Dupilumab Improves Itch and Skin Lesions in Adults With Prurigo Nodularis Regardless of Prior Use of Immunosuppressants or Phototherapy: Post Hoc Results From the PRIME and PRIME2 Clinical Trials

Shawn G. Kwatra[1], Gil Yosipovitch[2], Sonja Ständer[3], Brian S. Kim[4], Jérôme Msihid[5], Ashish Bansal[6], Renata Martinčová[7], Simmi Wiggins[8], Noah A. Levit[6], Ryan B. Thomas[6], Donia Bahloul[5]

[1]Johns Hopkins University, Baltimore, MD, USA; [2]University of Miami, Miami, FL, USA; [3]University Hospital Münster, Münster, Germany; [4]Icahn School of Medicine at Mount Sinai, New York, NY, USA; [5]Sanofi, Chilly-Mazarin, France; [6]Regeneron Pharmaceuticals, Inc., Tarrytown, NY, USA; [7]Sanofi, Prague, Czech Republic; [8]Sanofi, Reading, UK

INTRODUCTION

- Prurigo nodularis (PN) is a chronic, inflammatory skin disease characterized by multiple intensely itchy nodules on the extensor surfaces of the limbs and trunk that can severely impact quality of life[1-3]
- Dupilumab is the only US Food and Drug Administration approved systemic therapy for PN,[4] however immunosuppressants (IS) and phototherapy have been used off-label for the treatment of PN[5]
- Patients with prior IS/phototherapy treatment may represent a more severe and/or treatment-refractory population of patients with PN

OBJECTIVE

- **To report post hoc efficacy of dupilumab in patients with PN inadequately controlled with topical prescription therapies or when those therapies are not advisable, from two pooled phase 3 trials (LIBERTY-PN PRIME and PRIME2), with or without prior use of IS or phototherapy for PN**

METHODS

- LIBERTY-PN PRIME and PRIME2 are randomized, placebo-controlled, phase 3 studies of dupilumab treatment up to 24 weeks in adults with PN inadequately controlled on topical prescription therapies or when those therapies are not advisable. Patients were randomized 1:1 to dupilumab 300 mg every 2 weeks (Q2W, n = 153) or matched placebo (n = 158).
- This study investigated patients with or without prior use of phototherapy for PN, or IS for any reason. The primary efficacy outcomes were the proportion of patients with a ≥ 4-point improvement in weekly average Worst Itch Numerical Rating Scale (WI-NRS) from baseline to Week 24, and patients with an Investigator's Global Assessment (IGA) score of 0 or 1 (clear or almost clear) for PN stage (IGA PN-S) at Week 24.

METHODS (CONT.)

- Patients were not permitted the use of phototherapy or IS during the study period or up to 4 weeks before the screening visit.
- Safety outcomes included treatment-emergent adverse events (TEAEs)

RESULTS

Table 1. Prior IS or phototherapy use for PN.

Patients with prior IS or phototherapy use for PN, n (%)	Placebo (n = 158)	Dupilumab 300 mg Q2W (n = 153)	Overall (n = 311)
Prior phototherapy for PN			
Yes	13 (8.2)	12 (7.8)	25 (8.0)
No	145 (91.8)	141 (92.2)	286 (92.0)
Prior systemic IS			
Yes	56 (35.4)	58 (37.9)	114 (36.7)
No	102 (64.6)	95 (62.1)	197 (63.3)
Prior systemic IS or phototherapy for PN			
Yes	64 (40.5)	62 (40.5)	126 (40.5)
No	94 (59.5)	91 (59.5)	185 (59.5)
Standardized systemic medications previously used by ≥ 5% of patients with prior IS use, n (%)	**Placebo (n = 56)**	**Dupilumab 300 mg Q2W (n = 58)**	**Overall (n = 114)**
Ciclosporin	15 (26.8)	18 (31.0)	33 (28.9)
Methotrexate	13 (23.2)	14 (24.1)	27 (23.7)
Triamcinolone acetonide	4 (7.1)	14 (24.1)	18 (15.8)
Prednisolone	8 (14.3)	7 (12.1)	15 (13.2)
Methylprednisolone	6 (10.7)	8 (13.8)	14 (12.3)
Prednisone	6 (10.7)	5 (8.6)	11 (9.6)
Thalidomide	3 (5.4)	8 (13.8)	11 (9.6)
Betamethasone dipropionate;betamethasone sodium phosphate	3 (5.4)	3 (5.2)	6 (5.3)
Dexamethasone	2 (3.6)	4 (6.9)	6 (5.3)

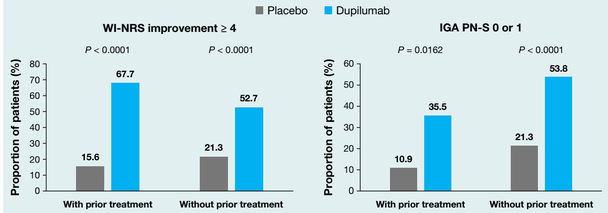
RESULTS (CONT.)

Table 2. Patient demographics and baseline characteristics.

	With phototherapy or prior systemic IS for PN			Without phototherapy nor prior systemic IS for PN		
	Placebo (n = 64)	Dupilumab 300 mg Q2W (n = 62)	Overall (n = 126)	Placebo (n = 94)	Dupilumab 300 mg Q2W (n = 91)	Overall (n = 185)
Age, mean (SD), years	48.9 (14.6)	49.1 (16.0)	49.0 (15.3)	48.7 (16.3)	50.8 (17.0)	49.8 (16.7)
Female, n (%)	41 (64.1)	44 (71.0)	85 (67.5)	58 (61.7)	60 (65.9)	118 (63.8)
Duration of PN (years), mean (SD)	5.91 (5.98)	5.09 (5.08)	5.51 (5.55)	5.12 (7.00)	6.08 (8.36)	5.59 (7.69)
Stable use of TCS/TCI, n (%)	38 (59.4)	41 (66.1)	79 (62.7)	53 (56.4)	50 (54.9)	103 (55.7)
WI-NRS score, mean (SD)	8.5 (1.1)	8.7 (1.0)	8.6 (1.0)	8.3 (1.0)	8.5 (0.9)	8.4 (1.0)
IGA-PN-S, n (%)						
Moderate	38 (59.4)	37 (59.7)	75 (59.5)	64 (69.6)	66 (72.5)	130 (71.0)
Severe	26 (40.6)	25 (40.3)	51 (40.5)	28 (30.4)	25 (27.5)	53 (29.0)

SD, standard deviation; TCS, topical corticosteroid; TCI, topical calcineurin inhibitor.

Figure. Proportion of patients with ≥ 4-point improvement in WI-NRS and IGA PN-S 0 or 1 at Week 24.



Prior treatment indicates prior use of IS or phototherapy for PN.

Table 3. Safety summary.

	With phototherapy for PN or prior systemic IS		Without phototherapy or prior systemic IS for PN	
	Placebo (n = 64)	Dupilumab 300 mg Q2W (n = 62)	Placebo (n = 93)	Dupilumab 300 mg Q2W (n = 90)
Any TEAE	34 (53.1)	43 (69.4)	55 (59.1)	54 (60.0)
Severe TEAE	3 (4.7)	4 (6.5)	6 (6.5)	1 (1.1)
Treatment-emergent SAE	5 (7.8)	2 (3.2)	7 (7.5)	5 (5.6)
Any TEAE leading to death	0	0	0	0
Any TEAE leading to permanent discontinuation of study drug	2 (3.1)	0	2 (2.2)	0
Any treatment-emergent other selected AE	9 (14.1)	6 (9.7)	9 (9.7)	10 (11.1)
TEAE related to IMP	11 (17.2)	10 (16.1)	10 (10.8)	16 (17.8)

AE, adverse event; IMP, investigational medicinal product; SAE; serious adverse event.

CONCLUSIONS

- **Patients treated with dupilumab experienced greater and clinically meaningful improvement in itch and achieved skin that was clear/almost clear of nodules at Week 24, regardless of prior use of IS/phototherapy for the treatment of PN**
- **Incidence of TEAEs was generally consistent among patients with and without prior IS or phototherapy**

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