Presentation #D2T01.4A

# 52-Week Safety and Disease Control With Ruxolitinib Cream in Children Aged 2–11 Years With Atopic Dermatitis: Results From the Phase 3 TRuE-AD3 Study

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# Presenting Author Disclosures

- Amy S. Paller has served as an investigator or consultant for AbbVie, Abeona, Apogee, Applied Pharma Research, Arcutis, Aslan, BioCryst, Boehringer Ingelheim, Bristol Myers Squibb, Dermavant, Galderma, Eli Lilly, Incyte Corporation, Janssen, Johnson & Johnson, Krystal Biotech, LEO Pharma, Mitsubishi Tanabe, Nektar, Primus, Procter and Gamble, Regeneron, Sanofi, Seanergy, TWI Biotech, and UCB

# Ruxolitinib Cream for Atopic Dermatitis

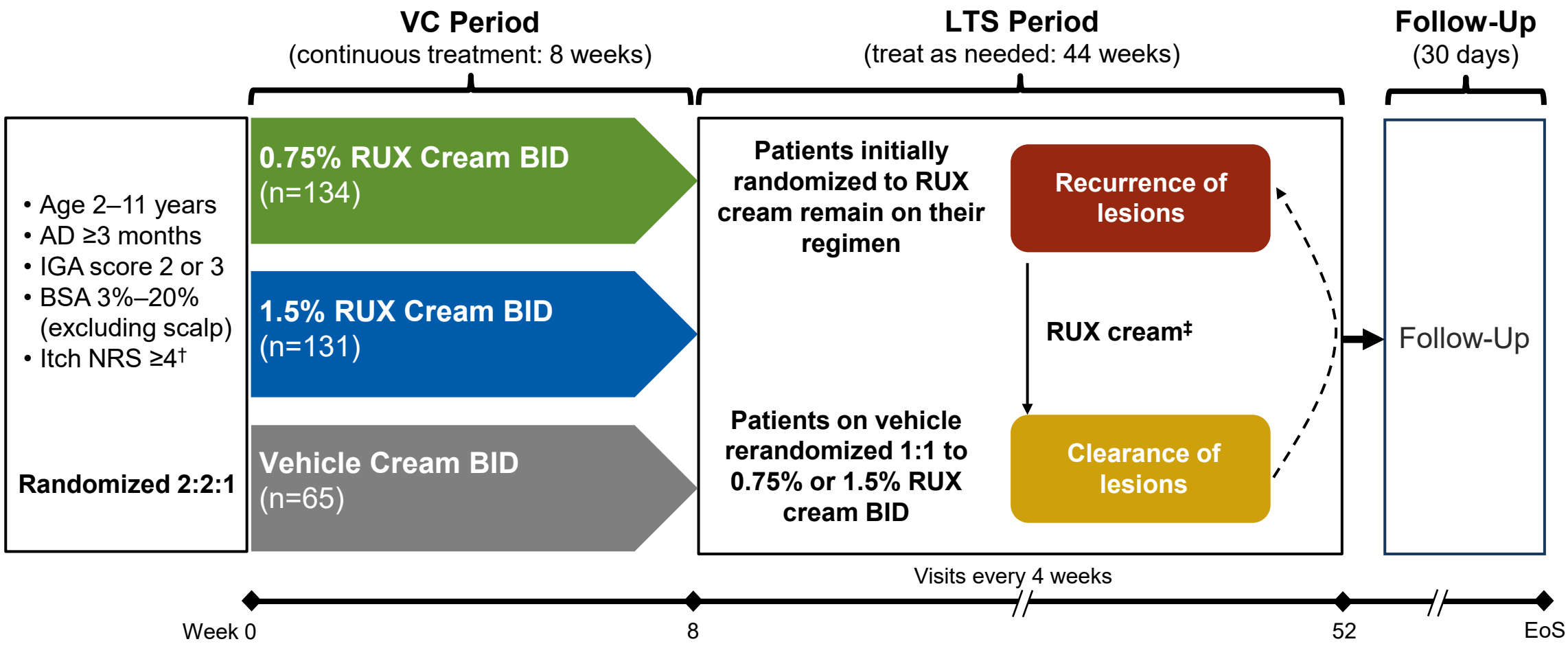
- AD is a chronic, highly pruritic, inflammatory skin disease with onset usually occurring in childhood[1,2]
- Twice-daily continuous application of RUX (JAK1/JAK2 inhibitor) cream for 8 weeks was well tolerated and demonstrated efficacy vs vehicle in patients with mild to moderate AD
  - Adults and adolescents aged ≥12 years (TRuE-AD1 and TRuE-AD2)[3]
  - Children aged 2–11 years (TRuE-AD3)[4]
- Subsequent as-needed application of RUX cream demonstrated long-term safety and disease control
  - Adults and adolescents with mild to moderate AD (TRuE-AD1 and TRuE-AD2)[5]
  - Children aged 2–11 years with moderate to severe AD (maximum-use study)[6]

**Objective:**
To evaluate the long-term safety and disease control of RUX cream in children aged 2–11 years with mild to moderate AD in the phase 3 TRuE-AD3 study (NCT04921969)

AD, atopic dermatitis; JAK, Janus kinase; RUX, ruxolitinib.

1. Silverberg JI, Simpson EL. *Dermatitis*. 2014;25(3):107-114. 2. Fuxench ZCC, et al. *J Invest Dermatol*. 2019;139(3):583-590. 3. Papp K, et al. *J Am Acad Dermatol*. 2021;85(4):863-872. 4. Eichenfield LF, et al. Presented at: EADV Congress: October 11-13, 2023; Berlin, Germany. 5. Papp K, et al. *J Am Acad Dermatol*. 2023;88(5):1008-1016. 6. Bissonnette R, et al. Presented at: RAD Conference: June 8-10, 2024; Chicago, IL.

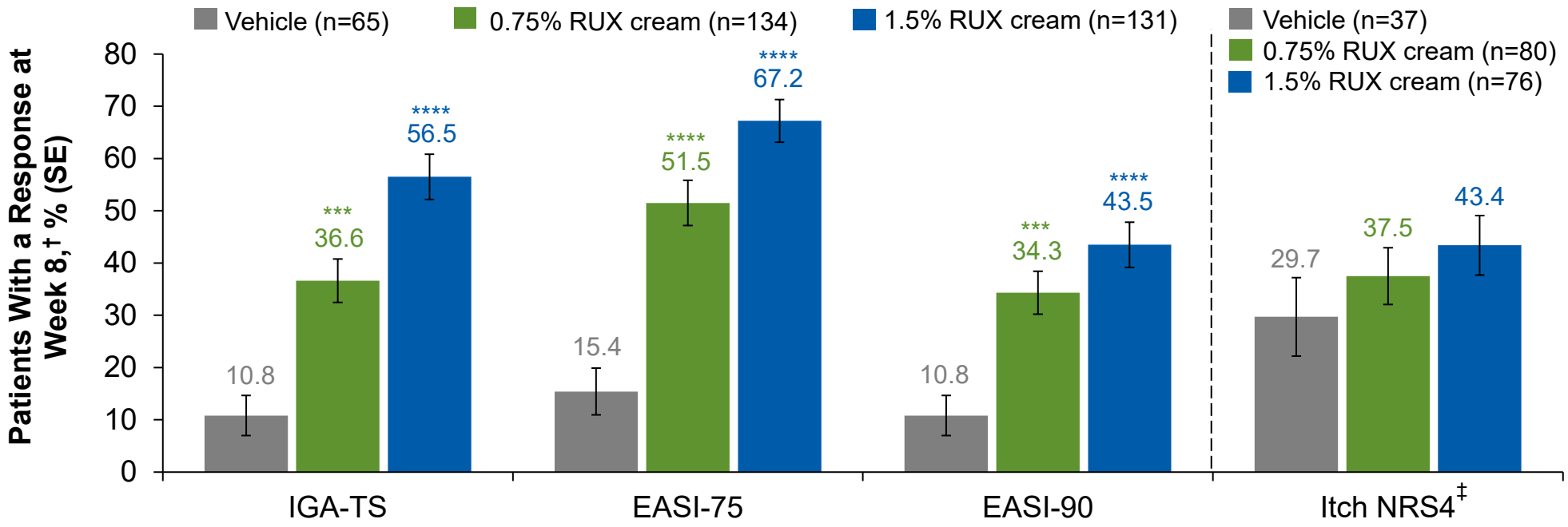
# TRuE-AD3 Study Design




BID, twice daily; BSA, body surface area; EoS, end of study; IGA, Investigator's Global Assessment; LTS, long-term safety; NRS, numerical rating scale; VC, vehicle controlled.
† Among patients aged 6–11 y.
‡ 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.

# Efficacy and Safety at Week 8 of the VC Period

- Significantly more patients who applied 0.75% and 1.5% RUX cream vs vehicle achieved IGA-TS, EASI-75, and EASI-90 at Week 8
- Among patients aged 6–11 years, Itch NRS4 at Week 8 was achieved by more patients for 0.75% and 1.5% RUX cream than for vehicle, although these differences were not statistically significant
- There were few application site reactions by Week 8 (4.5% for RUX cream vs 3.1% for vehicle; none serious)




EASI-75, ≥75% improvement in Eczema Area and Severity Index from baseline; EASI-90, ≥90% improvement in Eczema Area and Severity Index; IGA-TS, Investigator's Global Assessment treatment success (IGA score of 0/1 with a ≥2-point improvement from baseline); NRS4, ≥4-point reduction in numerical rating scale score.
*** *P*<0.001 vs vehicle; **** *P*<0.0001 vs vehicle; † Patients with missing data were imputed as nonresponders. ‡ Patients aged 6–11 y with baseline Itch NRS ≥4 were included in this analysis.

# Baseline Patient Demographics and Disease Characteristics

## *LTS-Evaluable Population†*

- Baseline clinical characteristics were similar across treatment groups

| Characteristic | Vehicle to 0.75% RUX Cream (n=25) | Vehicle to 1.5% RUX Cream (n=24) | 0.75% RUX Cream (n=119) | 1.5% RUX Cream (n=114) | All LTS Patients (N=282) |
|---|---|---|---|---|---|
| Age, median (range), y | 8.0 (2–11) | 5.5 (2–11) | 7.0 (2–11) | 6.0 (2–11) | 7.0 (2–11) |
| Female, n (%) | 15 (60.0) | 12 (50.0) | 67 (56.3) | 55 (48.2) | 149 (52.8) |
| White, n (%) | 14 (56.0) | 13 (54.2) | 69 (58.0) | 61 (53.5) | 157 (55.7) |
| Affected BSA, mean (SD), % | 8.3 (4.5) | 12.1 (5.8) | 9.9 (5.2) | 11.1 (5.6) | 10.4 (5.4) |
| Baseline IGA, n (%) | | | | | |
| 2 | 5 (20.0) | 7 (29.2) | 26 (21.8) | 27 (23.7) | 65 (23.0) |
| 3 | 20 (80.0) | 17 (70.8) | 93 (78.2) | 87 (76.3) | 217 (77.0) |
| Baseline EASI, mean (SD) | 7.4 (3.6) | 9.1 (5.3) | 8.6 (6.3) | 9.0 (4.6) | 8.7 (5.4) |
| Itch NRS score, mean (SD)‡ | 6.9 (1.7) | 6.4 (1.9) | 6.5 (1.8) | 7.0 (1.5) | 6.7 (1.7) |
| Duration of disease, median (range), y | 4.2 (0.4–11.2) | 4.9 (0.9–10.7) | 5.5 (0.3–11.3) | 4.6 (0.4–11.2) | 4.9 (0.3–11.3) |
| Prior therapy in last 12 mo, n (%) | 16 (64.0) | 18 (75.0) | 79 (66.4) | 75 (65.8) | 188 (66.7) |

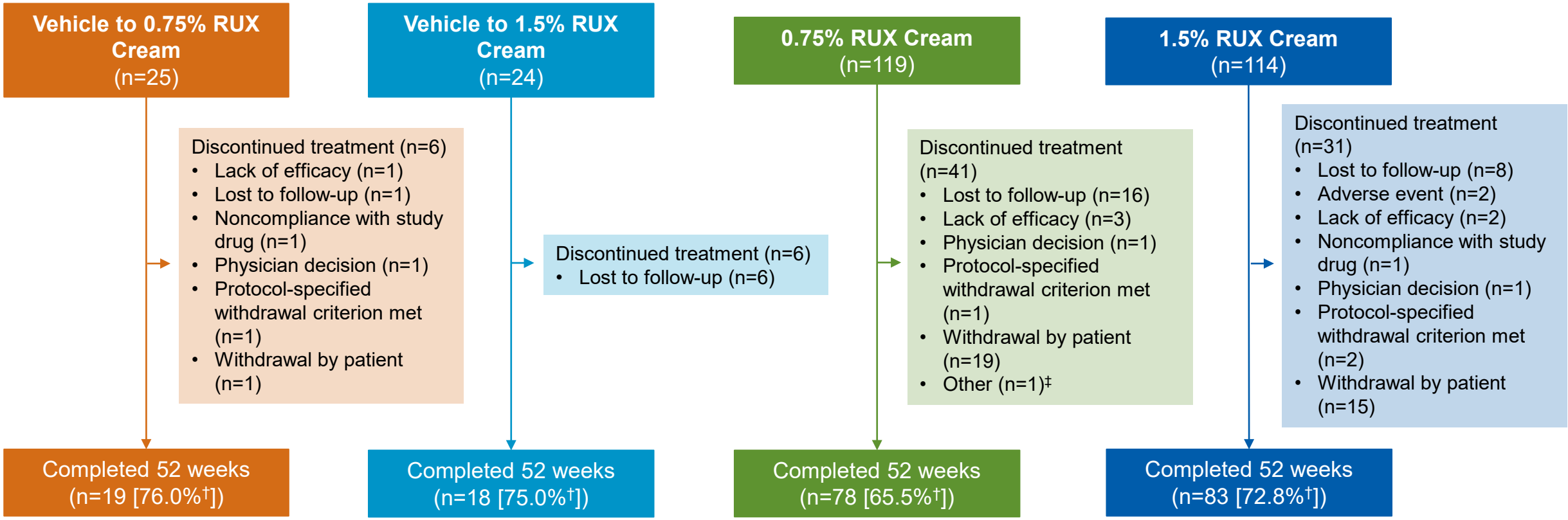
EASI, Eczema Area and Severity Index.

† Patients who applied ≥1 dose of RUX cream in the LTS period; ‡ For patients aged 6–11 years (vehicle to 0.75% RUX, n=19; vehicle to 1.5% RUX, n=12; 0.75% RUX, n=76; 1.5% RUX, n=66; all patients, n=173). Score is mean of ≥4 of the 7 days immediately prior to the baseline visit.

# Patient Disposition During the LTS Period

## *Treatment Discontinuations*

- >65% of patients† completed 52 weeks
- Very few patients discontinued RUX cream due to lack of efficacy or an adverse event

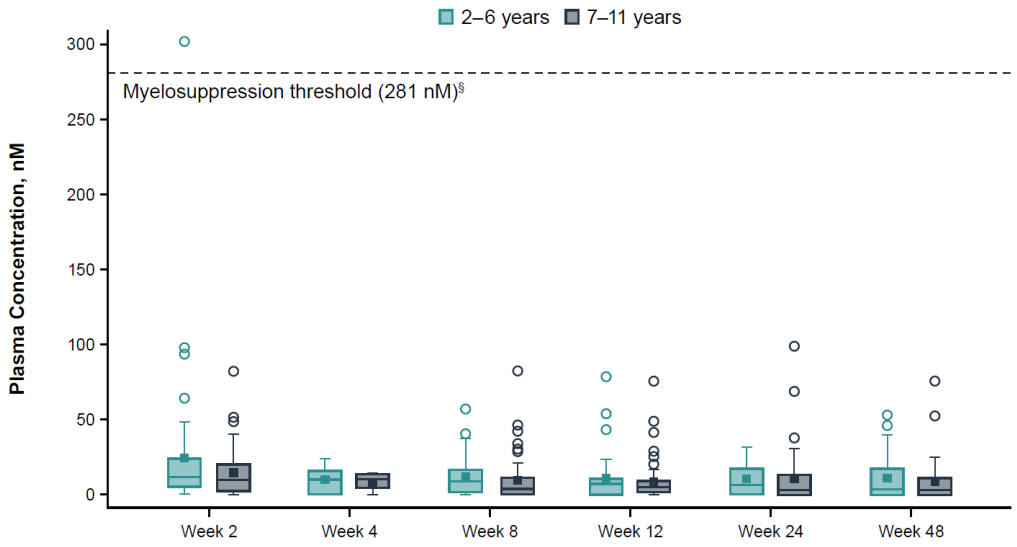



† Percentage of patients entering the 44-week LTS period.
‡ Not specified.

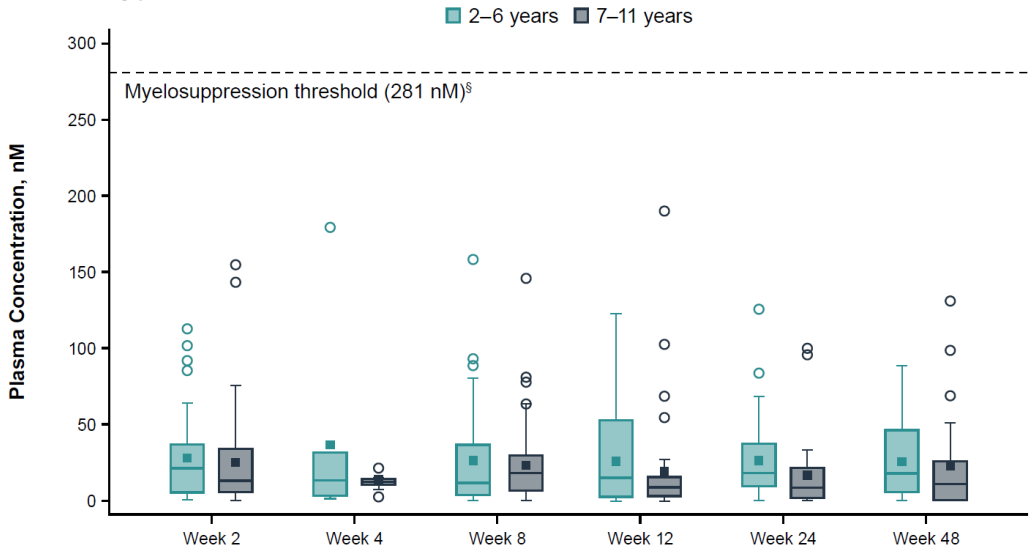
# Pharmacokinetics

- Mean RUX plasma concentrations remained low and were well below the level associated with myelosuppression (281 nM)
  - A single outlier was not of clinical concern†
- No accumulation of RUX was observed
- No differences were observed between age groups

**0.75% RUX Cream†**




**1.5% RUX Cream‡**




IQR, interquartile range; Q1, quartile 1; Q3, quartile 3; TEAE, treatment-emergent adverse event.
IQR, represented by boxes; medians, by dark lines; means, by squares; outliers, by circles; Q1–(1.5 x IQR) and Q3+(1.5 x IQR), by whiskers.
† A male patient aged 6 years had a RUX plasma concentration of 302 nM at Week 2, followed by 78 nM at Week 12. No TEAEs were reported, and hematology parameters remained within the normal range. ‡ Data for a 2-year-old male patient were excluded owing to an implausible RUX concentration of 1230 nM at Week 4; RUX concentration was <80 nM at all subsequent sampling time points. § Threshold associated with JAK-mediated myelosuppression using in vitro assays in whole blood in adults.[1]

1. Quintás-Cardama A, et al. *Blood*. 2010;115(15):3109-3117.

# Safety in the LTS Period

- Both strengths of RUX cream were well tolerated in any body region and associated with few application site reactions
- No new safety signals emerged with long-term treatment up to 1 year
- No meaningful differences were observed between patients aged 2–6 and 7–11 years

| n (%) | Vehicle to 0.75% RUX Cream (n=25) | Vehicle to 1.5% RUX Cream (n=24) | 0.75% RUX Cream (n=119) | 1.5% RUX Cream (n=114) | All LTS Patients (N=282) |
|---|---|---|---|---|---|
| Patients with TEAE | 9 (36.0) | 13 (54.2) | 57 (47.9) | 63 (55.3) | 142 (50.4) |
| Patients with treatment-related TEAE | 3 (12.0) | 0 | 6 (5.0) | 8 (7.0) | 17 (6.0) |
| Patients with application site reaction | 0 | 0 | 2 (1.7) | 1 (0.9) | 3 (1.1) |
| Patients with grade ≥3 TEAE† | 0 | 0 | 3 (2.5) | 3 (2.6) | 6 (2.1) |
| Patients with serious TEAE | 0 | 0 | 0 | 3 (2.6)‡ | 3 (1.1) |
| Patients with fatal TEAE | 0 | 0 | 0 | 0 | 0 |
| Patients with TEAE leading to discontinuation of study drug | 0 | 0 | 0 | 1 (0.9)§ | 1 (0.4) |

† No events were considered treatment related.
‡ Asthma occurred in 2 patients (considered unrelated to treatment and resolved without RUX interruption). Eczema herpeticum occurred in 1 patient (considered unrelated to treatment and resolved after 24 days).
§ Impetigo (grade 2; considered unrelated to treatment and was resolving at the time of the last study visit).

# Most Common TEAEs and Select TEAEs in the 52-Week Study

## Most Common TEAEs†

| n (%) | 0.75% RUX Cream (n=134) | 1.5% RUX Cream (n=130) |
|---|---|---|
| Upper respiratory tract infection | 18 (13.4) | 21 (16.2) |
| Nasopharyngitis | 7 (5.2) | 17 (13.1) |
| COVID-19 | 12 (9.0) | 9 (6.9) |
| Pyrexia | 10 (7.5) | 4 (3.1) |
| Otitis media | 5 (3.7) | 7 (5.4) |
| Asthma | 7 (5.2) | 4 (3.1) |
| Gastroenteritis viral | 4 (3.0) | 7 (5.4) |
| Pharyngitis streptococcal | 8 (6.0) | 3 (2.3) |
| Vomiting | 5 (3.7) | 6 (4.6) |
| Influenza | 6 (4.5) | 4 (3.1) |
| Application site pain‡ | 5 (3.7) | 4 (3.1) |
| Cough | 7 (5.2) | 2 (1.5) |
| Ear infection | 5 (3.7) | 4 (3.1) |

## Select TEAEs

- No folliculitis or herpes zoster
- 1 patient with eczema herpeticum
- No MACE, malignancies, or thromboses

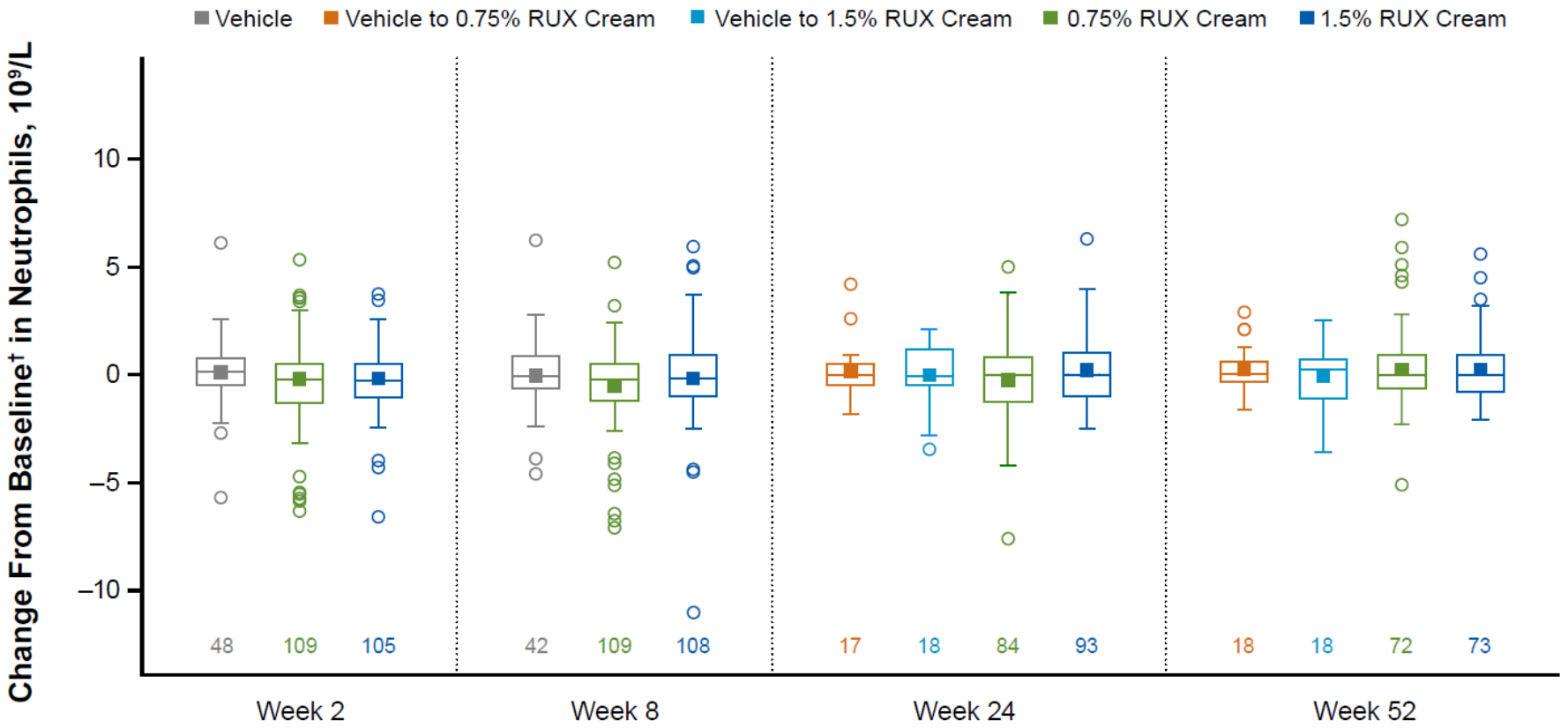
| n (%) | 0.75% RUX Cream (n=134) | 1.5% RUX Cream (n=130) |
|---|---|---|
| Diarrhea | 3 (2.2) | 5 (3.8) |
| Contact dermatitis | 2 (1.5) | 3 (2.3) |
| Headache | 1 (0.7) | 3 (2.3) |
| Nausea | 1 (0.7) | 0 |
| Serious infections | 0 | 1 (0.8)§ |
| Folliculitis | 0 | 0 |
| Herpes zoster | 0 | 0 |
| MACE | 0 | 0 |
| Malignancy | 0 | 0 |
| Thrombosis | 0 | 0 |

MACE, major cardiovascular event.

† TEAE in ≥9 patients (3.4%) across both RUX cream groups; ‡ Reported as burning, stinging, pain, or pain/discomfort at an application site; § Eczema herpeticum occurred on Day 324 in a patient aged 2 years with moderate AD with early onset and involvement of face and neck as risk factors; RUX cream and chronic, stable oral antihistamines were stopped 7 days prior for a TEAE of molluscum contagiosum.

# Key Hematologic Parameters

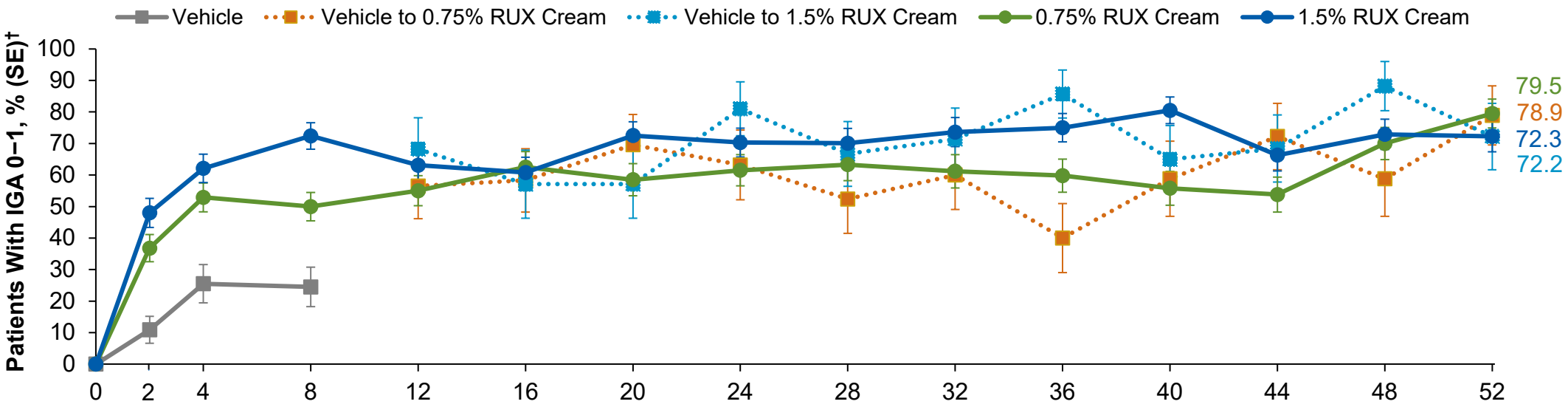
- There were no clinically meaningful changes in hemoglobin, platelet, and neutrophil (shown below) values during the 52-week study




IQR, represented by boxes; medians, by dark lines; means, by squares; outliers, by circles; Q1–(1.5 x IQR) and Q3+(1.5 x IQR), by whiskers.
† For vehicle to 0.75% RUX cream and vehicle to 1.5% RUX cream groups, the baseline measurement is the last assessment before commencing treatment in the LTS period.

# Achievement of Clear or Almost Clear Skin (IGA 0–1)

- Substantially more patients who applied RUX cream achieved clear or almost clear skin vs vehicle through Week 8; improvements were maintained or further improved with as-needed RUX cream through Week 52
  - Patients spent nearly half of the LTS period off treatment due to lesion clearance

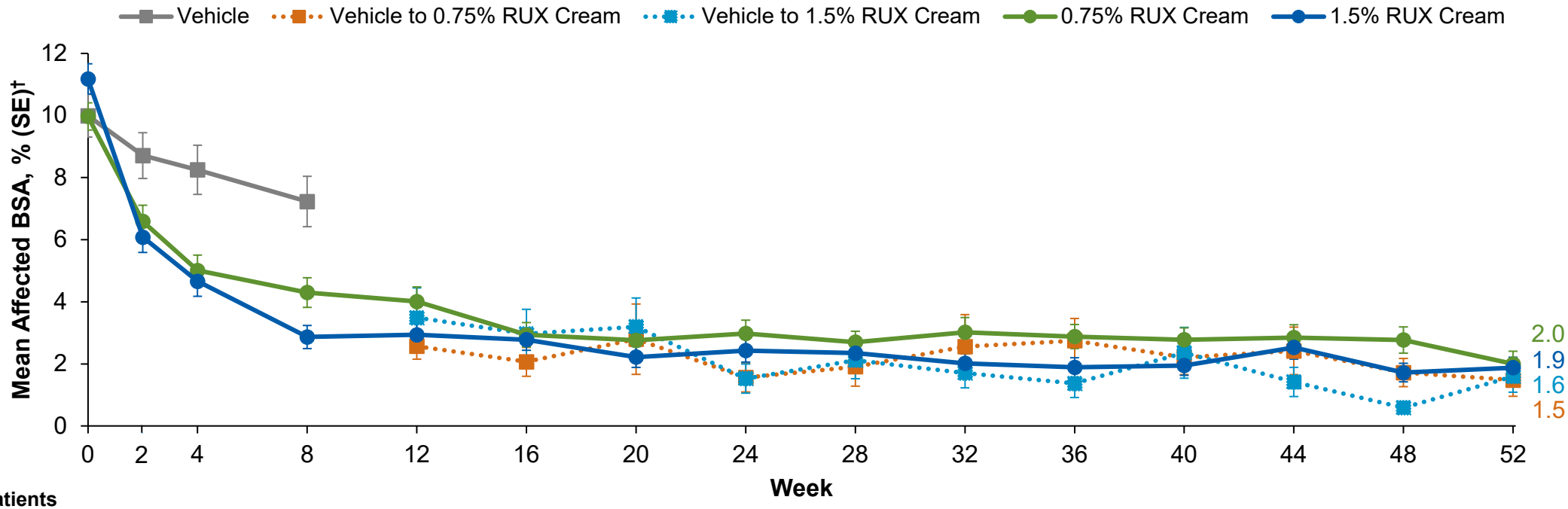



| Number of Patients | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Vehicle | 65 | 55 | 51 | 49 | | | | | | | | | |
| Vehicle to 0.75% RUX Cream | | | | | 23 | 24 | 23 | 19 | 21 | 20 | 20 | 17 | 18 | 17 | 19 |
| Vehicle to 1.5% RUX Cream | | | | | 22 | 21 | 21 | 21 | 21 | 21 | 21 | 20 | 19 | 17 | 18 |
| 0.75% RUX Cream | 134 | 125 | 121 | 122 | 109 | 96 | 94 | 96 | 90 | 85 | 87 | 86 | 80 | 80 | 78 |
| 1.5% RUX Cream | 131 | 125 | 124 | 116 | 103 | 102 | 102 | 101 | 97 | 91 | 92 | 87 | 89 | 85 | 83 |

† Week 12–52 data exclude 1 patient each in the 0.75% and 1.5% RUX cream groups who completed the study but did not receive treatment in the LTS period (maintained IGA and BSA of 0).

# Reduction of Lesion Extent (% Affected BSA)

- Affected BSA decreased substantially more with both strengths of RUX cream vs vehicle through Week 8, with maintained or lower values with as-needed use of RUX cream through Week 52

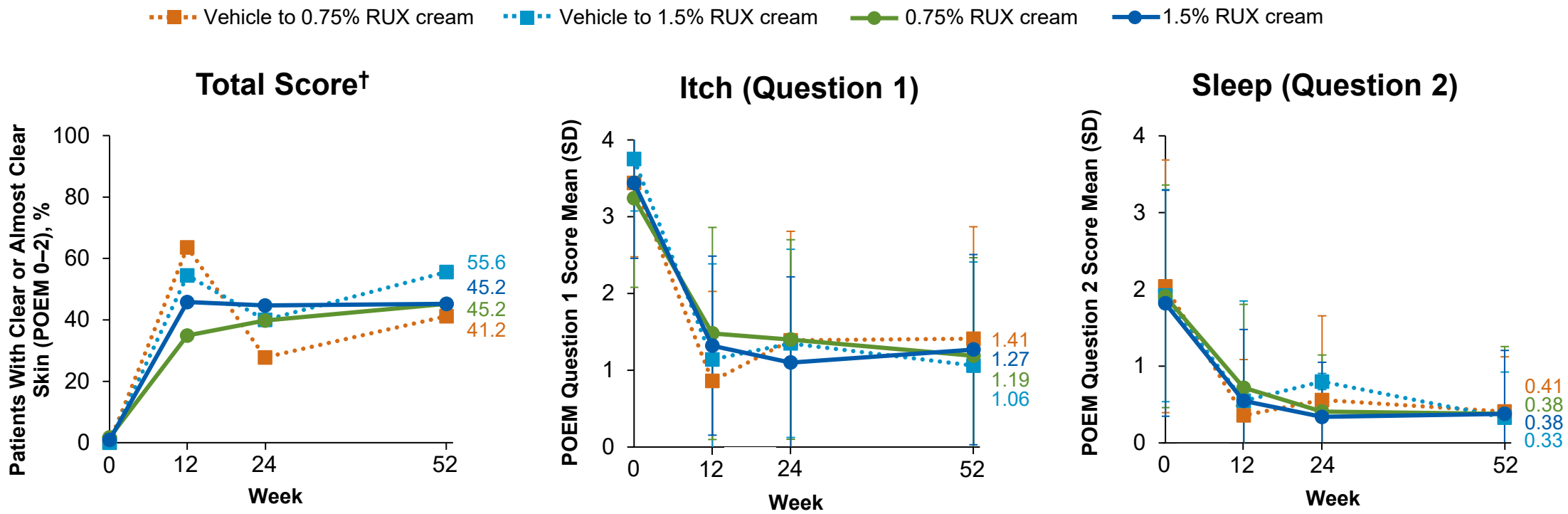



| Number of Patients | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Vehicle | 65 | 55 | 51 | 49 | | | | | | | | | |
| Vehicle to 0.75% RUX Cream | | | | | 23 | 24 | 23 | 19 | 21 | 20 | 20 | 17 | 18 | 17 | 19 |
| Vehicle to 1.5% RUX Cream | | | | | 22 | 21 | 21 | 21 | 21 | 21 | 21 | 20 | 19 | 17 | 18 |
| 0.75% RUX Cream | 134 | 125 | 121 | 122 | 109 | 96 | 94 | 96 | 90 | 85 | 87 | 86 | 80 | 80 | 78 |
| 1.5% RUX Cream | 131 | 125 | 124 | 116 | 103 | 102 | 102 | 101 | 97 | 91 | 92 | 87 | 89 | 85 | 83 |

† Week 12–52 data exclude 1 patient each in the 0.75% and 1.5% RUX cream groups who completed the study but did not receive treatment in the LTS period (maintained IGA and BSA of 0).

# Improvement in Patient-Reported Symptoms and Signs (POEM)

- Improvements in POEM score, including itch and sleep, persisted through Week 52




| Number of Patients | | | | |
|---|---|---|---|---|
| Vehicle to 0.75% RUX Cream | 25 | 22 | 18 | 17 |
| Vehicle to 1.5% RUX Cream | 24 | 22 | 20 | 18 |
| 0.75% RUX Cream | 118 | 106 | 88 | 73 |
| 1.5% RUX Cream | 112 | 96 | 94 | 73 |

| | | | | |
|---|---|---|---|---|
| 25 | 22 | 18 | 17 |
| 24 | 22 | 20 | 18 |
| 118 | 106 | 88 | 73 |
| 112 | 94 | 94 | 73 |

| | | | | |
|---|---|---|---|---|
| 25 | 22 | 18 | 17 |
| 24 | 22 | 20 | 18 |
| 118 | 106 | 88 | 73 |
| 112 | 96 | 94 | 73 |

† Mean (SD) baseline scores were 16.16 (7.52) for vehicle to 0.75% RUX cream, 17.42 (6.64) for vehicle to 1.5% RUX cream, 15.49 (6.48) for 0.75% RUX cream, and 15.34 (6.41) for 1.5% RUX cream.

# Conclusions

- In patients aged 2–11 years with mild to moderate AD, **RUX cream treatment for up to 1 year was well tolerated**, with a low incidence of application site reactions, 1 case of eczema herpeticum, and no observed cases of MACE, malignancy, thrombosis, herpes zoster, or folliculitis
- Low mean RUX plasma concentrations and a lack of effect on hematologic parameters suggest **systemic JAK inhibition is highly unlikely**
- **Children experienced effective long-term disease control from as early as 2 weeks**, with >60% of patients achieving clear or almost clear skin (IGA 0–1) and a low mean affected BSA (≤3%) for the majority of the 44-week as-needed treatment period
- Safety and efficacy results in children aged 2–11 years were **similar to phase 3 results in adolescents and adults[1,2] and maximum-use studies in children,[3] adolescents,[4] and adults[4]**

1. Papp K, et al. *J Am Acad Dermatol*. 2021;85(4):863-872. 2. Papp K, et al. *J Am Acad Dermatol*. 2023;88(5):1008-1016. 3. Bissonnette R, et al. Presented at: RAD Conference: June 8-10, 2024; Chicago, IL. 4. Bissonnette R, et al. *Am J Clin Dermatol*. 2022;23(3):355-364.

# Thank You For Your Attention

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