Dupilumab for Prurigo Nodularis: Real-World Outcomes Up to 104 Weeks from the DUPItaPN Study

Running title: Long-Term Real-World Outcomes of Dupilumab in Prurigo Nodularis

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Data availability: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Ethics statement: This work was based on the systematic and continuous collection of clinical data within routine practice across Italian dermatology centers. According to current AIFA guidance, registry-based data collection without predefined study endpoints is not classified as an observational study; therefore, Ethics Committee approval and individual informed consent were not required, except for the publication of patients' clinical photographs. All data were handled in compliance with applicable privacy regulations and anonymized prior to analysis.

Patient consent: The patient provided written informed consent for the publication of her clinical photographs and anonymized clinical data.

What is already known about this topic?

- Prurigo nodularis (PN) is a chronic, intensely itchy skin disorder that greatly affects quality of life.
- Dupilumab is approved for moderate-to-severe PN, but real-world long-term data, especially in patients with multiple comorbidities, are limited.

What does this study add?

- Dupilumab showed rapid, sustained improvement in itch, lesions, sleep, pain, and quality of life up to 104 weeks, with good safety even in elderly and comorbid patients.

Abstract

Background: Prurigo nodularis (PN) is a chronic, intensely pruritic skin disorder that markedly impairs quality of life. Dupilumab, an IL-4Rα antagonist, is approved for moderate-to-severe PN, but long-term real-world evidence remains limited.

Objectives: To evaluate the long-term effectiveness and safety of dupilumab in adults with PN, including those with multiple comorbidities, in a real-world multicenter setting.

Methods: Clinical data were collected from 26 Italian dermatology centers. Adults with PN refractory to topical therapies and/or phototherapy, and/or prior systemic treatments who received dupilumab for a minimum treatment duration of 12 weeks were included. Outcomes routinely assessed in practice—Worst Itch Numeric Rating Scale (WI-NRS), Investigator Global Assessment for PN-Stage (IGA PN-S), Sleep NRS, Skin Pain NRS, and Dermatology Life Quality Index (DLQI)—were analyzed at baseline and weeks 12, 24, 52, 76, and 104. Main endpoints were ≥4-point WI-NRS reduction and IGA PN-S 0/1 status. Predictors of response and safety were also evaluated.

Results: A total of 543 patients (mean age 65.7 years; 63.7% female) were included. Dupilumab induced rapid and sustained improvements: mean WI-NRS decreased from 8.7 to 2.7 at week 24 and to 1.7 at week 104 ($p < 0.001$); ≥4-point WI-NRS reduction was achieved by 86.4% and by 86.8% of patients at 24 and 104 weeks, respectively; IGA PN-S 0/1 by 62.8% and by 81.2% of patients at 24 and 104 weeks. DLQI improved from 17.4 to 2.6 ($p < 0.001$). Higher baseline WI-NRS predicted better outcomes, while psychiatric comorbidities and prior tricyclic antidepressant use predicted lower response. Dupilumab was well tolerated; discontinuation due to adverse events occurred in 2.9%, with no cancer progression or viral reactivation.

Conclusions: Dupilumab provided sustained, clinically meaningful benefits and a favourable safety profile over 104 weeks, supporting its role as a long-term treatment for moderate-to-severe PN, including in elderly and comorbid patients.

Introduction

Prurigo nodularis (PN), or nodular prurigo, is a chronic inflammatory skin disorder characterized by persistent pruritus and indurated nodules lasting ≥6 weeks[1]. These symptoms severely impair patients' quality of life and mental health[2]. Epidemiological studies report a prevalence of 6.5–111.0 per 100,000 (median 32.7) and an incidence of 2.9–20 per 100,000 person-years[3]. PN is strongly associated with psychiatric, endocrine, cardiovascular, renal diseases, and malignancies, resulting in a higher comorbidity burden than other chronic dermatoses[4]. Anxiety, depression, and suicidal ideation are particularly frequent[5].

The pathophysiology of PN is multifactorial and incompletely understood, involving neuronal sensitization, dermal fibrosis, and a self-perpetuating itch–scratch cycle. Given this complexity, therapy must balance efficacy and safety, especially in patients with comorbidities such as hypertension or renal impairment, and minimize drug interactions.[6] Although individualized treatment based on disease severity, quality-of-life impact, and comorbidities remains essential, recent expert consensus and clinical practice guidelines now outline structured therapeutic options for PN[7]. In mild cases, topical corticosteroids and calcineurin inhibitors remain first-line options.[8] For moderate-to-severe or refractory disease, systemic agents such as gabapentinoids, antidepressants, sedating antihistamines, or short-term corticosteroids may be used, though efficacy is limited and long-term safety concerns persist. Phototherapy, immunosuppressants, and neuromodulators represent additional, yet often suboptimal, alternatives.[9,10]

A major advance in PN therapy was the development of dupilumab, a fully human monoclonal antibody that binds the IL-4 receptor α subunit (IL-4Rα), thereby inhibiting signaling of both IL-4 and IL-13. By blocking these key type 2 inflammatory pathways, dupilumab reduces the activation of downstream JAK-STAT pathways, limits the recruitment of inflammatory cells, and disrupts the itch–scratch cycle, leading to both decreased pruritus and improvement of skin lesions.[11] In 2022, dupilumab became the first systemic therapy approved by the FDA and EMA for adults with moderate-to-severe PN, based on the LIBERTY-PN PRIME and PRIME2 phase 3 trials (n=151 and n=160).[12-15] In these studies, dupilumab achieved significantly higher WI-NRS response rates (60% vs 18.4%; 37.2% vs 22.0%) and greater reductions in nodule counts compared with placebo.

Real-world studies have since confirmed dupilumab's short- and mid-term effectiveness in PN across various populations.[16-18] However, evidence on long-term outcomes and large-scale safety remains limited. To address this gap, we conducted a multicenter Italian study to evaluate the long-term effectiveness and safety of dupilumab in adult PN patients.

Materials and methods

Study design

The systematic data collection was conducted across 26 Italian dermatology centers (Supplementary Table 1) to describe the long-term use of dupilumab in patients with PN, including those with relevant comorbidities. This retrospective, multicenter observational study adopted a predefined follow-up schedule up to week 104, with data locked in August 2025. Because patients started dupilumab at different times, the dataset reflects a cross-sectional snapshot of treatment exposure and clinical outcomes at the time of data closure. Adult patients (≥18 years) with a diagnosis of PN—defined by chronic pruritus lasting more than six weeks, signs of repeated scratching, and the presence of pruritic nodules—were routinely treated with dupilumab in outpatient settings according to clinical judgment.[19] Only patients with a minimum treatment duration of 12 weeks were included, ensuring sufficient treatment exposure. Patients with end-stage chronic kidney disease, severe hepatic impairment, or uncontrolled diabetes were excluded. No formal washout period was defined. Eligibility required lesions persisting ≥3 months, failure of topical therapies and/or phototherapy, ≥20 nodules, and pruritus NRS ≥7. Dupilumab was administered according to the Summary of Product Characteristics.[11] Data of patients treated with dupilumab, including demographic and clinical characteristics, history of atopic dermatitis or other atopic conditions, age at onset of atopic dermatitis, disease duration, comorbidities, and details of previous and ongoing therapies were collected. Disease severity was assessed using validated instruments, including the WI-NRS[20] (range 0–10), the Investigator Global Assessment for PN-Stage[21] (IGA PN-S, range 0 = clear to 4 = severe, ≥100 nodules), the Sleep-NRS[22] and Skin Pain-NRS[23] (both range 0–10), and the Dermatology Life Quality Index (DLQI, range 0–30). These measures were recorded at baseline and at follow-up visits (weeks 12, 24, 52, 76, and 104). Where available, laboratory parameters such as total IgE levels (kU/L), lactate dehydrogenase (U/L), and eosinophil count ($\times 10^9$/L) were also collected at baseline and during follow-up. The

primary measures of interest were the proportions of patients achieving a reduction of at least 4 points in WI-NRS and those reaching an IGA PN-S score of 0 or 1 during follow-up up to week 104. Additional analyses examined potential factors associated with clinical response. Safety was evaluated by describing adverse events and reasons for treatment discontinuation as routinely reported at each participating center. This study used aggregated, fully anonymized data that were collected as part of routine clinical care and provided by participating centres in non-identifiable, aggregate form. The dataset cannot be linked to individual patients. Therefore, in accordance with applicable institutional policies and national regulations, formal ethics committee approval and individual informed consent were not required.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation, while categorical variables were presented as numbers and percentages. Missing data were handled using the last observation carried forward method (LOCF). The Shapiro–Wilk test was applied to assess the distribution of continuous variables. Longitudinal comparisons were made using the Friedman test for repeated measures, and correlations between baseline IgE levels and clinical indices were assessed using Spearman's rank correlation coefficient. Univariate and multivariate analyses were conducted to explore whether baseline characteristics influenced the likelihood of achieving a ≥4-point WI-NRS reduction or an IGA PN-S score of 0 or 1. Statistical significance was set at $p < 0.05$, and all analyses were performed using STATA 11.2 software (StataCorp LP Inc., College Station, TX, USA).

Results

Baseline characteristics of dupilumab-treated patients

Data were collected from 543 patients treated with dupilumab monotherapy for at least 12 weeks. At the time of analysis, 519 patients had reached week 24, 417 week 52, 353 week 76, and 297 week 104. Baseline demographics characteristics are summarized in table 1. The study population was predominantly female (63.7%), with a mean age of 65.7 years and a mean body mass index of 26.7. The mean disease duration was 8.9 years, and 20.1% of patients reported a history of smoking. A history of atopic dermatitis was present in 32.6% of patients, allergic rhinitis in 17.8%, asthma in 10.5%, and allergic conjunctivitis in

5.3%. The most frequent systemic comorbidities were hypertension (42.9%), dyslipidemia, and cardiovascular disease. Notably, 36 patients had a past or current malignancy, 23 had chronic kidney disease, 14 had a history of hepatitis B or C infection, and 6 were HIV-positive and receiving therapy. Previous treatments most often included systemic corticosteroids (43.1%), while approximately one-quarter of patients had received systemic immunosuppressants or antidepressants. No patient received concomitant topical or systemic therapies for PN during the study period, as dupilumab was administered as monotherapy.

Effectiveness outcomes

Treatment with dupilumab led to a rapid and sustained improvement in itch severity. The mean WI-NRS score decreased significantly from 8.69 ± 1.41 at baseline to 3.78 ± 2.63 at week 12, and further to 2.67 ± 2.59 at week 24. Continued improvement was observed at later time points, with mean scores of 1.99 ± 2.39 at week 52, 1.79 ± 2.36 at week 76, and 1.72 ± 2.44 at week 104 ($p < 0.001$ for trend) (Table 2).

Skin clearance, defined as the proportion of patients achieving an IGA PN-S score of 0 or 1, demonstrated a slower but steady improvement over time. (Table 2)

At week 12, 43.2% of patients had already reached this threshold, and the proportion increased progressively with longer treatment exposure. By week 52, 76.9% of patients had achieved IGA 0–1, a rate that remained stable thereafter, with comparable values observed at weeks 76 and 104 (Figure 1).

Other disease-related symptoms displayed a comparable time course, with skin pain decreasing from a mean baseline score of 6.62 ± 2.41 to 2.49 ± 2.53 at week 12 and subsequently stabilizing around 1.0 during follow-up visits. Sleep quality showed parallel improvements, with Sleep-NRS decreasing from 7.09 ± 2.55 at baseline to 2.37 ± 2.75 at week 12, and further to 1.09 ± 2.12 at week 104. Quality of life improved substantially as reflected by the DLQI, which fell from 17.4 ± 6.94 at baseline to 6.69 ± 6.22 at week 12, 4.51 ± 5.75 at week 24, and continued to decrease to 2.57 ± 4.89 at week 104 ($p < 0.001$). These findings were consistent with categorical analyses. As shown in Figure 1, the proportion of patients achieving at least a 4-point reduction in WI-NRS from baseline increased from 68.9% at week 12 to 78.7% at week 24, and peaked at 87.7% by week 76, with 86.8% maintaining this response at week 104. This indicates that the vast majority of patients not

only improved but also sustained clinically meaningful itch relief throughout two years of treatment. Representative clinical images illustrate this evolution, showing improvement of nodular lesions and residual post inflammatory changes after 24 weeks of therapy compared with baseline (Figure 2).

Predictors of treatment response: univariate and multivariate analysis

Univariate logistic regression analyses identified several baseline variables significantly associated with clinical response, including reduction of at least four points in WI-NRS and achievement of IGA 0 or 1 (Supplementary Tables 2 and 3). At 12 weeks, higher baseline WI-NRS scores, presence of cardiovascular disease and previous topical or systemic antihistamine therapies were positively associated with ≥4-point reduction in WI-NRS, whereas prior use of tricyclic antidepressants was negatively associated (OR 0.15, $p<0.001$). Similar trends persisted at later time points, with a higher baseline WI-NRS consistently predicting greater reductions at 24, 52, 76, and 104 weeks. A higher sleep NRS at baseline also emerged as a significant predictor at 52 and 76 weeks. For achievement of IGA 0 or 1, prior tricyclic antidepressant use and psychiatric comorbidities were consistently associated with lower likelihood of response. Multivariate stepwise logistic regression analyses confirmed baseline WI-NRS as a strong independent predictor of ≥4-point reduction at all evaluated time points, together with cardiac comorbidities at 12–24 weeks, BMI at 24 weeks, and prior corticosteroid therapies at 76 weeks (Supplementary Table 4). Regarding IGA 0 or 1, baseline DLQI, prior tricyclic antidepressant use, and psychiatric comorbidities remained significant negative predictors, particularly at early (12–24 weeks) and mid-term follow-up. Overall, these analyses highlight baseline disease severity, comorbidities, and prior treatment history as key determinants of clinical response over time. Notably, neither the concomitant presence nor a history of atopic dermatitis had any impact on the likelihood of achieving a ≥4-point reduction in WI-NRS or attaining IGA 0/1.

Laboratory outcomes

Longitudinal evaluation of laboratory parameters demonstrated a progressive and statistically significant decline in total IgE concentrations over the course of dupilumab treatment. (Table 3) Mean IgE values decreased from 989 ± 1817 kU/L at baseline to 502 ± 1087 kU/L at week 24, 277 ± 569 kU/L at week 52, and further to 155 ± 186 kU/L at week

104 ($p < 0.001$). Eosinophil counts showed modest fluctuations over time, with a baseline mean of 0.47 ± 0.49 $\times 10^9$/L, a reduction to 0.29 ± 0.27 at week 24, and variable values at later assessments (0.41 ± 0.91 at week 52, 0.26 ± 0.22 at week 76, and 0.36 ± 0.51 at week 104) ($p = 0.010$). In contrast, LDH levels remained stable throughout follow-up, with no significant differences compared with baseline (mean 211 ± 81.5 U/L at baseline vs. 201 ± 63.2 U/L at week 104, $p = 0.525$). Correlation analyses at baseline showed that total IgE levels were only weakly associated with disease severity (supplementary table 5). A modest but statistically significant positive correlation was observed between total IgE and IGA PN-S scores ($\rho = 0.181$, $p = 0.009$), whereas no significant associations were detected with WI-NRS, skin pain, sleep disturbance, or DLQI. Conversely, strong correlations were evident among the clinical measures themselves. WI-NRS was significantly associated with IGA PN-S ($\rho = 0.262$, $p < 0.001$), skin pain ($\rho = 0.375$, $p < 0.001$), sleep disturbance ($\rho = 0.515$, $p < 0.001$), and DLQI ($\rho = 0.247$, $p < 0.001$). Similarly, sleep disturbance showed strong correlations with both skin pain ($\rho = 0.600$, $p < 0.001$) and a weak correlation with DLQI ($\rho = 0.344$, $p < 0.001$).

Adverse events and drop out

Among the 543 patients included in the study, the overall treatment discontinuation rate was 19.7% (n=107). The most common reason was loss to follow-up (9.7%, n=53), while a small proportion (0.7%, n=4) discontinued therapy voluntarily. Lack of efficacy, defined as insufficient control of pruritus or persistence of nodular lesions, accounted for 6.2% of discontinuations (n=34). Adverse events led to treatment interruption in 2.9% of cases (n=16), most frequently due to conjunctivitis (n=6), followed by psoriasis exacerbation (n=2), arthralgia (n=2), and single cases of myalgia, lymphadenopathy, fever, gingival erosions, anemia, and photodermatitis. Additional adverse events not requiring discontinuation included arthralgia (3 further cases), conjunctivitis (6), rosacea eruption (3), telogen effluvium (2), psoriasis (2), and isolated cases of dyslipidemia, oral candidiasis, oral ulcers, diarrhea, and facial erythema. Importantly, no cases of malignancy progression or reactivation of chronic viral infections (HCV, HBV, or HIV) were observed during dupilumab therapy.

Discussion

This multicenter, real-world systematic data collection offers long-term insights into the effectiveness and safety of dupilumab in prurigo nodularis, including patients with systemic comorbidities. To our knowledge, this is one of the largest cohorts reported to date, with over 500 patients followed for up to 104 weeks. Overall, our results reinforce and extend the evidence from pivotal randomized trials and previous real-world series demonstrating that dupilumab delivers durable benefits across key disease domains — including itch, skin clearance, sleep, pain, and quality of life. In our real-world cohort, response rates were not only comparable but in fact higher, with nearly 79% of patients achieving a ≥4-point WI-NRS reduction by week 24, compared with 60% in PRIME. Moreover, long-term follow-up up to two years showed that clinical responses deepened and were maintained, highlighting the durability of dupilumab's effect beyond the timeframe of the phase 3 trials. Our study also included patients with multiple comorbidities, who are typically excluded from clinical trials, and both effectiveness and safety outcomes remained favourable, further supporting the utility of dupilumab in routine clinical practice. Our results are also consistent with previously published real-life studies.[17,24] A more recent Chinese multicenter study on 73 patients demonstrated that by week 12, nearly 85% achieved PP-NRS4, while 37–47% reached IGA 0/1 at weeks 12–16, with parallel gains in quality of life. [16] These early improvements are consistent with the rapid antipruritic effects observed in our cohort, though our long-term data demonstrate further progressive benefits up to two years. Taken together, these real-world studies, together with our large multicenter experience, reinforce the external validity of clinical trial results and highlight dupilumab's sustained effectiveness and safety in diverse PN populations. From a laboratory perspective, dupilumab induced a progressive and significant decline in total IgE levels over two years, consistent with its mechanism of action on the IL-4/IL-13 signaling pathway. However, correlations between IgE and disease severity were weak in our cohort, underscoring that IgE cannot be used as a reliable biomarker for PN severity or treatment response. Interestingly, our results contrast with a recent retrospective study suggesting that elevated baseline IgE levels predicted greater relief from pruritus under dupilumab, raising the possibility of IgE as a biomarker for treatment stratification.[25] These discrepancies highlight the need for further prospective studies to clarify whether IgE truly has predictive value in PN or whether other

inflammatory markers may provide more reliable guidance. Eosinophil counts fluctuated modestly, without clear clinical significance, and LDH levels remained stable. Taken together, these findings suggest that, similar to atopic dermatitis, clinical parameters remain superior to serological markers for monitoring treatment outcomes in PN. An additional strength of our study is the exploration of potential predictors of treatment response. Logistic regression analyses revealed that baseline disease severity, as reflected by a higher baseline WI-NRS score, was the most consistent and independent predictor of clinically meaningful pruritus reduction across all time points, confirming that patients with higher symptom burden are most likely to benefit from dupilumab. Interestingly, cardiovascular comorbidities were also associated with better outcomes at earlier time points, though the biological plausibility of these associations remains unclear and may be confounded by demographic or clinical factors. An interesting finding of our regression analyses was the consistent identification of previous tricyclic antidepressant use and psychiatric comorbidities as negative predictors of dupilumab response. Rather than suggesting misdiagnosis in these cases, this observation may reflect the complex bidirectional interplay between psychogenic pruritus and PN, as PN can also arise as a complication of chronic pruritus with a psychiatric component. In such patients, a combined therapeutic strategy — including both dupilumab and antidepressant therapy — may be particularly relevant. Moreover, our results indicate that dupilumab can still be effective in patients with other pruritogenic comorbidities, which deserves emphasis. These findings raise an important practical question regarding timing and extent of etiological work-up: while a comprehensive assessment remains desirable, it may be most clinically useful to prioritize it in cases of suboptimal or absent response to dupilumab. Overall, our data support a nuanced, multidisciplinary approach that integrates dermatological and psychiatric perspectives while avoiding premature exclusion of patients from biologic therapy.

Baseline DLQI also emerged as a negative predictor for achieving IGA 0/1, reinforcing the interplay between quality of life impairment and therapeutic response. These findings align with previous observations in other inflammatory dermatoses,[26] where baseline severity and comorbidity burden modulate response to biologic therapy. Overall, our results emphasize the importance of comprehensive baseline assessment, including clinical history

and psychiatric evaluation, to better stratify patients and optimize treatment strategies in PN. Safety analysis confirmed the favourable tolerability of dupilumab. The discontinuation rate due to adverse events was low (2.9%), and most adverse events were mild or manageable, consistent with the known safety profile of dupilumab in other type 2 inflammatory diseases.[27] Conjunctivitis was the most frequently reported event, but severe ocular complications were not observed.[28] Importantly, no reactivation of chronic infections (HBV, HCV, HIV) occurred, and no progression or recurrence of malignancy was detected in patients with prior cancer, providing reassuring data for clinicians managing patients with these comorbidities.[29,30] Clinically relevant, dupilumab was also well tolerated in patients with chronic kidney disease, without signs of renal function deterioration or treatment-related complications, in keeping with previous real-world reports supporting its safety in this fragile population.[31] These findings are highly relevant given the high prevalence of systemic diseases in PN patients, which often complicates systemic treatment decisions and limits the use of immunosuppressants or corticosteroids. Dupilumab's targeted mechanism of action and absence of broad immunosuppression likely explain this favourable profile. Our results also highlight the importance of long-term follow-up in PN. Whereas short-term studies demonstrated early effectiveness, our two-year data indicate that responses are not only durable but also continue to deepen over time, particularly with respect to nodule clearance and QoL restoration. This has significant implications for clinical practice: patients and physicians should be aware that maximal benefits may require sustained treatment, and premature discontinuation could undermine outcomes. Moreover, the relatively low dropout rate due to inefficacy (6.2%) suggests that most patients can expect meaningful and lasting benefit. The strengths of our experience include the large sample size, extended follow-up, and the inclusion of patients with a broad spectrum of comorbidities, offering a reliable reflection of routine clinical practice. However, some limitations should be acknowledged. The retrospective design and inter-center variability may introduce biases, and data from the first 12 weeks of treatment were not captured. In addition, laboratory data at week 12 were not systematically collected. The inclusion of patients with ≥20 nodules, IGA 4, WI-NRS ≥7, and at least 12 weeks of dupilumab monotherapy likely selected more severe cases, limiting generalizability and potentially affecting outcomes. Moreover, the exclusion of patients with end-stage chronic

kidney disease, severe hepatic impairment, or uncontrolled diabetes may further limit the applicability of these findings to the overall PN population. PN's fluctuating course may overestimate long-term benefits, the absence of a control group prevents causal inference, and analyses of biomarkers such as IgE and eosinophils should be interpreted cautiously due to small sample sizes. Finally, while potential predictors of response emerged, these require confirmation in prospective, controlled settings to establish their value for guiding personalized treatment strategies. In conclusion, dupilumab provides durable improvements in pruritus, lesion clearance, sleep, pain, and quality of life in PN, with a favourable safety profile even in patients with comorbidities. These findings support the growing role of dupilumab as a key systemic treatment option for moderate-to-severe disease. Future research is warranted to identify biomarkers of response, explain reduced effectiveness in patients with psychiatric comorbidities, and evaluate the long-term impact of dupilumab on disease and healthcare burden.

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Figure legends

Figure 1. Proportion of patients achieving IGA PN-S 0 or 1 and proportion of patients with ≥4-point WI-NRS reduction from baseline over time, Percentages are shown for each assessment timepoint.

Figure 2. Clinical images of a patient with prurigo nodularis before and after treatment with dupilumab. (a–d) Baseline: before initiation of dupilumab therapy, showing widespread nodular lesions on the trunk and extremities (WI-NRS: 10; IGA-PN: 4). (e–h) After 24 weeks of treatment: marked improvement with mainly post inflammatory changes and residual scars visible (WI-NRS: 3; IGA-PN: 1). This case was intentionally selected because it represents an emblematic and clinically meaningful presentation of PN. The patient had applied adhesive patches over nodules to avoid scratching, demonstrating mechanical suppression of scratching and interruption of the itch–scratch cycle, central to PN pathophysiology. Additionally, she developed lesions on the mid-back by using external objects to reach otherwise inaccessible areas, highlighting the behavioral and neuro-sensory components of PN. This case provides a didactic visual example of disease mechanisms beyond classical distribution patterns.

Table 1. Baseline clinical characteristics of patients with prurigo nodularis undergoing dupilumab therapy. Data are presented as mean ± standard deviation (SD) for continuous variables and number and percentage for categorical variables.

Clinical characteristics	**ALL (N=543)**
General	
Female/male, n (%)	346 (63.7)/197 (36.3)
Age, mean (SD), years	65.7 (15.8)
BMI, mean (SD), kg/m2	26.7 (3.2)
Smokers, n (%)	114 (20.1)
Age of onset, mean (SD), years	56.6 (19.1)
Disease duration, mean (SD), years	8.9 (14.1)
Atopic Comorbidities, n (%)	
Atopic dermatitis	177 (32.6)
Allergic rhinitis,	97 (17.8)
Asthma	57 (10.5)
Allergic conjuntivitis	29 (5.3)
Comorbidities, n (%)	
Hypertension	233 (42.9)
Dyslipidemia	96 (17.6)
Cardiovascular disorders	92 (16.9)
Psychiatric comorbidities	89 (16.4)
Diabetes	79 (14.5)
Thyroid disorders	53 (9.7)
Previous or current carcinoma	36 (6.6)
Chronic renal failure	23 (4.2)
Previous or chronic HCV/HBV infection	14 (2.6)
HIV infection	6 (1.1)
Previous systemic therapy, n (%)	
Systemic steroid	232 (43.1)
Antihistamines	130 (23.9)
Tricyclic antidepressants	121 (22.2)
Immunosuppressants drugs	117 (21.5)
Narrow-band UVB	10 (1.8)

BMI, Body Mass Index;

Table 2. Therapeutic response of patients with prurigo nodularis during dupilumab treatment over time. *N* indicates the number of patients assessed at each visit using the Last Observation Carried Forward (LOCF) method. *P*-values were derived from the Friedman test for repeated measures to evaluate within-subject changes over time.

	Therapeutic response						
	Week 0	**Week 12**	**Week 24**	**Week 52**	**Week 76**	**Week 104**	**P-value***
	N=543	**N=543**	**N=519**	**N=417**	**N=353**	**N=297**	
WI-NRS, mean (SD)	8.69 (1.41)	3.78 (2.63)	2.67 (2.59)	1.99 (2.39)	1.79 (2.36)	1.72 (2.44)	<0.001
IGA PN-S, mean (SD)	3.42 (1.62)	1.68 (1.06)	1.24 (0.96)	0.92 (0.96)	0.82 (0.96)	0.78 (0.98)	<0.001
Skin Pain-NRS, mean (SD)	6.62 (2.41)	2.49 (2.53)	1.66 (2.28)	1.24 (2.03)	1.21 (2.16)	1.16 (2.13)	<0.001
Sleep-NRS, mean (SD)	7.09 (2.55)	2.37 (2.75)	1.59 (2.39)	1.10 (2.09)	1.06 (2.09)	1.09 (2.12)	<0.001
DLQI, mean (SD)	17.4 (6.94)	6.69 (6.22)	4.51 (5.75)	3.09 (5.02)	2.93 (4.99)	2.57 (4.89)	<0.001

WI-NRS, Worst Itch Numeric Rating Scale, DLQI, Dermatology Life Quality Index, NRS, numeric rating scale, N, number, SD, standard deviation

Table 3. Longitudinal changes in laboratory indices in patients with prurigo nodularis during dupilumab treatment. N indicates the number of patients for whom each laboratory index was available at each visit, assessed using the Last Observation Carried Forward (LOCF) method. P-values were derived from the Friedman test for repeated measures to evaluate changes in Total IgE, eosinophil count, and LDH over time.

	Therapeutic response					
	Week 0	**Week 24**	**Week 52**	**Week 76**	**Week 104**	**P-value***
	N=268	**N=105**	**N=72**	**N=44**	**N=38**	
Total IgE (kU/L), mean (SD)	989 (1817)	502 (1087)	277 (569)	264 (564)	155 (186)	<0.001
Eosinophil count, mean (SD)	0.47 (0.49)	0.29 (0.27)	0.41 (0.91)	0.26 (0.22)	0.36 (0.51)	0.010
LDH (U/L), mean (SD)	211 (81.5)	189 (46.4)	202 (43.7)	211 (55.5)	201 (63.2)	0.525

IgE, immunoglobulin E, LDH, Lactate Dehydrogenase, N, number, SD, standard deviation

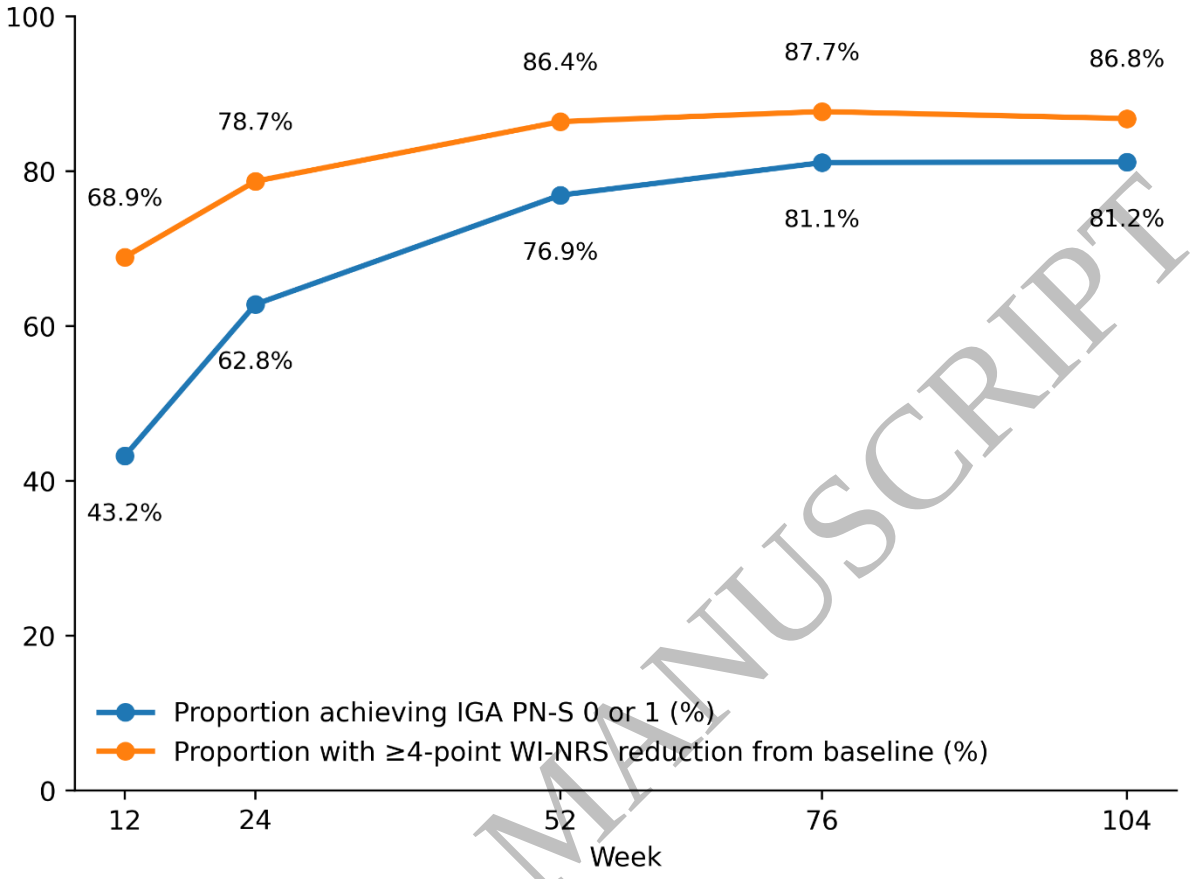

Figure 1
160x119 mm (x DPI)

Figure 2
165x93 mm (x DPI)