Dupilumab Efficacy on Itch and Skin Lesions in Adult Patients With Prurigo Nodularis May be Observed Concurrently or Independently Over 24 Weeks: Results From Two Phase 3 Trials

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INTRODUCTION

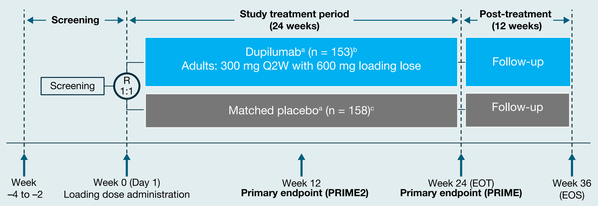
- Prurigo nodularis (PN) is a chronic inflammatory and pruritic skin disease. Clinically it is characterized by intense pruritus accompanied by hyperkeratotic nodules often associated with very low quality of life, including sleep disruption[1–3]
- The US Food and Drug Administration has recently approved dupilumab as the only treatment of PN[4] but it is unknown to what extent within-patient categorical improvements in itch and skin lesions occur concurrently or independently
- Two phase 3 clinical trials, LIBERTY PN PRIME and PRIME2, demonstrated dupilumab efficacy and safety in patients with PN[5,6]

OBJECTIVE

- **To report the efficacy of dupilumab on signs and symptoms in adult patients with PN who did and did not achieve the multicomponent endpoint**

STUDY DESIGN

Figure 1. Study design.



Key inclusion criteria
- Aged ≥ 18 to 80 years
- PN diagnosis for ≥ 3 months
- Average WI-NRS score ≥ 7 in the 7 days prior to Day 1 (daily assessed)
- ≥ 20 PN lesions at screening and Day 1
- History of failing a 2-week course of medium-to-superpotent TCS, or TCS not medically advisable
- 10% of mild active atopic dermatitis was allowed in the atopic population

Key exclusion criteria
- Severe renal conditions
- Active chronic or acute infection (except HIV infection)
- Known or suspected immunodeficiency
- Active malignancy or history of malignancy within 5 years before baseline
- Skin morbidities (except for PN and mild AD)
- PN secondary to medications
- PN secondary to medical conditions such as neuropathy or psychiatric disease

[a]Low-to-medium potency TCS/TCI as background therapy permitted (maintain dose from screening to EOT).
[b]One patient was not treated with IMP. [c]One patient in PRIME was randomized but not exposed to study intervention due to fear of being exposed to COVID-19.
AD, atopic dermatitis; EOS, end of study; EOT, end of treatment; IMP, investigational medicinal product; R, randomization; TCI, topical calcineurin inhibitor; TCS, topical corticosteroids. WI-NRS, Worst Itch Numerical Rating Scale.

STUDY DESIGN (CONT.)

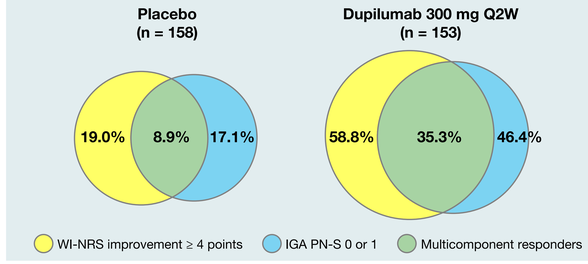
Study endpoints

- Multicomponent endpoint
  - Proportion of patients with a concomitant ≥ 4-point reduction in WI-NRS[a] from baseline and an IGA PN-S[b] score of 0 or 1 at Week 24
- Proportion of patients with a ≥ 4-point reduction in WI-NRS[a] from baseline at Week 24
- Proportion of patients achieving an IGA PN-S[b] score of 0 or 1 at Week 24
- Proportion of patients not achieving a ≥ 4-point reduction in WI-NRS from baseline nor an IGA PN-S score of 0 or 1 at Week 24

[a]**Worst-Itch Numerical Rating Scale (WI-NRS),** patient-reported outcome, worst pruritus in the past 24 hours (0 = no itch, 1–2 = mild pruritus, 3–6 = moderate pruritus, 7–9 = severe pruritus, 10 = very severe pruritus). Minimal important difference in WI-NRS depends upon the baseline score; for baseline WI-NRS ≥ 7, ≥ 4-point reduction is clinically meaningful[7]
[b]**Investigator's Global Assessment for PN Stage (IGA PN-S)[8],** clinician-assessed severity of disease, using a 5-point scale (0 = clear [no nodules], 1 = almost clear [1–5 nodules], 2 = mild [6–19 nodules], 3 = moderate [20–100 nodules], 4 = severe [> 100 nodules])

RESULTS

Figure 2. Proportion of patients with concomitant WI-NRS improvement from baseline by ≥ 4 points and IGA score 0 or 1 at Week 24.



- The proportion of patients treated with dupilumab vs. placebo who achieved a WI-NRS improvement by ≥ 4 points or an IGA PN-S score of 0 or 1 at Week 24 were 69.9% vs. 27.2%
- 23.5% of dupilumab-treated patients met only WI-NRS improvement by ≥ 4 points (and not an IGA PN-S score of 0 or 1), and 11.1% met only an IGA PN-S score of 0 or 1 (and not a WI-NRS improvement by ≥ 4 points) at Week 24

RESULTS (CONT.)

Table. Baseline demographic and clinical characteristics.

	Multicomponent responders		WI-NRS improvement ≥4 points		IGA PN-S 0 or 1		Non-responders	
	Placebo (n = 14)	Dupilumab 300 mg Q2W (n = 54)	Placebo (n = 30)	Dupilumab 300 mg Q2W (n = 90)	Placebo (n = 27)	Dupilumab 300 mg Q2W (n = 71)	Placebo (n = 115)	Dupilumab 300 mg Q2W (n = 46)
Age, mean (SD), years	41.7 (14.9)	52.4 (15.9)	45.0 (16.6)	51.1 (15.6)	41.1 (14.5)	49.9 (17.6)	50.7 (15.1)	51.2 (16.4)
Weight, mean (SD), kg	72.9 (19.6)	73.7 (17.8)	72.3 (18.1)	74.8 (16.1)	73.9 (22.7)	74.4 (18.5)	73.4 (17.7)	73.3 (18.9)
Female sex, n (%)	7.0 (50.0)	36.0 (66.7)	16.0 (53.3)	60.0 (66.7)	19.0 (70.4)	45.0 (63.4)	71.0 (61.7)	35.0 (76.1)
Race, n (%)								
White	11.0 (78.6)	31.0 (57.4)	20.0 (66.7)	51.0 (56.7)	18.0 (66.7)	40.0 (56.3)	66.0 (57.4)	23.0 (50.0)
Black or African American	0	1.0 (1.9)	1.0 (3.3)	5.0 (5.6)	1.0 (3.7)	4.0 (5.6)	6.0 (5.2)	3.0 (6.5)
Asian	3.0 (21.4)	20 (37.0)	8.0 (26.7)	32.0 (35.6)	7.0 (25.9)	25.0 (35.2)	40.0 (34.8)	17.0 (37.0)
Others or missing data[a]	0	1.0 (1.9)	0	2.0 (2.2)	0	2.0 (2.8)	2.0 (1.7)	3.0 (6.5)
Region, n (%)[b]								
Asia	1.0 (7.1)	17.0 (31.5)	6.0 (20.0)	28.0 (31.1)	5.0 (18.5)	20.0 (28.2)	36.0 (31.3)	16.0 (34.8)
Eastern Europe	5.0 (35.7)	7.0 (13.0)	6.0 (20.0)	11.0 (12.2)	7.0 (25.9)	11.0 (15.5)	8.0 (7.0)	2.0 (4.3)
Latin America	2.0 (14.3)	8.0 (14.8)	6.0 (20.0)	12.0 (13.3)	5.0 (18.5)	11.0 (15.5)	21.0 (18.3)	10.0 (21.7)
Western countries	6.0 (42.9)	22.0 (40.7)	12.0 (40.0)	39.0 (43.3)	10.0 (37.0)	29.0 (40.8)	50.0 (43.5)	18.0 (39.1)
Duration of PN, mean (SD), years								
< 3 years	9.0 (64.3)	27 (50.0)	18.0 (60.0)	39.0 (43.3)	19.0 (70.4)	36.0 (50.7)	49.0 (42.6)	24.0 (52.2)
≥ 3 years	5.0 (35.7)	27 (50.0)	12.0 (40.0)	51.0 (56.7)	8.0 (29.6)	35.0 (49.3)	66.0 (57.4)	22.0 (47.8)
History of atopy, n (%)[c]								
Ongoing mild AD	0	1.0 (1.85)	1.0 (3.33)	3.0 (3.33)	1.0 (3.7)	3.0 (4.2)	5.0 (4.3)	1.0 (2.2)
Stable use of TCS/TCI, n (%)[d]	5.0 (35.7)	35.0 (64.8)	12.0 (40.0)	54.0 (60.0)	10.0 (37.1)	44.0 (61.9)	74.0 (64.3)	28.0 (60.9)
WI-NRS (0–10), mean (SD)[e]	8.7 (1.0)	8.7 (0.9)	8.8 (0.9)	8.7 (0.9)	8.4 (0.8)	8.6 (0.93)	8.3 (1.1)	8.4 (0.9)
IGA PN-S (0–4), n (%)								
3	12.0 (85.7)	39.0 (72.2)	20.0 (66.7)	58.0 (64.4)	24.0 (88.9)	51.0 (71.8)	70.0 (60.8)	33.0 (71.7)
4	2.0 (14.3)	15.0 (27.8)	10.0 (33.3)	32.0 (35.6)	3.0 (11.1)	20.0 (28.2)	43.0 (37.4)	13.0 (28.3)

[a]Including American Indian or Alaska Native, Native Hawaiian or Pacific Islands, unknown; [b]Asia: China, Japan, South Korea, Taiwan; East Europe: Hungary, Russia; Latin America: Argentina, Chile, Mexico; Western countries: USA, Canada, France, Italy, Portugal, Spain, UK. [c]Defined as having a medical history of AD, allergic rhinitis/rhinoconjunctivitis, asthma, or food allergy. [d]Defined as maintaining the same medicine (low-to-medium potency TCS, or TCI) and maintaining the same frequency of treatment (once or twice daily) used from 2 weeks prior to screening. [e]0 = No itch and 10 = Worst imaginable itch.

CONCLUSIONS

- **More than one-third of dupilumab-treated patients achieved the multicomponent endpoint at Week 24, constituting concurrent responses on both itch and skin lesions. However, more than two-thirds had clinically meaningful improvement by Week 24, defined as either ≥ 4-point reduction in WI-NRS from baseline, IGA PN-S score 0/1, or both.**
- **Almost one-quarter of dupilumab-treated patients met only WI-NRS ≥ 4-point improvement at Week 24, suggesting that skin lesion improvement may lag behind improvement of itch.**
- **Safety was consistent with the known safety profile of dupilumab across approved indications.**

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