

A multicentric retrospective real-life study was conducted to assess the drug survival at 12 and 36 months of 191 patients with psoriasis involving critical areas (nail, palmoplantar, scalp, genital regions) undergoing treatment with risankizumab following the Italian Guidelines for the management of plaque psoriasis. The anti-IL-23 switch was performed in patients who recorded a primary or secondary failure to topical or systemic drugs. The study was performed in agreement with the principles established by the Declaration of Helsinki and informed consents were obtained from all the patients. Categorical data were described by absolute frequency and percentages. End-point of the survival analysis was represented by the need for therapy switch. The effectiveness of risankizumab in maintaining drug survival was assessed at 12-month and 36-month using Kaplan-Meier curves and the log-rank test was applied to evaluate the differences between curves. Univariate Cox regression was carried out for each risk factor to estimate Hazard Ratio (HR) with 95% confidence interval (95% CI). Significance was fixed at 0.05 and all analyzes were carried out with R version 3.4.1.

Results:

Drug survival at one year was 97.6% (95% CI: 95.3-100), instead, at three year it was 95% (95% CI: 91.4–98.8%). Seven patients discontinued risankizumab. Reasons for discontinuation were: i) secondary ineffectiveness (3 patients) with a mean time to discontinuation of 13 months; ii) primary ineffectiveness (2 patients); adverse events [occurrence of pancreatic carcinoma (1 patient) and development of an eczematiform eruption (1 patient)]. The log-rank test and Cox regression did not detect any differences in drug survival regarding BMI, gender, age, duration of disease, severity of the disease at baseline or previous exposure to biologics. The only

factor that showed a correlation with the risk of therapeutic switch was the presence of palmoplantar psoriasis, HR 4.72 (95% CI: 1.00-24.3, p=0.047) (Fig.1)

Conclusion:

The study highlights the prolonged efficacy of risankizumab in difficult-to-treat areas of psoriasis and emphasizes the importance of personalized therapeutic approaches. Understanding the factors influencing treatment outcomes in these complex regions can enhance patient care and long-term prognosis. Further research and clinical trials are needed to refine treatment strategies for challenging areas of psoriasis.

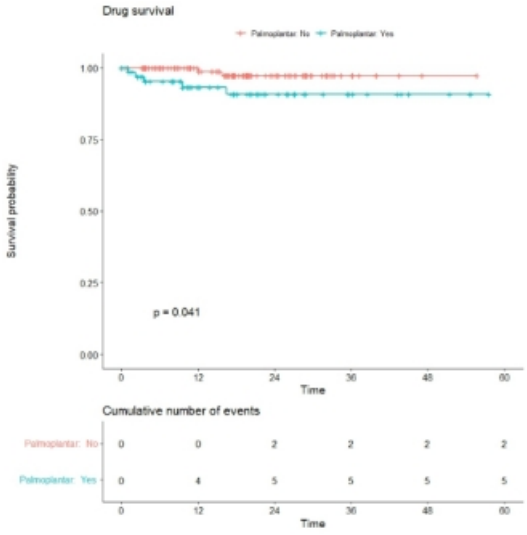

Fig.1: Kaplan Meyer curve of the drug survival of the population

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Abstract N°: 6567

Patientmanagement. Biosimilars as a replacement therapy for biologicals in psoriasis and hidradenitis suppurativa.

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Introduction & Objectives:

Biosimilars are similar to the reference drug in terms of quality, biological activity, safety and efficacy. Once the patent protection of a biological drug has expired, companies can launch the approved biosimilars on the market after proof of efficacy for a disease.

Materials & Methods:

259 outpatients with psoriasis (94%) or hidradenitis suppurativa [HS] (6%) treated at the Department of Dermatology of the University Medical Center Mainz were retrospectively examined with regard to disease burden, side effects and/or symptoms during and after switching from an original biological to a biosimilar and, if necessary, switching back to the original substance.

Results:

76.4% (198/259) of the patients had previously received the originator of adalimumab Humira® and 23.6% (61/259) the originator of etanercept Enbrel®. 79.5% (206/259) of patients were switched to a biosimilar. 94.2% (194/206) of this switched group presented again, with 78.9% (153/194) of the switched overall collective continuing the biosimilar therapy until the end of the survey period. 21.1% (41/194) of patients were switched back to the original substance or another medication, 19.3% (35/181) in psoriatic patients, 46.2% (6/13) in HS patients. Worsening of efficacy (68.3%), progression of arthritis (68.3%) and increased skin symptoms (56.1%) were the main reasons given for switching back, whereas fatigue, headaches, gastrointestinal complaints or pain on injection were rarely cited.

Conclusion:

We were able to show that biosimilar therapy was successful in around 80% of the population studied. In the event of an increase in symptoms or the occurrence of side effects, a switch back was necessary and mostly successful.

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Abstract N°: 6619

Biologic Therapies for Cutaneous Immune-Related Adverse Events: A Systematic Review

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Introduction & Objectives: The rate of occurrence for cutaneous immune-related adverse events (cirAEs) attributed to immune checkpoint inhibitors (ICIs) ranges from 30% to 60.1 The efficacy of biologic agents in treating cirAEs and impact of these therapies on cancer treatment outcomes are not yet fully understood. This systematic review aims to assess the role of biologic therapies in treating cirAEs in cancer patients on ICIs.

Materials & Methods: Adhering to PRISMA guidelines, we conducted a search of PubMed/MEDLINE, EMBASE, Web of Science, and Cochrane databases from their inception until September 1, 2023. The search utilized both Medical Subject Headings terms and keywords such as 'Cutaneous Immune-related Adverse Events,' 'Immune Checkpoint Inhibitors,' and 'Biologic Therapy.' We only included peer-reviewed observational studies in English that described cases of cirAEs treated with biologics.

Results: Thirty-two studies, discussing 109 patients with cirAEs, were eligible for inclusion. Immunobullous eruptions were the most prevalent cirAE (46.8%), followed by eczematous reactions (17.4%). Pembrolizumab and nivolumab, primarily administered for melanoma (37.5%, 33 out of 88 reported cases) and lung cancer (15.9%, 14 out of 88 reported cases), constituted the predominantly prescribed immunotherapies. Biologic medications, most notably dupilumab (51.4%, 56 out of 109 cases) and rituximab (22%, 24 out of 109 cases), have shown effectiveness in treating cirAEs with 92.7% of patients achieving clinical response (52.5% complete and 47.5% partial response). Specifically, 41% (32 out of 79 reported and actively on-treatment cases) of patients continued immunotherapy without interruption while managing cirAEs with biologics. In terms of cancer status, after the completion of biologic therapy, 47% (27 out of 57 reported cases) of these patients remained in a state of complete remission, partial remission, or disease-free from progression.

Conclusion: Our analysis demonstrated the robust efficacy of biologic medications in treating cirAEs during immunotherapy. Moreover, the data suggests the relative safety of using of biologics to manage cirAEs in cancer patients, although there is a significant proportion of cases with unreported cancer status. These results underscore the dual advantages of biologic medications: effective treatment of cirAEs and seeming lack of negative impact on cancer treatment or outcomes. Further studies with larger patient cohorts are necessary to validate these findings and overcome the limitations posed by underreporting of cancer status during biologic therapy.

References

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Abstract N°: 6731

Secukinumab Demonstrates Consistent Safety Profile in Patients With Psoriasis and Hidradenitis Suppurativa: Updated Pooled Safety Analysis From Clinical Trials

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Introduction & Objectives:

Secukinumab, a fully human anti-interleukin (IL)-17A monoclonal antibody, is approved for multiple immunological disorders, including moderate-to-severe plaque psoriasis (PsO), psoriatic arthritis (PsA), axial spondyloarthritis (axSpA; including ankylosing spondylitis and non-radiographic axSpA) and hidradenitis suppurativa (HS). Long-term safety of secukinumab was previously reported based on the pooled data from 47 clinical trials across approved indications of PsO, PsA and axSpA involving 27,765 patient-years (PYs) with a cut-off on 25 June 2022.1 Here, we report the updated safety profile of secukinumab in adult patients with PsO and HS.

Materials & Methods:

The pooled safety analysis included 43 phase I/II/III/IV clinical trials (PsO: 41 and HS: 2 trials) with patients who had received ≥1 dose of subcutaneous secukinumab (cut-off: December 2023). Adverse events (AEs) were reported as exposure-adjusted incidence rates (EAIRs)/100 PYs. All AEs were coded using the Medical Dictionary for Regulatory Activities (MedDRA; version 26.1) with individual AEs presented in MedDRA Preferred Terms (PT). The safety topics of interest for secukinumab (based upon reported treatment-emergent AEs) were assessed by standardised grouping with the use of system organ class (SOC), high-level group terms (HLGTs), high-level terms (HLTs) and Standardised MedDRA Queries (SMQs). Safety topics for which no MedDRA hierarchy or query existed were assessed with specific groups of events in a customised query for the analysis (customised MedDRA Query or CMQ).

Results:

A total of 13,842 patients (PsO [N=12,782] and HS [N=1060]) were included in the analysis. 16.6% and 85.0% of PsO patients were exposed to 150-mg and 300-mg secukinumab (including both regimens of every 2 [SECQ2W] and 4 weeks [SECQ4W]), respectively. All the patients with HS were exposed to 300-mg secukinumab (including SECQ2W and SECQ4W regimens). The most frequently reported AEs were nasopharyngitis (EAIR [95% CI]: 22.23 [21.47, 23.01]) and upper respiratory tract infection (EAIR [95% CI]: 6.11 [5.75, 6.49]) in patients with PsO. In the HS subset, headache was the most frequent AE (EAIR [95% CI]: 19.71 [16.78, 23.00]) followed by nasopharyngitis (EAIR [95% CI]: 14.39 [11.95, 17.19]). The incidence of paradoxical skin reactions such as dyshidrotic eczema was low in PsO (EAIR [95% CI]: 0.42 [0.33, 0.52]) and HS (EAIR [95% CI]: 1.08 [0.52, 2.00]) subset. No cases of pyoderma gangrenosum were identified in the PsO and HS subset. The incidence of serious and *Candida* infections was EAIR (95% CI): 1.52 (1.35, 1.71) and 2.93 (2.69, 3.19) in the PsO and EAIR (95% CI): 3.84 (2.67, 5.34) and 5.65 (4.21, 7.43) in the HS subset. EAIRs/100 PYs for inflammatory bowel disease, malignancies, major adverse cardiovascular events, and suicidal ideation/behaviour remained low across both indications. The EAIRs/100 PYs for AEs of special interest are reported in **Table 1**.

Conclusion:

This pooled safety data analysis, based on 43 phase I/II/III/IV clinical trials, demonstrated that secukinumab is well tolerated in patients with PsO and HS. Comparison of EAIR between PsO and HS should be cautiously interpreted due to the differences in population size, doses and duration of exposure for the two indications.

Reference

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Table 1. Summary of safety data from secukinumab in clinical trials (entire treatment period)

Variables	PsO Any secukinumab N = 12,782	HS Any secukinumab N = 1060
Exposure (days), mean (SD)	543.9 (508.96)	319.3 (90.54)
Exposure (days), median (min–max)	365.0 (1–2471)	364.0 (3–520)
Patient years	19,032.7	926.5
Death, n (%)	19 (0.15)	2 (0.19)
EAIR/100 PYs (95% CI)		
Any AE	224.00 (219.73, 228.34)	284.33 (265.78, 303.83)
Any serious AE	7.35 (6.96, 7.76)	9.17 (7.29, 11.38)
Most common AEs, EAIR (95% CI)		
Nasopharyngitis	22.23 (21.47, 23.01)	14.39 (11.95, 17.19)
Upper respiratory tract infections	6.11 (5.75, 6.49)	6.28 (4.75, 8.16)
Headache	7.42 (7.02, 7.84)	19.71 (16.78, 23.00)
Arthralgia	5.77 (5.42, 6.13)	4.75 (3.44, 6.40)
Diarrhoea	4.58 (4.27, 4.91)	8.41 (6.60, 10.56)
AEs of special interest, EAIR (95% CI)		
Serious infections and infestations[1]	1.52 (1.35, 1.71)	3.84 (2.67, 5.34)
Opportunistic infections[2]	0.18 (0.12, 0.25)	0.32 (0.07, 0.95)
Tuberculosis-related events[3]	0.04 (0.02, 0.08)	0.32 (0.07, 0.95)
Neutropenia[3]	0.86 (0.73, 1.00)	0.98 (0.45, 1.86)
IBD[3]		
IBD	0.01 (0.00, 0.04)	0.11 (0.00, 0.60)
Crohn's disease	0.09 (0.05, 0.14)	0.11 (0.00, 0.60)
Ulcerative colitis	0.12 (0.08, 0.18)	0.11 (0.00, 0.60)
MACE[3]	0.40 (0.31, 0.50)	0.22 (0.03, 0.78)
Candida infections[4]	2.93 (2.69, 3.19)	5.65 (4.21, 7.43)
Injection-site reactions[4]	1.63 (1.45, 1.82)	2.19 (1.34, 3.39)
Suicidal ideation/behaviour[5]		
Suicidal ideation	0.04 (0.02, 0.08)	0.22 (0.03, 0.78)
Suicide attempt	0.03 (0.01, 0.07)	0.11 (0.00, 0.60)
Completed suicide	0.01 (0.00, 0.04)	-
Malignancy[5]*	0.84 (0.72, 0.98)	0.43 (0.12,1.11)

*Malignancy: Malignant or unspecified tumours. [1]Rates for SOC; [2]Rates for CMQ; [3]Rates for MedDRA Query term for the analysis; [4]Rates for MedDRA HLT; [5]Rates for SMQ.

PTs included in:

a) Opportunistic infections - Aspergillus infection, bronchopulmonary aspergillosis, atypical mycobacterial infection, atypical mycobacterial pneumonia, mycobacterial infection, *Mycobacterium avium* complex infection, *Mycobacterium ulcerans* infection, *Candida* sepsis, gastrointestinal candidiasis, mucocutaneous candidiasis, oesophageal candidiasis, peritoneal candidiasis, systemic candidiasis, coccidioidomycosis, cryptococcosis, cytomegalovirus colitis, cytomegalovirus gastritis, cytomegalovirus hepatitis, *Trichosporon* infection, herpes simplex encephalitis, herpes simplex pharyngitis, herpes zoster cutaneous disseminated, herpes zoster meningitis, herpes zoster meningoencephalitis, meningoencephalitis herpetic, varicella zoster pneumonia, histoplasmosis, histoplasmosis cutaneous, opportunistic infection, isosporiasis, leishmaniasis, *Pneumocystis jirovecii* pneumonia, progressive multifocal leukoencephalopathy, pneumonia respiratory syncytial viral, respiratory syncytial virus bronchitis, respiratory syncytial virus infection, toxoplasmosis, bone tuberculosis, disseminated tuberculosis, intestinal tuberculosis, lupus vulgaris, lymph node tuberculosis, peritoneal tuberculosis, tuberculosis, tuberculosis gastrointestinal, tuberculous pleurisy.

b) Tuberculosis-related events - Joint tuberculosis, latent tuberculosis, Mycobacterium tuberculosis complex test positive, pulmonary tuberculosis, Mycobacterium test positive, and tuberculosis.

c) Neutropenia - Neutropenia, leukopenia, neutrophil count decreased, white blood cell count decreased, granulocytopenia, agranulocytosis, febrile neutropenia, neutropenic colitis.

d) *Candida* infections - Oral candidiasis, vulvovaginal candidiasis, *Candida* infection, skin candida, oesophageal candidiasis, genital candidiasis, balanitis candida, oropharyngeal candidiasis, gastrointestinal candidiasis, anal candidiasis, mucocutaneous candidiasis, nail candida, otitis externa candida, respiratory moniliasis and urinary tract candidiasis.

e) IBD - Ulcerative colitis, Crohn's disease, haemorrhagic diarrhoea, perirectal abscess, ulcerative proctitis and inflammatory bowel disease.

f) MACE - Myocardial infarction, stroke and cardiovascular death.

g) Malignancy - Basal cell carcinoma, squamous cell carcinoma, Bowen's disease, malignant melanoma in situ, malignant melanoma, breast cancer, prostate cancer, bladder cancer, keratoacanthoma, thyroid cancer, adenocarcinoma of colon, colon cancer, bladder transitional cell carcinoma, cutaneous T-cell lymphoma, anal fistula, anal fistula infection, cholangitis sclerosing, colitis erosive, intestinal pseudo-obstruction, pouchitis.

AE, adverse events; CI, confidence interval; CMQ, Customised MedDRA Query term; EAIR, exposure-adjusted incidence rate per 100 patient-years; HLT, high-level term; HS, hidradenitis suppurativa; IBD, inflammatory bowel disease; MACE, major adverse cardiovascular events; N, number of patients in the analysis; n, number of patients with a response; PsO, psoriasis; PT, preferred term; PY, patient-years; SD, standard deviation; SOC, system organ class; SMQ, standardised MedDRA query term.

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Abstract N°: 6778

Reassessing Sunscreen Efficacy: A Review of its Role in Skin Cancer Prevention and Low- and Middle-Income Countries

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Introduction & Objectives:

Sunscreen application is widely recommended as a primary measure for skin protection against harmful UV radiation. However, doubts regarding its efficacy in the general population have been raised by epidemiological studies. Our study aims to evaluate the association between sunscreen use and the risk of skin cancer.

Materials & Methods:

A comprehensive search strategy was employed to identify relevant studies in major databases. Studies examining the relationship between sunscreen use and skin cancer risk were included. Data extraction and analysis were conducted following with Keywords like: “Skin Cancer”, “Sunscreen” “Ealry Prevention”, and “Skin CancerAwareness” in research databases like: PUBMED, SCOPUS, MEDLINE, GOOGLE SCHOLAR.

Results:

Sunscreen application, along with protective clothing and seeking shade, is commonly employed as a preventive strategy against skin cancer and photoaging caused by excessive sun exposure. UV radiation comprises two types of rays: UVA and UVB, with distinct wavelengths and effects on the skin. While UVB primarily damages the DNA in the outer layers of the skin, leading to sunburn, UVA penetrates deeper into the dermis, causing minor damage such as tanning and wrinkles, as well as DNA mutations linked to cancer. Sunscreen formulations typically contain UV filters categorized as mineral (physical) or organic (chemical) filters. Physical filters, such as titanium dioxide (TiO2) and zinc oxide (ZnO), create a physical barrier on the skin to reflect UV rays, blocking approximately 5% of UV radiation while absorbing the remaining 95%.

Conclusion:

Despite the widespread recommendation for sunscreen use, particularly in low- and middle-income countries (LMICs), limited awareness about skin cancer persists due to inadequate knowledge and information dissemination in these regions. UV radiation is recognized as a significant environmental factor influencing human health, with even short exposures leading to extensive genome damage, while chronic exposure results in a high mutation burden in the skin.

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Abstract N°: 6820

Revealing patient characteristics and treatment outcomes in ultra-long biologic users for psoriasis.

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Introduction & Objectives:

Biologics are effective for psoriasis, but little is known regarding patients treated with one biologic for an "ultra-long" duration. Therefore, the aim of this study was to explore the prevalence, patient and treatment characteristics and treatment outcomes of "ultra-long users" of biologics for psoriasis.

Materials & Methods:

From the prospective, multicenter BioCAPTURE cohort, patients with psoriasis who received continuous treatment with the same biologic for ≥10 years were included. Baseline characteristics of these "ultra-long users" were determined and compared to the total BioCAPTURE population. Additionally, the frequency of concomitant systemic treatment use and dose adjustments administered, the trajectory of Psoriasis Area and Severity Index (PASI) scores, and drug survival rates beyond 10 years were analyzed.

Results:

In BioCAPTURE, 30.5% of the patients with the potential to reach a treatment episode of ≥10 years, actually achieved this treatment duration. These patients were treated with ustekinumab, etanercept, adalimumab and infliximab. The proportion of ultra-long users was highest for ustekinumab (37%). Ultra-long users had a longer disease duration and were diagnosed more often with psoriatic arthritis compared to the total BioCAPTURE population. A large percentage of ultra-long users (69.5%) had ≥1 comorbidities and 66% used no additional

systemic antipsoriatic therapy. Dose adjustments were often applied, varying from dose escalation (30%), to dose reduction (41%), or both (14%); only 16% consistently used the standard dose. The median PASI course for ultra-long users from month 6 onwards was continuously <3, with only a small proportion achieving complete clearance of their psoriasis (3.9-13.7% at the various time points). Drug survival beyond 10 years showed that >60% of this group was still treated with the same biologic after 15 years.

Conclusion:

Ultra-long use of the same biologic in patients with psoriasis was common in real-world practice, but varied between biologics. The median PASI around 2.5 throughout the 10 years treatment indicates that this value was an acceptable measure for patients and treating physicians. Remarkably, ultra-long use was reached also in patients having multiple comorbidities (including PsA) and a variety of dose adjustments of the biologics was applied. These results potentially assist in the decision-making regarding treatment choice, continuation and modification of biologics for psoriasis.

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Abstract N°: 6823

Treatment with tildrakizumab of hidradenitis and Fournier's gangrene triggered By multikinase inhibitors, in a male patient with metastatic hepatocellular carcinoma

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Introduction & Objectives:

Introduction & Objectives:

52 years old male patient with grade IV hepatocarcinoma and hepatitis B, treated with sorafenib. During the treatment, he suffered several adverse events including total corporal alopecia areata, Hurley grade III, suppurative hidradenitis and Fournier gangrene. Due to this last life-threatening adverse event (which appeared 10 months after introducing this drug), sorafenib was switched for lenvatinib while apremilast was also initiated without response in controlling cutaneous symptoms, so it was replaced by tildrakizumab 100 mg. During therapy with this anti-IL23, corporal hair was fully recovered, and both, suppurative hidradenitis and Fournier gangrene, were placed under control. Subsequently, tildrakizumab 100 mg was discontinued but a new Fournier gangrene episode occurred 6 months later. Then, tildrakizumab 100 mg was restarted and levantinib was stopped 4 months due to the progression of the liver disease. Afterwards, It was decided to initiate with 2 new drugs for liver disease and after 6 months without hidradenitis suppurative lesions or Fournier gangrene episodes, tildrakizumab is discontinued again. Currently, patient shows no signs or symptoms of hidradenitis suppurative lesions or Fournier gangrene episodes and either psoriasis and liver disease are both stable.

Conclusion:

This poster highlights the importance of being aware of the side effects of new oncological therapies. The sequential appearance of the 3 side effects and the fact that they disappeared after the discontinuation of the therapy with pd1-p21 and multikinase inhibitors seem to indicate a causal relationship.

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Abstract N°: 6995

Interlukin-17 inhibitor in Congenital Erythrokeratodermia Cardiomyopathy Syndrome

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Introduction & Objectives:

Desmoplakin (DSP) is the most abundant desmosomal protein and mainly found in tissues exposed to mechanical stress, such as the epidermis and heart. Erythrokeratodermia cardiomyopathy (EKC) syndrome is a rare congenital disorder caused by *DSP* mutation, which is characterized by woolly hair, ichthyosis, generalized erythrokeratodermia, failure to thrive, dental abnormalities, and dilated cardiomyopathy (OMIM 615821). It may be fatal in early childhood without prompt intervention. Here we report a case of EKC patient carrying a new mutation who responded well to interleukin- 17 inhibitor.

Materials & Methods:

We collected clinical photos and examination data of the children, as well as skin tissue specimens before and after treatment and performed H&E and immunofluorescence staining.

Results:

A 13-year-old Asian girl was referred to our department because of generalized erythroderma. She has had recurrent erythema, scales, and pustules since she was 1 year old, which improved after systemic administration of corticosteroids, methotrexate, or acitretin. At the age of 12, she was diagnosed with dilated cardiomyopathy, heart failure, and arrhythmias, and her heart function continued to deteriorate to the point where he needed to consider a heart transplant. When she come to us, a complete blood count revealed mild leukocytosis and neutrophilia, CT scan showed a marked enlargement of the cardiac silhouette. Skin histopathology showed parakeratosis and epidermal hyperplasia. During hospitalization, generalized pustules relapsed with transient fever. Generalized pustules psoriasis was diagnosed at first, and anti-interleukin-17 monoclonal antibody was administrated every four weeks after the guardian's consent. She was discharged with marked improvement in skin lesions. The progressive development of woolly hairs during follow-up prompted us to search for alternative diagnoses. Whole exome sequencing uncovered a heterozygous *de novo DSP* mutation c.1843G>C, which has never been reported before. Based on genetic testing and clinical manifestations, we revised the diagnosis to EKC syndrome. Skin lesions almost completely resolved after 10 months of treatment with no adverse events. Surprisingly, cardiac function continued to improve, with ejection fraction increased from 25% to 45%. In addition, DSP expression in epidermal was significantly upregulated compared with baseline.

Conclusion:

We reporte a new mutation in EKC syndrome. Our patient's lesions and cardiac function were significantly improved after treatment with interleukin-17 inhibitor. The partial recovery of DSP expression after interleukin-17 inhibitor indicated anti-inflammatory treatment may play a pivotal role in the recovery of skin barrier dysfunction and cardiac function. This case also provides new treatment option for EKC patients.

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Abstract N°: 6998

One Step Forward, Two Steps Back: Case series of anti-TNF paradoxical reactions

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Introduction & Objectives:

Anti-TNF agents represent a major breakthrough in the management of inflammatory diseases. Among the side effects of these agents are the so-called paradoxical effects. They represent new onset or exacerbation of a condition (symptom/disease), usually improved with TNF blockers. These paradoxical effects are mainly psoriasiform skin reactions, uveitis and granulomatous diseases. Infrequent and probably underreported, herein we report a case series of female patients undergoing anti-TNF treatment presenting with paradoxical reactions.

Materials & Methods:

Case 1: Pyoderma gangrenosum in a patient with seronegative rheumatoid arthritis under anti-TNF.

Case 2: Pustular psoriasis in a patient with psoriatic arthritis under anti-TNF treatment.

Case 3: Panniculitis due to adalimumab for psoriatic arthritis, in a patient treated with anti-TNF.

Results:

Case 1: Pyoderma gangrenosum in a female patient with seronegative rheumatoid arthritis, was treated with Guzelkumab and topical therapies.

Case 2: Pustular psoriasis in a female patient with psoriatic arthritis was initially treated with acitretin and strong potency topical corticosteroids. The biologic used upon regression of the lesions was Ixekizumab without further complications.

Case 3: Panniculitis due to adalimumab for psoriatic arthritis in a female patient was handled with conticosteroids and biologic switch to brodalumab.

Conclusion: The causal mechanism of occurrence is still a matter of debate, but may implicate an imbalance of cytokines toward interferons, chemokines and probably IL-17. These reactions may raise differential diagnosis problems. Symptoms resolve, most of the time, due to the discontinuation of the anti-TNF agent; but in some cases, it is a biologic class switch effect that could lead to the withdrawal of anti-TNF agents and paradoxical effects.

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Abstract N°: 7087

Clinical observation of ofatumumab for the treatment of pemphigus vulgaris: A single-center cohort study

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Introduction & Objectives:

The therapeutic strategy for the treatment of pemphigus vulgaris (PV) needs optimization because of the deficiencies of glucocorticoid and rituximab. Ofatumumab, a fully human anti-CD20 monoclonal antibody administered subcutaneously, may provide a convenient and safe option for PV treatment. This study aims to evaluate the effectiveness of ofatumumab in patients with PV, while observing the severe adverse reactions.

Materials & Methods:

This is a cohort study. After strict screening and signing informed consent, eligible PV patients received ofatumumab subcutaneous injection (20mg twice, 2 weeks apart), in addition to glucocorticoids tapering dependent on the disease conditions. The control group were generated using propensity score matching (PSM) in a 1:2 ratio from patients treated with glucocorticoids alone or combined with traditional immunosuppressants with critical data. The primary end point was prednisone dosages tapering to 0.2mg/kg/d at month 6. Secondary end points were pemphigus disease area index (PDAI) activity score and its change percentage at month 6.

Results:

Twenty-two patients received ofatumumab and PSM was performed based on gender, age, BMI, severity, and disease duration, and 44 matched patients were included in the control group. The PDAI activity scores at baseline were 22.5±14 in the ofatumumab group and 22.3±14.1 in the control group (p=0.815). The initial prednisone dosage was 41.4±16 mg/d in the ofatumumab group versus 36.8±16.3 mg/d in the control group. At month 6, there were no significant difference in the proportion of patients achieving lesions clear-up (PDAI scored 0) between two groups, while 10 of 22 (45.5%) patients in the ofatumumab group achieved the treating goal of prednisone dosages lower than 0.2 mg/kg/d, versus 7 of 44 (15.9%) in the control group (p=0.010). The PDAI change percentage was 92% in ofatumumab group and 84% in control group (p=0.247). Notably, at month 1, the PDAI activity score declined more significantly in ofatumumab group (Figure 1). No serious adverse reaction was observed in ofatumumab group.

Conclusion:

At month 6, there were significantly higher proportion of patients who received a maintaining dosage of 0.2mg/kg/d than the control group with similar treating outcomes between the two groups. The application of ofatumumab (20mg twice, 2 weeks apart) may facilitate early recovery of lesions in patients with PV and rapid reduction of prednisone dosages. Further studies are needed to evaluate its effectiveness in producing complete remission and explore the regimen in patients with different clinical characteristics.

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Abstract N°: 7130

JAK1 inhibitors: A promising option for patients with autoimmune skin diseases

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Introduction & Objectives:

Introduction: Autoimmune skin diseases are refractory types of dermatology, such as pemphigoid, pemphigus, lupus erythematosus and lichen planus. Patients with such disorders often require long-term oral glucocorticoids therapy, which could be accompanied by poor response and complications. The Janus kinase (JAK)-signal transducers and activators of transcription (STAT) signaling pathway is stimulated by cytokines and involved in many important biological reactions, such as cell proliferation, differentiation, apoptosis, and immune regulation. JAK1 inhibitors have been used in the treatment of a variety of inflammatory skin diseases, such as atopic dermatitis and psoriatic arthritis. The development of autoimmune skin diseases also involves the JAK1 signaling pathway.

Objective: To observe the efficacy and safety of the JAK1 inhibitors in the treatment of autoimmune skin diseases.

Materials & Methods:

Seven Chinese patients were treated with the oral selective JAK-1 inhibitor (abrocitinib or upadacitinib), with a good safety profile, for pemphigus(n=2), pemphigoid with psoriasis (n=1), systemic lupus erythematosus(n=2), Behcet's disease (n=1), and lichen planus(n=1) respectively.

Results:

In patients with pemphigus, the lesions of the trunk and limbs were significantly improved after two weeks of treatment, and the lesions of the head and mucosa were significantly improved after 4 weeks. In the pemphigoid patient with psoriasis, the lesions of the trunk and limbs were significantly improved after one week of treatment, and the facial lesions were significantly improved after three weeks. Mucocutaneous lesions and joint pain in patients with systemic lupus erythematosus improved significantly after 2 weeks of treatment. The lesions in patients with lichen planus improved significantly after 2 weeks of treatment. In the patient with Behcet's disease, there was significant improvement in limb lesions after two weeks of treatment and in mucous lesions after four weeks.

After 2 weeks of treatment, the lesions improved significantly in all cases. The patients did not report discomfort during treatment, and no adverse effects were observed. Except for one pemphigus patient who developed folliculitis, the other patients did not report discomfort during treatment and no adverse effects were observed.

Conclusion:

The JAK1 inhibitors are promising potential therapeutic agents for autoimmune skin diseases, with the favorable safety profiles.

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Abstract N°: 7165

Switching to an Adalimumab Biosilimar: Real-World Evidence from Saudi Arabia

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Introduction & Objectives:

Biosimilars (BSMs) are becoming increasingly relevant in dermatology. The introduction of BSMs to medical care has classically faced barriers and been met with apprehension. Many RCTs on BSMs have been published. However, studies on the outcome of switching to monoclonal-antibody (Mab) - BSMs in Saudi Arabia (KSA) and Arab countries are still completely lacking. In the latter half of 2022, the Saudi Ministry of Health (MOH) enforced a mandatory switch of all patients (PTs) on adalimumab (ADA) originator (ORG) to a ADA-BSM (Code: GP2017). ADA is approved by the Saudi FDA for moderate-severe plaque psoriasis (PSO) with/-out arthritis (PsA) and hidradenitis suppurativa (HS).

Objectives:

- To describe the characteristics of the ADA PTs cohort in a dermatology department in KSA including those who were switched to ADA-BSM.
- To report the reasons for discontinuation (D/C) after switching to ADA-BSM.
- To analyse the impact of mandatory switching to ADA-BSM on efficacy & drug survival.

Materials & Methods:

This is a retrospective, single-center study. Medical Records and ADA request records for the period between Jun 2022 and Aug 2023 were reviewed. 94 saudi PTs were either already on, or were started on ADA for approved dermatological indications. Four PTs, were excluded, due to lack of documented response and loss of follow-up. For the remaining 90 PTs, data on demographics, indication, prior treatments, level of primary response, reasons for pausing or discontinuing ADA were collected until Oct 2023.

Results:

23% of PTs had HS, whereas 65% had PSO, with an additional 12% having PSO/PsA. The majority (90%) of patients were bio-naive. The peak dermatological response across all skin conditions was clustered into 4 categories (complete clinical response 39 %, Minimal Disease Activity 34 %, Partial Response 26%, No Response 1%) with significantly more partial responders in the HS subgroup (43%, $P<0.01$). (Fig. 1) Until Oct 2023, 16 PTs were taken off ADA, either temporarly (=3) or permanently (=13). All 16 PTs had PSO with 2 PTs also suffering from PsA. No HS patients have been taken off ADA-BSM in this period. Reasons for D/C included loss of follow-up, primary irresponsiveness, secondary loss of response (=3, all had partial peak response), temporary pause in therapy excluding side effects, and unavailabilty (Fig. 2). 2 out 3 primary non-responders have lacked response ADA-ORG before being switched to ADA-BSM. Out 5 PTs who lost follow-up, 4 had complete or almost complete clinical response at their last visit. Adverse drug reactions leading to ADA D/C have not been detected in our cohort.

Conclusion:

The overwhelming majority of PTs experienced continued response and drug survival after switching. Interestingly, all 3 secondary non-responders (3.3%) had declining response to ADA-ORG prior to switching. Despite higher rates of partial response, HS PTs receiving ADA were kept on ADA, largely due to lack of approvals for other biologics in KSA during the study period. To our knowledge, this is first study to provides real-world evidence on the outcome of switching to a Mab-BSM in an Arab country. In conclusion, our study suggests that switching to ADA-BSM in Arab countries can safely and successfully with significant cost reduction for the public sector. Larger, detailed studies are required to study the effects on regional and country levels.

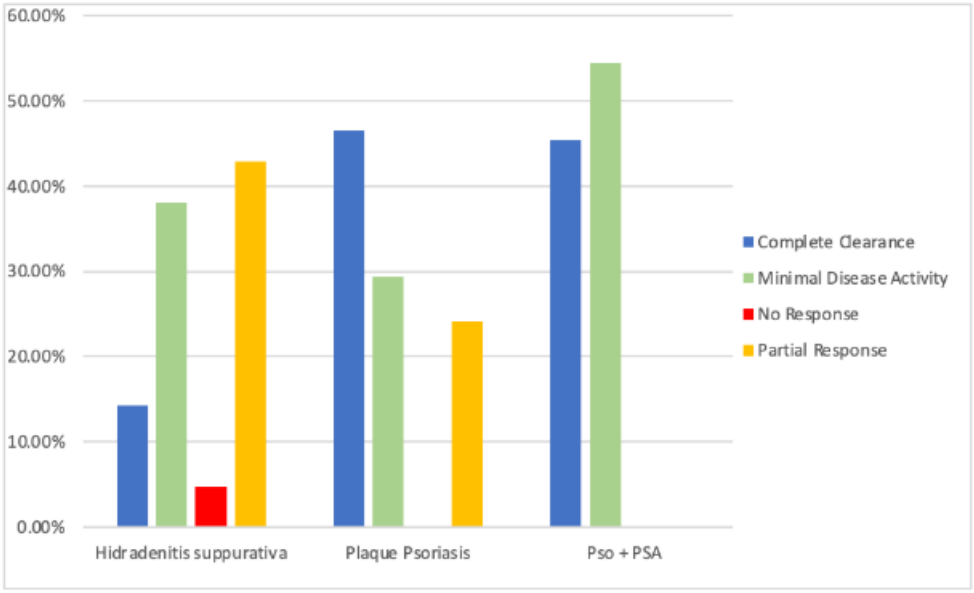

Figure 1: clustered-response rates to ADA for each diagnosis

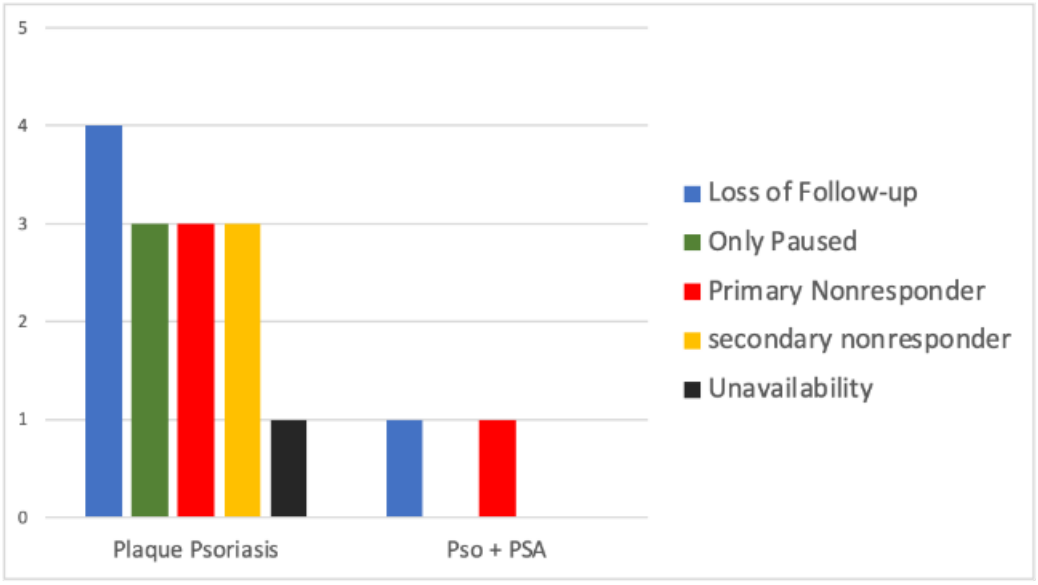

Figure 2: Reasons for D/C of ADA-BSM for PSO and PSO with PsA

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Abstract N°: 7216

A paradoxical psoriasis and pyoderma gangrenosum development after the treatment of ankylosing spondylitis with Certolizumab

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Introduction & Objectives: A 52-year-old female patient admitted to our clinic with complaints of open wounds in the left pretibial area . She also had circumscribed, psoriasiform lesions in various parts of the body for 2 months. Areas with a mild plaque style and desquamation appearance with psoriasis were detected also on the scalp. She stated that systemic and oral antibiotic treatment from various doctors for the open wound area in pretibial area were prescribed before and topical antifungal creams were used.

Her clinical history included left nephrectomy ,ankylosing spondylitis and hypertension. There was a history of using methotrexate and certalizumab treatments for ankylosing spodilitis. No bacterial colonisation was detected in the wound microbial culture.

Materials & Methods: Skin biopsies were obtained from the patient's complaint areas.

In biopsy taken from the margin of wound, inflammatory cells rich in PNLs were detected in the dermis. No microorganism was detected in specific staining with PAS. The patology was reported as sterile dermal abscess. This lesion was diagnosed as pyoderma gangrenosum.

During this period, the patient was prescribed 0.5 mg / kg methylprednisolone, topical steroid and antibiotic combined creams for the wound area with the pre-diagnosis of pyoderma gangrenosum. Topical steroids were added to the hair, hand-foot and other lesions. Topical antifungal therapy was stopped.

For the pyoderma gangrenosum lesion on the left pretibial region Intravenous immunoglobulin therapy was planned. Intravenous immune globulin (IVIG) was administered for 2 months. The pyodermic area in the patient's lower knee area regressed. Since resolution occured and didn't flare up again in the follow-up IVIG and the systemic steroid was stopped.

However, during this period, the psoriasiform lesions on the hands, sides of the feet and scalp did not regress. Skin biopsy taken from this area was reported as minimal mononuclear inflammatory cell infiltration, superficial hyper-parakeratosis, spongiosis . This lesions were diagnosed as psoriasis with the clinical and pathological clues.

The patient's psoriasiform lesions were resistant to topical steroids. She had hypertensive condition. Her lesions were refractory to the current methotrexate treatment. She had increased liver function tests in his last examinations. She was switched from certalizumab pegol treatment to secukinumab treatment as a biological treatment for psoriasiform lesions. **

Results: The exacerbation of the patient's lesions stopped and improvement was achieved with treatment.

IVIG treatment in pyoderma gangrenosum is used as an effective treatment in cases where systemic steroids and other immunosuppressant drugs are unresponsive or contraindicated.

Considering the possible development of paradoxical psoriasis after certolizumab pegol switching of treatment agent with secukinumab was preffered for the patient. The possible reason of development of

psoriasis can be the reduction of TNFα during anti-TNF treatment and its decreased suppressive effect on IFNγ

Conclusion: It can be evaluated that the effective use of new generation of systemic therapies would be beneficial in the treatment of multiple isochronous systemic diseases.

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Abstract N°: 7226

Pemphigus Vulgaris Treatment in Chronic Renal Failure Patient with Intravenous Immunoglobulin (IVIG).

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Introduction & Objectives:

A 60-year-old woman presented to our outpatient clinic with a complaint of widespread rash on the body. Dermatological examination revealed generalized eroded bullae on the erythematous background. She was diagnosed with end-stage chronic renal failure(CRF) due to infection secondary to recurrent nephrolithiasis, hyperlipidemia and diabetes mellitus. She was receiving hemodialysis 3 days a week due to CRF. The patient has been using Calcitriol, Escitalopram, Insulin glargine, Calcium carbonate and Atorvastatin.

In the anamnesis, it was reported that she had been followed up from an external center for 3 months and the previous biopsy and DIF findings were compatible with pemphigus vulgaris. She was followed up with topical corticosteroids but there was progression in the symptoms. The patient was hospitalized and a blood sample was sent for an indirect immunofluorescent (IIF) test. During hospitalization, considering the patient's known comorbid diseases and on-going hemodialysis, 16 mg prednisone low dose oral and topical sodium fusidate 20 mg/day for the whole body were started. When the patient's IIF result was positive at 1/200 and decreasing titers, disease activation was evaluated as high. The regression of the patient's complaints with low dosage prednisone treatment was insufficient and high doses of long-term prednisone treatment could not be given in our patient. For adjuvant treatment, mycophenolate mofetil or azathioprine was not evaluated as an option due to chronic renal failure. In addition, rituximab was not considered in our patient due to a history of recurrent infections leading to CRF and higher rates of opportunistic infections with rituximab. The patient was started on 2 gram/kg/day Intravenous Immunoglobulin (IVIG) treatment and the infusion divided into 10 days instead of 5 days.

Materials & Methods:

-

Results:

The patient's complaints completely regressed with IVIG treatment and has been followed-up without any symptoms.

Conclusion:

IVIG is preferred as a safe and effective treatment modality in patients with pemphigus vulgaris with multiple comorbidities, end-stage chronic renal failure, and high risk of opportunistic infection. Since the high weight molecules in IVIG therapy can affect renal functions, we believe that a slower and longer IVIG infusion may be a protective strategic method in CRF and pemphigus vulgaris patients.

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Abstract N°: 7320

Optimization of Treatment for Plaque Psoriasis Patients with Secondary Loss of Response to Secukinumab

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Optimization of Treatment for Plaque Psoriasis Patients with Secondary Loss of Response to Secukinumab

Introduction & Objectives:

Secukinumab is known for its efficacy and safety in treating moderate-to-severe plaque psoriasis. However, some patients experience a secondary loss of response to the standard dosage (300 mg every 4 weeks), leading to recurring rashes during stable treatment. The causes of this diminished response are unclear but may include insufficient dosage or decreased drug sensitivity. Treatment optimization through off-label dose escalation, such as shortening the dosing interval, could provide benefits, though there is limited empirical evidence.

This work focus on investigating the potential causes of secondary loss of response to secukinumab and evaluate the efficacy and safety of shortening the dosing interval to 300 mg every 2 weeks in patients with a secondary loss of response.

Materials & Methods:

1. We enroll 22 patients with moderate-to-severe plaque psoriasis who experienced a secondary loss of response to secukinumab. As a control group, 66 patients who met treatment targets of secukinumab were matched in a 1:3 ratio. We then collected possible factors related to the secondary loss of response, including
2. Triggering factors: Obesity, smoking, alcohol consumption, fatigue, infections, stress, etc.;
3. Disease characteristics: Special types of psoriasis, such as involvement of hard-to-treat areas (e.g., scalp, palms, soles, nails, genitals), joint involvement, and seasonal patterns.
4. Treatment habits: Early intervention, irregular use of secukinumab, and previous treatment history.

All patients underwent at least 16 weeks of secukinumab treatment. A secondary loss of response was defined as a relapse after achieving PASI 75 or BSA <3 and IGA 0/1, where the condition worsened (with a loss of PASI 75 or a rise to BSA ≥3 and IGA ≥2). In contrast, those with current PASI <3 or IGA 0/1 were considered reaching the treatment target.

1. The 22 patients with a secondary loss of response underwent 12 weeks of secukinumab treatment at 300 mg every 2 weeks. Efficacy and safety outcomes were recorded and analyzed.

Results:

\1. Patients who experienced a secondary loss of response showed higher rates of extended dosing intervals (40.1% vs. 6%; $p < 0.05$), fatigue (27.3% vs. 12.1%; $p < 0.05$), and involvement of special areas (59.1% vs. 41%; $p < 0.05$), compared to the control group. The loss-of-response group also had higher BMI (27.5 vs. 26.3), but the difference was not statistically significant.

\2. After 12 weeks, 19 of the 22 patients (86.4%) achieved PASI <3 with IGA 0/1, with 3 patients (13.6%) achieving complete clearance of skin lesions. The average DLQI at 12 weeks was 2.6. Only one patient experienced a generalized rash 4 weeks after shortening the dosing interval, leading to treatment discontinuation. No adverse

reactions were reported from other patients.

Conclusion:

Irregular use of secukinumab, particularly extending the dosing interval, along with fatigue, special area involvement, and obesity, are potential causes of the secondary loss of response to secukinumab. Reducing the dosing interval to 300 mg every 2 weeks demonstrates promising short-term efficacy and safety for patients experiencing secondary loss of response. Clinicians may consider this approach before discontinuing secukinumab or switching to other biologics when faced with similar cases in practice.

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Abstract N°: 7424

Lichen planus pemphigoides and dupilumab: efficacy and safety up to 28 weeks

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Introduction & Objectives: Lichen planus pemphigoides (LPP) is a rare autoimmune disease characterized by the presence of both lichen planus (LP) and bullae or blisters. The pathogenesis involves autoantibodies against different epitopes of type XVII collagen, while diagnosis is based on the clinical examination and immunopathological features. Treatment lacks standardization and corticosteroids, dapsone and acitretin represent the most used first-line therapies . Off-label use of immunomodulators has been proposed for refractory cases, with two LPP cases treated with dupilumab that have been reported in literature, yet without any evidence of long-term responses.

Materials & Methods: A 54-year-old female presented to our department with a 3-year history of violaceous plaques with polygonal configuration and bullae of the face, neck and upper arms associated with severe itching and worsened by sun exposure. A biopsy performed at on the right ventral wrist showed linear disposition pattern of IgG in the basement membrane zone, necrosis in basal keratinocytes and dense lichenoid lymphocytic infiltrate, that led to a diagnosis of lichen pemphigoid. The patient, due to her marked request of a non-steroidal systemic treatment, was initially treated with dapsone 100mg/day and then with methotrexate 15 mg/week and folic acid 5mg/week, with mild control of itch but continuous onset of new cutaneous lesions.

Results: In consideration of the medical history and poor response to previous treatments, off-label subcutaneous injections of dupilumab 300 mg (2 vials at time 0, then 1 vial every 2 weeks) were introduced. Concomitant topical Clobetasol was prescribed and daily Sun Protection Factor (SPF) 50+ was recommended. Baseline total IgE were elevated (1093 kU/L); at week (W) 0 the itch measured through the Numerical Rating Scale (NRS) was 9/10 and the sleep itch was 8/10, which decreased at W4 to 6/10 (-33%) and 8/10 (-11%), respectively. At W12 the itch decreased to 3/10 (-66%) and sleep itch was normalized to 0/10 (100% of improvement), with the same results maintained during the last visit performed at W28. Quality of life measured through the Dermatology Life Quality Index (DLQI) moved from 24/30 at W0 to 15/30 at W4 (-30%), 11/30 at W12 (-43%) and 8/30 at W28 (-53%). Moreover, a progressive improvement of skin lesions in terms of new bullae was registered, with sporadic remaining plaques on the wrists and legs. No side effects were reported during the observation period.

Conclusion: LPP is an autoimmune condition whose optimized therapy algorithm still needs to be established. Dupilumab, binding the alpha subunit of the IL-4 receptor, results in downregulating the IL-4 and IL-13 cytokine pathways. LPP pathogenesis linked to auto-antibodies against BP180 NC16A would be sustained by a dysregulation of type 2 inflammation, leading to a favorable response in the case of the resulting Th2 inhibition. Long-term use of dupilumab has been validated in conditions clinically closed to LPP such as bullous pemphigoid (BP) and LP, but the experience on LPP is limited to 15 weeks of treatment. Our clinical evidence suggested that dupilumab would be an efficacy and safe strategy up to 28 weeks to treat recalcitrant cases of LPP, with further studies on this issue that will be necessary to corroborate our preliminary findings.

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Abstract N°: 7479

Tumor necrosis factor-alpha inhibitor-associated psoriatic alopecia and palmoplantar pustulosis in a patient with ulcerative colitis

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Introduction & Objectives:

Tumor necrosis factor-alpha inhibitors (TNFis) are used to treat multiple inflammatory diseases including inflammatory bowel disease, rheumatoid arthritis, and psoriasis, among others. This family of medications can cause various side effects, some as common as injection-site reactions and others as rare as the paradoxical induction of psoriasiform skin lesions. Paradoxical reactions can be defined as the appearance or exacerbation during treatment with a biologic agent of a pathological condition that usually responds to this class of drug. Paradoxical reactions in patients treated with TNFis have an estimated prevalence of 1.5% to 5%. Such reactions usually present as psoriasiform eruptions on the trunk and extremities along with flexural and palmoplantar involvement (palmoplantar pustulosis). When affecting the scalp, new-onset psoriasis induced by TNFi can result in non-scarring or scarring alopecia. Although the paradoxical reaction was first reported in 2003, this TNFi-associated psoriatic alopecia (TiAPA) has been recently reported with increasing frequency. Close surveillance of patients treated with newly available biologic drugs is necessary to detect new and undescribed paradoxical reactions.

Materials & Methods:

Case report

Results:

Case report

Conclusion:

We report a 29-year-old woman who developed TiAPA and palmoplantar pustulosis after 6 months of treatment with infliximab for ulcerative colitis. Patient was switched out of class to ustekinumab after discontinuation of infliximab. Treatment was escalated with the addition of UVB phototherapy and topical therapy (calcipotriol/betamethasone dipropionate foam, emollient and keratolytic agent – urea). The patient's TNFis-induced skin lesions completely resolved within 6 months of initiating this treatment regimen.

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Abstract N°: 7489

Analysis of survival data of 225 patients treated with BRAF-MEK inhibitors as a function of dose reductions during therapy

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Introduction & Objectives: In 2015, 2 BRAF-MEK inhibitor combination therapies became available to delay resistance and prolong overall survival compared to monotherapy. However, in clinical trials dose reductions were used in 33% of patients due to side effects. Our objective was to assess the efficacy of BRAF-MEK inhibitor therapy in 225 patients between 2015 and 2022 as a function of dose reductions applied

Materials & Methods: 172 patients received Dabrafenib-trametinib and 53 patients received Vemurafenib-cobimetinib therapy at the Department of Dermato-Oncology of the National Institute of Oncology. Mutation analysis was performed with the cobas® BRAF V600 test at the Department of Molecular Pathology of the National Institute of Oncology, from primary tumours or metastases. Tumor control, therapeutic response was evaluated according to RECIST version 1.1. Kaplan-Meier analysis was used for statistical analysis of progression-free survival and overall survival significance was determined by log-rank test. Adverse events were classified according to CTCAE 4.03 terminology. Dose modification was performed according to the protocol.

Results: During dabrafenib-trametinib therapy, 37 patients (21%) required dose reduction. >Gr 3 adverse events were observed in 14.5% (n=25) of patients. Overall survival of dose-reduced patients showed significantly better survival in the group of dabrafenib-trametinib therapy by Kaplan-Meier analysis p=0.0028 (13 months vs 48 months). PFS showed weak significance p=0.0270 (9 months vs 16 months) with better median survival of dose-reduced patients.Dose reduction was used in addition to vemurafenib-cobimetinib in 19 patients (35.8%). When comparing patients who received dose reduction with patients who received full-dose vemurafenib-cobimetinib target therapy, no significant difference was found in overall survival (18 vs 29) P=0.3625 or progression-free survival P=0.3148 (14 vs 10). >Gr3 adverse events were detected in 35% of 19 patients.

Conclusion: Based on our results, we found a positive association between adverse events and efficacy using Kaplan-Meyer analysis in the group of patients receiving dabrafenib-trametinib therapy. Survival of dose-reduced patients in subgroup analyses has not been investigated in the literature, and no data on this in trials of registrational studies. Further analyses using multivariate statistical methods are needed to refine the results.

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Abstract N°: 7609

Is it a guideline or a rule? Comparing regional practices in atopic dermatitis & psoriasis management

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Is it a guideline or a rule? Comparing regional practices in atopic dermatitis & psoriasis management

Introduction & Objectives:

This multi-centre audit aims to determine key differences between biologic initiation in atopic dermatitis (AD) vs psoriasis patients between two large regional centres.

Materials & Methods:

We looked at 50 patients from each centre, drawn evenly between psoriasis and AD, selected from clinics in October 2023. We recorded demographics such as age and gender, history of prior conventional systemic treatments and UV phototherapy pre-biologics initiation, cumulative duration on conventional systemic medications before transitioning to biologic therapy, the last immunosuppressant preceding biologic introduction, rationale for cessation, the choice of first biologic, duration between discontinuation of conventional systemic therapy and initiation of first biologic, causes for any delays, EASI/PASI score when decision made to commence biologic and most recent EASI/PASI score.

Results:

Within Centre A, a tertiary eczema clinic, AD patients were on conventional systemic medications for an average of 2 years and 2 months. The average time taken to commence the biologic after their last systemic medication was 2.4 months. The average EASI prior to biologic initiation was 20.9, reducing to 5.82 in recent scores. For Centre B, a regional biologic clinic, AD patients were on conventional systemic medication for an average of 2 years and 6 months and time taken to commence the biologic after their last systemic medication was 3 months. The corresponding EASI scores were 23.61 and 2.25, respectively.

For psoriasis patients in Centre A, a tertiary psoriasis clinic, the average pre-biologic systemic medication duration was 4 years, with a 3 month interval from last conventional systemic to biologic initiation. Average PASI score was 14.3 prior to biologic initiation, reducing to 3.96 in recent scores. In Centre B, a regional biologic clinic, psoriasis patients had an average systemic medication duration of 4 years and 6 months, with a 1.74 month interval before biologic commencement. The respective PASI scores were 11.81 and 1.56.

Conclusion:

These findings underscore discernible variations in prescribing practices between two UK centres, whilst noting a more conservative approach in AD patients' biologic initiation. A lower threshold for commencing biologics in psoriasis compared to AD was noted in both centres. In centre A patients with AD are on conventional systemics for a shorter period of time prior to commencing a biologic. Reasons for this may be influenced by prescriber confidence, the well-established history of biologics in psoriasis, National Institute for Health and Care Excellence (NICE) guidelines specifying criteria for PASI scores in psoriasis (but not for eczema), and unique characteristics of local patient populations.

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Abstract N°: 7918

Differentiating early responders, late responders, and nonresponders during real life dupilumab treatment using a personalized biomarker approach

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Introduction & Objectives:

Dupilumab, an anti-IL4R monoclonal antibody, is an effective treatment for atopic dermatitis (AD), but fewer than 50% of patients achieve complete/near complete clearance at 16 weeks, with variable response and durability. Further, it is unclear which patients respond early versus later. In this real-world study, we sought to identify biomarkers for early response, late response, no response, and response maintenance to dupilumab.

Materials & Methods:

67 moderate-to-severe AD patients treated with dupilumab (39 early responders, 11 late responders, 17 nonresponders) were evaluated at two follow-up visits (FU1, FU2; mean interval 8.9 months), with clinical scores and serum samples collected at each visit, alongside serum from age/sex-matched healthy controls. Early responders achieved an investigator global assessment (IGA) of 0/1 or a ≥2 point reduction from baseline at both follow-ups; late responders met these criteria only at FU2; nonresponders did not meet responder criteria and/or were dissatisfied with treatment/adverse events at both follow-ups. Serum was analyzed using OLINK high-throughput proteomics; differentially expressed proteins (DEPs) were defined as fold-change (FCH) >1.3 and $P<0.05$.

Results:

At baseline, no significant differences were observed in patient characteristics, clinical severity, or past medical history.

At both follow-up visits (FU1 [47 (26 Up, 21 Down)] and FU2 [59 (39 up, 20 down)]) early responders had similar protein expression profiles to healthy subjects. Late responders showed 45% improvement in proteomic dysregulation from FU1 to FU2 [from 114 (101 Up, 13 Down)] to [42 (23 Up, 19 Down) vs N].

Late responders showed upregulation of many Th1 (e.g., IFNγ, CXCL9, CXCL10), Th2 (e.g., IL4, CCL7), Th17/22 (e.g., S100A12), and T cell activation/migration/DC (e.g., CD40LG, XCL1, IL16) pathways (all $P<0.05$) in FU1, with robust downregulation/normalization of these biomarkers at FU2.

The nonresponders showed a worsening of their blood proteome between FU1 [103 (93 Up, 10 Down)] and FU2 [229 (223 Up, 6 Down)] visits. Uniquely to nonresponders, key Th1 and other biomarkers (e.g. CXCL9, CXCL10, OX40) remained significantly upregulated vs. controls at both FU1 and FU2 ($P<0.05$). Spearman analysis revealed strong and positive correlations between changes in clinical severity (i.e. EASI, IGA, BSA) between FU2 and FU1 and changes in blood biomarkers, including those belonging to T cells/dendritic-cells/NK cells (e.g., CD27, CD5, CD83, IL7R, FASLG), and Th2 pathways (e.g., TSLP) (all $R\geq0.35$, $P<0.05$).

Conclusion:

Our study reveals distinct systemic biomarker profiles linked to the timing and maintenance of dupilumab response in moderate-to-severe AD patients. Early responders show early normalization and stability in their blood proteomic profile, while late responders exhibit continuous changes in Th1, Th2, and Th17/22 pathways. Nonresponders have persistent upregulation of specific biomarkers, suggesting potential targets for refining therapeutic strategies.

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Abstract N°: 7987

Durability of response to nemolizumab in patients with moderate-to-severe prurigo nodularis: Results from a randomised placebo-controlled withdrawal Phase 3b study

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Introduction & Objectives:

Nemolizumab, a first-in-class interleukin-31 receptor alpha antagonist, demonstrated clinically meaningful and statistically significant improvements in itch and skin nodules in adults with moderate-to-severe prurigo nodularis (PN) in two phase 3 pivotal studies (OLYMPIA 1: NCT04501666 and OLYMPIA 2: NCT04501679 of 24- and 16-week treatment periods, respectively) and in an interim analysis (up to 52 weeks) of an open-label long-term extension (LTE) study (OLYMPIA LTE: NCT04204616). Here we report results from a phase 3b study (OLYMPIA DURABILITY: NCT05052983), which aimed to assess the long-term durability of response over a 24-week period following withdrawal of nemolizumab in patients with PN who had previously responded to 52-week open label treatment in the LTE study.

Materials & Methods:

A phase 3b multicentre, randomised, double-blind, placebo-controlled, parallel-group, withdrawal study was conducted** in adults with PN who participated in the OLYMPIA LTE study with uninterrupted dosing for 3 months before the Week (W) 52 visit and achieved a clinical response (i.e., Investigator's Global Assessment [IGA] score of 0/1 [clear/almost clear] and ≥4-point improvement in weekly average Peak Pruritus Numerical Rating Scale [PP NRS] score from baseline of the lead-in study) at W52. In OLYMPIA DURABILITY, patients were randomised 1:1 to either continue the same dosing regimen received in the LTE study (i.e., nemolizumab 30 mg/60 mg [depending on baseline weight </≥90 kg] administered every 4 weeks [Q4W]) or to placebo Q4W (withdrawal arm). If a patient met either criterion for relapse (defined as ≥4 points increase in PP NRS score and/or ≥2 points increase in IGA score from baseline) at any point during the treatment period, the patient had to exit the study and could re-enter the LTE study. Patients who completed the study through Week 24 were eligible to re-enrol in the LTE study. The primary endpoint was time from baseline to relapse.

Results:

Of 34 patients, 18 continued nemolizumab (mean [SD] age: 59.9 [14.1] years; mean [SD] body weight: 80.3 [15.0] kg; female: 77.8%) and 16 were withdrawn from nemolizumab and received placebo (mean [SD] age: 59.1 [13.4] years; mean [SD] body weight: 77.0 [16.0] kg; female: 81.3%). The nemolizumab arm had significantly less protocol-defined relapse vs the withdrawal arm, i.e. (3/18 [16.7%] vs 12/16 [75.0%]; hazard ratio [95% CI]: 0.125 [0.034-0.462]). The median (95% CI) time to relapse in patients after a clinical response at W52 was 112.5 (84.0-161.0) days for patients in the withdrawal arm, while for patients in the nemolizumab arm the median time to relapse was undetermined due to low relapse rate until Week 24.

Treatment-emergent adverse events (TEAEs) were reported in 12/18 (66.7%) and 10/16 (62.5%) of patients in the nemolizumab and withdrawal arms, respectively, of which most were mild-to-moderate in severity. Serious TEAEs were reported in 2/18 (11.1%) patients in the nemolizumab arm and in none in the placebo arm. None of serious TEAEs were assessed as related to study drug. Neutralizing antidrug antibodies were not detected in any of the arms at W24.

Conclusion:

Clinical responders to nemolizumab at week 52 had significantly lower relapse rates when continuing on nemolizumab than those withdrawn. These findings support the continued use of nemolizumab beyond 52 weeks of treatment among patients who are clinical responders.

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Abstract N°: 8009

Efficacy and safety of ESK-001, a highly selective oral TYK2 inhibitor, in moderate-to-severe plaque psoriasis: Phase 2 results through week 28

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Introduction & Objectives: ESK-001 is an oral, highly selective allosteric TYK2 inhibitor being developed for patients with moderate-to-severe plaque psoriasis. The Phase 2 ESK-001 program consists of a completed randomized, placebo-controlled, dose-ranging study (STRIDE, NCT05600036) and an ongoing open-label extension study (OLE, NCT05739435) in patients completing STRIDE. Herein, efficacy and safety results of ESK-001 through Week 28 in the OLE are reported.

Materials & Methods: STRIDE was a randomized, double-blinded, placebo-controlled, 12-week study in patients with moderate-to-severe psoriasis, evaluating five ESK-001 dose groups, from 10 mg QD to 40 mg BID compared to placebo. The OLE study is ongoing and evaluating long-term safety and efficacy in patients from all dose groups completing STRIDE, with patients allocated 1:1 to receive long term ESK-001 40 mg QD or 40 mg BID. The primary endpoint was safety and efficacy endpoints included PASI 75/90/100 and sPGA 0/1. All clinical data through Week 28 were analyzed, with response rates reported using as observed (AO) and modified non-responder imputation (mNRI) methods.

Results: The primary and key secondary endpoints in STRIDE were met ($p<0.0001$) at Week 12 for the top dose levels with clear dose-dependent effects. Clinical efficacy was mirrored by decreased expression of pathogenic cytokines within lesions, including IL-23 and IL-17A, which returned to non-lesional levels at Week 12. In the OLE, efficacy increased substantially in a dose-dependent manner through Week 28 (**Table**). In the 40 mg BID group, 83% (mNRI)/93% (AO) of patients achieved PASI 75 and 63% (mNRI)/72% (AO) achieved PASI 90. sPGA 0/1 responses increased from 59% at Week 12 to 68% (mNRI)/76% (AO) at Week 28 in the 40 mg BID group. Median % changes in PASI from baseline to Week 28 were 95% (40 mg BID) and 89% (40 mg QD). Patients within each OLE dose arm achieved similar levels of efficacy by Week 28 regardless of their initial dose in STRIDE including placebo. ESK-001 was generally safe and well-tolerated in STRIDE, with a similar safety profile in the OLE. TEAE frequency and severity were similar across study arms, with the majority being mild-to-moderate and self-limited. No deaths, treatment-related AEs associated with classic JAK inhibitor labeling, or clinically significant laboratory or ECG trends were observed. In both STRIDE and the ongoing OLE, the most common TEAEs were URTIs, nasopharyngitis, and headache.

Table: Increased Efficacy Responses with Longer Exposure to ESK-001

	40 mg BID	40 mg QD
	STRIDE **Week 12**	**OLE** **Week 28**
	NRI (N=39)	AO (N=71)
PASI 75 (%)	64	93
PASI 90 (%)	39	72
PASI 100 (%)	15	35
sPGA 0/1 (%)	59	76

Conclusion: In STRIDE and OLE, Phase 2 studies in patients with moderate-to-severe plaque psoriasis, the oral selective TYK2 inhibitor ESK-001 demonstrated clear dose-dependent efficacy. At the highest dose, 40 mg BID, maximal clinical responses were safely achieved at Week 28. Indirect comparisons of historical data suggest that ESK-001 has the potential for best-in-class efficacy, with efficacy in the range reported for many biologic therapies for psoriasis.

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Abstract N°: 8055

Efficacy and safety of the oral interleukin-1 receptor-associated kinase 4 (IRAK4) inhibitor zabedosertib in adult patients with moderate-to-severe atopic dermatitis – Results of the phase 2a DAMASK study

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Introduction & Objectives:

Interleukin-1 receptor-associated kinase 4 (IRAK4) is a key mediator of interleukin-1 receptor and toll-like receptor signaling. Its inhibition has potential for a broad anti-inflammatory effect and represented an attractive target in atopic dermatitis (AD). Here we report the results of a Phase 2a proof-of-concept study with the oral IRAK4 inhibitor zabedosertib (BAY1834845) in adult patients with moderate-to-severe AD (DAMASK: NCT05656911).

Materials & Methods:

The DAMASK study was a double-blind, placebo-controlled, parallel-group study conducted at 22 sites in seven countries in Europe and the US. Adults with moderate-to-severe AD who were inadequately controlled by topical corticosteroids (TCS) or for whom TCS were medically not advisable received zabedosertib 120 mg twice daily or placebo for 12 weeks with a daily background use of emollients. Primary endpoint was the Eczema Area and Severity Index (EASI)-75 response at week 12. Main secondary endpoints included the validated Investigator Global Assessment scale (vIGA-AD) response at week 12 (vIGA-AD 0 or 1 with at least a 2-grade reduction from baseline), change from baseline in body surface area (BSA) affected by AD, response in the Peak Pruritus Numerical Rating Scale (NRS; achievement of a ≥4-point-improvement in the weekly average of the Peak Pruritus NRS 0–10 score from baseline), as well as safety and tolerability of zabedosertib.

Results:

A total of 77 patients were randomised and treated in a 2:1 ratio (verum vs placebo).**Efficacy**: the proportion of EASI-75 responders at week 12 in the zabedosertib arm was not statistically different from placebo (32.3% vs 37.4%). No statistically significant differences for vIGA-AD response (15.9% vs 28.5%), change from baseline in BSA affected by AD (−13.3% vs −20.3%), or Peak Pruritus NRS response (16.4% vs 25.0%) between the zabedosertib arm and placebo were observed. **Biomarkers**: blood-based disease biomarkers, such as thymic stromal lymphopoietin and chemokine (C-C) ligand 17, as well as gene expression analysis from skin biopsies did not signal a therapeutic effect by zabedosertib. **Safety**: treatment-emergent adverse events (TEAEs) were reported in 44.2% vs 28.0% of study participants in the zabedosertib and placebo arms, respectively, with nasopharyngitis

being the only TEAE occurring in more than 5% of participants. There were no relevant differences between zabedosertib and placebo regarding the percentage of participants with TEAEs related to study intervention, adverse event (AE) intensity, or AEs leading to discontinuation of study drug. No serious AE, severe AE, or death was reported, and there were no clinically relevant findings for laboratory investigations, vital signs and electrocardiogram parameters.

Conclusion:

In this Phase 2a study, zabedosertib, a development candidate targeting IRAK4 in AD, was well tolerated with no safety concerns, but no treatment effect across the efficacy endpoints was observed and no significant differences in biomarkers were detected. These results contrast with the clear pharmacodynamic effect of zabedosertib in a recent proof-of-mechanism study (1) and suggest that inhibition of IRAK4 is not a promising approach for the treatment of AD. Other immune-mediated diseases with different molecular involvement of IRAK4, including other inflammatory skin diseases, may still be targeted successfully with zabedosertib.

Reference

1. Jodl SJ, et al. *Clin Transl Sci.* 2024;17(3):e13771.