Vixarelimab reduced pruritus, improved nodules, and was well-tolerated in patients with Prurigo Nodularis in a Phase 2a, randomized, double-blind, placebo-controlled study

Top Level Results

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Howard Sofen discloses participation as a clinical investigator for Kiniksa Pharmaceuticals, Galderma, and Menlo

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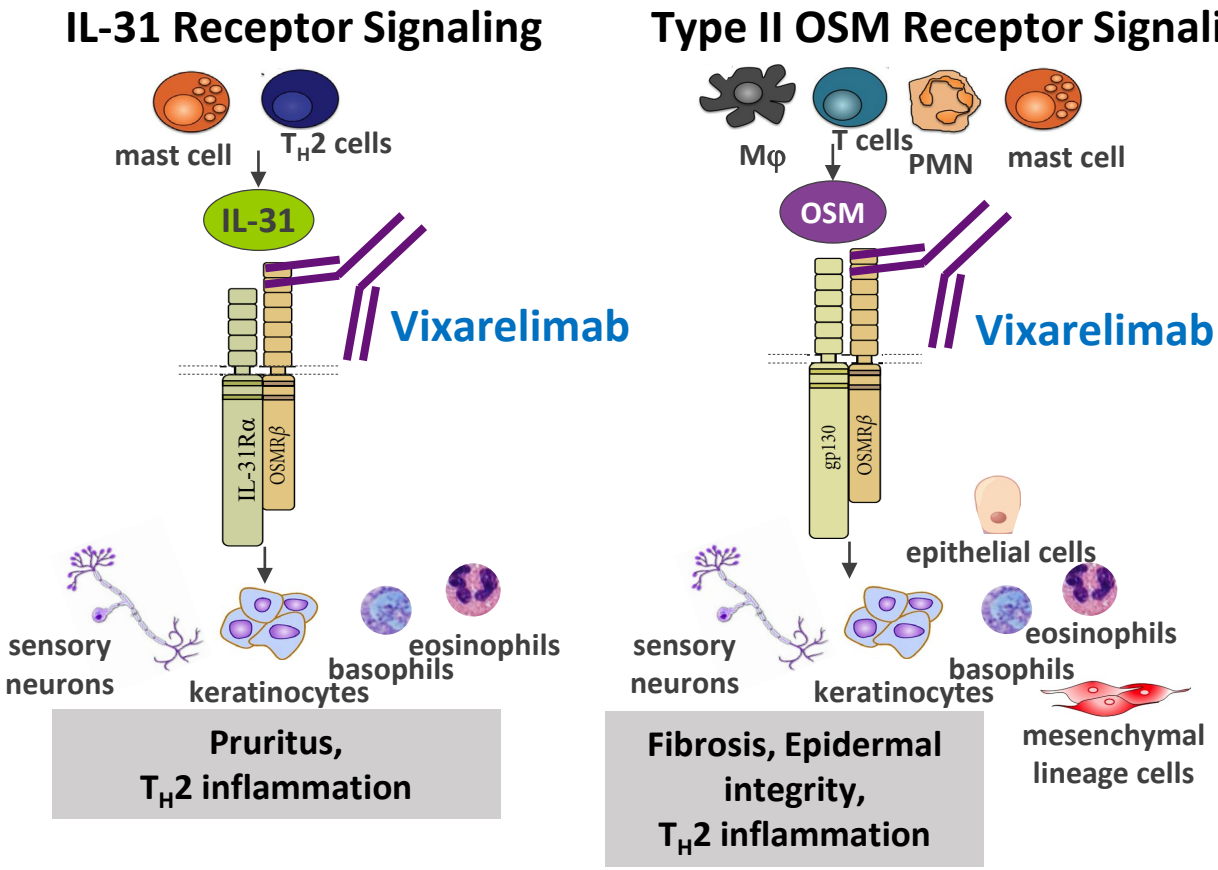
Introduction

- Prurigo nodularis (PN):
  - Chronic skin disease
  - Symmetrically distributed, intensely pruritic hyperkeratotic papules and nodules
  - Etiology unknown
- Symptomatology implicates pruritic pathways, and its histologic features point to epidermal proliferation, inflammation, and fibrosis
- Vixarelimab (KPL-716), a human monoclonal OSMRβ antibody, inhibits both:
  - Interleukin-31
  - Oncostatin M

Vixarelimab inhibits IL-31 and OSM signaling via a single epitope (OSMRβ)

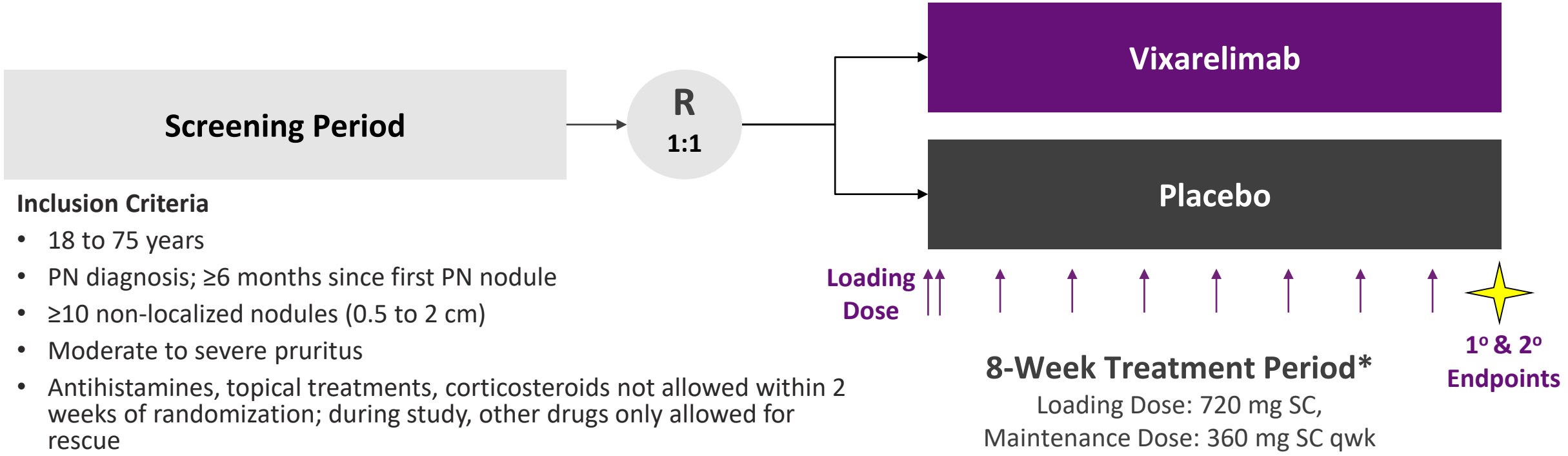


IL = interleukin, LIF, leukemia inhibitory factor, OSM = oncostatin M, T_H2 = type 2 T helper cell.
Image adapted from Richards C. ISRN Inflammation. 2013;2013:1-23.
[1]Gandhi et al. Presented at Society for Investigative Dermatology, 2019.

Objective

To assess the efficacy and safety of vixarelimab in patients with prurigo nodularis

Multinational, Randomized, Double-Blind, Placebo-Controlled Phase 2a Study



Inclusion Criteria

- 18 to 75 years
- PN diagnosis; ≥6 months since first PN nodule
- ≥10 non-localized nodules (0.5 to 2 cm)
- Moderate to severe pruritus
- Antihistamines, topical treatments, corticosteroids not allowed within 2 weeks of randomization; during study, other drugs only allowed for rescue

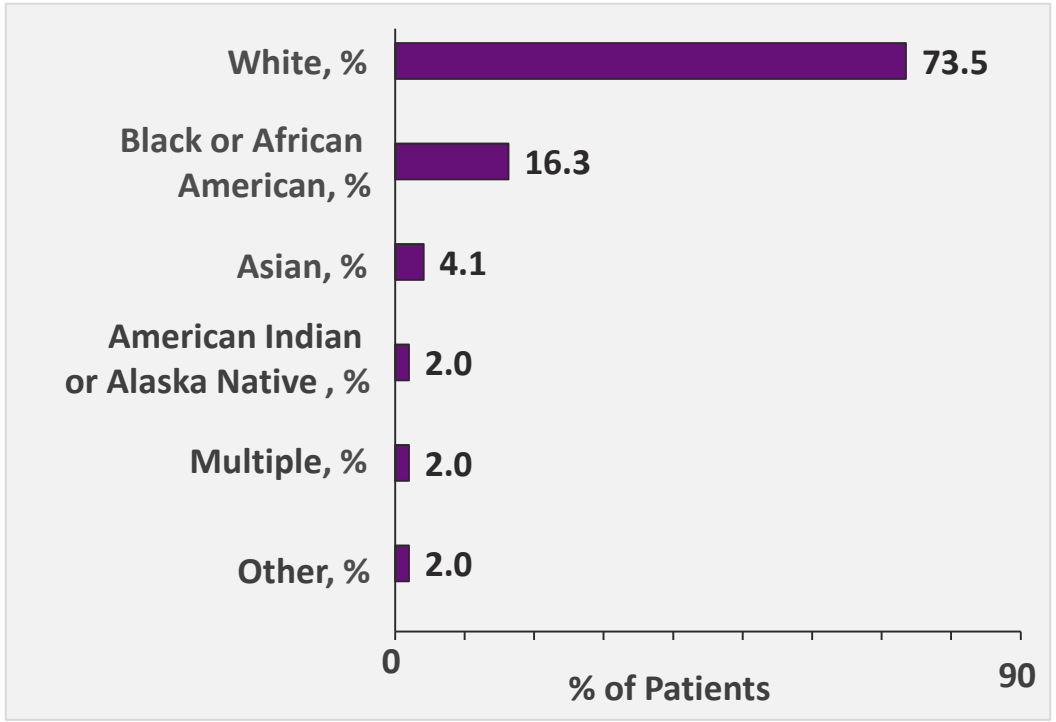
1° Efficacy Endpoint	• % change from baseline vs placebo in weekly average Worst Itch-Numeric Rating Scale (WI-NRS)
Secondary Endpoints	• Proportion with ≥4-point reduction from baseline in weekly average WI-NRS • Severity of disease by PN-Investigators Global Assessment score (PN-IGA)

*A second cohort with a planned 16-week treatment period was also analyzed at the 8-week timepoint, and is included in this 8-week analysis

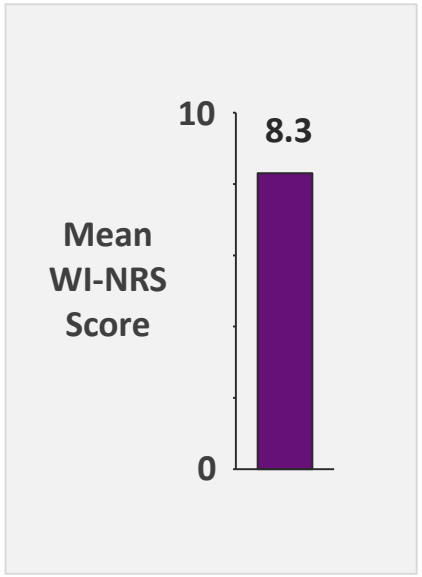
Baseline Demographics and Clinical Characteristics

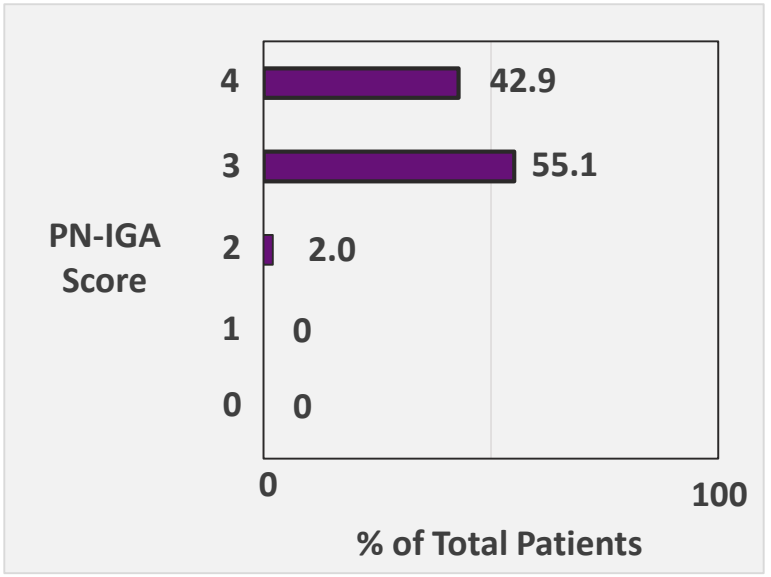
Demographics	Vixarelimab (n=23)	Placebo (n=26)	Total (n=49)
Age (Mean Years)	52	64	58
Sex (Male/Female)	10/13	10/16	20/29

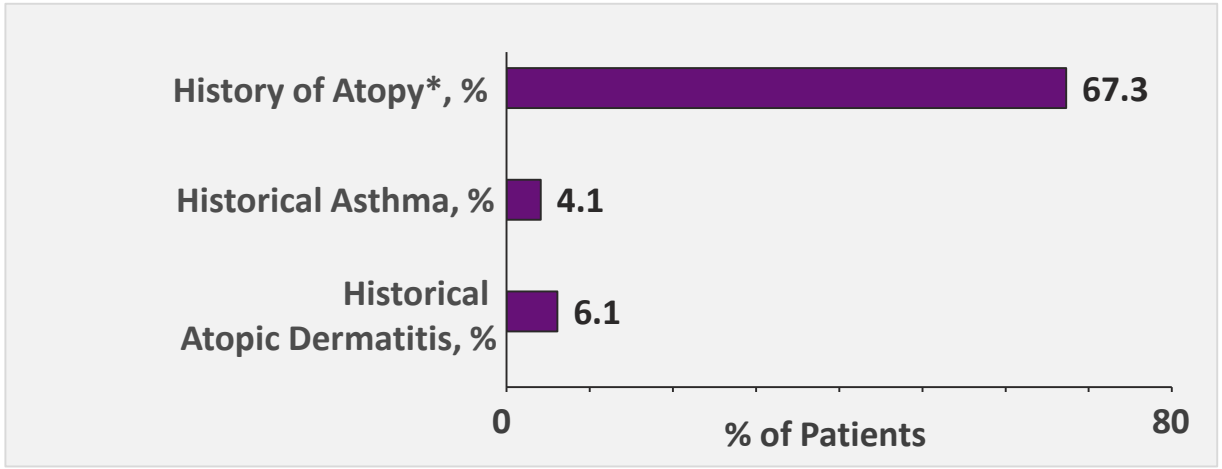
Race (n=58)



Clinical Characteristics at Baseline (n=58)

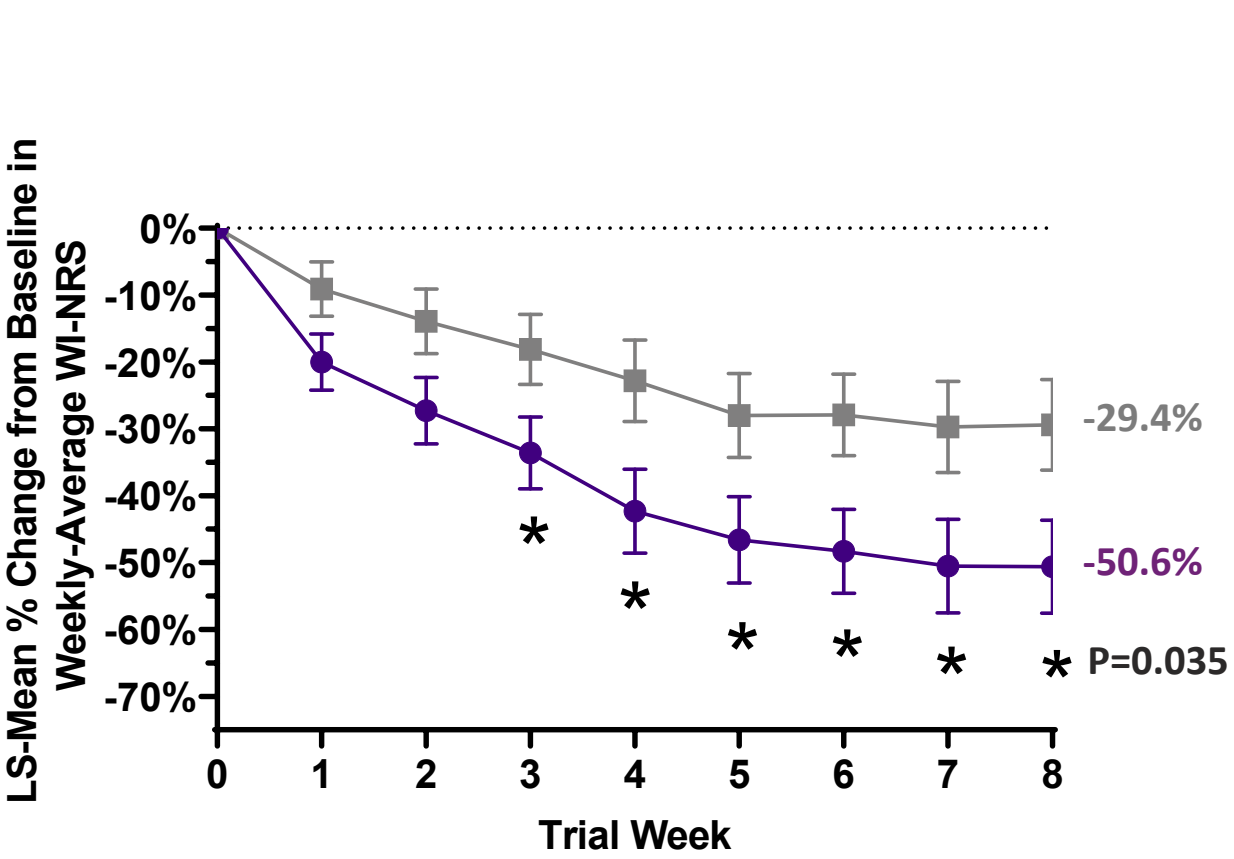


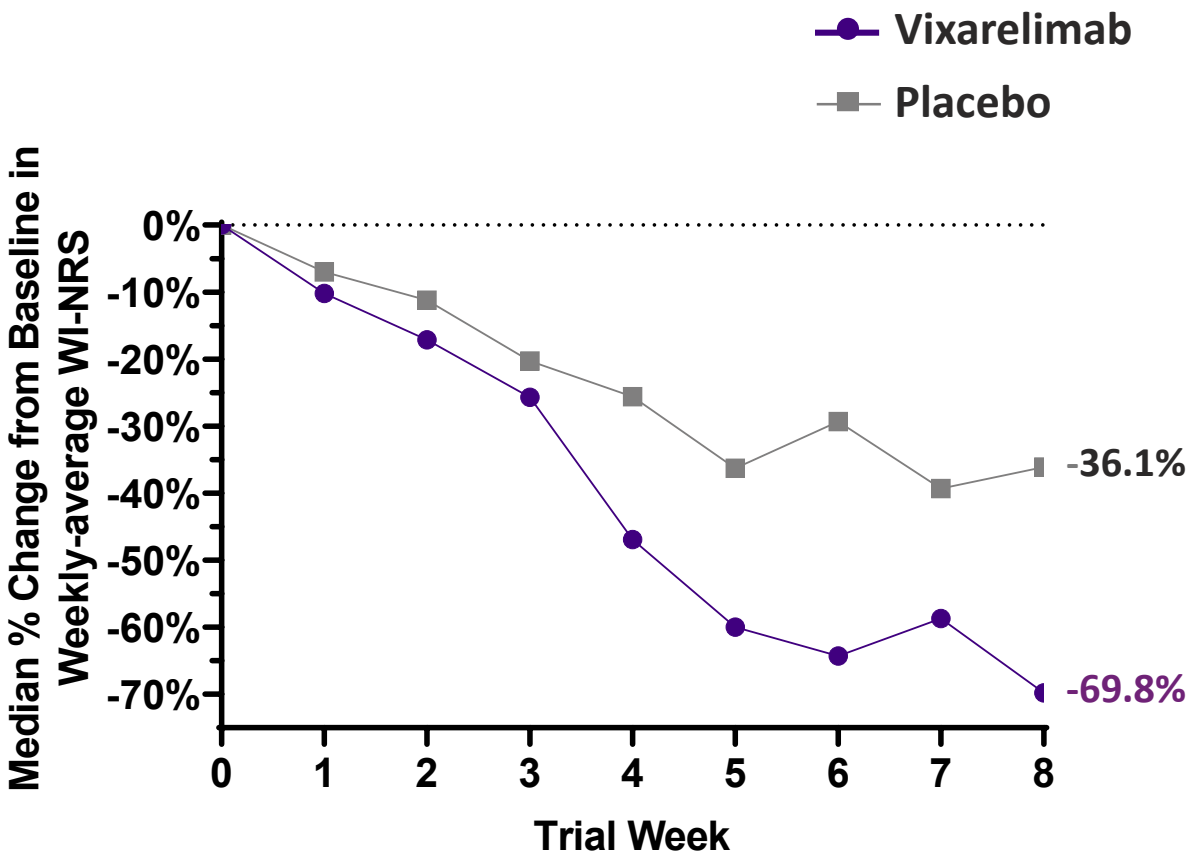




*Primarily defined as seasonal allergies

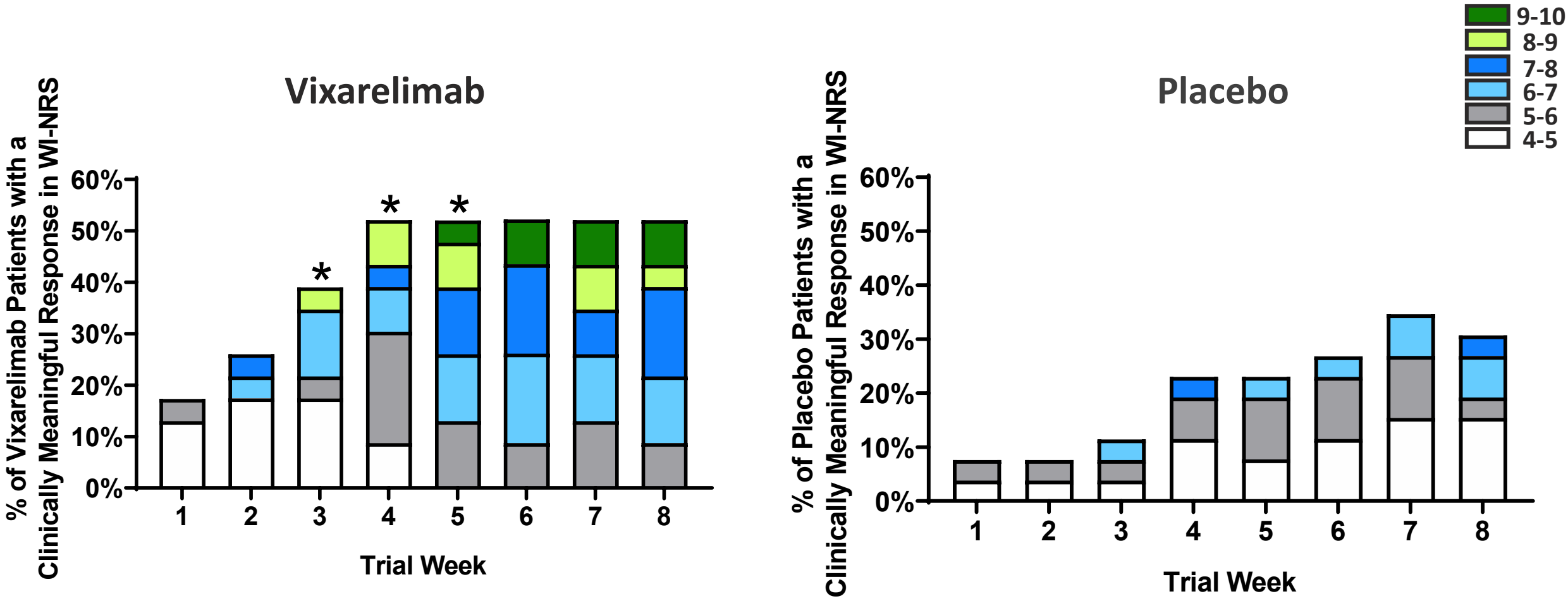
Vixarelimab Significantly Reduced Weekly-Average WI-NRS versus Placebo





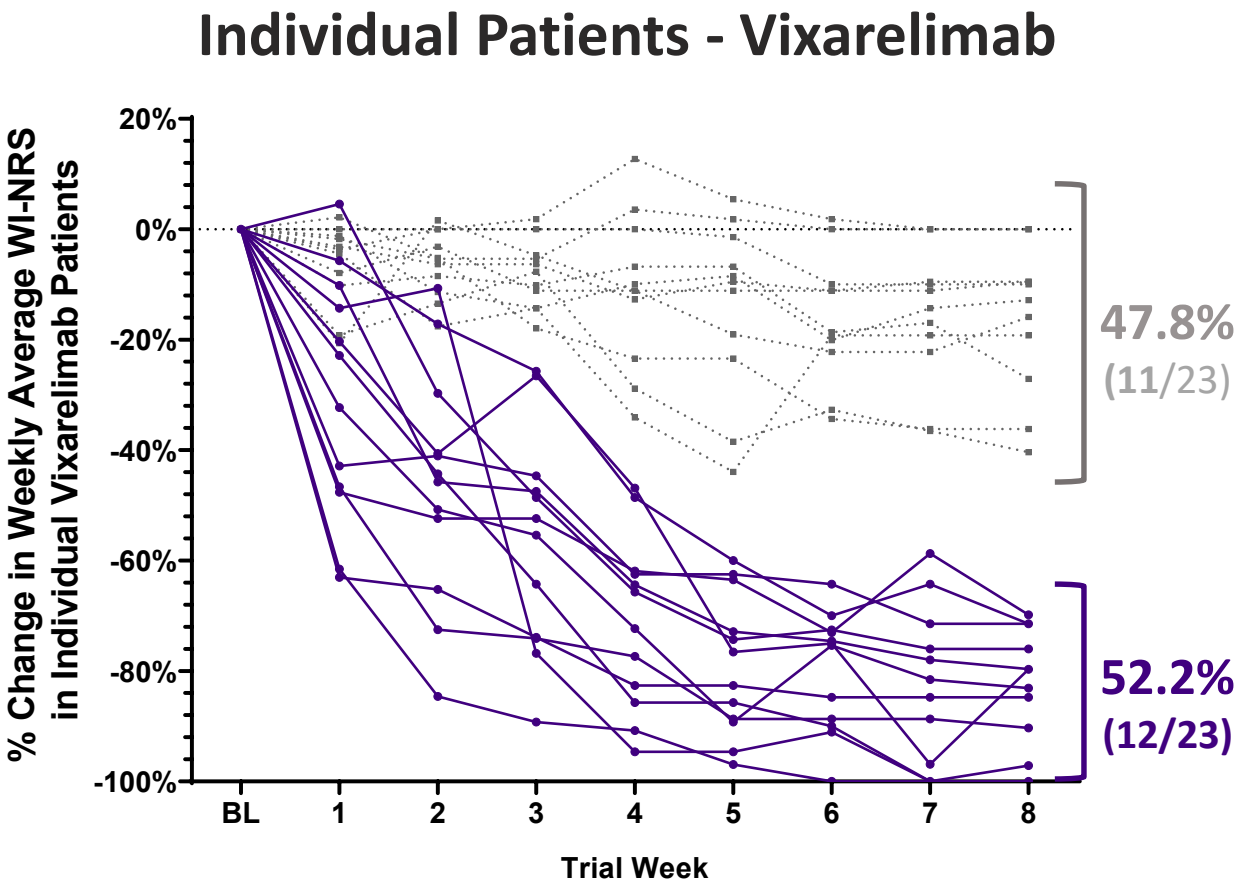
*p < 0.05;
Data were calculated using the last observation carried forward analysis
WI-NRS, Worst-Itch Numeric Rating Scale; LS, least squares

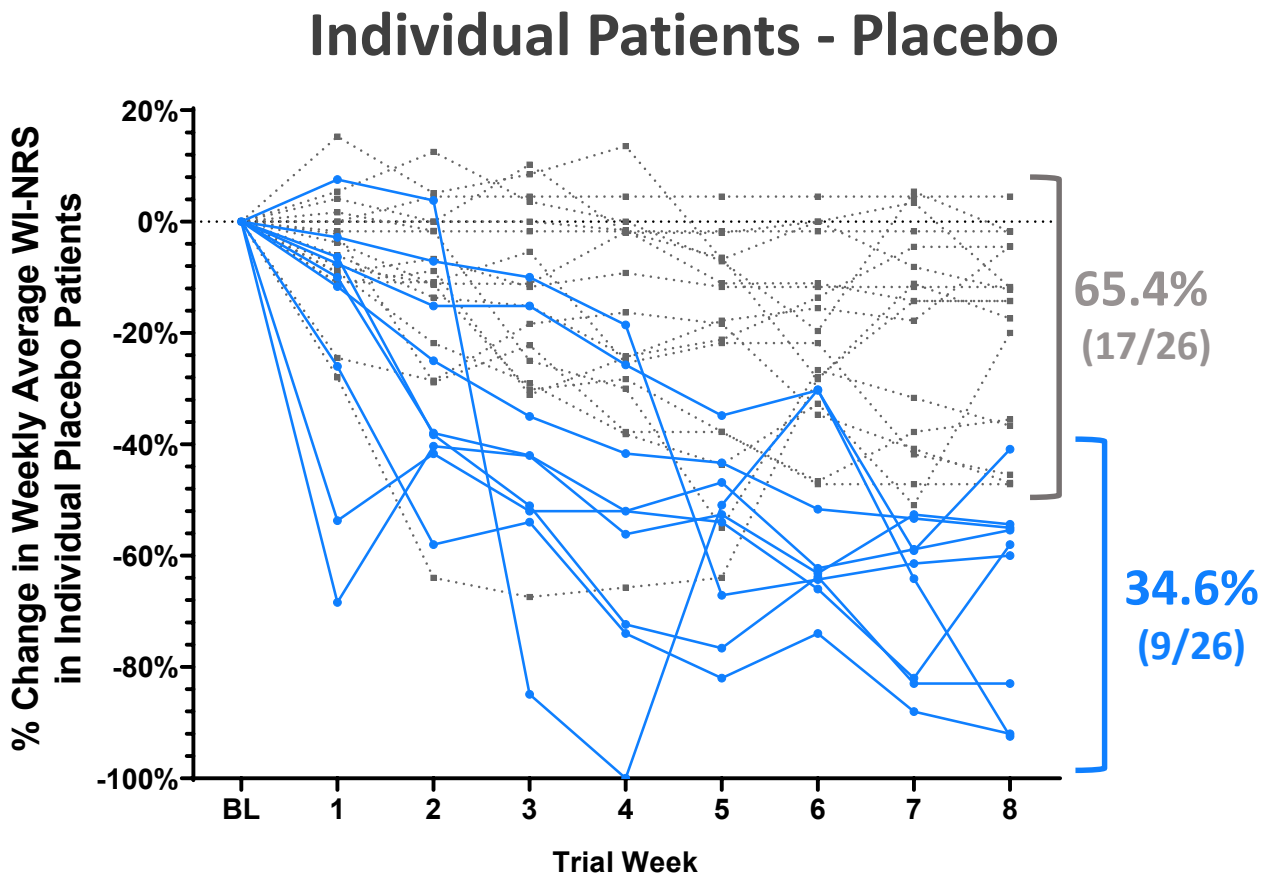
Vixarelimab: Majority With Clinically Meaningful ≥4-Point WI-NRS Reduction



*p < 0.05; WI-NRS, Worst-Itch Numeric Rating Scale; LS, least squares

Vixarelimab: Majority With Clinically Meaningful ≥4-Point WI-NRS Reduction





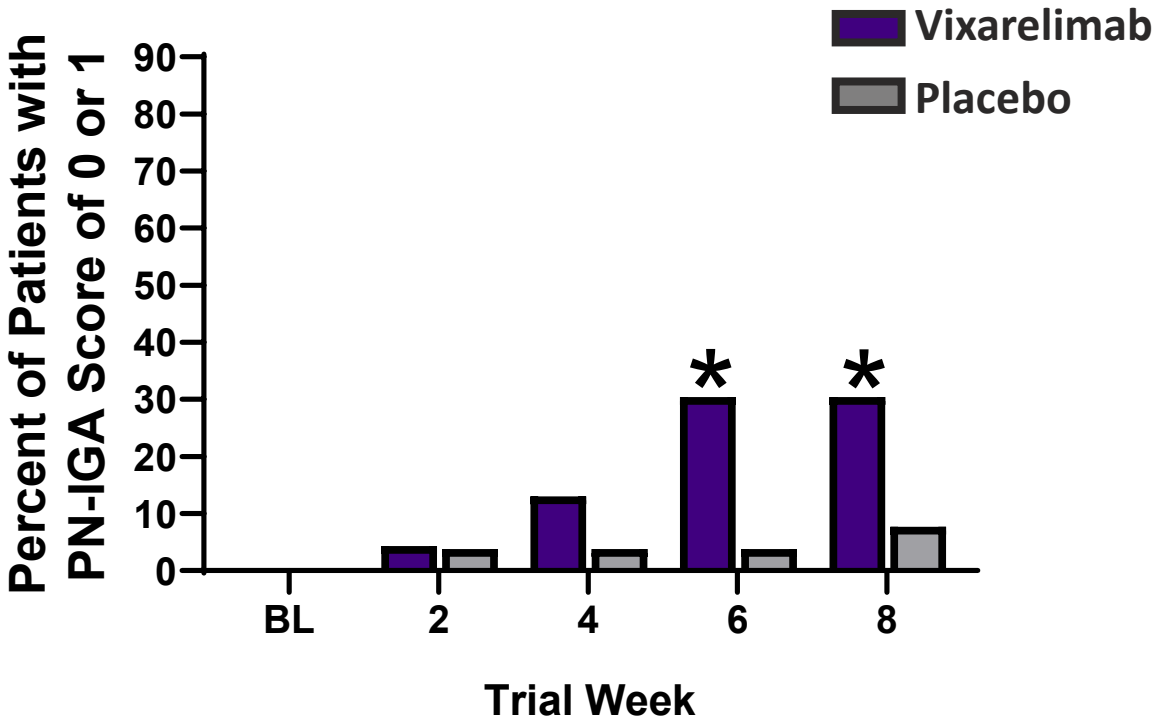
WI-NRS, Worst-Itch Numeric Rating Scale

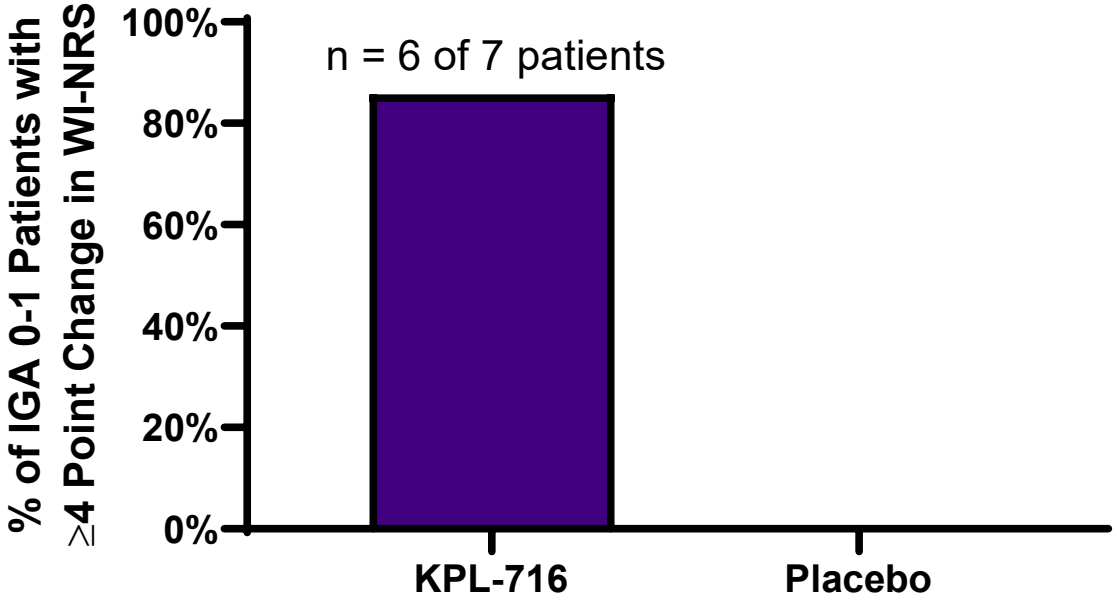
WI-NRS Reduction ≥4 Points - Vixarelimab

WI-NRS Reduction ≥4 Points - Placebo

WI-NRS Reduction <4 Points

Vixarelimab: More Patients With Clear/Almost Clear Lesion Score (IGA 0/1)





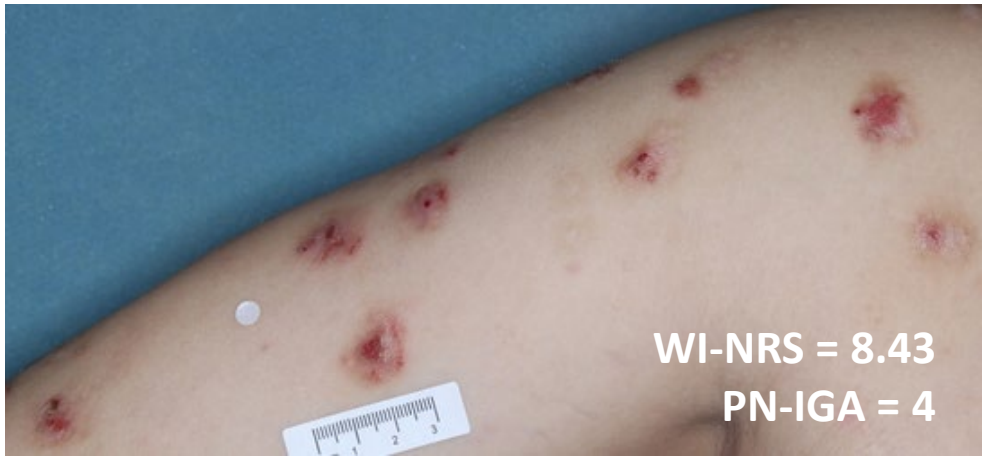
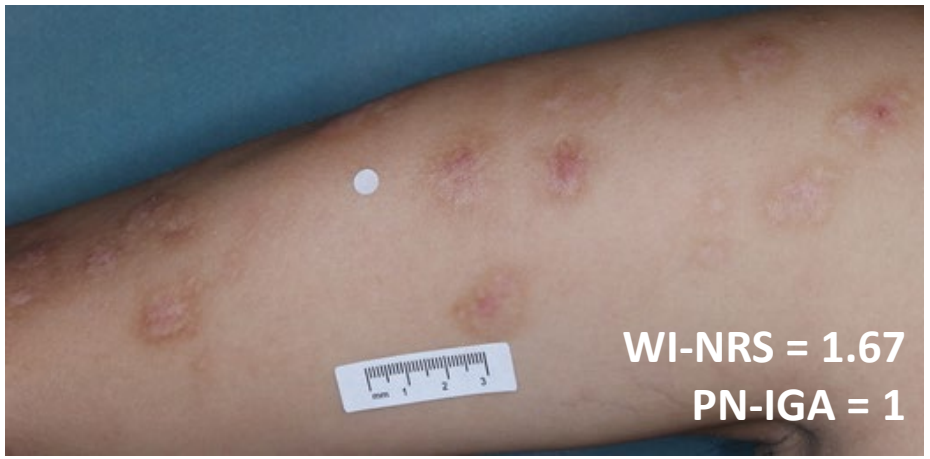
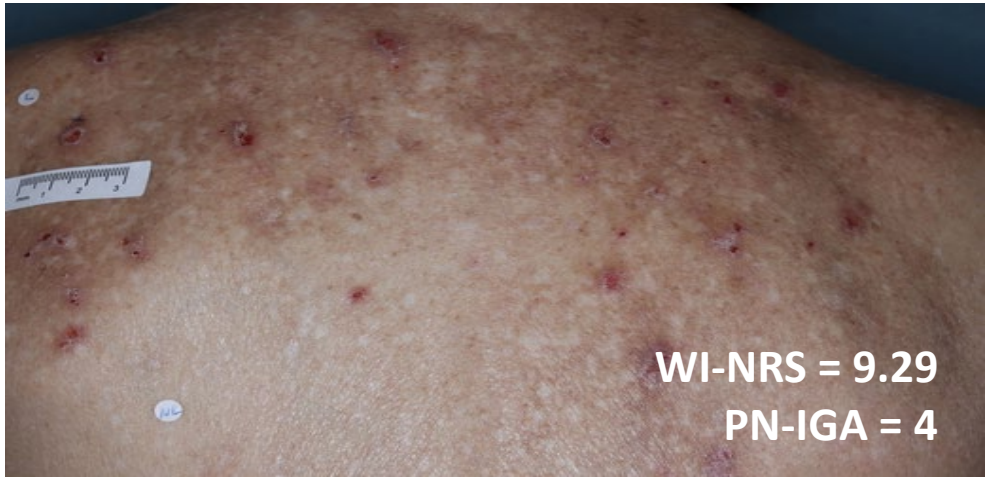
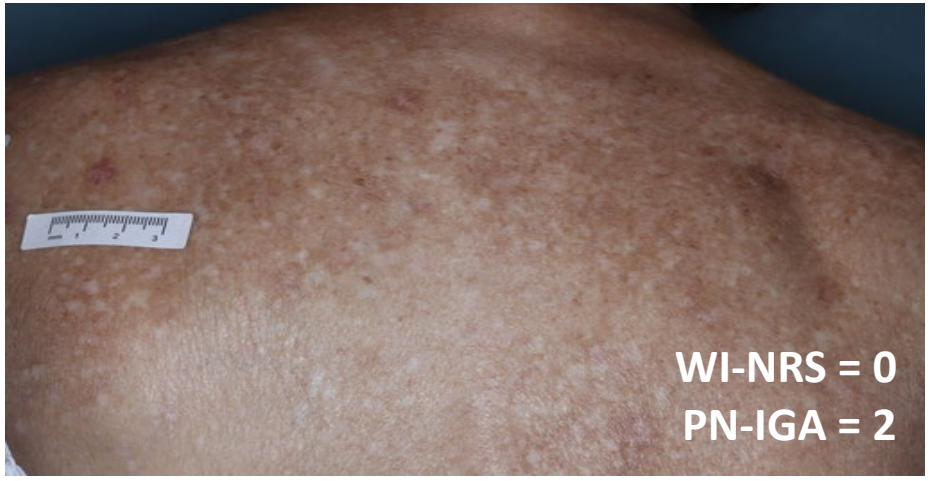
*p < 0.05 ;PN-IGA = prurigo nodularis-investigator's global assessment

Key Points

Concordant Effect of Vixarelimab on PN-IGA and Pruritus

- Vixarelimab: 85.7% achieved both 0-1 on PN-IGA scale and 4-point response on WI-NRS
- Placebo: 0% achieved both 0-1 on PN-IGA scale and 4-point response on WI-NRS

Nodule Resolution at Week 8 in Vixarelimab Recipients (Representative Images)

	Day 1	Week 8
Vixarelimab Recipient 1	 WI-NRS = 8.43 PN-IGA = 4	 WI-NRS = 1.67 PN-IGA = 1
Vixarilemab Recipient 2	 WI-NRS = 9.29 PN-IGA = 4	 WI-NRS = 0 PN-IGA = 2

Vixarelimab was Well-Tolerated in Prurigo Nodularis Patients*

	Vixarelimab (n=23)	Placebo (n=26)
Any Adverse Event (n)	82.6% (19)	65.4% (17)
Treatment-emergent Adverse Event (TEAE) (n)	82.6% (19)	65.4% (17)
Drug-Related TEAE (n)	39.1% (9)	30.8% (8)

None of the following occurred during the study: serious TEAE, drug-related serious TEAEs, TEAE leading to treatment discontinuation, drug-related TEAE leading to treatment discontinuation, serious TEAE leading to treatment discontinuation, drug-related serious TEAE leading to treatment discontinuation, TEAE leading to death

Adverse Events of Interest in ≥5% of Patients	Vixarelimab (n=23)	Placebo (n=26)
Infections and Infestations (n)	30.4% (7)	46.2% (12)
Upper Respiratory Tract Infection (n)	17.4% (4)	3.8% (1)
Nasopharyngitis (n)	4.3% (1)	7.7% (2)
Urinary Tract Infection (n)	0	11.5% (3)
Skin and Subcutaneous Tissue Disorders	26.1% (6)	15.4% (4)
Skin Burning Sensation	0	7.7% (2)

Key Points

- No serious adverse events
- No atopic dermatitis flares
- All AEs were mild and transient

*Safety data are limited to first 56 days (8-week treatment period)

Vixarelimab Improved Signs and Symptoms of Prurigo Nodularis in Phase 2a

Conclusions:

- Primary efficacy endpoint, LS-mean change from baseline weekly-average WI-NRS, was met:
  - Week 8: -50.6% (vixarelimab) vs. -29.4% (placebo); mean difference 21.1%; p = 0.035
- Median reduction in pruritus (WI-NRS) at Week 8: -69.8% (vixarelimab) vs. -36.1% (placebo)
- Greater clear or almost clear attainment (PN-IGA score of 0/1) in vixarelimab recipients
  - Week 8: 30.4% (vixarelimab) vs 7.7% (placebo); p = 0.032
  - Nodule improvement as early as Week 4
- Vixarelimab was well-tolerated
  - No dose-limiting adverse experiences
  - No serious adverse events or atopic dermatitis flares

Key Point

This study is the first to provide data regarding the efficacy and safety of dual inhibition of IL-31 and OSM pathways via OSMRβ in treatment of prurigo nodularis