Dermatology Practical & Conceptual

Dupilumab: an Additional Arrow in the Quiver for Prurigo Nodularis? Data From a Real-Life Setting

Roberta Di Caprio[1], Stefano Caccavale[1], Eugenia Veronica Di Brizzi[1], Caterina Mariarosaria Giorgio[1], Aleksandra Stefaniak[1], Giuseppe Argenziano[1], Anna Balato[1]

1 Dermatology Unit, University of Campania "Luigi Vanvitelli", Naples, Italy

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Corresponding Author: Stefano Caccavale, MD, Dermatology Unit, University of Campania "Luigi Vanvitelli", Via Pansini 5, 80131 Naples, Italy. ORCID ID: 0000-0001-7433-9283. E-mail: stefano85med@libero.it

ABSTRACT

Introduction: Prurigo nodularis (PN) management remains a significant challenge due to its chronicity, treatment resistance, and scarcity of approved treatments and to its impact on patients' quality of life.

Objective: The aim of this study was to assess PN therapeutic management in a real-life setting.

Methods: In this prospective observational study, 90 patients diagnosed with moderate-to-severe PN were included. Patients were each prescribed therapies available for PN according to symptom severity, consistent with treatment guidelines; only those undergoing systemic therapies were included. Disease severity was evaluated through the measurements of Investigator's Global Assessment (IGA) score, Numeric Rating Scale (NRS) for pruritus, and Dermatology Life Quality Index (DLQI) at the beginning of the study (week 0 – W0) and after a 6-month period of treatment (W24).

Results: At W0, patients were prescribed antidepressants (41.0%), dupilumab (34.0%), antihistamines (23.0%), phototherapy (4.0%) or nemolizumab (2.0%). At W24, patients on dupilumab achieved an IGA score of 0 or 1 and a ≥4-point NRS reduction, more than those on antidepressants (44.5% vs 16.7% and 54.4% vs 16.7%, respectively). The average DLQI score was reduced by 14 points in the dupilumab group, compared to a 6-point reduction in the antidepressant group.

Conclusions: Our findings reflect the real-world practice of treating PN and support the use of dupilumab as a new effective treatment option, with significant improvements in pruritus, quality of life, and disease severity compared to antidepressant therapy, suggesting its potential as a preferred therapeutic option for PN.

Introduction

Prurigo nodularis (PN) is an inflammatory skin condition with highly pruritic, hyperkeratotic papules or nodules arising in the setting of chronic pruritus, which can greatly impact patients' quality of life [1,2]. These nodules, often resulting from a relentless itch-scratch cycle, can lead to significant skin thickening and lichenification [3]. The prevalence of PN is not well documented, but it is known to affect both sexes and all races, with a slight predominance in middle-aged and elderly individuals [1]. PN pathogenesis is multifactorial and not yet fully understood. It is thought to involve a complex interplay between neurogenic, immunologic, and psychogenic factors. Neurogenic factors include increased nerve growth factor expression, and increased nerve fiber density in pruritic skin, which can lead to heightened itch perception. Immunologic factors involve elevated levels of circulating and skin-resident Th2 cells, mast cells, and eosinophils, which contribute to inflammation and pruritus. Psychogenic factors such as stress and anxiety can also exacerbate pruritus and scratching behavior, leading to a vicious itch-scratch cycle [4-6].

PN management remains a significant challenge due to the chronic nature of the disease, treatment resistance, and its substantial impact on patients' quality of life [7]. Traditional treatments consist of topical corticosteroids (TCS) and selective topical calcineurin inhibitors (TCI) administered either alone or with antihistamines, followed by phototherapy and other systemic treatments (gabapentin, antidepressants, corticosteroids, or immunosuppressants) [8]. However, these treatments often provide incomplete relief and can have undesirable side effects, such as skin atrophy caused by the long-term topical corticosteroid use and sedation caused by antihistamines [9].

Dupilumab, a fully human monoclonal IgG4 antibody, has recently emerged as a promising new treatment option for PN. It blocks interleukin (IL)-4 and IL-13 signaling by specifically binding to IL-4 receptor alpha subunit shared by both IL-4 and IL-13 receptor complexes and has demonstrated good efficacy and safety in a variety of diseases with type 2 inflammation, like atopic dermatitis and asthma [10,11]. Based on favorable results from clinical trials substantiating type 2 cytokines IL-4 and IL-13 implication in steering the pathogenesis of PN, dupilumab has been approved by the U.S. Food and Drug Administration (FDA) as the first specific drug for the treatment of PN [12]. However, data on dupilumab efficacy from real-world studies are lacking, and the range and degree of the disease burden and how it impacts treatment satisfaction in patients with PN remains not well investigated.

Objective

Our aim was to conduct a prospective observational study to assess the therapeutic management of PN in a real-life setting.

Methods

Study Design

This prospective observational study was conducted over a 27-month period (October 2021–December 2023) and involved 90 consecutive patients diagnosed with PN at the Dermatology Unit, University of Campania Luigi Vanvitelli, Naples, Italy. Patient demographic details are shown in Table 1.

Inclusion criteria were: males or females aged 18–80 years at the time of signing the informed consent, a minimum of 10 PN lesions in total on both legs, and/or both arms and/or trunk at screening visit, and patients with PN who are inadequately controlled on topical prescription therapies or when those therapies are not advisable.

Moreover, as regarded patients scheduled with dupilumab, those who did not respond to or showed contraindications

Table 1. Clinical and Demographic Patient Characteristics.

	N	%
Population	90	100
Sex		
male	35	39
female	55	61
Age, y		
≤ 18	1	1
> 18≤35	5	6
> 35≤65	44	49
> 65	40	44
Comorbidities		
Diabetes	15	16.7
Dyslipidemia	23	25.5
Hypertension	33	36.7
Heart diseases	4	4.4
Others	27	30
IGA		
1	22	24.4
2	36	40
3	19	21.2
4	13	14.4
NRS		
0-5	17	18.9
6-10	73	81.1
DLQI		
≤2	9	10
>2≤10	45	50
>10	36	40

Abbreviations: DLQI: Dermatology Life Quality Index; IGA: Investigator's Global Assessment score; NRS: Numeric Rating Scale.

or side effects to at least one conventional systemic therapy according to Italian law were included.

Exclusion criteria were: active chronic or acute infection (except well-controlled HIV infection), PN secondary to medications or medical conditions, such as neuropathy or psychiatric disease, known or suspected immunodeficiency, severe renal conditions, moderate-to-severe atopic dermatitis (AD) within six months before the screening visit, or documented diagnosis of moderate-to-severe AD from screening visit to randomization visit, active malignancy or history of malignancy within five years of baseline.

At enrollment, clinical and demographic data, including sex, age, comorbidities, and previous treatments, were collected. To date, guidelines for the treatment of PN have been published only by the Japanese Dermatological Association (JDA) and by the International Forum for the Study of Itch (IFSI) [13]. Both recommend a step-by-step treatment approach (step 1: TCS, TCI, and H1 antihistamines; step 2: topical capsaicin, intralesional corticosteroids, and UV therapy; step 3: gabapentin, pregabalin, or antidepressants in case of predominating neuropathic characteristics versus cyclosporine or methotrexate in cases of predominant inflammation; step 4: neurokinin 1 receptor (NK1R) antagonist, μ-opioid receptor antagonists, dupilumab, nemolizumab (currently under investigation) [8]. Enrolled patients could be prescribed any of the aforementioned available therapies, according to symptom severity, consistent with treatment guidelines. The entry into the study did not influence the therapeutic decision.

Clinical response was closely monitored throughout the treatment period to aid in the evaluation of the therapy efficacy. For all patients, disease severity was evaluated through the measurements of Investigator's Global Assessment (IGA) score [14], Numeric Rating Scale (NRS) for pruritus [15], and Dermatology Life Quality Index (DLQI) [16], at the beginning of the study (week 0 [W0]) and after 6-month period of systemic treatment (W24). The IGA score is a 5-point scale used to rate the severity of the disease. The NRS is a patient-reported outcome measure used to assess the severity of itching. The DLQI, because of its self-explanatory questions, is one of the most commonly used tools for the assessment of health-related quality of life (HRQoL) in dermatology. The DLQI score ranges from 0 to 30 points, with a lower score indicating better HRQoL. According to the classification of DLQI score proposed by Hongbo et al. [17], 0 to 1 point indicates normal QoL, 2–5 points indicate slightly, 6–10 points severely, 11–20 points very severely, and 21–30 extremely severely impaired HRQoL.

The baseline characteristics (e.g., IGA, NRS, DLQI, comorbidities) between the two subgroups treated with dupilumab or antidepressants were similar and quite comparable.

The study was conducted in accordance with the principles of the Declaration of Helsinki and Good Clinical Practice guidelines. All patients provided informed consent before participating in the study.

Statistical Analysis

The data are expressed in the form of mean for continuous variables, while categorical variables are presented as numbers and percentages. Data that passed the normality test were analyzed using a two-tailed t-test; otherwise, the Mann-Whitney test was used to calculate statistical differences. Statistical significance was established at $P<0.05$. Bonferroni test correction for multiple comparisons was applied for the analysis of IGA improvement, ≥4 points NRS, and DLQI reduction from baseline between patients on dupilumab and patients on antidepressant treatment. Statistical analyses were performed using GraphPad Prism 6.0 (GraphPad Software Inc, La Jolla, CA, USA) or SAS software v 9.3 (SAS Institute Inc., Cary, NC, USA).

Results

In all, 90 patients, 35 (39%) males and 55 (61%) females, aged 18–80, were enrolled into the study. Among the participants, 15 (16.7%) patients had diabetes, 23 (25.5%) dyslipidemia, 33 (36.7%) hypertension, and four cardiovascular diseases (4.4%). Other comorbidities were present in 27 (30%) of the patients. Baseline demographic and clinical data are summarized in Table 1. PN was diagnosed in 73% of cases by clinical evaluation only, while the remaining 27% by a combination of clinical and histological examinations. The distribution of the pruritic nodules varied among the patients, with the upper limbs 59 (66%), lower limbs 51 (57%), and trunk 48 (53.3%) being the most commonly affected areas. The back (N=17, 18.9%) and face (N=13, 14.4%) were less commonly affected.

Regarding disease severity indices, at baseline (W0), 22 (24.4%) patients presented Grade 1 IGA Score, 36 (40.0%) had Grade 2, 19 (21.2%) had IGA 3, and 13 (14.4%) had IGA4. Moreover, 17 (18.9%) patients had NRS itching score between 0–5, while the remaining 73 (81.1%) between 6–10, suggesting a moderate-to-very severe level of pruritus. The mean DLQI score at baseline was 16.2, indicating a very large effect of the disease on patients' life. In detail, DLQI ≤2 was observed in nine (10%), DLQI >2≤10 in 45 (50%), and DLQI >10 in 36 (40%) patients(Table 1).

All patients had previously under gone various treatments for PN, including topical corticosteroids (N=55, 61.1%), antihistamines (N=40, 44.4%), antidepressants (N=49, 54.4%, of whom 94% amitriptyline, 4% mirtazapine, and 2% escitalopram), systemic corticosteroids (N=9, 10.0%), and other immunosuppressants (N=7, 7.8%). At W0, patients

were prescribed as follows: 37 (41.0%) antidepressants, 30 (34.0%) dupilumab, 21 (23.0%) antihistamines (57.0% sedating and 43.0% non-sedating), four (4.0%) phototherapy, and two (2.0%), nemolizumab (Figure 1). The latter were two patients referred by the dermatologist to participate in a clinical trial evaluating the efficacy and safety of nemolizumab for the treatment of PN (NCT04921345). Thus, since 75% of patients were in treatment with antidepressants or dupilumab, the subsequent analysis was performed on this subpopulation. At W24, after six months of treatment, IGA 0–1 was attained by 14 (44.5%) patients on dupilumab, indicating clear or almost clear skin, compared to six (16.7%) of those on antidepressants (Figure 2; $**P<0.01$).

Furthermore, 16 (54.4%) patients receiving dupilumab had a ≥4-point NRS reduction compared to six (16.7%) patients on antidepressant therapy (Figure 3; $**P<0.01$) [14]. In terms of the impact on quality of life, the average DLQI score at W24 was reduced by 14 points in the dupilumab group, compared to a 6-point reduction in the antidepressant one (Figure 4, $***P<0.1$). Patients withdrawing from the study were defined as non-responders according to the non-responder imputation method.

Discussion

In this prospective observational study, we assessed the therapeutic management of PN in a real-world setting since it still poses considerable challenges for both patients and physicians. Indeed, until FDA approval of dupilumab as the first specific biologic agent for the treatment of PN, these patients were often treated with a multimodal, long-term regimen of both topical and systemic therapies; however, treatment effectiveness was poor [7-9]. When treating PN, the primary goal is to reduce pruritus and break the itch-scratch cycle, thereby allowing the skin to heal. In support of this, first, a correct diagnostic approach is mandatory to identify dermatological or systemic diseases associated with PN and to choose the best therapy for the patient. The approval of dupilumab has changed the scenario of PN management [19]. Data from recent clinical trials have demonstrated its effectiveness in alleviating both itching and nodule development

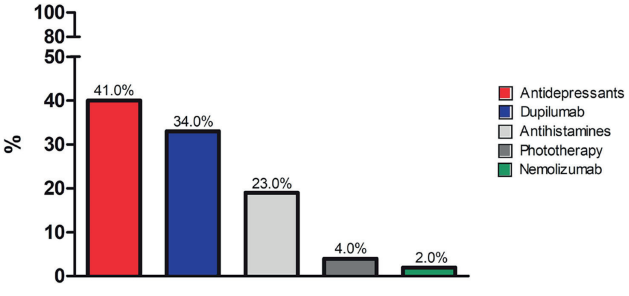

Figure 1. Percentage of patients receiving different systemic therapies at week 0.

as well as in enhancing overall quality of life. Indeed, in two parallel phase 3 trials of similar design, LIBERTY-PN PRIME and PRIME2, dupilumab resulted in a ≥4-point Worst Itch (WI)-NRS reduction in 60% and 18% of patients (PRIME) or 57.7% and 19.0% (PRIME2) at week 24, in the dupilumab and placebo arms, respectively [12]. Moreover, IGA of clear-to-almost clear (0–1) was achieved in 48% vs 18.4% as well as in 44.9% *vs* 15.9% in the two trials, respectively. Dupilumab-treated patients also had significant improvements in QoL, as measured by mean change in DLQI score from baseline to week 24: PRIME, -12.0; PRIME2, -13.2. [12]. Thus, these data confirmed the involvement of an activated Th2 cytokine pathway in PN pathogenesis. However, although randomized controlled trials allow assessing treatment efficacy, their applicability is restricted to ideal conditions, and this limits their ability to portray what happens in the real world. Moreover, as strict inclusion and exclusion criteria might limit generalizability and applicability of trial results to the broader PN population, disease treatment remains difficult and unsatisfactory. In our real-life setting, 40.0% of patients presented Grade 2 and 21.2% Grade 3 IGA scores at baseline; 81.1% had an NRS itching score between 6–10, suggesting a moderate-to-severe disease with a very high level of pruritus.

In line with the literature, topical corticosteroids, antidepressants, and antihistamines were the treatments most frequently used previously. At W0, patients enrolled in the study were prescribed with antidepressants (41.0%), dupilumab (34.0%), antihistamines (23.0%), phototherapy (4.0%), or nemolizumab (2.0%). We therefore decided to verify the improvement of the selected study indices in the two most represented treatment groups (antidepressants and dupilumab). Our results demonstrated a significantly greater reduction in all disease parameters in the patients treated with dupilumab compared to those treated with antidepressants. In particular, after 24 weeks of treatment, 44.5% of dupilumab-treated patients achieved an IGA score of 0 or 1, indicating clear or almost clear skin, vs 16.7% of those on antidepressants. Moreover, regarding pruritus and scratching, 54.4% of patients receiving dupilumab had a ≥4-point NRS reduction compared to 16.7% of patients on antidepressant therapy. As expected, pruritus relief greatly improved patients' QoL. Indeed, the mean DLQI score at W24 was reduced by 14 points in the dupilumab group, compared to the 6-point reduction we found in the antidepressant group. These findings are partially in line with previous studies.

In a real-world observational study, Zhang et al. demonstrated a significant reduction in IGA score, mean NRS Itch Intensity (NRSI), and DLQI, from 3.75, 8.625 and 15.13 to 1.50, 1.563, and 4.625, respectively, in eight adult patients diagnosed with PN after 16 weeks of treatment

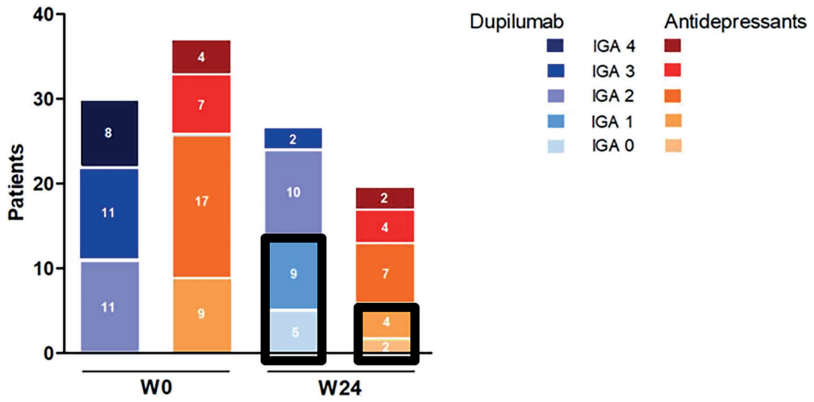

Figure 2. Improvement in IGA and IGA activity score at week 24 (W24). Statistical analysis was performed using the Mann-Whitney test (with Bonferroni correction) between the two most represented treatment groups (antidepressants and dupilumab), ***P*<0.01. The rectangles highlight patients achieving IGA0–1 in both dupilumab (5+9=14 patients) and antidepressants (2+4=6 patients) groups.

Figure 3. Percentage of patients who achieved NRS improvement (reduction) by ≥4 points from baseline (W0) at week 24 (W24), respectively. Statistical analysis was performed using the Mann-Whitney test (with Bonferroni correction) between the two most represented treatment groups (antidepressants and dupilumab), ***P*<0.01.

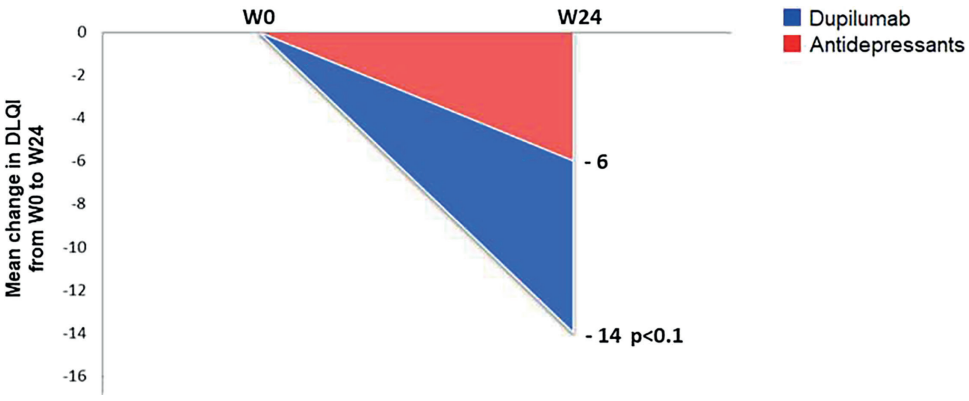

Figure 4. Mean DLQI reduction from baseline (W0) at week 24 (W24), respectively. Statistical analysis was performed using the Mann-Whitney test (with Bonferroni correction) between the two most represented treatment groups (antidepressants and dupilumab), ****P*<0.1.

with dupilumab [20]. Similarly, Chiricozzi et al. reported a reduction in IGA for at least 2 grades in 82.6% of the patients after 16 weeks of treatment [21]. In a retrospective cohort study, Pruritus Peak (PP)-NRS and DLQI significantly improved in all the 45 enrolled patients from baseline to 16 weeks after dupilumab treatment ($P< 0.001$ for both [22]. Moreover, compared to antidepressants, dupilumab has been proven to elicit fast and notable symptom reduction in PN patients. Zhai et al. observed a mean NRSI reduction of 7.89 points after only two weeks of dupilumab, whereas Beck et al. reported a pruritus improvement to nearly 0 in terms of NRSI in 12 weeks of treatment [23,24]. In addition, beyond clinical symptom relief, patients' mental health and quality of life also saw subjective improvements after biological therapy. Conversely, antidepressants' effects on chronic pruritus are variable and may appear modest in patients with PN. Kouwenhoven et al. showed that systemic treatment with gabapentin and/or antidepressants decreased the median average pruritus NRS score from 7.0 to 5.5 in 31 patients with severe chronic pruritus after 4 weeks and remained stable with up to 24 weeks of treatment [25]. However, the common side effects of antidepressants result in considerable rates of discontinuation. After initiation of gabapentin and/or antidepressants, vertigo and drowsiness were most frequently and particularly present in the first few days of treatment [26]. Moreover, even if previous clinical trials for gabapentin in neuropathic pain did not find a higher incidence of these adverse reactions in older adults, clinicians should be careful in these patients with preexisting dizziness or somnolence, with adjusted dosing, patient instructions, and close follow-up [27].

Limitations

Our study presents some limitations. First, the sample size of the enrolled patients, although higher than others, was relatively small, which may limit the generalizability of the findings and results. Second, the study was conducted over a 6-month period, which may not be sufficient to evaluate the long-term efficacy and safety of the treatments. In this regard, Paganini et al. have recently demonstrated the effectiveness of dupilumab in all the parameters considered for the disease, up to week 84 of treatment [19].

Conclusion

Our findings reflect the real-world practice of treating PN and support the use of dupilumab as a new effective treatment option, with significant improvements in pruritus, quality of life, and disease severity compared to antidepressant therapy. However, further large-scale, longer-term studies are needed to confirm these findings and to evaluate the long-term efficacy and safety of dupilumab in the management of PN.

References

1. Huang AH, Williams KA, Kwatra SG. Prurigo nodularis: Epidemiology and clinical features. *J Am Acad Dermatol*. 2020; 83(6): 1559-1565. DOI: 10.1016/j.jaad.2020.04.183. Epub 2020 May 23. PMID: 32454098.
2. Ferreira BR, Misery L. Psychopathology Associated with Chronic Pruritus: A Systematic Review. *Acta Derm Venereol*. 2023; 103:adv8488. DOI: 10.2340/actadv.v103.8488. PMID: 37606153; PMCID: PMC10461306.
3. Wong LS, Yen YT. Chronic Nodular Prurigo: An Update on the Pathogenesis and Treatment. *Int J Mol Sci*. 2022;23(20):12390. DOI: 10.3390/ijms232012390. PMID: 36293248; PMCID: PMC9604302.
4. Williams KA, Huang AH, Belzberg M, Kwatra SG. Prurigo nodularis: Pathogenesis and management. *J Am Acad Dermatol*. 2020; 83(6):1567-1575. DOI: 10.1016/j.jaad.2020.04.182. Epub 2020 May 24. PMID: 32461078.
5. Garcovich S, Maurelli M, Gisondi P, et al. Pruritus as a Distinctive Feature of Type 2 Inflammation. *Vaccines (Basel)*. 2021;9(3):303. DOI: 10.3390/vaccines9030303. PMID: 33807098; PMCID: PMC8005108.
6. Shao Y, Wang D, Zhu Y, et al. Molecular mechanisms of pruritus in prurigo nodularis. *Front Immunol*. 2023;14:1301817. DOI: 10.3389/fimmu.2023.1301817. PMID: 38077377; PMCID: PMC10701428.
7. Kowalski EH, Kneiber D, Valdebran M, Patel U, Amber KT. Treatment-resistant prurigo nodularis: challenges and solutions. *Clin Cosmet Investig Dermatol*. 2019;12:163-172. DOI: 10.2147/CCID.S188070. PMID: 30881076; PMCID: PMC6400231.
8. Müller S, Zeidler C, Ständer S. Chronic Prurigo Including Prurigo Nodularis: New Insights and Treatments. *Am J Clin Dermatol*. 2024;25(1):15-33. DOI: 10.1007/s40257-023-00818-z. Epub 2023 Sep 17. PMID: 37717255; PMCID: PMC10796623.
9. Whang KA, Kang S, Kwatra SG. Inpatient Burden of Prurigo Nodularis in the United States. *Medicines (Basel)*. 2019; 6(3):88. DOI: 10.3390/medicines6030088. PMID: 31405223; PMCID: PMC6789607.
10. Le Floc'h A, Allinne J, Nagashima K, et al. Dual blockade of IL-4 and IL-13 with dupilumab, an IL-4Rα antibody, is required to broadly inhibit type 2 inflammation. *Allergy*. 2020;75(5): 1188-1204. DOI: 10.1111/all.14151. Epub 2020 Jan 3. PMID: 31838750; PMCID: PMC7317958.
11. Pappa G, Sgouros D, Theodoropoulos K, et al. The IL-4/-13 Axis and Its Blocking in the Treatment of Atopic Dermatitis. *J Clin Med*. 2022;11(19):5633. DOI: 10.3390/jcm11195633. PMID: 36233501; PMCID: PMC9570949.
12. Yosipovitch G, Mollanazar N, Ständer S, et al. Dupilumab in patients with prurigo nodularis: two randomized, double-blind, placebo-controlled phase 3 trials. *Nat Med*. 2023;29(5): 1180-1190. DOI: 10.1038/s41591-023-02320-9. Epub 2023 May 4. PMID: 37142763; PMCID: PMC10202800.
13. Satoh T, Yokozeki H, Murota H, et al. 2020 guidelines for the diagnosis and treatment of prurigo. *J Dermatol*. 2021;48(9):e414-e431. DOI: 10.1111/1346-8138.16067. Epub 2021 Jul 27. PMID: 34314056.
14. Reich A, Riepe C, Anastasiadou Z, et al. Itch Assessment with Visual Analogue Scale and Numerical Rating Scale: Determination

of Minimal Clinically Important Difference in Chronic Itch. *Acta Derm Venereol.* 2016; 96(7):978-980. DOI: 10.2340/00015555-2433. PMID: 27068455.

15. Phan NQ, Blome C, Fritz F, et al. Assessment of pruritus intensity: prospective study on validity and reliability of the visual analogue scale, numerical rating scale and verbal rating scale in 471 patients with chronic pruritus. *Acta Derm Venereol.* 2012; 92(5): 502-507. DOI: 10.2340/00015555-1246. PMID: 22170091.
16. Finlay AY, Khan GK. Dermatology Life Quality Index (DLQI) a simple practical measure for routine clinical use. *Clin Exp Dermatol.* 1994; 19(3):210-216. DOI: 10.1111 /j.1365-2230.1994.tb01167.x. PMID: 8033378.
17. Hongbo Y, Thomas CL, Harrison MA, et al. Translating the science of quality of life into practice: What do dermatology life quality index scores mean? *J Invest Dermatol.* 2005; 125(4):659-664. DOI: 10.1111/j.0022-202X.2005.23621.x. PMID: 16185263.
18. Riepe C, Osada N, Reich A, et al.. Minimal Clinically Important Difference in Chronic Pruritus Appears to be Dependent on Baseline Itch Severity. *Acta Derm Venereol.* 2019; 99: 1288-1290. DOI: 10.2340/00015555-3332. PMID: 31580464.
19. Paganini C, Talamonti M, Maffei V, et al. Dupilumab for Treatment of Prurigo Nodularis: Real-Life Effectiveness for up to 84 Weeks. *J Clin Med.* 2024; 13(3):878. DOI: 10.3390 /jcm13030878. PMID: 38337572; PMCID: PMC10856572.
20. Zhang Z, Li S, Wang Y, Zhao J. A real-world observational study of dupilumab treatment in adult patients with prurigo nodularis. *An Bras Dermatol.* 2023; 98(4):440-448. DOI: 10.1016/j. abd.2022.09.008. Epub 2023 Mar 23. PMID: 36966024; PMCID: PMC10334323.
21. Chiricozzi A, Gori N, Ippoliti E, et al. Long-term therapeutic response to dupilumab in patients affected by prurigo nodularis: A real-world retrospective study. *J Eur Acad Dermatol Venereol.* 2024;38(10):e892-e895.DOI: 10.1111/jdv.19980. Epub 2024 Mar 27. PMID: 38534078.
22. Fang HY, Lian CH. The effectiveness and safety of dupilumab in the management of refractory prurigo nodularis in 45 Chinese patients: A real-life observational study. *J Dermatol.* 2023; 50(8):1084-1087. DOI: 10.1111/1346-8138.16803. Epub 2023 Apr 23. PMID: 37088954.
23. Zhai LL, Savage KT, Qiu CC, et al. Chronic Pruritus Responding to Dupilumab-A Case Series. *Medicines (Basel).* 2019; 6(3):72. DOI: 10.3390/medicines6030072. PMID: 31261951; PMCID: PMC6789555.
24. Beck TC, Wilson EM, Wilkes E, et al. Kappa opioid agonists in the treatment of itch: just scratching the surface? *Itch (Phila).* 2023; 8(4):e0072. DOI: 10.1097/itx.0000000000000072. Epub 2023 Dec 6. PMID: 38099236; PMCID: PMC10720604.
25. Kouwenhoven TA, van de Kerkhof PCM, Kamsteeg M. Gabapentin and oral antidepressants for chronic pruritus: a prospective cohort study evaluating efficacy and side effects in daily dermatological practice. *J Dermatolog Treat.* 2023; 34(1):2274291. DOI: 10.1080/09546634.2023.2274291. Epub 2023 Oct 31. PMID: 37905412.
26. Sreekantaswamy SA, Mollanazar N, Butler DC. Gabapentinoids for Pruritus in Older Adults: A Narrative Review. *Dermatol Ther (Heidelb).* 2021; 11(3):669-679. DOI: 10.1007/s13555 -021-00513-z. Epub 2021 Mar 15. PMID: 33721214; PMCID: PMC8163906.
27. Serpell MG. Neuropathic Pain Study Group. Gabapentin in neuropathic pain syndromes: a randomised, double-blind,