Barzolvolimab Demonstrates Safety and Clinically Meaningful Activity in Moderate-Severe Prurigo Nodularis

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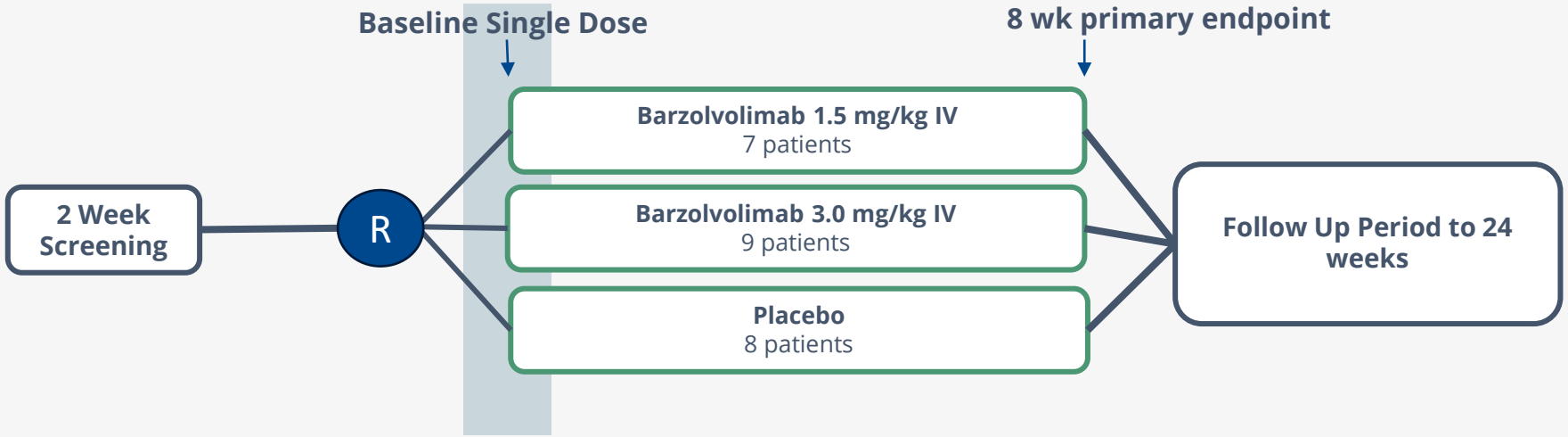
Background

- Prurigo nodularis (PN) is a chronic inflammatory skin disease characterized by intensely pruritic nodules
- Mast cells (MCs) have been hypothesized to play a role in chronic itch and neuroinflammation of PN [1,2]
- Mast cells require engagement of their KIT receptors by stem cell factor (SCF) for activation, tissue recruitment and survival
- Barzolvolimab (CDX-0159), an anti-KIT monoclonal antibody, was well-tolerated, and demonstrated improvement in itch and urticarial lesions accompanied by depletion of skin mast cells in chronic urticarias [3,4]
- Here we report safety and clinical activity data of a Phase 1b single dose trial of barzolvolimab in patients with moderate to severe PN (NCT04944862)

[1]Liang Y, et al. *J Cutan Pathol.* 2000;27(7):359-366. [2] Meixiong J, et al. *Immunity.* 2019;50(5):1163-1171 e1165.

[3]Terhost-Molawi, D, et al. *Allergy.* 2022; 00: 1-11. [4]Maurer, M, et al. EAACI 2023 oral presentation.

Study Design and Status: Phase 1b Study in Prurigo Nodularis



- Randomized, double-blind, placebo-controlled, single dose study in adults with moderate to severe PN
  - WI-NRS ≥7 at baseline
  - IGA≥3 at baseline
- Primary endpoint is safety profile; secondary endpoints include changes from baseline in Worst Itch-Numerical Rating Scale (WI-NRS) & Investigator Global Assessment (IGA), PK, and serum tryptase
  - Patients followed for safety and efficacy endpoints to 24 weeks
  - ***Primary timepoint for evaluation of clinical activity was 8 weeks***
- 24 patients randomized (evaluable: n=23 safety; n=22 efficacy)

Demographics and Baseline Characteristics

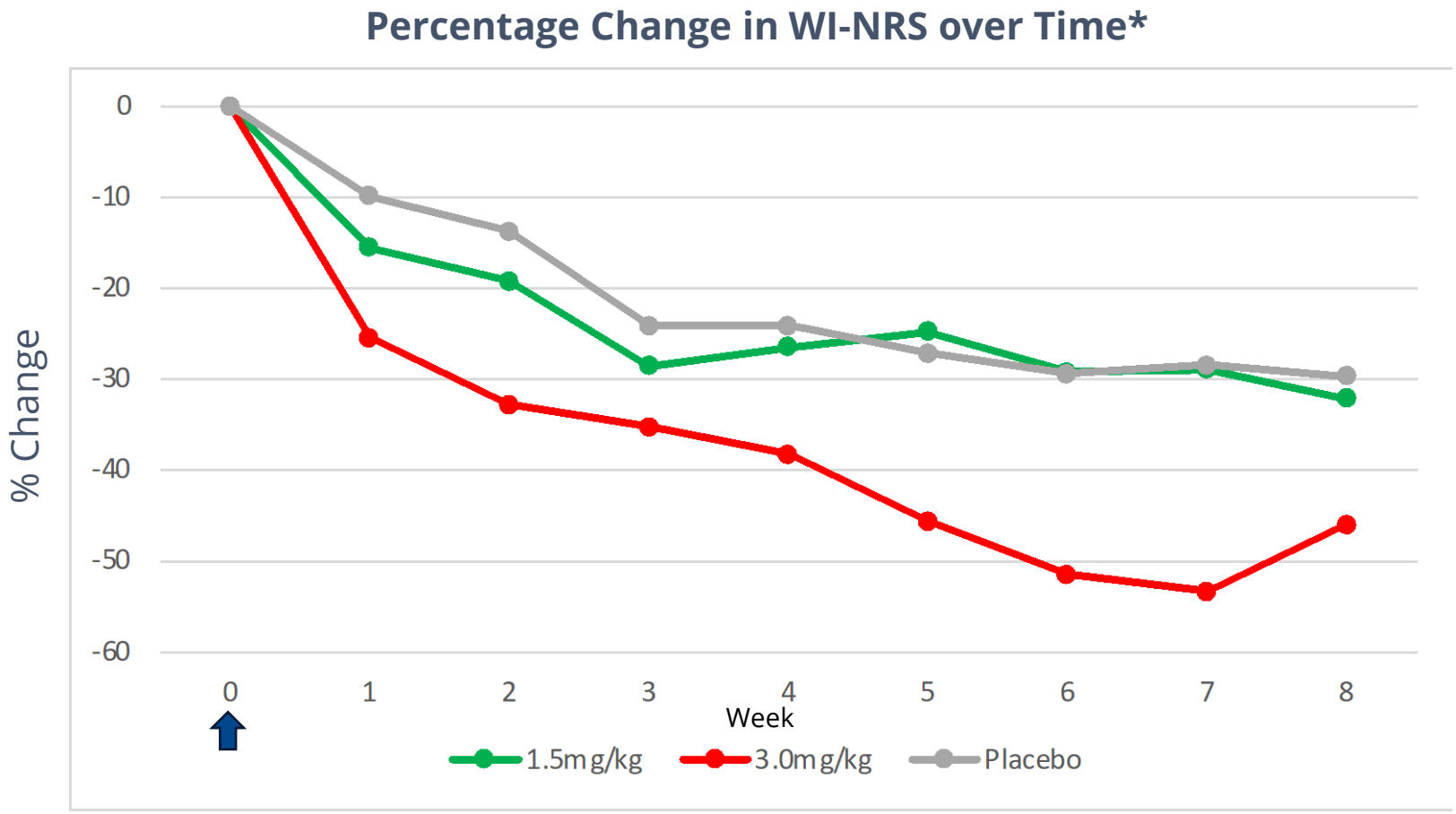
Baseline Characteristic	1.5 mg/kg N=7	3.0 mg/kg N=8	Placebo N=8	Total N= 23
Age years	65 (56-69)	60 (29-63)	55.5 (18-75)	60 (18-75)
Sex Female, n (%)	4 (57)	6 (75)	2 (25)	12 (57)
Race White, n (%)	3 (43)	5 (63)	6 (75)	14 (61)
Black n (%)	4 (57)	3 (37)	2 (25)	9 (39)
Ethnicity Hispanic n (%)	1 (14)	0 (0)	1 (13)	2 (9)
Weight (kg)	89.4 (68.5-103.4)	84.6 (48-117)	84.6 (57.5-137)	85.9 (48-137)
PN duration years	9.7 (1-21.9)	7.3 (0.3-21.1)	9.7 (0.4-32.1)	8.5 (0.3-32.1)
WI-NRS weekly average	8.6 (7.4-10)	8.4 (7.5-10)	8.7 (7.3-10)	8.6 (7.3-10)
IGA	3.1(3-4)	3.3 (3-4)	3.4 (3-4)	3.3 (3-4)
Tryptase (ng/ml)	6.2 (4.4-7.9)	5.3 (3.2-11.2)	5.4 (2.8-7.6)	6.0 (2.8-11.2)

Mean (range) are presented unless otherwise indicated

Barzolvolimab was Well Tolerated

- Adverse Events (AEs) were generally mild to moderate in intensity and considered unrelated to treatment
- Through 8 weeks:
  - One patient who received 3.0 mg/kg had an anaphylactic reaction (resolved without sequelae)
  - Two patients had unrelated SAEs reported (DVT/pulmonary embolism/pneumonia in placebo patient and dizziness in a 1.5 mg/kg patient)
  - No AE was reported in more than one barzolvolimab treated patient
  - Hematology results were consistent with prior studies
- Generally, AEs seen during the 24-week follow-up period were consistent with comorbidities commonly observed in the PN population

Rapid and Meaningful Reduction in WI-NRS Following a Single Dose of Barzolvolimab 3.0 mg/kg



*Similar response observed out to 16 weeks.

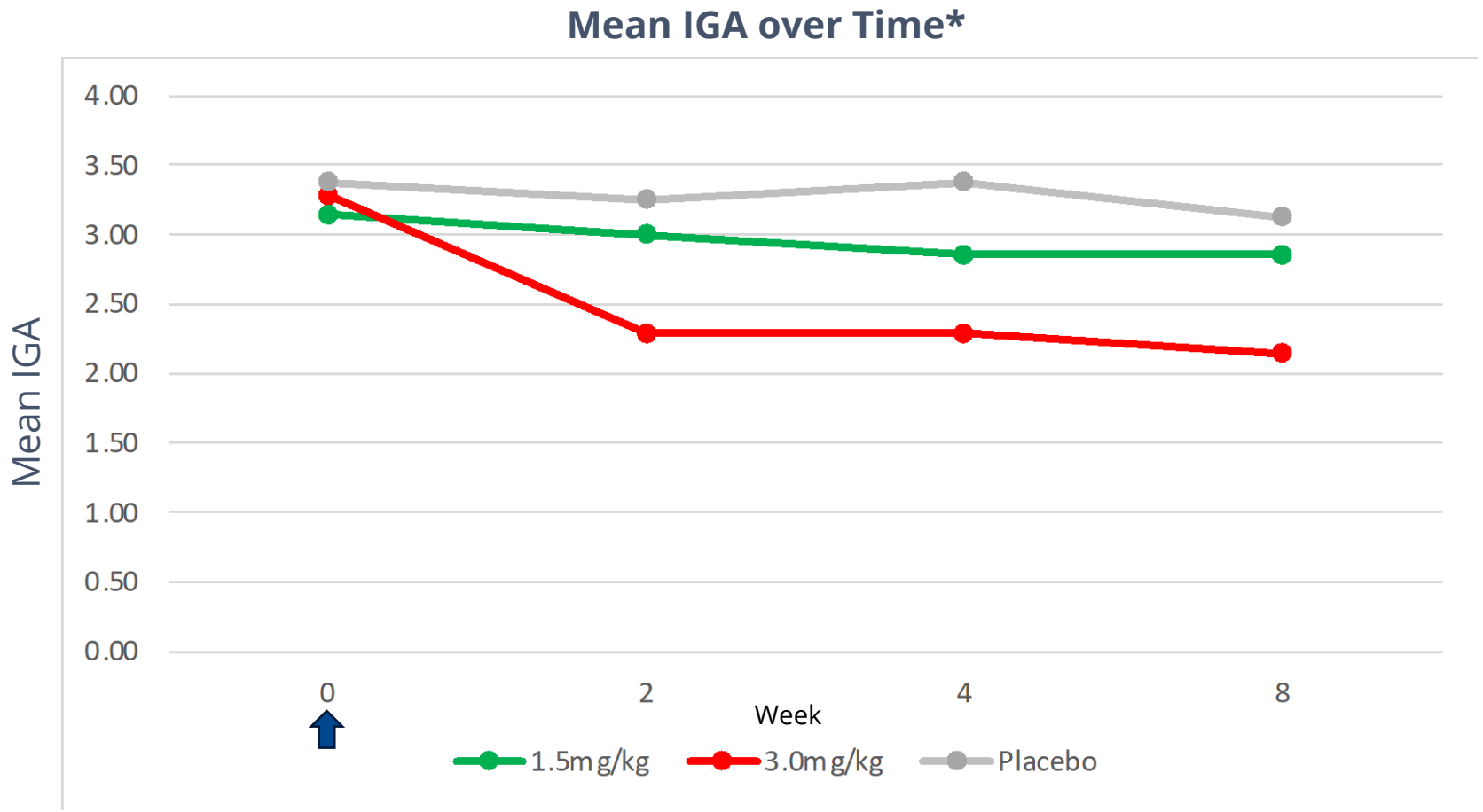
↑ Single dose administered at Week 0

Clinically Meaningful Reduction in WI-NRS Following a Single Dose of Barzolvolimab 3.0 mg/kg

Proportion % of Subjects with ≥4-point decrease in WI-NRS

Dose	Week 01	Week 02	Week 03	Week 04	Week 05	Week 06	Week 07	Week 08
1.5 mg/kg	0	14	29	14	29	29	29	43
3.0 mg/kg	14	29	29	29	57	71	57	57
placebo	0	0	13	13	25	38	38	25

Early, Durable Healing of PN lesions Following a Single Dose of Barzolvolimab 3.0 mg/kg



*Similar response observed out to 16 weeks.

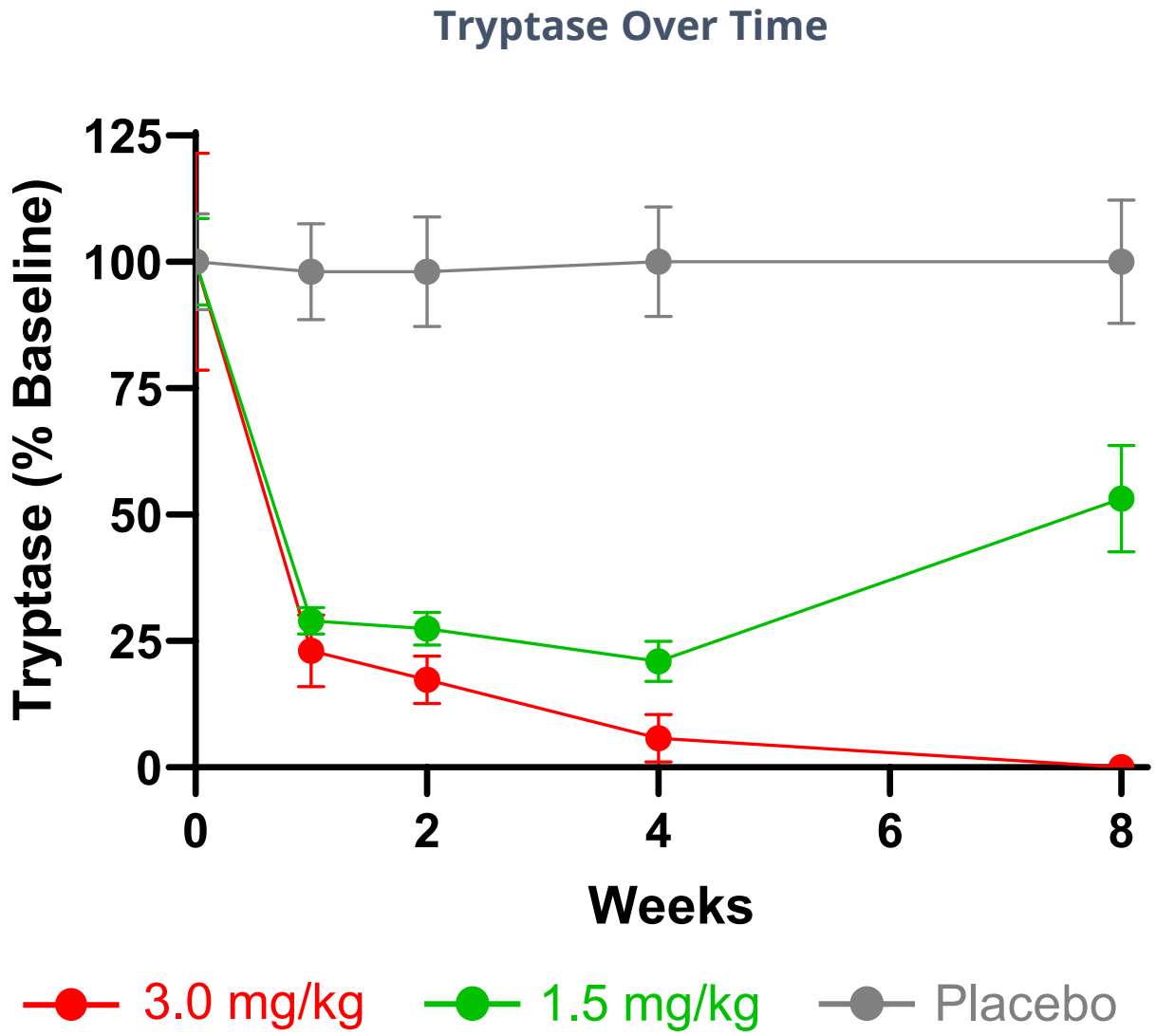
Single dose administered at Week 0

29% of Patients Treated with Barzolvolimab 3.0 mg/kg Achieved Clear or Almost Clear Skin by Week 8

Proportion % of Subjects with IGA 0/1

Dose	**Baseline**	**Week 2**	**Week 4**	**Week 8**
1.5 mg/kg	0	0	0	0
3.0 mg/kg	0	14	14	29
placebo	0	0	0	0

Tryptase is Profoundly and Durably Suppressed by Barzolvolimab 3.0 mg/kg



Summary and Discussion

- Barzolvolimab was generally well tolerated in patients with PN
- A single dose of 3.0 mg/kg demonstrated clinically meaningful activity in PN at 8 weeks
  - 57% experienced a clinically meaningful reduction in itch from baseline
  - 29% achieved clear or almost clear skin by IGA
  - Response observed as early as 1 week after dosing
  - Clinically meaningful activity persisted to 16 weeks
- Clinical activity was associated with profound serum tryptase reduction, which was sustained at the 3.0 mg/kg dose
- The encouraging safety and clinical activity warrant further study of barzolvolimab in PN
- These data support a potential role for mast cells in the pathogenesis of PN and other disease states involving chronic itch