Abstract #6746
Presented at the 32nd European Academy of Dermatology and Venereology (EADV) Congress
11–14 October 2023, Berlin, Germany

A Phase 3 Study of Ruxolitinib Cream in Children Aged 2–<12 Years with Atopic Dermatitis (TRuE-AD3): 8-Week Analysis

Lawrence F. Eichenfield, MD,[1] Linda F. Stein Gold, MD, PhD,[2] Eric L. Simpson, MD, MCR,[3] Andrea L. Zaenglein, MD,[4] April W. Armstrong, MD, PhD, MPH,[5] Megha M. Tollefson, MD,[6] Weily Soong, MD,[7] Lara Wine Lee, MD, PhD,[8] Alim R. Devani, MD,[9] Seth B. Forman, MD,[10] Dareen D. Siri, MD,[11] Brett Angel, MD,[12] Howard Kallender, PhD,[12] Qian Li, PhD,[12] Amy S. Paller, MD[13]

[1]University of California San Diego, San Diego, CA, USA; [2]Henry Ford Health System, Detroit, MI, USA; [3]Oregon Health & Science University, Portland, OR, USA; [4]Penn State/Hershey Medical Center, Hershey, PA, USA; [5]David Geffen School of Medicine at University of California at Los Angeles, Los Angeles, CA, USA; [6]Mayo Clinic, Rochester, MN, USA; [7]AllerVie Health, Birmingham, AL, USA; [8]Medical University of South Carolina, Charleston, SC, USA; [9]Dermatology Research Institute, Calgary, Alberta, Canada; [10]ForCare Clinical Research, Tampa, FL, USA; [11]Midwest Allergy Sinus Asthma SC, Normal, IL, USA; [12]Incyte Corporation, Wilmington, DE, USA; [13]Northwestern University Feinberg School of Medicine, Chicago, IL, USA

Disclosures

- LFE has served as an investigator, consultant, speaker, or data safety monitoring board member for AbbVie, Amgen, Arcutis, Aslan, Bristol Myers Squibb, Castle, Dermavant, Eli Lilly, Forte Biosciences, Galderma, Incyte, Janssen, LEO Pharma, Novartis, Ortho Dermatologics, Pfizer, Regeneron, Sanofi Genzyme, Trialspark and UCB

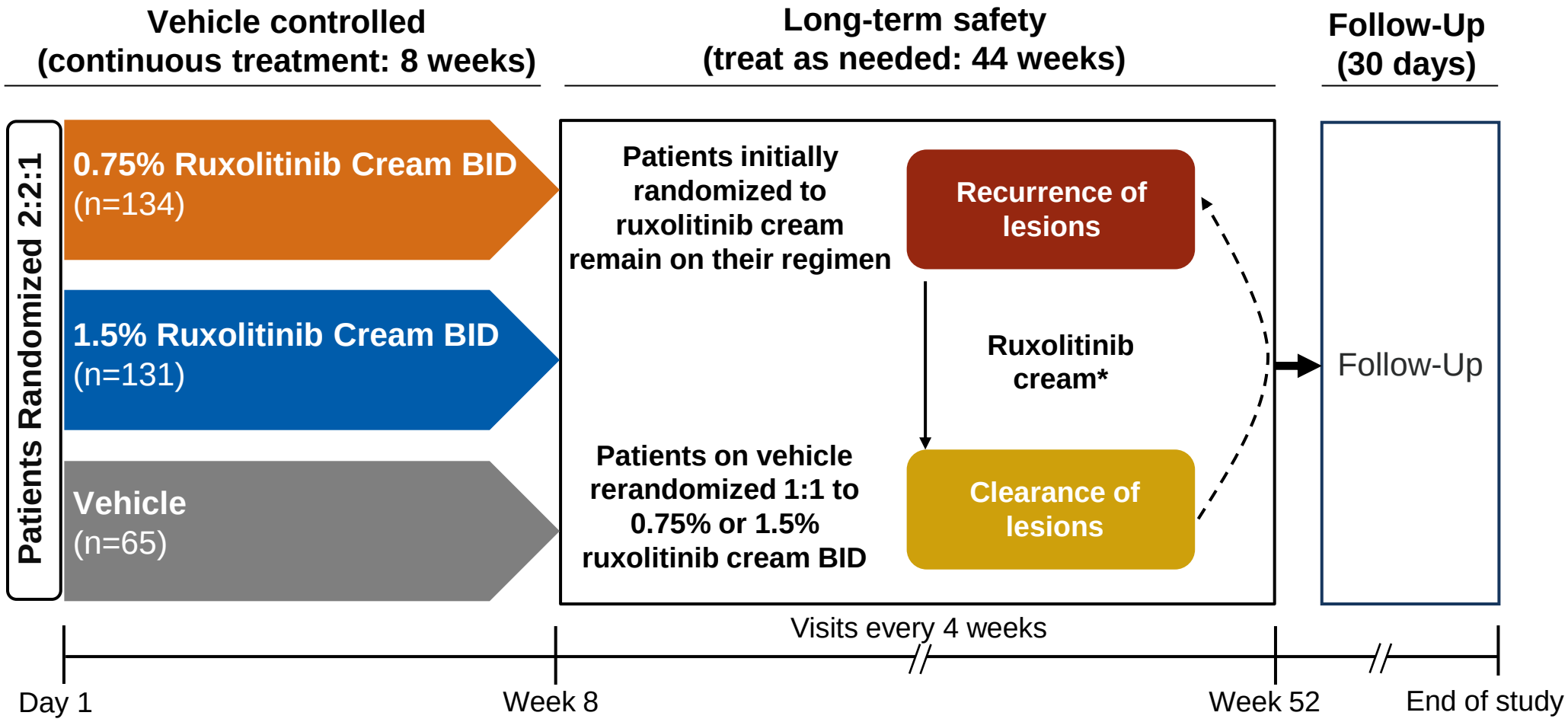
Atopic Dermatitis in Children

- AD is an inflammatory skin condition affecting up to 23% of children globally[1-2]
- Ruxolitinib cream is a selective JAK1/JAK2 inhibitor approved in the United States for the treatment of mild to moderate AD in adolescents and adults[3]
- In two pivotal phase 3 randomized studies of identical design (TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745651]), ruxolitinib cream demonstrated anti-inflammatory and antipruritic activity and was well tolerated in adolescents and adults[4]
- In a pilot pediatric PK/safety study (NCT03257644), ruxolitinib cream was well tolerated in patients aged ≥2 years with AD, with no effect on hematologic parameters or bone biomarkers and with low mean plasma concentrations, and efficacy was consistent with TRuE-AD1/TRuE-AD2 results[5]
- **Objective:** To evaluate the efficacy, safety, and PK of ruxolitinib cream in patients aged 2 to <12 years with mild to moderate AD in a randomized phase 3 study (TRuE-AD3 [NCT04921969])

AD, atopic dermatitis; JAK, Janus kinase; PK, pharmacokinetics.

1. Odhiambo JA, et al. *J Allergy Clin Immunol*. 2009;124(6):1251-1258; 2. Silverberg JI, et al. *Ann Allergy Asthma Immunol*. 2021;126(4):417-428.e2; 3. OPZELURA™ (ruxolitinib cream). Full Prescribing Information, Incyte Corporation, Wilmington, DE, 2023; 4. Papp K, et al. *J Am Acad Dermatol*. 2021;85(4):863-872; 5. Leung DYM, et al. *Ann Allergy Asthma Immunol*. 2023;130(4):500-507.e3.

Study Design



BID, twice daily; BSA, body surface area; NRS, Numerical Rating Scale.
* Patients self-evaluated recurrence of lesions between study visits and treated lesions with active AD (≤20% BSA). If lesions cleared between study visits, patients stopped treatment 3 days after lesion disappearance. If new lesions were extensive or appeared in new areas, patients contacted the investigator to determine if an unscheduled additional visit was needed.

Study Endpoints

- **Primary Endpoint**
  - Percentage of patients achieving IGA-TS (score of 0 or 1 with ≥2-grade improvement from baseline) at Week 8
- **Secondary Endpoints**
  - Percentage of patients achieving EASI75 through Week 8 vs baseline
  - Percentage of patients with itch NRS4 through Week 8 vs baseline (among patients aged 6 to <12 years)
  - Time to achieve itch NRS4
  - Safety and tolerability
- **Other Endpoints**
  - C_{ss} of ruxolitinib

C_{ss}, steady-state plasma concentration; EASI, Eczema Area and Severity Index; EASI75, ≥75% improvement in EASI; IGA-TS, Investigator's Global Assessment–treatment success; NRS2, ≥2-point improvement in NRS from baseline; NRS4, ≥4-point improvement in NRS from baseline.

Eligibility Criteria

- **Key Inclusion Criteria**
  - Patients aged 2 to <12 years with AD ≥3 months
  - IGA score of 2 or 3
  - 3%–20% affected BSA (excluding scalp)
  - Baseline itch NRS score ≥4 (for patients aged 6 to <12 years)
- **Key Exclusion Criteria**
  - Unstable course of AD
  - Other types of eczema
  - Immunocompromised status
  - Use of a biologic within 12 weeks or 5 half-lives (whichever was longer) of baseline
  - Use of AD systemic therapies within 4 weeks of baseline
  - Phototherapy within 2 weeks of baseline
  - Use of AD topical therapies (except bland emollients) within 1 week of baseline
  - Previous treatment with a JAK inhibitor

Demographics Among Patients Aged 2 to <12 Years

- 330 patients (median [range] age, 6.0 [2–11] years) were enrolled
- Baseline demographics were similar across treatment groups

Demographic Characteristic	Vehicle (n=65)	0.75% Ruxolitinib Cream (n=134)	1.5% Ruxolitinib Cream (n=131)	Total (N=330)
Age, median (range), y	6.0 (2–11)	6.0 (2–11)	6.0 (2–11)	6.0 (2–11)
2–6, n (%)	33 (50.8)	68 (50.7)	66 (50.4)	167 (50.6)
7–<12, n (%)	32 (49.2)	66 (49.3)	65 (49.6)	163 (49.4)
Female, n (%)	38 (58.5)	73 (54.5)	68 (51.9)	179 (54.2)
Race, n (%)				
White	37 (56.9)	75 (56.0)	68 (51.9)	180 (54.5)
Black	19 (29.2)	45 (33.6)	42 (32.1)	106 (32.1)
Asian	3 (4.6)	7 (5.2)	11 (8.4)	21 (6.4)
Other	6 (9.2)	6 (4.5)	9 (6.9)	21 (6.4)
Not reported	0	1 (0.7)	1 (0.8)	2 (0.6)
Country, n (%)				
United States	65 (100)	129 (96.3)	122 (93.1)	316 (95.8)
Canada	0	5 (3.7)	9 (6.9)	14 (4.2)

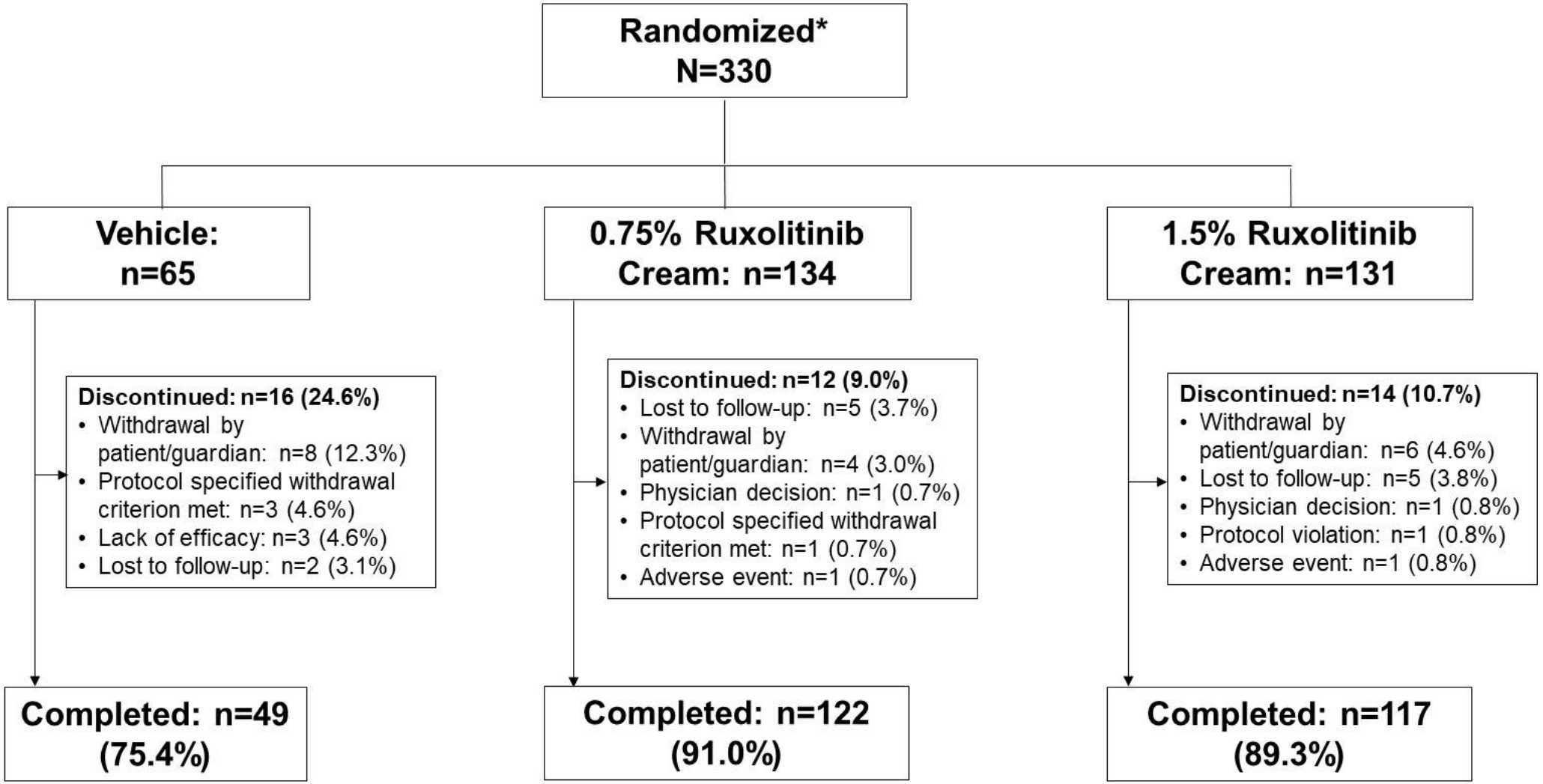
Baseline Clinical Characteristics Among Patients Aged 2 to <12 Years

- Baseline clinical characteristics were similar across treatment groups

Clinical Characteristic	Vehicle (n=65)	0.75% Ruxolitinib Cream (n=134)	1.5% Ruxolitinib Cream (n=131)	Total (N=330)
Affected BSA, mean (SD), %	10.0 (5.54)	10.0 (5.11)	11.2 (5.58)	10.5 (5.40)
Baseline EASI, mean (SD)	8.6 (5.47)	8.4 (6.11)	8.9 (4.57)	8.6 (5.40)
>7, n (%)	36 (55.4)	62 (46.3)	80 (61.1)	178 (53.9)
Baseline IGA, n (%)				
2	16 (24.6)	31 (23.1)	31 (23.7)	78 (23.6)†
3	49 (75.4)	103 (76.9)	100 (76.3)	252 (76.4)
Itch NRS score, mean (SD)*	6.5 (1.79)	6.6 (1.78)	6.9 (1.55)	6.7 (1.70)
Itch NRS score ≥4, n (%)*	37 (97.4)	80 (94.1)	76 (98.7)	193 (96.5)
Duration of disease, median (range), y	4.4 (0.4–11.2)	5.2 (0.3–11.3)	4.7 (0.4–11.2)	4.8 (0.3–11.3)
Had prior therapy in last 12 mo, n (%)	46 (70.8)	86 (64.2)	90 (68.7)	222 (67.3)

* For patients aged 6–<12 years (vehicle, n=38; 0.75% ruxolitinib cream, n=85; 1.5% ruxolitinib cream, n=77; total, n=200). Score is mean of at least 4 of the 7 days immediately prior to the baseline visit.
† Capped at 25%.

Patient Disposition During the VC Period



* All randomized patients were included in the efficacy analysis. One patient in the 1.5% ruxolitinib cream treatment group did not apply any treatment and was excluded from the safety analysis.

Safety

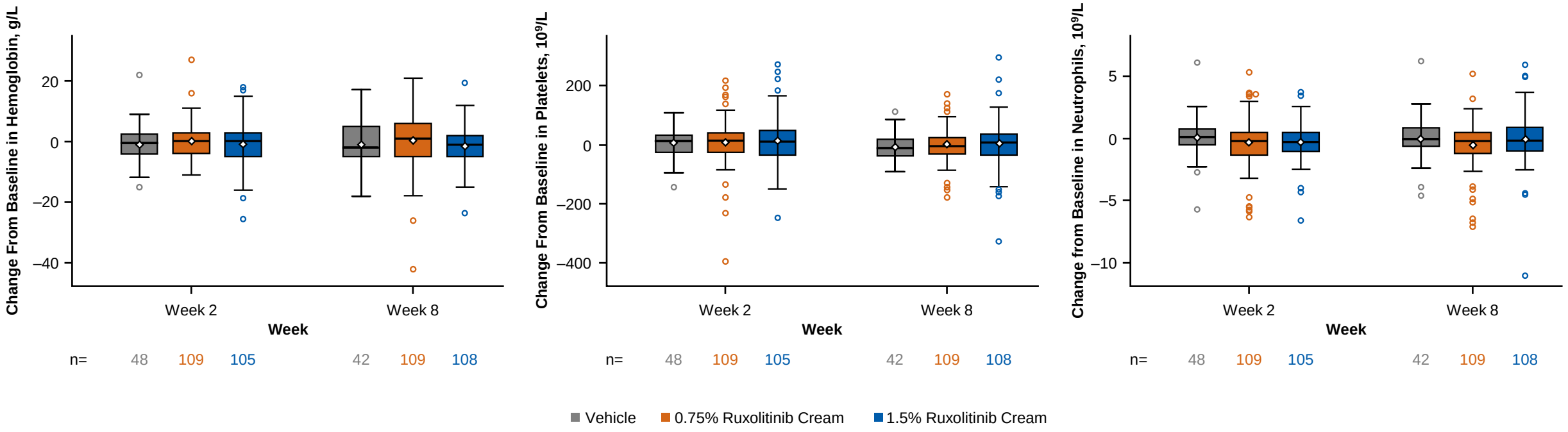
- Both strengths of ruxolitinib cream were well tolerated and associated with few application site reactions
- No serious AEs or deaths were reported
- No TEAEs suggestive of systemic JAK inhibition (eg, serious infections, MACE, malignancies, or thromboses) were observed

	Vehicle (n=65)	0.75% Ruxolitinib Cream (n=134)	1.5% Ruxolitinib Cream (n=130)	Total Ruxolitinib Cream (n=264)
Patients with TEAE, n (%)*	18 (27.7)	35 (26.1)	48 (36.9)	83 (31.4)
Treatment-related TEAE, n (%)	2 (3.1)	7 (5.2)	7 (5.4)	14 (5.3)
Most common treatment-related TEAEs, n (%)†				
Application site pain	0	4 (3.0)	3 (2.3)	7 (2.7)
Application site erythema	0	0	2 (1.5)	2 (0.8)
Application site irritation	0	1 (0.7)	1 (0.8)	2 (0.8)
Discontinuation due to a TEAE, n (%)‡	0	1 (0.7)	1 (0.8)	2 (0.8)
Dose interruption due to a TEAE, n (%)	4 (6.2)	4 (3.0)	1 (0.8)	5 (1.9)

AE, adverse event; MACE, major acute cardiovascular event; TEAE, treatment-emergent adverse event.
* No serious AEs were observed during the vehicle-controlled period; 2 had a Grade 3 TEAE (bilateral adenoid hypertrophy/bilateral tonsil hypertrophy/sleep apnea; worsening of AD).
† Occurring in ≥2 patients who applied either strength of ruxolitinib cream.
‡ Discontinuations due to: Grade 3 worsening of AD, unlikely related to study drug; Grade 2 application site pain, likely related to study drug.

Key Hematological Parameters

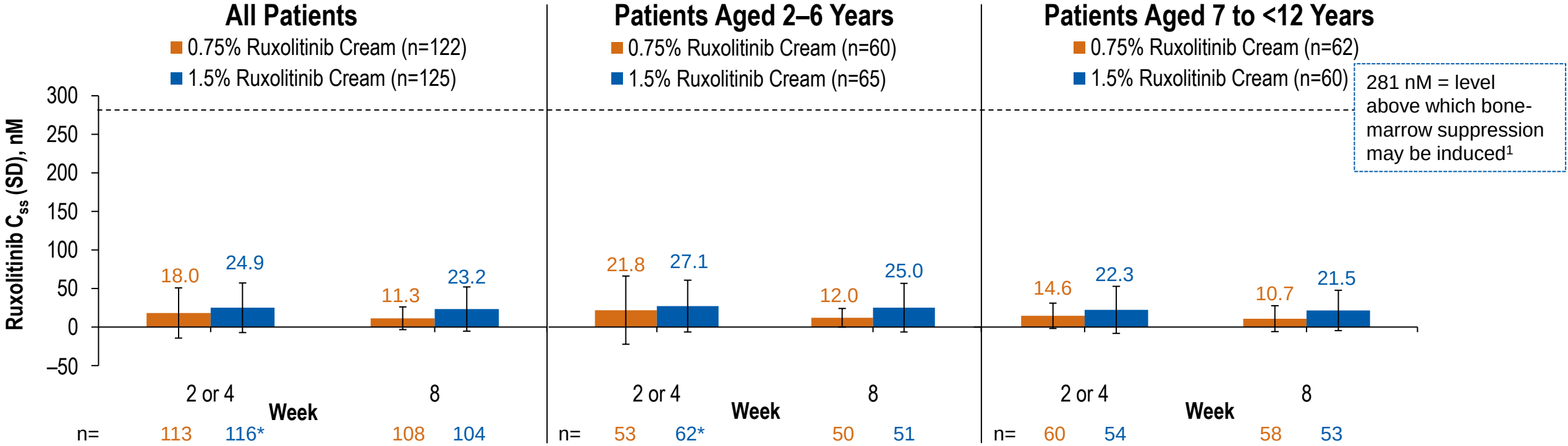
- No substantial changes from baseline in mean hemoglobin, platelet, and neutrophil values were observed in patients applying either strength of ruxolitinib cream



IQR, interquartile range; Q1, quartile 1; Q3, quartile 3.
IQR, represented by boxes; medians, by dark lines; means, by white diamonds; outliers, by circles; Q1–(1.5 x IQR) and Q3+(1.5 x IQR), by whiskers.

Pharmacokinetics

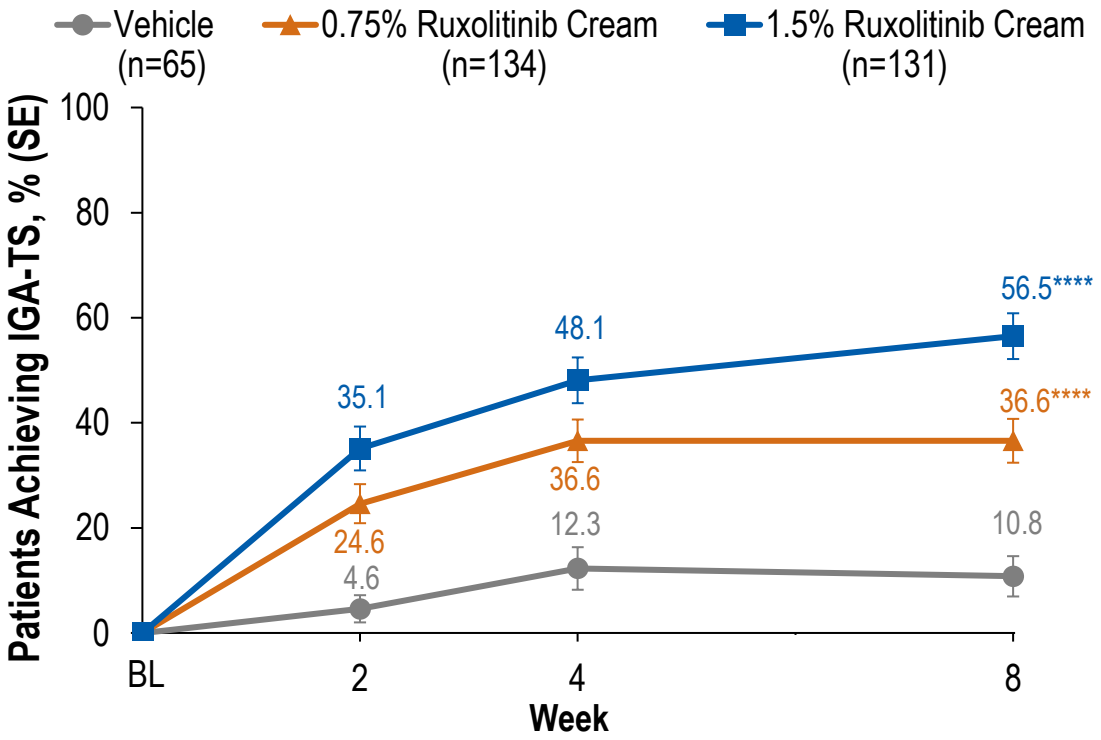
- Mean plasma concentrations of ruxolitinib at Weeks 2 or 4 and Week 8 were well below that associated with myelosuppression (281 nM)[1]
  - No accumulation was observed over 8 weeks
  - No differences were observed between the 2 age groups

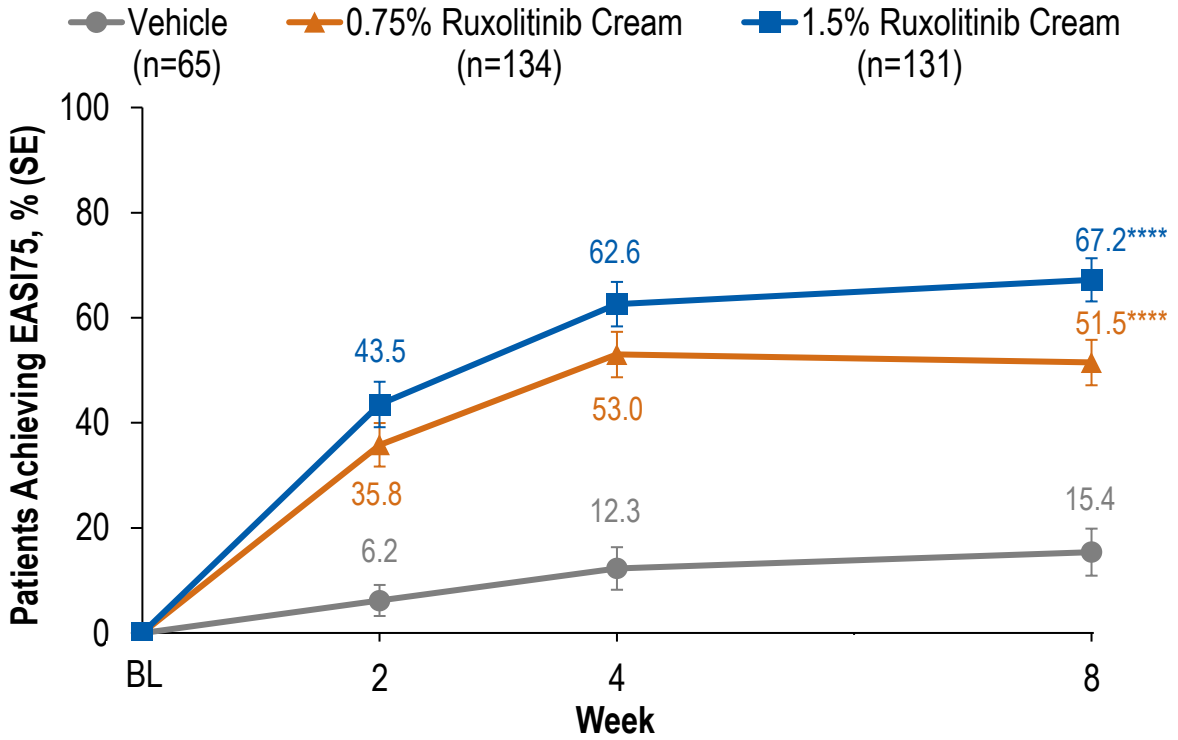


IC_{50}, half-maximal inhibitory concentration; pSTAT3, phosphorylated signal transducer and activator of transcription 3.
* Data for a 2-year-old male patient were excluded due to an implausible ruxolitinib C_{ss} of 1230 nM at Week 4. The subsequent (Week 8) ruxolitinib C_{ss} for this patient was 33.0 nM.
1. Quintas-Cardama A, et al. *Blood*. 2010;115(15):3109-3117. The IC_{50} of ruxolitinib for thrombopoietin-stimulated pSTAT3 inhibition (a proxy parameter to assess JAK-related myelosuppression in bone marrow) is 281 nM.

Percentage of Patients Achieving IGA-TS (Primary Endpoint) and EASI75

- Clinical improvement was observed in patients applying 0.75%/1.5% ruxolitinib cream vs vehicle at Week 2, with efficacy increasing through Week 8 for IGA-TS and EASI75

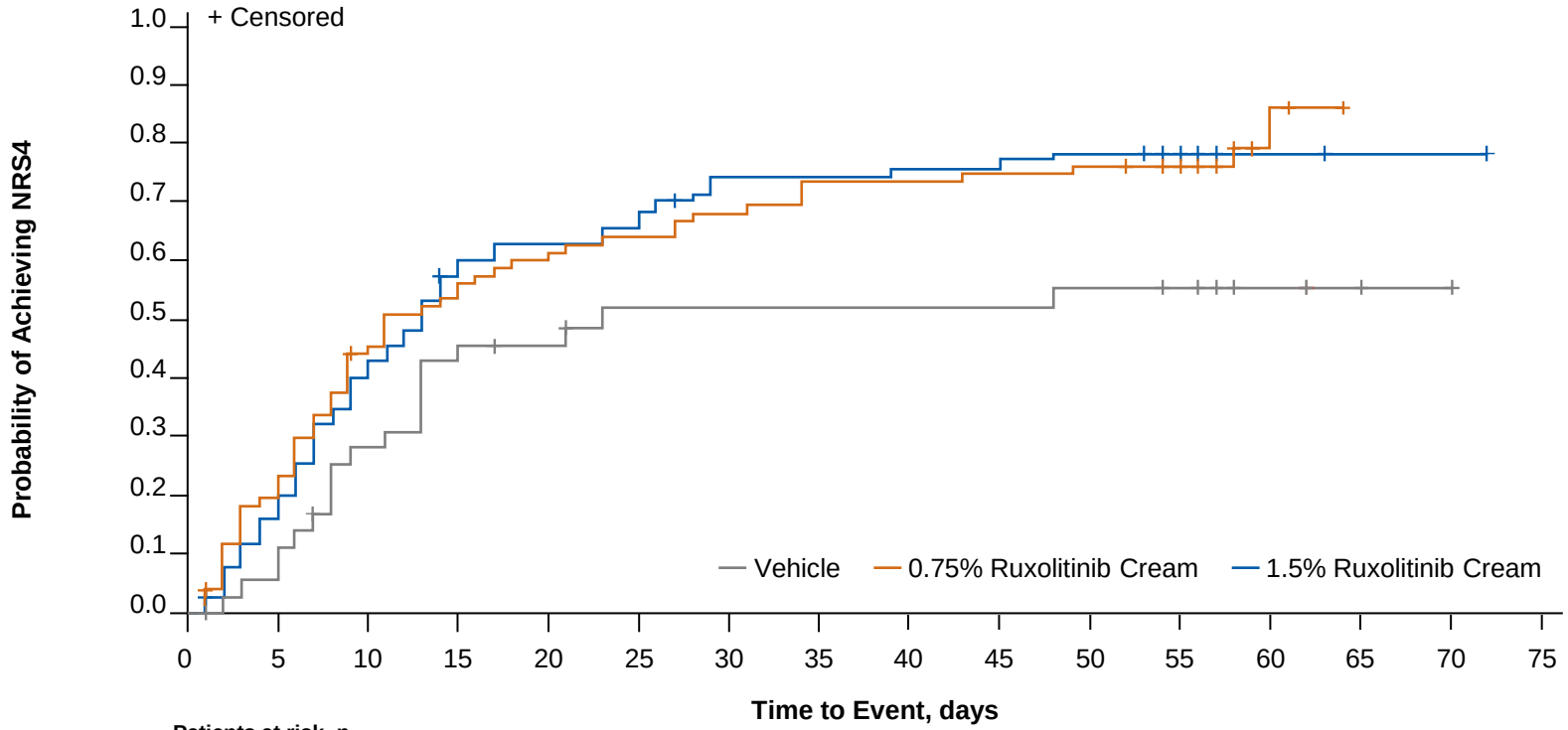




BL, baseline.
**** *P* ≤0.0001 vs vehicle.

Time to Achieve NRS4

- In patients aged 6 to <12 years with a baseline daily itch NRS ≥4 (n=192), median time to achieve NRS4 was 11.0/13.0 days vs 23.0 days (HR, 1.74/1.77; *P*<0.05 vs vehicle for both)

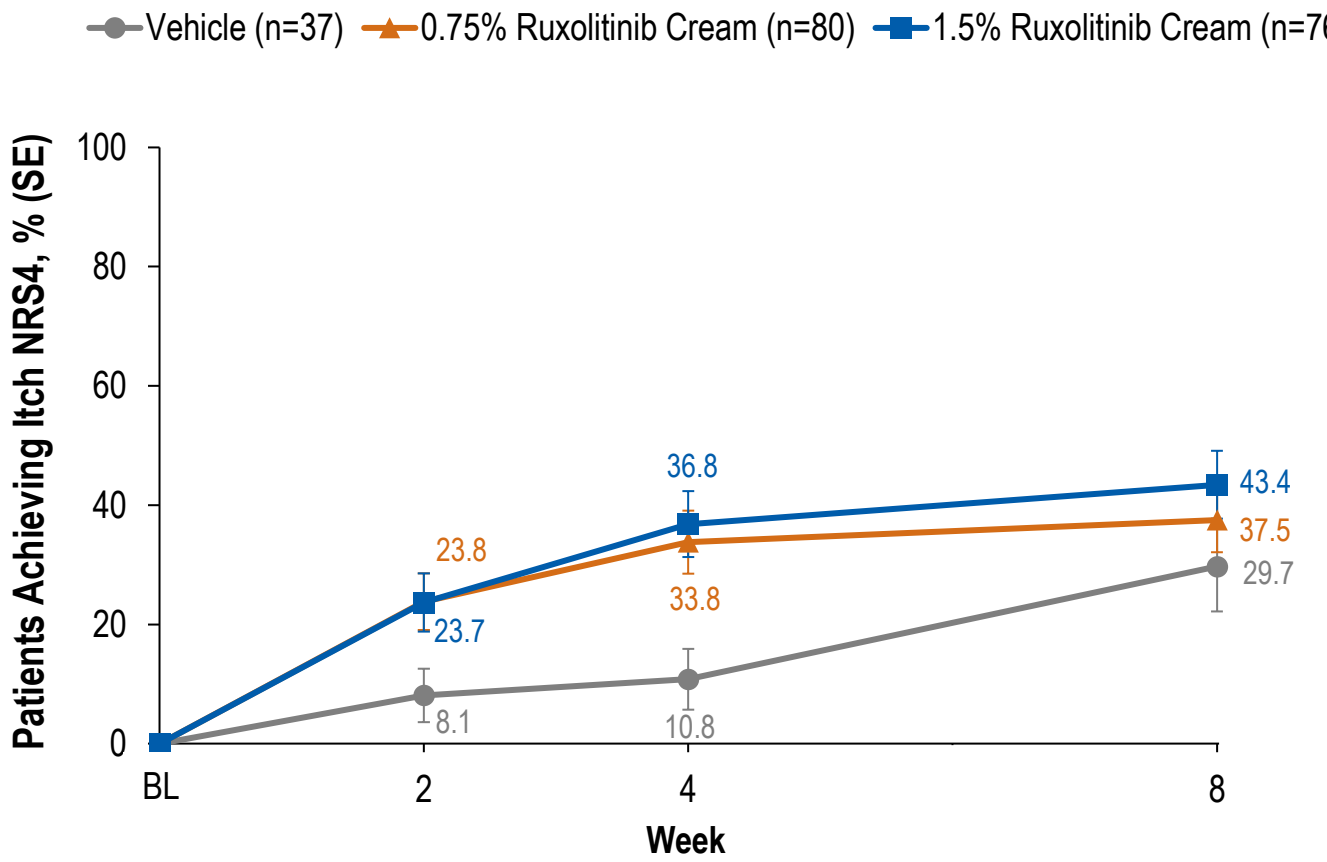


Patients at risk, n

Vehicle	37	34	25	20	18	14	14	14	14	14	13	12	3	2	1
0.75% Ruxolitinib Cream	79	62	42	35	30	27	24	20	20	19	18	15	3	0	
1.5% Ruxolitinib Cream	76	63	45	31	27	25	18	18	17	17	15	13	2	1	1	0

Percentage of Patients Achieving Itch NRS4

- Itch NRS4 at Week 4 and Week 8 was achieved by 33.8%/36.8% vs 10.8% and 37.5%/43.4% vs 29.7% of patients aged 6 to <12, respectively



Conclusions

- In patients aged 2 to <12 years with mild to moderate AD, ruxolitinib cream was well tolerated, and no serious infections, MACE, malignancies, or thromboses were observed
- Low mean ruxolitinib plasma C_{ss} and a lack of impact on hematologic parameters suggest systemic JAK inhibition is highly unlikely
- Ruxolitinib cream achieved significant efficacy vs vehicle at Week 8 for IGA-TS and EASI75
- Ruxolitinib cream led to early and sustained itch relief relative to vehicle in patients aged 6 to <12 years
- Results in children aged 2 to <12 years were similar to phase 3 results in adolescents and adults[1] and maximum-use data in children[2]

1. Papp K, et al. *J Am Acad Dermatol*. 2021;85(4):863-872; 2. Forman SB, et al. "A Maximum-Use Trial of Ruxolitinib Cream in Children Aged 2 to <12 Years With Atopic Dermatitis: 8-Week Analysis of Safety, Pharmacokinetics, Efficacy, and Patient-Reported Outcomes". Presented at: European Academy of Dermatology and Venereology (EADV) 32nd Congress, 11–14 October 2023, Berlin, Germany.

Thank You

- We thank the study investigators, patients, and their families for their participation in this study