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

Abstract N°: 112

Dupilumab in Adult Patients with Moderate-to-severe Prurigo Nodularis: 6-months Real-world Follow-up Results from the French Early Access Program

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Introduction & Objectives:

Prurigo nodularis (PN) is a chronic inflammatory skin condition characterized by intensely pruritic papulonodular lesions impacting quality of life. Dupilumab is the first biologic approved for the treatment of adults with moderate-to-severe PN. Dupilumab reduces type-2 inflammation by inhibiting interleukin (IL)-4 and IL-13. This interim analysis of a French early-access program (EAP) describes adult PN patients' characteristics, efficacy, and safety of dupilumab 300 mg injection administered every 2 weeks with an initial dose of 600 mg.

Materials & Methods:

Patients with moderate (≥20 nodules) to severe (>100 nodules) PN enrolled in EAP between 2022-November-11 and 2024-January-28 were included in this analysis. Patient demographics, disease characteristics, and treatment patterns were recorded at the time of EAP request. Changes in Worst-Itch Numerical Rating Scale (WI-NRS), Investigator's Global Assessment for PN-Stage (IGA PN-S), Dermatology Life Quality Index (DLQI) scores and incidence of adverse drug reactions (ADRs) at 3 (M3) and 6 months (M6) are presented here.

Results:

A total of 178 eligible patients were enrolled, with a mean (standard deviation [SD]) age of 63.4 (17.4) years and 62.4% of patients were female. Mean (SD) total number of nodules at diagnosis was 52.8 (40.5) and mean (SD) time since diagnosis was 3.98 (6.25) years. All patients had prior topical corticosteroids therapy, 28.7% (n/N=51/178) of patients had no comorbidities, and 15.2% (27/178) of patients had atopic comorbidities such as asthma and atopic dermatitis. 56.2% (100/178) of patients had only non-atopic comorbidities; hypertension and diabetes being the most frequent.

Out of 178 patients, 115 were confirmed as treated with dupilumab. At baseline, mean (SD) WI-NRS score was 7.2 (2.1), 71.7% (76/106) of patients had severe-to-very severe pruritus (WI-NRS ≥7), 32.7% (35/107) of patients had an IGA PN-S score of 4, and mean (SD) DLQI score was 13.1 (6.8).

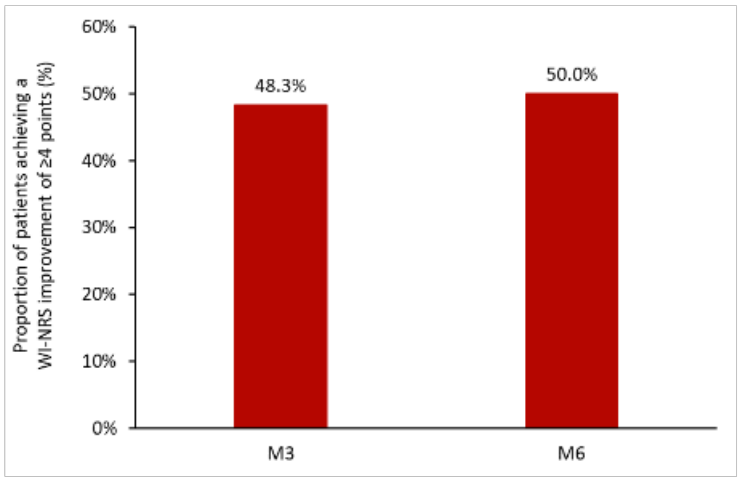
After treatment initiation, WI-NRS score improved by ≥4 points from baseline in 48.3% (29/60) of patients at M3, 50.0% (18/36) of patients at M6 **(Figure 1)**; 16.1% (10/62) and 46.2% (18/39) of patients achieved a WI-NRS score of 0/1 at M3 and M6, respectively; 41.5% (27/65) and 68.4% (26/38) of patients achieved an IGA PN-S score of 0/1 at M3 and M6, respectively **(Figure 2)**. Additionally, the mean (SD) DLQI score improved by 6.3 (6.4) and 7.9 (7.6) points, at M3 and M6, respectively.

At least one ADR was reported in seven patients, including herpes zoster infection (n=2), injection site reactions (n=1), and weight increase (n=1). Three patients permanently discontinued treatment due to inefficacy, headache, and pruritus (n=1 each). No conjunctivitis was reported.

Conclusion:

In this interim real-world data analysis from French EAP in adult patients with PN, improvements in clinical outcomes and safety of dupilumab were consistent with known dupilumab efficacy and safety profile. Of note, this cohort had a large proportion of patients with non-atopic comorbidities or without any comorbidities.

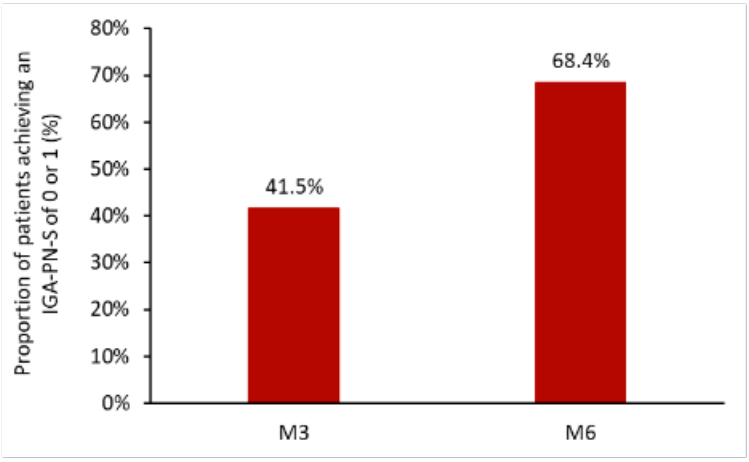
Figure 1: Proportion of patients achieving a WI-NRS improvement of ≥4 points from baseline at M3 and M6



	M3	M6
Number of patients	29/60	18/36

M3, 3 months; M6, 6 months; WI-NRS, Worst-Itch Numerical Rating Scale.

Figure 2: Proportion of patients achieving an IGA-PN-S of 0 or 1 at M3 and M6



	M3	M6
Number of patients	27/65	26/38

IGA-PN-S, Investigator's Global Assessment for PN-Stage; M3, 3 months; M6, 6 months.

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Abstract N°: 354

Itch Severity and Insomnia Risk in Patients with Severe Prurigo Nodularis and Other Dermatologic Conditions

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Introduction & Objectives:

Prurigo nodularis (PN), is a debilitating, inflammatory skin disease characterized by extremely pruritic, hyperkeratotic nodules. PN can significantly impair patients' quality of life due to severe pruritus and/or profound sleep disturbances.

The primary objective of our study was to assess insomnia and sleep disturbance among patients with PN and to compare it with patients with moderate to severe atopic dermatitis (AD), moderate to severe psoriasis, rosacea, and patients with non-melanoma skin cancers (NMSC). We also sought to evaluate the potential correlation between the intensity of itching and the severity of insomnia and sleep disturbances.

Materials & Methods:

This was a retrospective study. The medical records of 177 unique patients from a university-based dermatology clinic were retrospectively reviewed. A total of 40 patients with PN were included and were matched (for gender and age) with 137 individuals with various dermatological conditions other than PN as following: 40 with moderate to severe AD, 40 with moderate to severe psoriasis, 24 with rosacea and 33 patients with NMSC.

We employed the Athens Insomnia Scale (AIS), a validated tool comprising eight questions, each rated on a scale of 0 to 3, where 3 signifies the most severe impact on sleep and 0 indicates no disturbance. The total score ranges from 0 to 24, with a cut off of 6 points or more defining the presence of insomnia and sleep disturbance. Additionally, all participants were assessed for itch severity using the Peak Pruritus Numerical Rating Scale (PP-NRS). This scale ranges from 0 to 10, where participants were asked to rate their itch at the worst moment during the previous 24 hours. A score of 0 represents 'no itch' and 10 represents the 'worst itch possible.'

To investigate the potential correlation between itching severity and insomnia/sleep disturbance severity, we classified these conditions into three categories: severely itchy dermatoses (PN and AD combined), psoriasis, and rosacea. Two sample t-test and Spearman correlation analysis were conducted on Microsoft Excel, and RStudio was used to generate graphs.

Results:

The mean age of the study patients was 46.4 years (SD=12.2) with 115 (65%) females. PN had the highest mean PP-NRS score at 8.7, compared to AD (6.4), PsO (5.85), Rosacea (1.25) and was not available for NMSC. The mean PP-NRS score for PN was statistically significantly higher compared to all other conditions ($p<0.001$). PN also exhibited the highest mean AIS score at 14.95, compared to AD (12.2), PsO (10.2), Rosacea (2.4) and NMSC (3.8). Furthermore, the mean AIS score for PN was also statistically significantly higher when compared individually with each of the other indications ($p<0.001$).

Additionally, a statistically significant correlation was observed between PP-NRS and AIS scores in patients with severely itchy dermatoses (PN and AD combined) ($p=0.002$), as well as in those with psoriasis ($p<0.001$).

Conclusion:

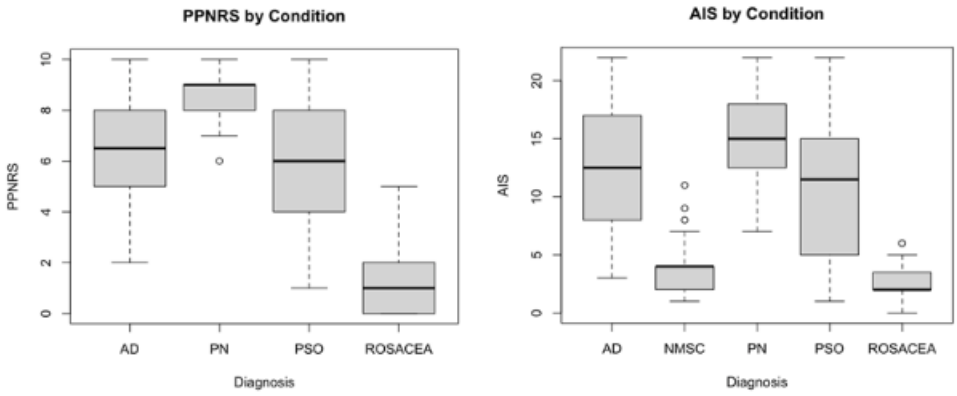
Patients with PN experience heightened pruritus and sleep disturbances compared to other dermatologic diseases. Notably, A positive correlation exists between pruritus and sleep disturbances in PN/AD and psoriasis cohorts. These observations underscore the importance of clinical recognition of these symptoms and advocate for continued investigation into therapeutic modalities that concurrently target pruritus and insomnia.

Appendix 1: Mean PPNRS/AIS Scores by Condition, and Correlation between AIS/NRS

Condition	Mean PP-NRS (0-10)	Mean AIS (0-24)	AIS Interpretation
PN	8.7	14.95	Moderate insomnia
AD	6.4	12.25	Mild insomnia
PsO	5.85	10.20	Mild insomnia
Rosacea	1.25	2.42	No insomnia
NMSC	NA	3.76	No insomnia

Condition	AIS/NRS Spearman Coefficient	Interpretation
PN and AD	0.48 (p = 0.002)	Strong correlation
PsO	0.60 (p = 0.00004)	Strong correlation
Rosacea	-0.13 (p = 0.56)	Negligible

Appendix 2: Box plots for AIS and PPNRS by Condition



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Abstract N°: 509

Paraneoplastic pruritus in lymphoid malignancies – A case series

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Paraneoplastic pruritus in lymphoid malignancies – A case series

Introduction & Objectives:

Pruritus can be a clue towards several systemic diseases. It is essential to look for malignancies in patients presenting with long-standing pruritus and poor response to therapy. Clinical history about symptoms like fever and weight loss and examination for lymphadenopathy can be helpful to detect a lymphoproliferative neoplasm. Pruritus in such cases can precede the clinical diagnosis of malignancy by several months to years. On the other hand, some cases can develop pruritus after diagnosis and initiation of chemotherapy. We here report a series of five cases of chronic, intractable** pruritus who were suffering from various lymphoid malignancies.

Materials & Methods:

All patients presenting with chronic pruritus were evaluated thoroughly for presence of any underlying systemic disease. After detailed history taking and clinical examination, appropriate laboratory tests, imaging and histopathological studies with immunohistochemical markers were advised.

Results:

We encountered five cases (2 males, 3 females) over a period of 8 months who presented with chronic, intensely pruritic skin lesions associated with various lymphoid malignancies. Age of patients ranged from 25 to 87 years. Duration of pruritus at the time of presentation ranged from 6 weeks to 1 year. On examination, there were multiple, hyperpigmented, excoriated, papulonodular lesions distributed symmetrically over trunk and extremities. Case 1, 2 and 3 had generalized lymphadenopathy with multiple enlarged lymph nodes affecting the cervical, axillary and inguinal region, while case 4 had massive cervical lymphadenopathy. An excisional lymph node biopsy in all four cases revealed the following malignancies - mantle cell lymphoma (case 1), small lymphocytic lymphoma (case 2), primary follicular dendritic cell sarcoma (case 3) and Hodgkin's lymphoma (case 4). The patients were prescribed a combination of second-generation antihistamine (fexofenadine) in morning, pregabalin in evening, topical steroids and emollients along with chemotherapy for the underlying lymphoid malignancy. Three of these cases are currently receiving chemotherapy with relief in pruritus except for case 3 who succumbed to his illness soon after diagnosis. In these cases, onset of pruritus was prior to diagnosis of malignancy and skin biopsy was not suggestive of lymphoproliferative disease. However, case 5 was already a known case of Hodgkin's lymphoma who developed itchy papular eruption over body 3 months after diagnosis and initiation of chemotherapy. Her skin biopsy revealed dermal eosinophilic infiltrate and diagnosed with eosinophilic dermatosis of hematologic malignancy. In addition to fexofenadine, pregabalin, topical steroids and emollients, she was additionally treated with doxycycline after which her pruritus reduced considerably.

Conclusion:

Chronic pruritus can be associated with several systemic conditions including malignancy. It is essential to evaluate such patients thoroughly. Clinical findings like fever, weight loss and lymphadenopathy are important clues to detect a lymphoproliferative neoplasm. It is also essential to note that as this pruritus is paraneoplastic, biopsy from skin lesions might not establish the diagnosis. Treatment of the underlying malignancy helps to reduce the pruritus, although patients may require additional therapy as well.

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Abstract N°: 1140

A capricious and recurrent vulvar pruritus on a psychiatric background

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Introduction & Objectives: Vulvar pathology is varied and can be infectious, inflammatory or tumoral. Localized vulvar pruritus can be of organic or psychological origin and can sometimes constitute a real problem of etiological diagnosis for the dermatologist.

Materials & Methods: We report the case of recurrent vulvar pruritus with a negative etiological assessment in a young woman with a psychiatric pathology.

Results: young woman aged 31, single, with a history of depression under treatment. Consulted for chronic vulvar pruritus, capricious and resistant to treatments with antimycotics and topical corticosteroids. The dermatological examination revealed a discreet vulvar erythema with a whitish vaginal discharge; the rest of the examination was without abnormalities. The bacteriological and mycological study of the vaginal sample was sterile, the assessment of pruritus (hemogram, inflammatory assessment, fasting blood sugar, renal assessment, liver assessment, thyroid assessment, parasitological examination of stools, dosage of total and specific IgE) was strictly normal . Histological study of a skin biopsy showed signs of psoriasis. The patient was placed on strong topical corticosteroids with good progress over 3 months.

Conclusion: Our case shows the interest in pushing further investigations in the face of chronic pruritus in psychiatric fields and not having the ease of retaining the term psychogenic as an etiology.

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Abstract N°: 1172

Clinicopathological characteristics and etiopathogenic aspects of chronic prurigo among Egyptian patients.

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Introduction & Objectives:

Prurigo is a common skin disease that has a spectrum ranged from acute to subacute and chronic form. Chronic prurigo (CP) is characterized by the presence of pruritus for at least 6 weeks. It is commonly described as prurigo nodularis but this is actually describing only the nodular lesions. The etiopathogenic aspects of CP are usually undetermined but could be regarded to allergic, systemic, neurological or dermatological origin.

In this study, we demonstrated the clinical spectrum, pathological features and possible etiological factors that could be related to such disorder.

Materials & Methods:

A prospective randomized study that enrolled all patients who were complaining from chronic itching for at least 6 weeks. Demographic data, clinical characteristics, pathological spectrum, routine and specific investigations were performed for each patient. The results were analyzed and data was summarized.

Results:

The study included 114 patients, with predominance of female patients (63.2%). The disease was more common (50%) among patients over 60 years while patients ranged between 40 to 60 years show the least incidence (20.2%). Female patients were predominant among all age groups (25 Vs 9, 13 Vs 10 and 34 Vs 23 respectively).

The duration of the disease ranged from 8 months to 4 years and they were categorized into 3 age groups. Patients who had lesions less than 1 year constituted 15.8% with predominance of females (11 vs 7) while patients with a disease ranged from 1-3 years constituted the major group (63.2%) with predominance of female patients (54 Vs 18).

The lesions were mostly distributed on the trunk and extremities (60.5%) with predominance of female patients (39 Vs 30) while male patients constituted the major group (14 Vs 4) in the disease localized to the extremities.

Histological evaluation shows four classes; The predominant was the pseudo-perforating pattern (38.6%), followed by chronic spongiotic dermatitis (31.6%), then dermal fibrosis (15.8%) and lastly dermal hypersensitivity reaction (14%). Tissue eosinophilia was significant in dermal hypersensitivity reaction and chronic spongiotic dermatitis.

Laboratory investigations show elevated serum IgE in 79.8% without significant correlation with blood eosinophilia (only elevated in 9.6%) or TRUE (patch test (only positive in 30.7%).

Conclusion:

To our knowledge, this is the first report described the characteristics of CP among Egyptian patients. The disease is commonly affected females with common generalized distribution and long-standing duration. The histological class of pseudo-perforation may be confused with perforating dermatoses. There was a significant correlation with

elevated serum IgE level; we recommended to be considered as a routine investigation in those patients.

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Abstract N°: 1527

Serological biomarkers of immune-cell activity and tissue destruction are associated with disease severity in patients with Prurigo Nodularis

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Introduction & Objectives:

Prurigo nodularis (PN) is a subtype of chronic prurigo that causes a highly pruritic, chronic disease characterized by hyperkeratotic, crusted, or excoriated, light red to bright-red nodules. This leads to an impaired quality of life due to severe itch and the chronic skin lesions. The pathogenesis of PN is not well-described, but activation of immune-cells, including T-cells and neutrophils, and tissue fibrosis and destruction has been associated with the inflammatory processes in the skin lesions.

The objective of this study was to investigate the association between serological biomarkers of immune cell activity and tissue destruction with disease severity in patients with PN.

Materials & Methods:

A subset of baseline samples from consenting patients with PN (NCT03181503) were included in the study analysis. In serum from 59 patients with PN (61% female), biomarkers reflecting immune cell activity (C4G, ELP-3, Cpa9-HNE), tissue fibrosis (PRO-C3, PRO-C6), tissue destruction (C3M, C4M, C6M, CRPM, PRO-C11) and dermal-epidermal junction (PRO-C7) were measured.

Differences in biomarker levels between groups of patients classified by disease severity, determined by the Investigator's Global Assessment (IGA), moderate and severe, were assessed using the Kruskal-Wallis test. A PCA analysis of the biomarker measurements was performed.

Results:

The biomarkers measuring T-cell activity (C4G), neutrophil activity (CPa9-HNE and EL-P3) together with epidermal basement membrane tissue destruction (C4M), presented higher levels in patients with severe PN by IGA scores compared to moderate PN ($p=0.007$, $p=0.010$, $p=0.013$, and $p=0.047$, respectively). None of the other biomarkers were significantly associated with disease severity by the IGA score. When performing a PCA analysis, the first four dimensions explained in total 70% of the variance. Dimension-1 reflected immune-cell activity driven by C4G, CPa9-HNE and ELP-3, Dimension-2, driven by tissue formation (fibrosis) by PRO-C3 and PRO-C6, Dimension-3 driven by tissue destruction by C3M, C4M and C6M, and Dimension-4 driven by dermal-epidermal junction damage by PRO-C7. Patients with severe PN had higher levels of the immune-cell activity markers of the first principal component, compared to moderate ($p=0.0026$).

Conclusion:

We identified blood-based biomarkers of immune-cell activity and tissue destruction to be associated with disease severity in patients with PN. In addition, biomarkers of fibrosis were detected, which should be studied in larger clinical trials to monitor early signs of disease remission. Further investigations should elucidate whether the biomarkers can be used as tools in patient stratification including evaluation of treatment response in clinical studies.

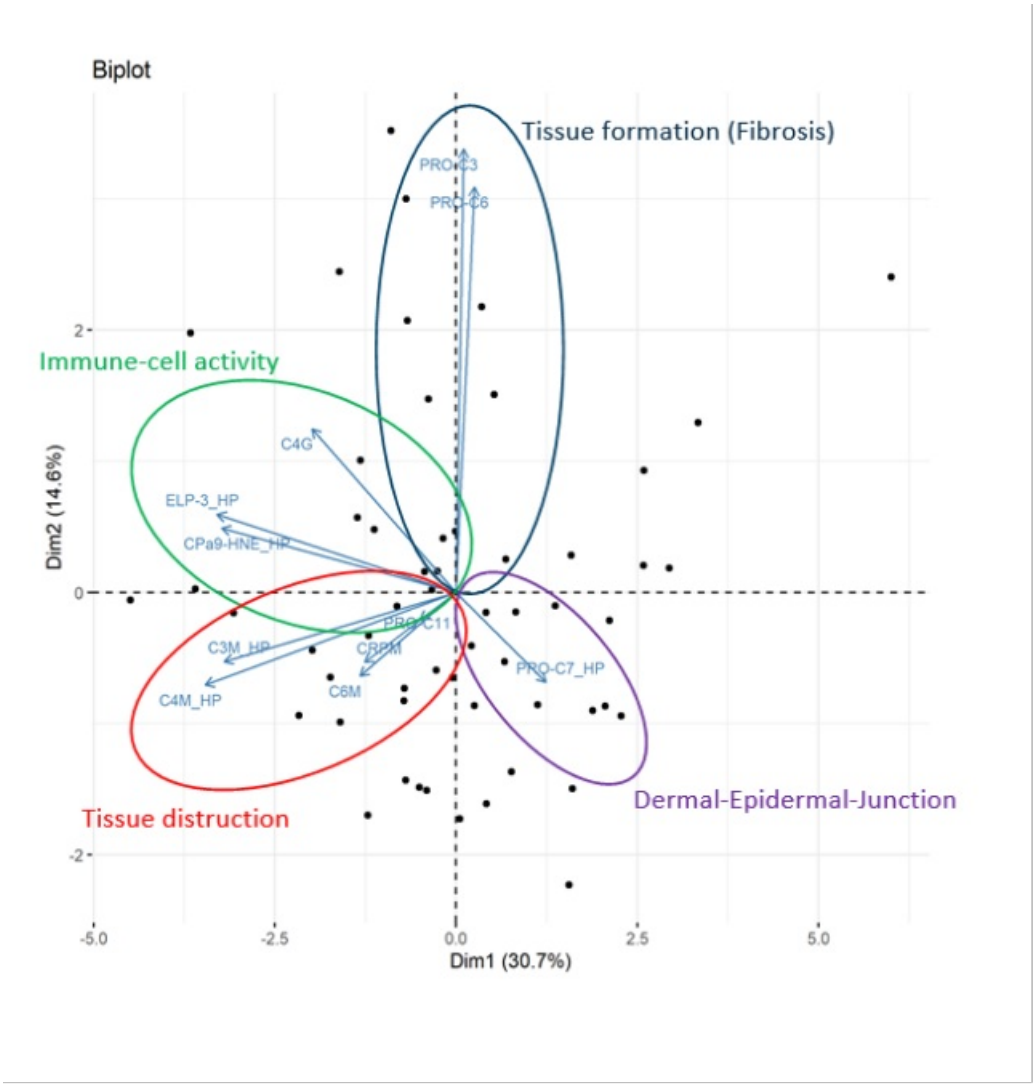

Figure 1. Biplot of the principal component analysis (PCA).

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Abstract N°: 1541

Itch intensity assessment in atopic dermatitis with different itch instruments and time frames - are there differences?

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Introduction & Objectives:

Chronic Pruritus (CP) is a cardinal symptom and major burden in atopic dermatitis (AD). Several instruments to determine pruritus intensity have been established. We aim at determining the validity of different itch instruments with different time frames in patients with AD.

Materials & Methods:

In a monocentric, open-label study, adult patients with moderate to severe AD having at least a mild itch (worst itch (WI) intensity ≥ 3/10 in the last 24h on the numeric rating scale (WI-NRS/24h)) were included. Patients received an in-label therapy with dupilumab 300mg s.c. Q2W for 16 weeks. Worst itch intensity was measured by NRS/last 24h, visual analogue scale (VAS, 0-10)/last 24h and VAS/last 4 weeks and verbal rating scale (VRS, 0-4)/last 24h. Quality of life (Dermatology life quality index; DLQI, 0-30), anxiety and depression (hospital anxiety and depression scale; HADS) were also assessed. All instruments were completed at baseline (BL) and at week 16 (W16).

Results:

49 patients (16 females; mean age, 41.1 years (32; [19-78])) were enrolled. Patients suffered from chronic pruritus for an average of 19 years (21; 19-78), showing an impaired QoL (DLQI average, 12.98 ((11; 3-30)). WI-NRS/24h was 7.46 (8; 2-10), WI-VAS/24h 6.87 (7; 2.1-10), WI-VAS/4 weeks 7.85 (8.3; 2.9-10) and WI-VRS/24h 2.52 (2; 1-4). The itch intensity scales correlated significantly among each other whereas the correlation strength of WI-VAS/4 weeks was only moderate at BL ($p < 0.001$; WI-NRS/24h / WI-VAS/24h, $r = 0.851$; WI-NRS/24h / WI-VAS/4 weeks, $r = 0.606$; WI-NRS/24h / WI-VRS/24h, $r = 0.717$; WI-VAS/24h / WI-VAS/4 weeks, $r = 0.698$; WI-VAS/24h / WI-VRS/24h, $r = 0.737$; WI-VAS/4 weeks/ WI-VRS, $r = 0.531$). All itch intensity scales (24h and 4 weeks) significantly decreased at W16 compared to BL ($p < 0.001$), with a mean reduction in pruritus intensity of 77.82%. At W16, WI-NRS/24h, WI-VRS/24h, WI-VAS/24h and WI-VAS/4 weeks correlated significantly among each other ($p < 0.001$; WI-NRS/24h / WI-VAS/24h, $r = 0.813$; WI-NRS/24h / WI-VAS/4 weeks, $r = 0.859$; WI-NRS/24h / WI-VRS/24h, $r = 0.768$; WI-VAS/24h / WI-VAS/4 weeks, $r = 0.779$; WI-VAS/24h / WI-VRS/24h, $r = 0.669$; WI-VAS/4 weeks / WI-VRS/24h, $r = 0.584$). The reduction in itch intensity was paralleled by a significant improvement of QoL ($p < 0.001$ (D 8.8)). Additionally, HADS was significantly reduced (HADS, depression $p = 0.001$ (D 2.6), anxiety $p = 0.012$ (D 1.7)). WI intensity and DLQI correlated at BL ($p < 0.001$; NRS/24h / DLQI, $r = 0.550$; VAS/24h / DLQI, $r = 0.590$; VAS/4 weeks / DLQI, $r = 0.511$; VRS/24h / DLQI, $r = 0.510$) and W16 ($p < 0.001$; NRS/24h / DLQI, $r = 0.797$; VAS/24h / DLQI, $r = 0.827$; VAS/4 weeks / DLQI, $r = 0.769$; VRS/24h / DLQI, $r = 0.689$). There was no correlation with WI intensity and HADS.

Conclusion:

Different itch intensity scales (NRS, VAS and VRS) and recall periods lead to similar results in effectively evaluating the itch intensity in this trial. Though WI-NRS/24h is the gold standard in clinical trials, using other scales gives valid results; all itch intensity assessment tools showed a sensitivity to change and correlated with the DLQI.

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Abstract N°: 1759

Sensory symptoms as an early manifestation of active vitiligo: a case control clinical and molecular study

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Introduction & Objectives:

Vitiligo is one of the most common cutaneous disorders of depigmentation. Vitiligo is a complex disease, involving genetic and environmental factors together with metabolic and immune alterations. There is some evidence in support of the neurohumoral pathogenesis. Vitiligo is generally asymptomatic and is not considered as a pruritic condition. However, some patients may experience itching, which can occur even before the appearance of the patches.

Aim of the work: To assess sensory symptoms in early active vitiligo patients (segmental, non-segmental or mixed) and to measure 3 neuropeptides expression in their lesional skin [neuropeptide Y(NPY), calcitonin gene related peptide (CGRP) and nerve growth factors (NGF)] to correlate neuropeptide levels, sensory symptoms, and functions, with criteria of disease activity.

Materials & Methods:

A case control study in which 85 patients, aged above 18 years old, were recruited from vitiligo outpatient clinic and classified into either active vitiligo group or stable vitiligo group. Patients were screened for itching or other abnormal neurological sensations as paresthesia and numbness. A Three- millimeter punch biopsy was taken from the edge of the skin lesion to assess the neuropeptides levels by ELISA. Also, a normal control group was included.

Results:

24.7% of patients had sensory symptoms and distributed as: 18.8% with itching, 2.4% with paresthesia and 3.5% with numbness. 51.8% of patients were active cases had no sensory affection and 23.5% of cases were stable without sensory affection. The levels of NGF, CGRP and NPY were significantly highest among normal skin compared to stable vitiligo and to active vitiligo skin, it was lowest among active vitiligo skin (p=0.001, 0.016 and 0.01 respectively). There was no statistically significant difference between the measured neuropeptides expression and associated sensory affection in the studied vitiligo cases.

Conclusion:

One third of the patients reported sensory symptoms predominantly itching that started few days preceding the appearance of new lesions thus it can be described as a prodroma of the disease activity. The levels of neuropeptides were highest in normal skin and lowest in active disease and this can be explained by neurogenic inflammation and enzymatic termination of the neuropeptide activity by peptidases. Further research including drugs that control neuropeptide release should be targeted.

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Abstract N°: 2716

Pruritus and its association with malignancy and mortality in patients with dermatomyositis and polymyositis between 2000 and 2021: a nationwide matched cohort study

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Introduction & Objectives:

Dermatomyositis (DM) is an autoimmune disease featuring progressive symmetrical proximal muscle weakness and characteristic skin manifestations, including pruritus. Pruritus is the most common initial symptom, correlating with increased cutaneous severity and significantly impacting quality of life. Its role as a prognostic factor varies, showing an association with favorable outcomes in some diseases and poorer outcomes in others. The study investigates the potential link between pruritus and cancer risk in DM patients, exploring whether pruritus increases cancer risk or affects overall survival.

Materials & Methods:

Our study conducted a nationwide cohort analysis of patients with dermatomyositis (DM) and polymyositis (PM) using Taiwan's National Health Insurance Research Database (NHIRD) to assess the cancer association and mortality rates of DM and PM from 2000 to 2021. Patients were divided into pruritus or non-pruritus groups based on whether they had been prescribed anti-pruritic agents. The groups were matched by date of birth (±2 years) and gender in a 1:1 ratio (pruritus vs. non-pruritus). Hazard ratios (HRs) and 95% CIs were estimated using Cox proportional Hazard models.

Results:

During the period from 2000 to 2021, after being matched by date of birth and gender from the two groups, 1293 DM/PM patients in both groups underwent further analysis. Overall, at the end of our follow-up, two hundred twenty-five cases (17.40%) in the pruritus group and one hundred thirty-three cases (10.29%) in the non-pruritus group ($p < 0.0001$) were associated with malignancy. Among them, nasopharyngeal cancer, lung cancer, colorectal cancer, and breast cancer were the most common cancer types. For all-cause mortality, there were 458 (35.42%) deaths in the pruritus group and 538 (41.61%) deaths in the non-pruritus group (p=0.0003). The presence of pruritus during disease course was associated with a higher risk of developing cancer (HR=1.512, 95%CI:1.122-2.037). Furthermore, older age at onset, including between 40 and 65-year-old and above 65-year-old (HR: 3.454, 95%CI:2.114-5.644; HR:4.964, 95%CI:2.842-8.670, respectively), male gender (HR:1.527, 95%CI: 1.151-2.024), diabetes mellitus (HR:2.154, 95%CI:1.547-3.000), and hypertension (HR:1.824, 95%CI:1.364-2.440) were significantly associated with malignancy.

Conclusion:

Our study provides the first general population-based evidence that patients with dermatomyositis and polymyositis who suffered from pruritus had a higher risk of developing malignancy. Comprehensive malignancy surveillance should be warranted in these patients.

Table 1 Distributions of baseline characteristics in dermatomyositis cohort by pruritus, 2000-2021.

	Pruritus	Non-pruritus	p-value
	N=1293	N=1293	
Male, n (%)	445 (34.42)	445 (34.42)	-
Age at index date, year, n (%)			
mean (std)	51.2 (14.45)	51.3 (14.61)	0.15
median (Q1-Q3)	52 (41-62)	52 (41-62)	
min, max	18, 88	18, 88	
< 40	275 (21.27)	283 (21.89)	0.48
40-65	797 (61.64)	787 (60.87)	
> 65	221 (17.09)	223 (17.25)	
Co-morbidities, n (%)			
Diabetes mellitus	189 (14.62)	202 (15.62)	0.44
Hypertension	367 (28.38)	383 (29.62)	0.44
Interstitial lung disease	209 (16.16)	251 (19.41)	0.03
Vasculitis	14 (1.08)	7 (0.54)	0.13
Arthritis	69 (5.34)	83 (6.42)	0.24
Post-herpes virus infection	41 (3.17)	51 (3.94)	0.29
Varicella, zoster	132 (10.21)	109 (8.43)	0.12

Table 2 Distributions of cancer and all-cause mortality in dermatomyositis cohort by pruritus, 2000-2021.

	Pruritus	Non-pruritus	p-value
Overall	N=1293	N=1293	
Cancer[#]			
Overall period	225 (17.40)	133 (10.29)	<0.0001
Ever registered in 5 years prior to index date	91 (7.04)	66 (5.10)	0.04
Ever registered in 10 years after index date	144 (11.14)	73 (5.65)	<0.0001
All-cause mortality	458 (35.42)	538 (41.61)	0.0003
Dermatopolymyositis and other dermatomyositis	N=757	N=629	
Cancer[#]			
Overall period	165 (21.80)	90 (14.31)	0.02
Ever registered in 5 years prior to index date	72 (9.51)	49 (7.79)	0.23
Ever registered in 10 years after index date	101 (13.34)	46 (7.31)	0.04
All-cause mortality	273 (36.06)	303 (48.17)	0.05
Polymyositis	N=536	N=664	
Cancer[#]			
Overall period	60 (11.19)	43 (6.48)	0.10
Ever registered in 5 years prior to index date	19 (3.54)	17 (2.56)	1.000
Ever registered in 10 years after index date	43 (8.02)	27 (4.07)	0.03
All-cause mortality	185 (34.51)	235 (35.39)	0.21

Patients had records in cancer registry data in a period between 5 years prior to and 10 years after the index date.

Table 3 Post cancer risk in dermatomyositis cohort without baseline cancer, 2000-2021.

	Crude HR (95% CI)		
	Overall	Dermatopolymyositis and other dermatomyositis	Polymyositis
Pruritus (Yes vs. No)	**1.512 (1.122-2.037)**	1.396 (0.958-2.034)	1.383 (0.845-2.265)
Male vs. female	**1.527 (1.151-2.024)**	**1.653 (1.170-2.335)**	1.296 (0.793-2.118)
Age at index date, year			
< 40	1.0	1.0	1.0
40-65	**3.454 (2.114-5.644)**	**3.339 (1.828-6.100)**	**3.690 (1.580-8.617)**
> 65	**4.964 (2.842-8.670)**	**5.057 (2.567-9.962)**	**4.873 (1.824-13.018**
Co-morbidities (Yes vs. No)			
Diabetes mellitus	**2.154 (1.547-3.000)**	**2.460 (1.655-3.655)**	1.734 (0.944-3.182)
Hypertension	**1.824 (1.364-2.440)**	**1.916 (1.336-2.749)**	**1.877 (1.147-3.073)**
Interstitial lung disease	0.907 (0.607-1.353)	0.634 (0.376-1.070)	1.540 (0.823-2.880)
Vasculitis	2.304 (0.572-9.288)	2.266 (0.560-9.177)	0.000 (0.000-.)
Arthritis	0.673 (0.332-1.366)	0.601 (0.246-1.469)	0.809 (0.254-2.576)
Post-herpes virus infection	0.653 (0.243-1.759)	0.458 (0.113-1.853)	1.099 (0.269-4.495)
Varicella, zoster	1.149 (0.708-1.867)	1.338 (0.781-2.291)	0.625 (0.196-1.990)

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Abstract N°: 2745

Efficacy of hypnotherapy in chronic idiopathic pruritus: a prospective monocentric pilot study

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Introduction & Objectives:

There is a high unmet demand for chronic idiopathic pruritus (CIP). Hypnosis-derived techniques can decrease itch in experimental settings; however, clinical evidence for this outcome is scarce. This study aimed to evaluate the efficacy of medical hypnosis in CIP.

Materials & Methods:

This was a prospective, single-centre study. Twelve patients with CIP were enrolled after undergoing a full etiological examination to rule out any dermatological or general underlying condition. Five standardized hypnotherapy sessions were performed at 2-week intervals by a board-certified expert, using a 45-minute standardized procedure. A clinical evaluation was performed before each hypnotherapy session. The primary endpoint was an improvement in the pruritus Numerical Rating Scale (NRS) score (ranging from 0 to 10) at day-84 (d84), 4 weeks after the end of treatment. The improvement in the NRS score at day-140 (d140), 12 weeks after the end of treatment was a secondary endpoint. Other secondary endpoints included the Verbal Rating Scale (VRS; 0-4) pruritus score, Sleep Numerical Rating Scale (SNRS; 0-10), Dermatology Life Quality Index (DLQI; 0–30), and Hospital Anxiety and Depression Scale (HAD; 0–21) scores, at d84 and d140. We carried out a modified Intent-to-Treat (mITT) analysis that included all patients who had received at least one evaluation. P-values were adjusted and results were expressed as mean ± standard deviation (SD).

Results:

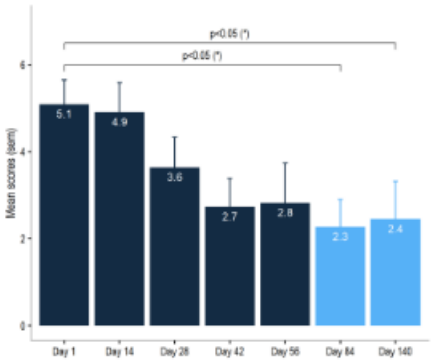
Eleven of the 12 study participants were included in the statistical analyses as one was lost to follow-up. In all the patients, general clinical examination, computed tomography scan and blood tests revealed no aetiology. Dermatological examination showed itching related lesions for 4 participants (36.4%). Six out of the 11 participants were females (54.5%) and five were men (45.4%). The mean age was 61.4±11.8 (SD) years old. The mean NRS pruritus score was 5.1±1.9 at baseline and 2.3±2.1 at d84, showing a decrease of more than 50% ($p<0,05$) (Figure 1). At d140, the mean NRS pruritus score was 2.5±2.9 ($p<0,05$) (Figure 1), confirming the maintenance of the improvement almost 3 months after the last session of hypnotherapy. The mean DLQI score was 6.6±6.5 at baseline, 2.5±4.0 at d84 and 3.6±7.3 at d140, showing a significant improvement at d84 ($p<0,05$) and the persistence of such a benefit at d140 ($p<0,05$). The mean VRS pruritus score was 2.0±0.8 at baseline and 1.1±0.8 at d84, showing a trend toward significance ($p=0.099$). There was no significant improvement of the SNRS score, however the mean SNRS score at baseline suggested a low impact of pruritus on sleep. There was no significant improvement of the HAD score, however the mean HAD score at baseline suggested only a borderline state of anxiety and depression. There were no adverse events related to the treatment.

Conclusion:

A standardized five-session hypnotherapy protocol for patients with CIP provided relief from pruritus for up to 3 months after the last session.

Figure 1.

Improvement in the pruritis score based on the Numerical Rating Scale (ranging from 0 to 10). Results are expressed as mean ± standard error of the mean (SEM). P-values are adjusted.



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Abstract N°: 2763

Single Cell Deciphering of Keloidal Pruritis Reveal Fibroblast and Schwann Cell Interplay though Midkine Paracrine

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Single Cell Deciphering of Keloidal Pruritis Reveal Fibroblast and Schwann Cell Interplay though Midkine Paracrine

Introduction & Objectives:

Keloids are a typical skin fibroproliferative disease that can cause severe aesthetic and functional concerns. Pain and pruritus are the most common clinical symptoms of keloids. Schwann cells variation and neuropathy within keloids play a role in these uncomfortable sensations, but the mechanisms underlying remain unclear.

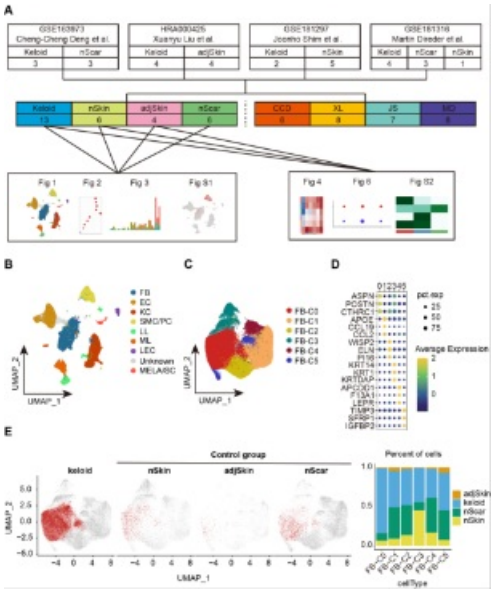
Materials & Methods:

The activity of fibroblasts and Schwann cells was investigated by integrating single-cell RNA sequencing (scRNA-seq) data of keloids. The results of bioinformatics analysis were validated by in vitro cell culture and clinical samples. Selected molecule was verified for its correlation with pain and itch, and used to treat cells to study its role in keloids.

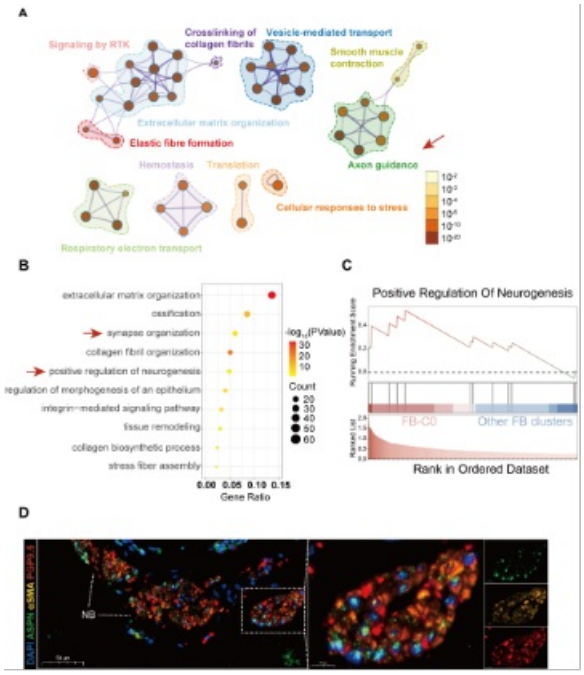
Results:

Our scRNA-seq analysis revealed specific types of fibroblasts and Schwann cells with increased proportions in keloids and function related to neurogenesis. We found active interactions between these two cell types, and eventually focusing on MDK, which is positively correlated with the patient's pain and itching level. Moreover, MDK treatment promoted Schwann cells proliferation and transition to a repair phenotype.

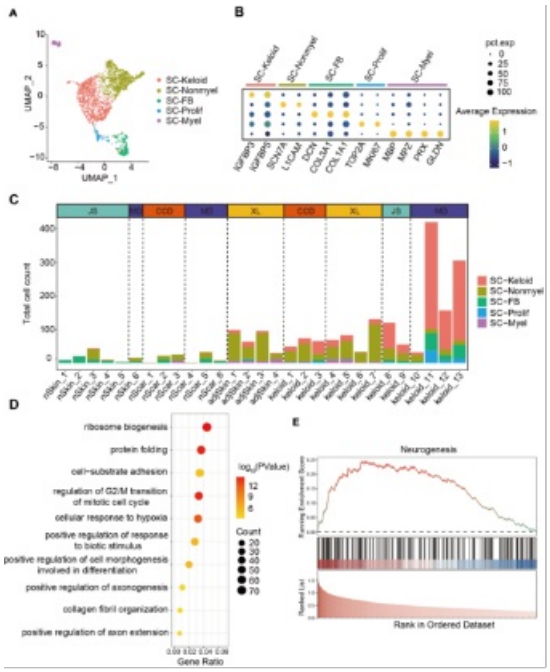
1. **scRNA-seq reveals the presence of a major fibroblast subtype in keloids**



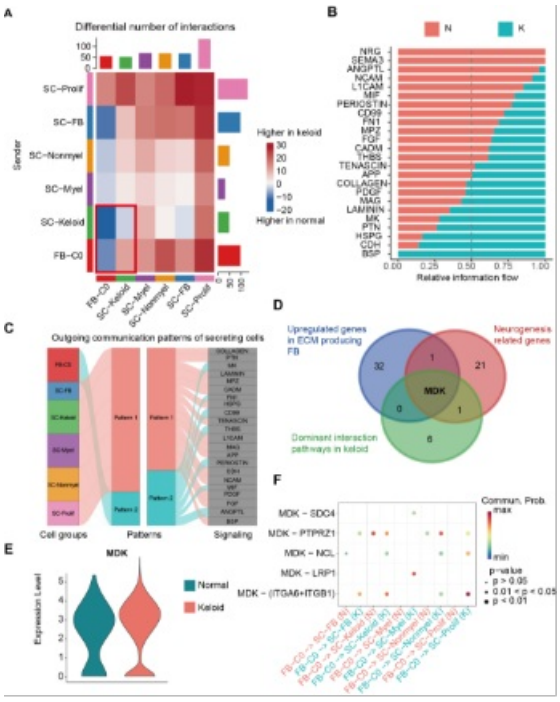
1. **Identification of matrix-producing FB subtype with neurogenesis function**



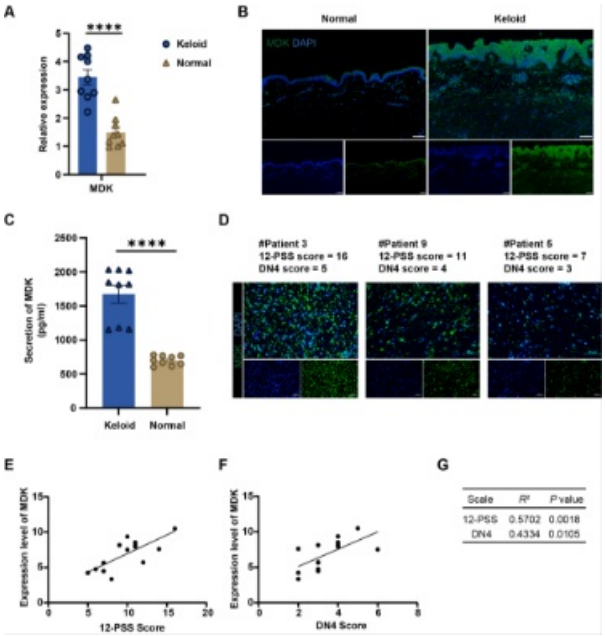
1. **Identification of subtypes of Schwann cells in keloids**



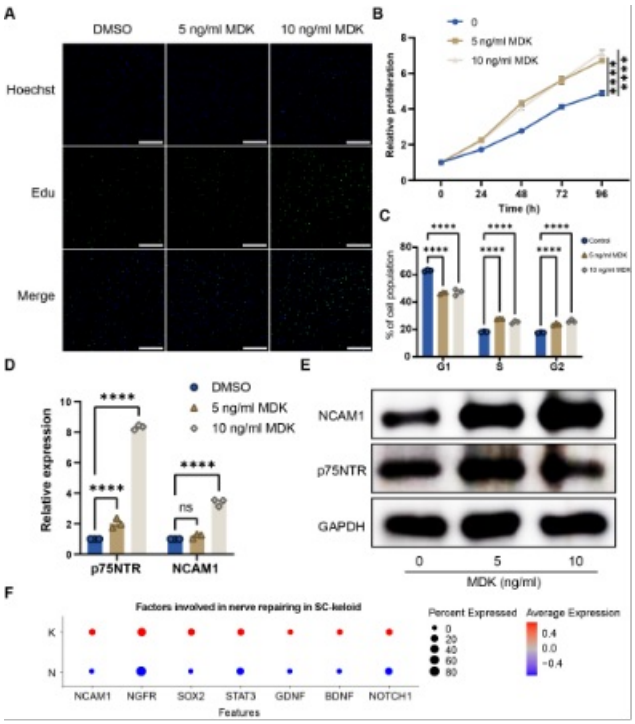
1. **Potential interactions in FB-C0 and Schwann cell subpopulations**



1. **Correlations were seen between MDK and the symptoms of keloids**



1. **MDK promotes Schwann cell proliferation and transformation to a repair phenotype**



Conclusion:

Our study further uncovers the underlying Schwann cell-related mechanisms of keloid pain and itchiness and suggests a potential therapeutic strategy to alleviate the uncomfortable symptoms of keloid patients.

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Abstract N°: 3030

Dupilumab breaks the "itch-scratch cycle" in Chronic Prurigo

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Introduction & Objectives:

The pathophysiology of chronic prurigo (CP) remains incompletely elucidated; nonetheless, an "itch-scratch cycle" is considered responsible for disease chronicity. Currently, dupilumab is approved in moderate to severe CP in adults eligible for systemic therapy. Real-world data remain scarce and complete and sustained disease resolution after dupilumab treatment are infrequently described.

Our goal is to report our cohort treated with dupilumab for CP with emphasis in three patients achieving complete control that persisted after dupilumab discontinuation.

Materials & Methods:

Retrospective and prospective unicentric cohort study of adult CP patients treated with dupilumab in the approved dosage with a minimal follow-up of 12 weeks, evaluating Investigator Global Assessment (IGA), Prurigo Activity Score (PAS), Worst Itch Numeric Rating Scale (WI-NRS) and Dermatology Quality of Life Index (DLQI).

Results:

Nine Caucasian patients (5M/4F, age 49±13.2), with disease duration of 4 years (IQR 2.1; range 1.4–21), 4 with concomitant AD, 3 with confirmatory biopsy were included. Dupilumab was used 6 months (IQR 10; range 3–30) with the following median results:

Baseline: IGA 4; PAS 3; WI-NRS 8.3; DLQI 11.5;

Week 12: IGA 2; PAS 1; WI-NRS 2.7; DLQI 1.0;

Week 52: IGA 0; PAS 0; WI-NRS 1.0; DLQI 0.5.

Apart from minor conjunctival erythema and allergic rhinitis in one patient, no adverse effects were reported. Out of these nine patients, three (1F/2M, mean age 45, with a mean disease duration of 9.6 years, 2 with concomitant minor AD) discontinued dupilumab at 3, 6 and 18 months after complete response. After a follow-up of 12, 24 and 6 months, respectively, they are still free of itch and CP lesions with no need to further treatment.

Conclusion:

Our study, albeit limited, corroborates the efficacy and safety of dupilumab in the management of CP. Moreover, with three patients (33%) achieving enduring and complete disease remission following dupilumab discontinuation, we may assume dupilumab has the potential to disrupt the "itch-scratch cycle", at least within a subset of patients with CP.

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Abstract N°: 3304

Rilzabrutinib reduces biomarkers related to itch and disease severity in chronic spontaneous urticaria and atopic dermatitis

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Introduction & Objectives: Itch is an irritating skin sensation and burdensome symptom observed in dermatological conditions, such as chronic spontaneous urticaria (CSU) and atopic dermatitis (AD). Itch can be triggered by endogenous or exogenous pruritogens. Mast cells and basophils are thought to play key roles in itch signalling pathways through histamine release. Non-histaminergic signalling is mediated by various compounds including cytokines, such as interleukin-31 (IL-31). Pruritogens activate sensory neurons upon binding to their receptor, such as histamine H1 and H4, Mas-related G protein-coupled (MRGP) receptors, and neurokinin receptors. These receptors convey an itch signal to the thalamus via dorsal root ganglia cells, eliciting scratching behaviour. Rilzabrutinib is an oral, reversible, covalent drug that inhibits Bruton's tyrosine kinase (BTK), which is expressed in B cells and myeloid-lineage cells, including mast cells. Here, we evaluate the effect of BTK inhibition with rilzabrutinib on biomarkers associated with itch and disease severity in CSU and AD.

Materials & Methods: Data from two, Phase 2, randomised, double-blind, placebo-controlled studies evaluating the efficacy and safety of rilzabrutinib are included: 1) the RILECSU dose-ranging study with rilzabrutinib 400 mg/day, 800 mg/day, or 1200 mg/day, or matching placebo in patients with moderate-to-severe CSU (NCT05107115); and 2) a proof-of-concept study with 2 rilzabrutinib dose regimens of 800 mg/day or 1200 mg/day, or matching placebo in patients with moderate-to-severe AD (NCT05018806).

Results: In the RILECSU study,** rilzabrutinib 1200 mg/day demonstrated a significant improvement in weekly Itch Severity Score (ISS7) vs placebo at Week 12 (least squares mean, -9.58 vs -6.31; *P*=0.0181). Median serum levels of IL-31 and soluble MRGP receptor X2 (sMRGPRX2) decreased from baseline vs placebo at Week 12 (IL-31, -8.1% vs 15.4%; sMRGPRX2, -22.8% vs -4.5%). In the AD study, a consistent trend favouring rilzabrutinib in patients achieving Peak Pruritus Numerical Rating Scale (PP-NRS) ≥4 was confirmed by a rapid and significant improvement in relative change in weekly average of daily PP-NRS scores. This improvement was seen as early as Week 1 with rilzabrutinib 1200 mg/day and Week 2 with 800 mg/day. Median total thymus and activation-regulated chemokine serum levels decreased from baseline vs placebo at Week 16 with rilzabrutinib 1200 mg/day (-34.5% vs -11.4%) and 800 mg/day (-21.7% vs 7.6%).

Conclusion: Significant improvements in weekly ISS7 and relative change in weekly average of daily PP-NRS scores were observed with rilzabrutinib in patients with CSU and AD, respectively. Rilzabrutinib reduces biomarkers associated with itch and disease severity in CSU and AD, suggesting that rilzabrutinib has the potential to treat itch-related conditions.

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Abstract N°: 3457

Persistent prurigo revealing intestinal giardiasis

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Introduction & Objectives: Intestinal giardiasis is an uncommon digestive parasitosis in our Moroccan context, a frequent cause of pale diarrhea and vomiting.

Materials & Methods: We present a clinical case of persistent and recurrent prurigo in a child who revealed this parasitosis.

Results: Clinical case: 7-year-old boy, with personal (atopic dermatitis) and familial atopic. Consulted for an itchy rash. Clinical examination found erosive papulo-vesicles on erythematous skin, hyperpigmented sequelae lesions on a background of cutaneous xerosis. The diagnosis of prurigo was made. The etiological assessment revealed an allergy to dust mites and intestinal giardiasis. The patient was put on oral metronidazole with symptomatic treatment of prurigo. The evolution was favorable with remission after 15 days of treatment.

Conclusion: Faced with any immunoallergic reaction including prurigo, a parasitological examination of the stools is highly necessary and useful.

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Abstract N°: 3614

Itch perception in chronic spontaneous urticaria may be associated with systemic inflammation and psychiatric comorbidities

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Department of Medicine, University of Cape Town, Cape Town, South Africa

Introduction & Objectives:

Chronic Spontaneous Urticaria (CSU) seriously impacts patients' lives. One major driver is the often severe, debilitating itch. The aim of this study was to examine the association between itch severity and clinical characteristics of CSU.

Materials & Methods:

Patients with CSU, enrolled in the Chronic Urticaria Registry (CURE) by UCARE centers worldwide, were categorized into groups of self-reported itch severity (none, mild, moderate, severe), based on the last seven days before enrollment. We used Pearson's chi-squared test and the Kruskal-Wallis test with pairwise comparisons and Bonferroni correction for group comparisons. Ordinal logistic regressions were then performed to investigate the association between demographic and clinical factors and perceived itch severity.

Results:

A total of 3045 patients (female: n=2263, 74.3%; median age: 42; IQR [32-55] years) were included. Patients reported no (n=498, 16.4%), mild (n=768, 25.2%), moderate (n=990, 32.5%), or severe itch (n=789, 25.9%).

Autoimmune diseases (11.1% of all cases) were more frequent in patients with severe itch ($p<0.001$). The proportion of patients with concomitant chronic inducible urticaria (CIndU: 21%) or an atopic condition (allergic rhinitis, 20.7%; asthma, 11.2%; atopic dermatitis, 5.2%; food allergy, 4.9%) did not differ significantly across itch severity groups ($p>0.05$), as was the case for hypertension, metabolic syndrome, gastrointestinal, or myeloproliferative diseases ($p>0.05$). Depression and anxiety were observed in 8.3% (n=242/2932) and 12.7% (n=375/2949) of cases, respectively, with a higher proportion of patients belonging to the groups with moderate and severe itch ($p<0.001$). Patients with more severe itch scored significantly higher on the Chronic Urticaria Quality of Life Questionnaire (CU-Q2oL; $p<0.001$). Sleep disturbances were reported by almost half of the patients (n=1384/2861, 48.4%), with a substantially higher prevalence among those experiencing severe itch (85%, $p<0.001$). Ordinal regression analyses revealed a positive association between itch severity and general discomfort/malaise (n=524/2387, 22.0%; beta: 0.355, 95% CI [0.144-0.566], $p<0.001$) and recurrent unexplained fever (n=147/2387, 6.2%; beta: 0.482, 95% CI [0.140-0.824], $p=0.006$). Moreover, there was an association between depression and experiencing more severe itch (beta: 0.376, 95% CI [0.099-0.653], $p=0.008$). We also recorded a significant positive association between itch severity and elevated erythrocyte sedimentation rate (n=279/1627, 17.1%; beta: 0.453, 95% CI [0.041-0.864], $p=0.031$), as well as elevated leukocytes counts (n=223/2265, 9.8%; beta: 0.861, 95% CI [0.276-1.447], $p=0.004$).

Conclusion:

Our data suggests that systemic inflammation and psychiatric comorbidities may play an influential role in itch perception in CSU. Future studies are needed to confirm these results and to investigate whether these conditions were pre-existing or developed during CSU.

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Abstract N°: 4003

Goodbye to pruritus! Dupilumab as a hero in the oncological battle

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Introduction:

Refractory pruritus in cancer patients represents a significant therapeutic challenge, impacting quality of life and showing limited efficacy of conventional treatments. In this context, dupilumab, an interleukin (IL) 4 and IL 13 inhibitor, has emerged as a promising therapeutic option. We present the case of a patient with advanced colon cancer and intractable pruritus who responded significantly to dupilumab treatment, underscoring its potential in addressing this symptom in the clinical context.

Case report:

We report the case of a 76-year-old man with advanced colon cancer who received multiple cycles of intravenous chemotherapy with folinic acid, fluorouracil, and oxaliplatin (FOLFOX regimen), 5-fluorouracil, irinotecan and capecitabine for 6 years. Following diagnosis in 2019, he developed pruritus characterized by excoriations and lichenification on the chest and neck associated with scratching. The clinical presentation varied in intensity but remained constantly present for years. Multiple biopsies were performed ruling out other pathologies and showing a spongiotic pattern with lichenoid damage, suggestive of possible toxicodermia secondary to chemotherapy. Clinical orientation leaned more towards an etiology secondary to the tumor process as the pruritus remained unchanged when changing chemotherapy. During this time, he underwent treatment with corticosteroids, antidepressants, and phototherapy, with partial control. The pruritus persisted, reaching an itch visual analog scale (VAS) score of 8/10 in March 2023, despite being treated with aprepitant. It was decided to initiate dupilumab 300 mg every 2 weeks, reducing discomfort with itch VAS scores of 0-1 within a month. Improvement was sustained in successive follow-ups to the present.

Conclusion:

Refractory pruritus in cancer patients poses a significant clinical challenge due to its impact on quality of life and the limited efficacy of conventional treatments. In this case, the patient presented with chronic pruritus associated with advanced colon cancer and the chemotherapy received over several years. Despite multiple therapeutic interventions, including corticosteroids, antidepressants, and phototherapy, the pruritus persisted, negatively affecting his quality of life and emotional well-being. Dupilumab, an IL-4 and IL-13 inhibitor, emerged as a promising therapeutic option in this context. The rapid and sustained improvement in pruritus observed in this case suggests a possible role of dupilumab in modulating the inflammatory response associated with oncologic disease and its treatment. It is postulated that refractory pruritus in cancer patients may be multifactorial, with contributions from paraneoplastic, metabolic, and pharmacological factors. The ability of dupilumab to block IL-4 and IL-13 signaling may interfere with several of these mechanisms implicated in the pathogenesis of pruritus, resulting in notable clinical improvement.

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Abstract N°: 4017

CLE-400: Topical α2-Adrenergic Agonist Being Developed as a Novel Mechanism for Treating Chronic Pruritus Associated with Notalgia Paresthetica

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Introduction & Objectives:

Notalgia paresthetica (NP) is a chronic peripheral neuropathy primarily characterized by localized back pruritus and possibly associated dysesthesias, including sensations of pain, numbness, and tingling. The symptoms of NP are typically unilateral and located medial or inferior to the scapula within the middle-upper back. NP is an often overlooked and underdiagnosed condition(1), and there are no approved treatments for it(2).

CLE-400 is a topical gel, comprising detomidine, an α2 adrenergic agonist, being developed to alleviate itch in localized chronic pruritus conditions. The activation of the α2 adrenergic receptors in the skin could produce anti pruritic and analgesic effects by inhibiting the excitability and neural signaling from the peripheral nociceptors to the brain. Our aim is to evaluate the efficacy and safety of CLE-400 in preclinical models and in clinical studies.

Materials & Methods:

CLE-400 antipruritic effect was examined in the chloroquine-inducted itch model in mice. Three doses of CLE-400 were administered topically once daily for 5 days, and the number of scratches was recorded for 30 min following chloroquine injection on the 5th day.

CLE-400 effect in peripheral neuropathy was tested in the peripheral neuritis trauma (PNT) model in pigs. In this study 3 doses were administered topically BID for 14 days and mechanical sensitivity in the affected skin area was measured using the Von Frey (VF) assessment.

The safety, tolerability, and pharmacokinetics of CLE-400 was evaluated in Phase 1 Single-Ascending-Dose and Multiple-Ascending-Dose studies in healthy volunteers. Currently, a phase 2 study in patients with NP is ongoing in the US, to study the efficacy, safety and tolerability of 4 weeks of treatment with CLE-400.

Results:

Topical application of CLE-400 significantly suppressed chloroquine-induced scratching behaviors in mice at all dose levels. In addition, CLE-400 exhibited a dose-dependent analgesic effect in the PNT model, that started as early as 1 hour post-dose, and was enhanced following repeated dosing during treatment period.

Phase 1 studies have shown that detomidine exposure increases proportionally with the dose, and the PK profile supports once daily administration. CLE-400 was safe and well tolerated, supporting proceeding to Phase 2.

Conclusion:

CLE-400 has demontrated anti pruritic and analgesic effects in preclinical models. Phase 1 study results supported proceeding to Phase 2, to further assess the efficacy and safety of CLE-400 in Notalgia Paresthetica patients.

While α2 adrenergic agonists are well established as systemic treatment of cardiovascular and psychiatric disorders , this trial of CLE-400 for Notalgia Parasthetica represents the first clinical study of this mechanism of action for the topical treatment of chronic, localized pruritus.

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Abstract N°: 4602

The impact of chronic pruritus on the quality of life and quality of sleep

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Introduction & Objectives:

Pruritus is defined by the unpleasant sensation that causes the desire to scratch. This sensation can occur anywhere on the body and can range from mild to severe. Chronic pruritus refers to persistent itching that lasts for six weeks or longer, it can be distressing and often requires medical attention to identify and address the underlying cause. Our study aims to describe the impact of chronic pruritus on the quality of life of the patients and their quality of sleep.

Materials & Methods:

We conducted a cross-sectional and descriptive study, gathering patients with chronic pruritus, aiming to evaluate the impact of their condition on the quality of life of their family using the Dermatology Life Quality Index (DLQI) and the Skindex-29. The patients completed a 10-cm visual analog score (VAS) indicating the overall severity of their itching over the previous 2 weeks. Pittsburgh Sleep Quality Index (PSQI) was used for the evaluation of sleep quality and sleep disturbances.

Results:

We collected 112 patients suffering from chronic pruritus, with a mean age of 54.5 ± 10.2 years, with a clear female predominance (63.5%). Regarding the underlying diagnosis, inflammatory causes were reported in 45.1%, neuropathic etiologies were reported in 20,6%, chronic pruritus of undetermined origin was reported in 18,7%, and secondary to systemic diseases were noted in 15,6%. The average length of itch history was 16 ± 5,6 months.

Concerning the quality of life, the mean value of the Dermatology Life Quality Index DLQI was 15 ± 3 which corresponded to a significant impact on the quality of life of our patients. The Skindex-29 values varied: the mean value of the emotional impact was 33.4 ± 5%, the function impact was 25.8 ± 7% and the symptom was 52.5 ± 11%. The mean value of the visual analog score VAS indicating the severity of itching was 6 ± 2 points which is associated with moderate itch and 4 ± 1 for sleep disturbance which is associated with mild sleep loss. According to the Pittsburgh Sleep Quality Index (PSQI), the average score was 14.1 ± 2.8 and therefore the overall sleep quality for the majority (68.1 %) fell within a categorically defined range for “poor” sleepers.

Conclusion:

This study underscores the significant burden of chronic pruritus on both the quality of life and sleep patterns of affected individuals. The findings emphasize the necessity for comprehensive management strategies aimed at alleviating pruritus-related symptoms to improve overall well-being and sleep quality in those afflicted by this condition. Further research and clinical interventions are warranted to enhance understanding and address the multifaceted impacts of chronic pruritus on individuals’ lives.

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Abstract N°: 5157

Efficacy of Dupilumab in the Treatment of Prurigo Nodularis: A Systematic Literature Review andAnalysis

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Introduction & Objectives:

Prurigo nodularis (PN) is a persistent and debilitating skin condition marked by multiple firm nodules and papules, commonly observed on the extensor surfaces of the limbs and the trunk. These lesions are accompanied by intense itching, significantly impairing the individual's quality of life. The development of skin lesions is attributed to persistent and repetitive rubbing or scratching, primarily induced by pruritus, thus perpetuating a relentless itch-scratch cycle. PN presents challenge for treatment due to low efficacy of traditional treatment. This study aims to assess the efficacy of dupilumab in the treatment of PN.

Materials & Methods:

We conducted a thorough literature review using the EMBASE and MEDLINE databases, utilizing search terms such as "prurigo," "prurigo nodularis," and "dupilumab." Our search strategy encompassed a wide range, incorporating both EMTREE and MESH approaches. Inclusion criteria comprised original trials, case reports, and case series published in English up to April 2024. 90 results were identified in EMBASE, 9 in MEDLINE and 150 in both databases and given further analysis with additional manual research. After analysis of titles and abstracts 27 researches was involved into the review. After analysis of full texts 5 papers (comprising four retrospective cohort studies and one clinical trial) including 415 patients were included into final analysis.

Results:

Patients across all studies showed notable improvements in various assessment scores following treatment with dupilumab. In one clinical trial, the achievement rate of Investigator Global Assessment (IGA) scores reaching 0/1 compared to placebo ranged from 44.9% to 48.0%, in contrast to 15.9% to 18.4% for the placebo group. Dermatology Life Quality Index (DLQI) scores demonstrated a decrease from baseline (ranging from 13.3 to 25.2) after 16 to 24 weeks to values between 0.9 and 11.4. Similarly, Pruritus Numeric Rating Scale (P-NRS) scores decreased from initial values of 7.5 to 8.9 to between 0.8 and 2.7. Across two studies, the total Hospital Anxiety Depression Scale (HADS) score decreased from initial scores of 14.4 to 16.0 to final scores ranging from 1.0 to 10.4. Adverse events were reported in 0% to 65.3% of patients, with conjunctivitis being the most frequently observed adverse event, ranging from 0% to 29.6%

Conclusion:

PN poses significant challenges in terms of effective treatment. While various treatment modalities such as topical corticosteroids, calcineurin inhibitors, UV light therapy, immunosuppressive agents, and systemic neuromodulators are commonly prescribed, their efficacy remains inconclusive with associated undesirable side effects. The persistent and intense itching experienced by PN patients often proves resistant to conventional therapies, which highlights the need for novel therapy. Recently, dupilumab was approved as the first biological systemic therapy indicated in PN. Dupilumab, a fully human monoclonal antibody, functions by inhibiting the shared receptor component for interleukin IL-4 and IL-13. Clinical studies have demonstrated dupilumab's superiority over placebo across various metrics, suggesting its potential as a safe and effective treatment option

for PN. The advent of biologic therapies like dupilumab, which target the underlying pathological mechanisms of PN, offers the promise of enhanced therapeutic benefits compared to traditional approaches with a favorable safety profile.

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Abstract N°: 5372

Dupilumab Is Efficacious in Patients With Prurigo Nodularis Regardless of History of Atopic Comorbidities: Pooled Results From Two Phase 3 Trials (LIBERTY-PN PRIME and PRIME2)

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Introduction & Objectives:

Prurigo nodularis (PN) is a chronic inflammatory skin condition characterized by severely itchy skin nodules. Nearly half of affected adult patients have a history of (or current) atopic comorbidity, such as atopic dermatitis (AD). The objective is to report the efficacy of dupilumab in patients with PN with or without history of atopic comorbidities, in a pre-specified analysis of pooled data from two phase 3 trials.

Materials & Methods:

In the randomized, double-blind, placebo-controlled, 24-week studies, LIBERTY-PN PRIME (NCT04183335) and PRIME2 (NCT04202679), adults with PN inadequately controlled by topical prescription therapies, were randomized 1:1 to dupilumab 300 mg every 2 weeks or matched placebo. Atopic patients were defined as patients with a physiciandocumented history, or current diagnosis, of at least one of the following atopic comorbidities: AD, allergic rhinitis/rhinoconjunctivitis, asthma, or food allergy. Efficacy was assessed from baseline to Week 24 through the Worst Itch Numerical Rating Scale (WI-NRS; 0–10), and the Investigator's Global Assessment for PN-Stage score (IGA PN-S; 0–4).

Results:

311 patients were randomized (dupilumab n=153, atopic/non-atopic N=67/86; placebo n=158, atopic/non-atopic N=68/90). At Week 24, significantly more atopic and nonatopic dupilumabtreated patients achieved a ≥4-point improvement in WI-NRS (58.2%/59.3%), and an IGA PN-S score of 0 or 1 (52.2%/41.9%) vs placebo (20.6%/17.8% [nominal $P<0.0001$/$P<0.0001$] and 16.2%/17.8% [nominal $P<0.0001$/$P=0.0005$], respectively). The proportion of patients achieving concomitant ≥4-point improvement in WINRS and IGA PN-S score of 0 or 1 was higher for both dupilumabtreated atopic and nonatopic patients (37.3%/33.7%) vs placebo (7.4%/10.0% [nominal $P=0.0057$/$P<0.007$]). Overall safety was consistent with the known dupilumab safety profile, with no remarkable differences between atopic and non-atopic patients.

Conclusion:

Dupilumab treatment improves itch and skin lesions in PN patients with and without a history of atopic comorbidities, indicating that underlying type 2 inflammation is present in patients with PN regardless of their history of atopic comorbidities.

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Abstract N°: 5614

Daily practice experience of dupilumab treatment in patients with prurigo nodularis: a 28-week evaluation of clinical effectiveness and safety from the BioDay registry

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Introduction & Objectives:

Dupilumab - a fully human IgG4 monoclonal antibody directed against interleukin (IL)-4 and IL-13 - is the first available targeted treatment option for adults with moderate-to-severe prurigo nodularis (PN). Although safety and efficacy have been demonstrated in phase III clinical trials, there is a paucity of real-world data. This study aims to evaluate the 28-week efficacy and safety of dupilumab in a prospective, multicenter cohort of adult patients with PN.

Materials & Methods:

Adult patients treated (February 2023 – April 2024) with dupilumab for PN with bilateral distribution of at least 20 nodules were enrolled in the Dutch prospective multicenter BioDay registry. Data were collected prior to the start of treatment (baseline), after 16 weeks and after 28 weeks of treatment. Efficacy was assessed using clinical outcome measures such as the Investigator Global Assessment for PN-Stage (IGA PN-S) and patient-reported outcome measures such as the weekly average itch Numeric Rating Scale (NRS). In addition, adverse events were evaluated.

Results:

Thirty-two patients with PN were included. The mean age was 62.4 (standard deviation 15.9) years, 56.3% (n=18) were female and 50.0% (n=16) of patients had a history of atopy. The (causative) disease associated with PN was mostly unknown (75.0%, n=24) or atopic dermatitis (AD; 18.8%, n=6). Data on the 28-week efficacy and safety of approximately 26 patients will be presented. Preliminary results based on 16-week efficacy (n=19) and 28-week efficacy (n=11) show a reduction in median IGA PN-S from 3.0 (interquartile range (IQR) 3.0-4.0) at baseline, to 2.0 (IQR 1.0-3.0) at week 16, and 1.0 (IQR 1.0-2.0) at week 28. The median weekly average itch NRS decreased from 8.0 (IQR 7.0-9.0) to 4.0 (IQR 3.0-7.0) and 3.0 (IQR 1.0-6.0) at weeks 16 and 28, respectively. Similarly, the median weekly average sleep disturbance NRS decreased from 5.0 (IQR 3.0-8.0) to 2.0 (IQR 0.0-4.0) at week 16 and 0.0 (IQR 0.0-1.0) at week 28. The proportion of patients achieving the absolute cut-off score of NRS itch ≤4 and IGA PN-S 0/1 was 63.2% (n=12/19) and 27.8% (n=5/18) at 16 weeks of treatment, and 63.6% (n=7/11) and 54.5% (n=6/11) at 28 weeks, respectively (Figure 1). The most frequently reported adverse events were ocular surface disease (OSD; 18.8%, n=6) and arthralgia (9.4%, n=3). A limited number of patients (9.4%, n=3) discontinued dupilumab treatment due to either side effects (n=1), ineffectiveness (n=1), or patient preference (n=1).

Conclusion:

Preliminary results from the BioDay registry show that dupilumab effectively reduces both skin lesions, itch and sleep disturbance in patients with moderate-to-severe PN in daily practice, consistent with phase III clinical trials.

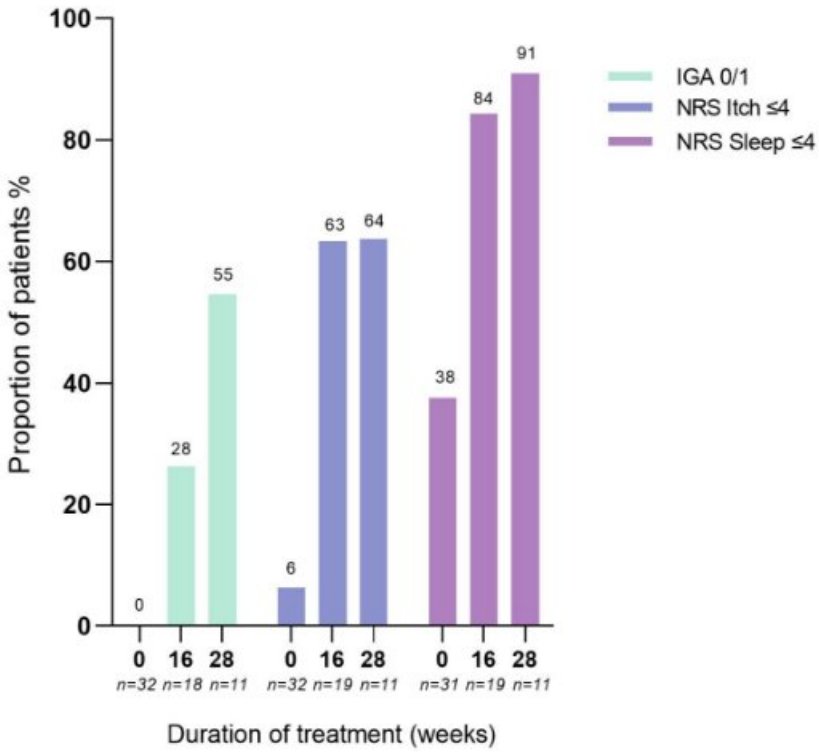

Figure 1. Proportion of patients achieving absolute cut-off score IGA PN-S 0/1, NRS itch ≤4 and NRS sleep disturbance ≤4 at baseline, 16 weeks and 28 weeks of treatment. Abbreviations: IGA PN-S, Investigator Global Assessment for PN-Stage; PN, prurigo nodularis; NRS, Numeric Rating Scale

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Abstract N°: 6157

Treatment of uraemic Pruritus with NB-UVB (TL01) : About 22 cases

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Introduction & Objectives:

Uremic pruritus occurs in patients having chronic renal failure, with or without dialysis. Several treatments exist. Narrow band UVB phototherapy (NB-UVB TL01) has been tried mainly in cases that are refractory to usual treatments. We aimed to evaluate the efficience of this treatment option through our study.

Materials & Methods:

Retrospective study carried out over a period of 32 years (1990-2022) including patients followed at our dermatology department for confirmed uremic pruritus treated with NB-UVB (TL01).

Results:

Twenty-two cases were assessed(15H/7F). The mean age was 63 years (26-81 years)

All patients were treated for stage 5 chronic kidney disease (GFR < 15 ml/min/1.73 m^2) with a mean duration of progression of 10 years. Twenty patients were on haemodialysis with a mean duration of progression of 5 years. The intensity of pruritus was assessed by the WI-NRS scale: mild in 5 patients (23%), essentially moderate in 15 patients (68%) and severe in 2 patients (9%).

Regarding treatment, the mean number of NB-UVB sessions was 28 (2 sessions per week in 59 % cases and 3 sessions per week in 41% cases). The protocol was to start with a loading dose equal to 70% of the minimal erythematous dose (MED) with an increase of 0.1J/cm2 per session.

We started with 0.3J/cm2 in phototype III patients and maximum dose (MD) was1.4 J/cm2. In phototype IV we started with 0.4J/cm2 and MD was 1.6J/cm2. The start dose in phototype V was 0.5J/cm2 and MD was 2J/cm2 . The cumulative dose varied from 1.9 to 64.3 J/cm2 with an average of 21.68 J/cm2. Progression was marked by an improvement in pruritus in only 45% of cases after an average period of 1 month : minimal in 30% of cases, moderate in 57% and significant in 13%. In cases where the response to treatment was satisfactory, recurrence after discontinuation of treatment was observed in 6 patients (27% of cases) within 1 month to 1 year. Transient erythema was observed in 4 patients and did not require discontinuation of treatment.

UVB phototherapy has an immunosuppressive action by inhibiting pro-inflammatory mediators (IL1 / TNF alpha) and an action of attenuation of Th1 mediated responses.

The main studies in the literature comparing the efficacy of NB-UVB(TL01) and broadband UVB in uraemic pruritus have shown a moderate and similar efficacy with a lower risk of side effects in NB-UVB(TL01).

Conclusion:

The aim of uremic pruritis treatment is to control the disease and improve the quality of life. NB-UVB(TL01) can be an effective therapeutic option in refractory cases in conjonction with other treatments, mainly emollients.

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Abstract N°: 6199

From chronic pruritus to renal oncocytoma

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Introduction: Chronic pruritus is a major and distressing symptom of many diseases among the adult population. It can be associated with various systemic conditions, including neoplastic diseases. We describe an interesting case of chronic itching in a woman as a manifestation of an underlying renal oncocytoma revealed by elevated tumor marker 15-3 (CA15.3).

Observation: A 57-year-old woman presented with a 6 months history of generalized pruritus. Physical examination revealed excoriated papules associated with post-inflammatory hyperpigmented scars on the trunk and lower limbs**.** A diagnostic workup for chronic pruritus with complete blood count, renal, hepatic, serum protein electrophoresis, antinuclear antibody, LDH and thyroid function tests did not reveal any abnormalities. However, the CA15-3 concentration was found to be high, at 189 U/mL (normal < 30). Mammography and breast ultrasound did not reveal any abnormalities. An abdominal and pelvic computed tomography (CT) scan was performed showing a large** mass in the right kidney (15cm×12cm). Based on these findings, the patient was referred to a urologic surgeon and underwent right radical nephrectomy with complete excision of the mass. On anatomopathological examination, the tumor was composed of a uniform population of plump cells with abundant granular acidophilic cytoplasm and non-anaplastic nuclei arranged in alveolar-type nests or trabeculae. These features are characteristic of a benign renal oncocytoma. The pruritus resolved completely without recurrence following chirurgical therapy and the skin lesions healed within two weeks. Four months after surgery, the CA 15-3 level was within the normal range at 27U/mL.

Discussion: Chronic pruritus is one of the symptoms that can significantly alter the quality of life. Recent literature suggests that work up for generalized chronic itching with unclear etiology should include complete blood count, renal, hepatic, and thyroid function tests, and imaging, such as chest x-ray and chest CT scan. In recent years there has been a growing interest in circulating tumor biomarkers for diagnostic purposes and also to improve the predictive power of factors in prognostic models. Tumor marker 15-3, also known as cancer antigen 15-3, is a circulating antigen expressed by human breast carcinoma cells. It has been useful as a breast cancer marker. Renal oncocytoma (RO) is currently considered within the spectrum of benign tumors of the kidney. In our case, a RO caused the elevated CA 15-3 levels in a patient without breast cancer. To our knowledge, we are the first to report a patient with chronic pruritus and elevated CA 15-3 leading to the detection of a renal tumor.

Conclusion: Our case highlights the association between chronic pruritus and neoplastic diseases, demonstrating an unusual presentation marked by elevated tumor markers.

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Abstract N°: 8081

Efficacy and safety of oral povorcitinib in patients with prurigo nodularis: 40-week results from a randomized, double-blind, placebo-controlled phase 2 study

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Introduction & Objectives:

Prurigo nodularis (PN) is a chronic inflammatory skin disease characterized by intensely itchy lesions resulting from chronic scratching. Pathogenesis of PN has been linked to proinflammatory cytokines and chemokines that signal through the JAK/STAT pathway, with JAK1 signaling particularly important for itch. Povorcitinib is an oral, small-molecule, selective JAK1 inhibitor. This analysis of the extension period (EXT) of a phase 2 study (NCT05061693; EudraCT 2021-006329-23) evaluated longer-term efficacy and safety of response-based povorcitinib dosing in patients (pts) with PN.

Materials & Methods:

Adults with PN for ≥3 months, ≥20 pruriginous lesions in ≥2 body regions, Investigator's Global Assessment (IGA) score ≥3, and mean Itch numerical rating scale (NRS) score ≥5 were randomized to once-daily povorcitinib (15, 45, or 75 mg) or placebo for 16 weeks (wks). Thereafter, pts received once-daily povorcitinib 45 or 75 mg during the 24-wk EXT. Primary endpoint was ≥4-point improvement in Itch NRS (Itch NRS4) at Wk 16. Secondary endpoints were time to Itch NRS4, percentage of pts achieving IGA treatment success (IGA-TS; IGA 0/1 [clear/almost clear] and ≥2-grade improvement from baseline) at Wk 16, and safety. Pts achieving both Itch NRS4 and IGA-TS (composite response) without missing data and without rescue therapy during the placebo-controlled period were considered responders and received the 45-mg dose during the EXT; nonresponders received 75 mg. Data with observed values were used in the EXT.

Results:

The primary endpoint was met; Wk 16 Itch NRS4 was achieved by significantly more pts receiving povorcitinib (15 mg, 36%; 45 mg, 44%; 75 mg, 57%) vs placebo (8%; all $P<0.01$). Time to Itch NRS4 was dose-dependent, with a median of 19 days for povorcitinib 75 mg vs not estimable for placebo. The majority of Wk 16 composite responders (84.0%; 21/25) originated from the 45 mg and 75 mg treatment groups. The most common reason for composite non-response at Wk 16 with the higher povorcitinib doses was achieving Itch NRS4 but not achieving IGA-TS.

Of 146 randomized pts, 124 were included in the EXT. In the full Wk 16 nonresponder subgroup, povorcitinib 75 mg resulted in increasing composite responses from 2% at Wk 16 to 41% by Wk 40. Itch NRS4 and IGA-TS responders also increased from 34% and 11% at Wk 16 to 70% and 51% by Wk 40, respectively. Forty-eight

percent of patients originally receiving placebo who switched to povorcitinib 75 mg achieved composite responses after 12 wks of treatment in the EXT. Among Wk 16 responders, 63% (12/19) achieved composite responses at Wk 40 and individual Itch NRS4 and IGA-TS responses were largely unchanged (89% each).

Povorcitinib was generally well tolerated during the EXT at both 45 and 75 mg doses, with few grade ≥3 treatment-emergent adverse events (AEs) or serious AEs (responders, 3.6% and 3.6%, respectively; nonresponders, 7.3% and 6.3%).

Conclusion:

Once-daily oral povorcitinib had a meaningful and sustained response in patients with recalcitrant PN, leading to improvements in itch and lesions. Itch NRS4 responses were more pronounced with the higher povorcitinib doses. However, IGA-TS responses may take longer than 16 wks to achieve. No new safety concerns were identified. These results suggest povorcitinib is a promising, novel treatment for PN. Phase 3 studies are currently enrolling.