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

DUPILUMAB

Brian S. Kim, MD[1]; Krystal Ngo, Pharm D[2*]; Margarida Gonçalo, MD, PhD[3]; Tsukasa Ugajin, MD, PhD[4]; Amy Praestgaard, MSc[2]; Melanie Makhija, MD[2]; Joseph Zahn, MD[5]; Ashish Bansal, MD, MBA[5]; Simmi Wiggins, PhD[6]

[1]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [2]Sanofi, Cambridge, MA, USA; [3]Department of Dermatology, University of Coimbra, Coimbra, Portugal; [4]Department of Dermatology, Tokyo Medical and Dental University, Tokyo, Japan; [5]Regeneron Pharmaceuticals Inc., Tarrytown, NY, USA; [6]Sanofi, Reading, UK

Background

- Prurigo nodularis (PN) is a chronic inflammatory disease characterised by severely itchy cutaneous nodules that substantially affects quality of life and is often inadequately controlled with topical medications[1–3]
- PN is often diagnosed with comorbid atopic diseases, such as atopic dermatitis (AD), and nearly half of adult patients with PN have a history of atopy or current atopic comorbidity[4]
- Two independent, randomized, phase 3 clinical trials, LIBERTY-PN PRIME (NCT04183335) and PRIME2 (NCT04202679), demonstrated the efficacy and safety of dupilumab in both atopic and non-atopic PN patients inadequately controlled with topical therapies or when those therapies were not advisable[5]

Methods

Study design

- **Population:** Adult patients with PN inadequately controlled with topical prescription therapies or for whom those therapies are inadvisable
- **Subgroups:** Atopic patients and non-atopic patients
  - Atopic patients were defined as patients with a physician-documented history of atopic comorbidities defined as AD, allergic rhinitis/rhinoconjunctivits, asthma, or food allergy, or a current diagnosis of at least one of these atopic comorbidities, per investigator judgement
  - Atopic and non-atopic PN populations were each capped at 60% of the total enrolled population
  - Of the atopic population enrolled, mild, active AD was capped at 10% (patients with moderate-to-severe AD were excluded)
- **Treatment:** Dupilumab 300 mg every 2 weeks (q2w) or matched placebo for 24 weeks; low-to-medium potency topical corticosteroids/topical calcineurin inhibitors (TCS/TCI) or antidepressants were permitted if patients were on a stable regimen prior to screening and enrolment, provided they expected the dose to not be changed throughout the study
- **Statistical methods:** *P*-values were calculated using Chi-square test. Non-responder imputation methodology[a] was used

Efficacy endpoints

- Proportion of patients with ≥ 4-point reduction in WI-NRS[b] from baseline at Week 12 and Week 24
- Proportion of patients with IGA PN-S[c] score 0 or 1 at Week 12 and Week 24
- Proportion of patients with concomitant ≥ 4-point reduction in WI-NRS[b] from baseline and IGA PN-S[c] score 0 or 1 at Week 12 and Week 24

[a]Patients who received the prohibited medications/procedures and/or rescue medications that impacted efficacy before each timepoint were considered non-responders, and missing data at each timepoint were considered non-responders.
[b]**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 reduction is clinically meaningful.
[c]**Investigator's Global Assessment for PN stage of disease (IGA PN-S)**, 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]).

Objective

- **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: LIBERTY-PN PRIME and PRIME2**

Conclusions

- **Dupilumab treatment for 24 weeks improves itch and skin lesions in patients with both atopic and non-atopic PN compared with placebo**
- **These observations suggest that interleukin-4 receptor alpha (IL-4Rα) signaling is involved in PN regardless of patient history of atopic comorbidities**
- **Overall safety was consistent with the known dupilumab safety profile, with no remarkable differences between atopic and non-atopic patients**

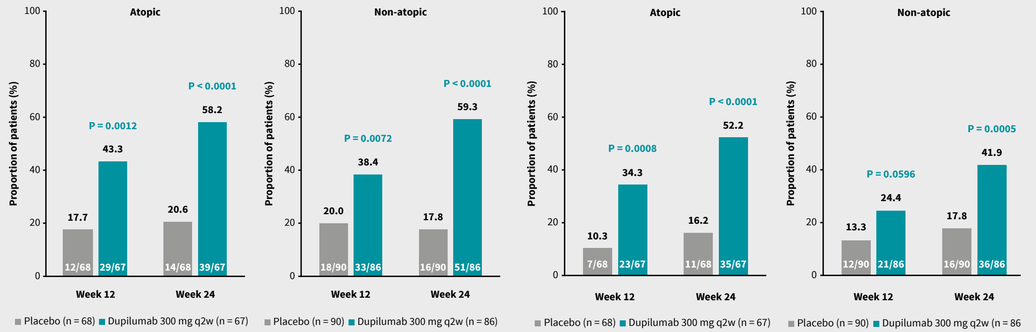
Results

Table 1. Baseline demographics and disease characteristics by history of atopy.

	Atopic		Non-atopic	
	Placebo (n = 68)	Dupilumab 300 mg q2w (n = 67)	Placebo (n = 90)	Dupilumab 300 mg q2w (n = 86)
Demographics				
Age (years), mean (SD)	47.4 (16.3)	46.8 (15.7)	49.9 (15.1)	52.7 (16.9)
Weight (kg), mean (SD)	73.5 (17.5)	76.3 (17.7)	73.2 (19.3)	73.2 (17.0)
Female sex, n (%)	44 (64.7)	47 (70.1)	55 (61.1)	57 (66.3)
Race, n (%)				
White	38 (55.9)	33 (49.3)	55 (61.1)	50 (58.1)
Black or African American[a]	2 (2.9)	7 (10.4)	6 (6.7)	4 (4.7)
Asian	26 (38.2)	26 (38.8)	26 (28.9)	28 (32.6)
Other or missing data[b]	2 (2.9)	1 (1.5)	3 (3.3)	4 (4.7)
Region, n (%)[c]				
Asia	21 (30.9)	22 (32.8)	25 (27.8)	25 (29.1)
Eastern Europe	6 (8.8)	7 (10.4)	10 (11.1)	10 (11.6)
Latin America	7 (10.3)	7 (10.4)	23 (25.6)	18 (20.9)
Western countries	34 (50.0)	31 (46.3)	32 (35.6)	33 (38.4)
Disease characteristics				
Duration of PN (years), mean (SD)	4.7 (5.4)	6.5 (7.9)	6.0 (7.3)	5.0 (6.6)
Ongoing mild atopic dermatitis, n (%)	7 (10.3)	6 (9.0)	0	0
Stable use of TCS/TCI[d], n (%)	43 (63.2)	41 (61.2)	48 (53.3)	50 (58.1)
WI-NRS[e] [0–10], mean (SD)	8.4 (1.1)	8.6 (1.0)	8.4 (1.0)	8.6 (0.9)
IGA PN-S[f] [0–4], n (%)				
3	42 (61.8)	50 (74.6)	60 (66.7)	53 (61.6)
4	26 (38.2)	17 (25.4)	28 (31.1)	33 (38.4)
DLQI[g] [0–30], mean (SD)	16.6 (7.1)	18.3 (6.3)	17.3 (7.3)	17.7 (7.1)
Skin pain NRS[h] [0–10], mean (SD)	6.9 (2.3)	7.5 (2.1)	7.3 (2.4)	7.0 (2.7)
Sleep NRS[i] [0–10], mean (SD)	4.5 (2.3)	3.9 (2.2)	4.0 (2.4)	4.7 (2.5)
Total HADS[j] [0–42], mean (SD)	14.8 (8.0)	15.4 (7.8)	15.4 (8.4)	15.3 (8.1)

[a]36.4% of USA patients were Black or African American; [b]Including American Indian or Alaska Native, Native Hawaiian or Pacific Islanders, and unknown; [c]Asia: China, Japan, Republic of Korea, Taiwan; East Europe: Hungary, Russia; Latin America: Argentina, Chile, Mexico; Western countries: USA, Canada, France, Italy, Portugal, Spain, and UK. [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. [f]0 = no nodules, 1 = 1–5 nodules, 2 = 6–19 nodules, 3 = 20–99 nodules, 4 = 100 or more nodules. [g]0–1 = no effect, 2–5 = small effect, 6–10 = moderate effect, 11–20 = very large effect, 21–30 = extremely large effect. [h]0 = no pain and 10 = worst imaginable pain. [i]0 = worst possible sleep and 10 = best possible sleep. [j]≤ 7 = normal, 8–10 = possible case, ≥ 11 probable case of anxiety/depression (scale for each anxiety and depression is 0–21). DLQI, Dermatology Life Quality Index; HADS, Hospital Anxiety and Depression Scale; NRS, Numerical Rating Scale; q2w, every 2 weeks; SD, standard deviation; TCI, topical calcineurin inhibitor(s); TCS, topical corticosteroid(s).

Figure 1. Proportion of patients achieving ≥ 4-point improvement from baseline in WI-NRS by history of atopy.

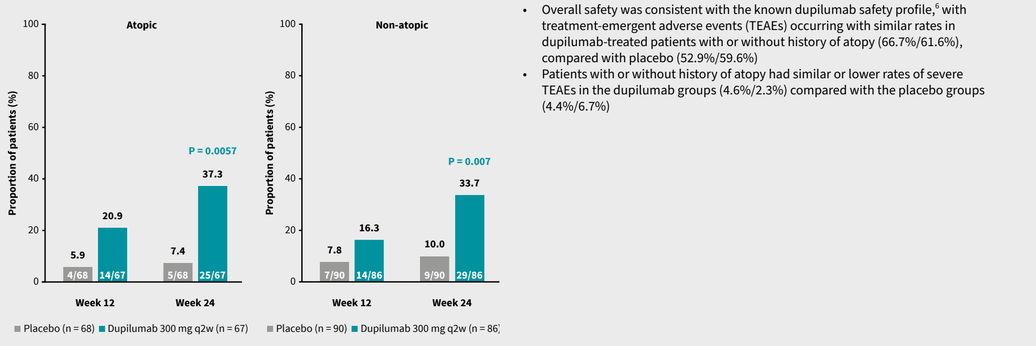


q2w, every 2 weeks; WI-NRS, Worst-Itch Numerical Rating Scale.

Figure 2. Proportion of patients achieving an IGA PN-S score of 0 or 1 by history of atopy.

q2w, every 2 weeks; IGA PN-S, Investigator's Global Assessment for PN stage of disease; PN, Prurigo Nodularis.

Figure 3. Proportion of patients with concomitant ≥ 4-point improvement from baseline in WI-NRS and IGA PN-S score 0 or 1 by history of atopy.



q2w, every 2 weeks; IGA PN-S, Investigator's Global Assessment for PN stage of disease; PN, Prurigo Nodularis; WI-NRS, Worst-Itch Numerical Rating Scale.

Safety

- Overall safety was consistent with the known dupilumab safety profile,[6] with treatment-emergent adverse events (TEAEs) occurring with similar rates in dupilumab-treated patients with or without history of atopy (66.7%/61.6%), compared with placebo (52.9%/59.6%)
- Patients with or without history of atopy had similar or lower rates of severe TEAEs in the dupilumab groups (4.6%/2.3%) compared with the placebo groups (4.4%/6.7%)

*This author has been included to serve as a presenter.

References: 1. Williams KA, et al. *J Am Acad Dermatol.* 2020;83:1567–75. 2. Zeidler C, et al. *Acta Derm Venereol.* 2018;98:173–9. 3. Pereira MP, et al. *J Eur Acad Dermatol Venereol.* 2020;34:2373–83. 4. Iking A, et al. *J Eur Acad Dermatol Venereol.* 2013;27:550–7. 5. Yosipovitch G, et al. *Nat Med.* 2023; https://doi.org/10.1038/s41591-023-02320–9. 6. Yosipovitch G, et al. Poster presented at *RAD* 2022.

Acknowledgements: Research sponsored by Sanofi and Regeneron Pharmaceuticals Inc. ClinicalTrials.gov Identifiers: NCT04183335 and NCT04202679. Medical writing support was provided by Benjamin Danet, PhD, of Excerpta Medica. Editorial assistance was provided by Tejaswi Ramisetty, Pharm D, of Sanofi, and was funded by Sanofi and Regeneron Pharmaceuticals Inc., according to the Good Publication Practice guideline.

Disclosures: Kim BS: AbbVie, Almirall, Amagma, Argenx, AstraZeneca, Bellus Health, Blueprint Medicines, Boehringer Ingelheim, BMS, Cara Therapeutics, Daewoong Pharmaceutical, Eli Lilly, Genzyme, GSK, Guidepoint Global, Incyte, Janssen, LectureLinx, LEO Pharma, OM Pharma, Pfizer, RecensMedical, Regeneron Pharmaceuticals Inc., Shaperon, Trevi Therapeutics, WebMD – consultant; Locus Biosciences – may hold stock and/or stock options in the company. **Gonçalo M:** AbbVie, LEO Pharma, Lilly, Novartis, Pfizer, Sanofi, Takeda – advisory board member and/or speaker. **Ugajin T:** AbbVie, Kyorin Pharmaceutical, Mitsubishi Tanabe Pharma, Takeda – lectures. **Praestgaard A, Makhija M, Wiggins S, Ngo K:** Sanofi – employees, may hold stock and/or stock options in the company. **Zahn J, Bansal A:** Regeneron Pharmaceuticals Inc. – employees and shareholders.

Presented at San Diego Dermatology Symposium (SDDS 2024), San Diego, CA, February 2–4, 2024. Data included in this poster were originally presented at the 25th World Congress of Dermatology (WCD); Suntec City, Singapore; July 3–8, 2023.