Ruxolitinib Cream 1.5% Twice Daily for the Treatment of Extensive Atopic Dermatitis in Children Aged 2–11 Years: 52-Week Results From a Maximum-Use Trial

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Background

- Ruxolitinib cream, a topically administered selective Janus kinase (JAK) 1/2A inhibitor, demonstrated anti-inflammatory and anti-pruritic activity in a phase 3 trial in children aged 2 to 11 years with atopic dermatitis (AD; NCT01949190) and was well tolerated through 8 weeks of therapy, consistent with phase 3 adult/adolescent data (TRuE-AD2; NCT01374536/NCT01374651).5
- In previous reports of this maximum-use trial (MUsT) in children aged 2 to 11 years with 20%–35% affected body surface area (BSA; Ruxolitinib 0.1% cream), 1.5% ruxolitinib cream was generally well tolerated, with rapid anti-inflammatory and anti-pruritic effects and improvements in patient-reported outcomes (PROs) observed with continuous treatment to Week 4 and maintained with as-needed treatment from Weeks 4 to 8.7

Objective

- Here, long-term results from as-needed treatment with 1.5% ruxolitinib cream in children with extensive, moderate to severe AD in a MUsT (NCT01503432) are presented

Methods

- The study design has been described previously (Figure 1).8
- Patients: Overall, 29 patients were enrolled and applied daily cream (27 patients continued into the study period)

Results

- Safety, tolerability, and exposure to ruxolitinib cream were assessed through Week 52
- Disease control and PRO outcomes with as-needed treatment from Week 4 through Week 52 were assessed
- Data were summarized using descriptive statistics, reported as means and standard deviations
- All patients who applied ≥1 dose of 1.5% ruxolitinib cream were included in the analyses

Exposure

- During the 4-week, continuous-use, maximum-use period in patients with mean (SD) 56.0% (20.2%) affected BSA at baseline (range of 30.0%–92.0% affected BSA), the mean (SD) steady-state plasma concentration (C_caption_brief] of ruxolitinib was 98.2 (148) nM, well below 281 nM (the half-maximal concentration of JAK-1/2 inhibition established for adults)9–11.
- Two patients had >60% affected BSA and C_caption_brief] ≥281 nM; however, no treatment-related TEAEs or laboratory abnormalities were reported in either patient
- The median amount of ruxolitinib cream applied per day decreased from the continuous-use, maximum-use period through the as-needed period (Table 3; correlated with the low percentage affected BSA being treated during the as-needed use period)

Efficacy and Disease Control

- Mean percentage affected BSA decreased from 58.0% at baseline to 11.4% at Week 4, and was maintained through Week 52 (Figure 2A)
- Investigator’s Global Assessment–Treatment success (IGA-TS) was achieved by 53.8% of patients at Week 4 and was generally sustained through Week 52 with as-needed therapy (Figure 2B)

- Patient-reported outcomes (PROs) improved from baseline in PROs assessing disease severity, quality of life, and sleep, occurred as early as Week 2 and were sustained through Week 52 (Figures 3 and 4)

Conclusions

- In patients aged 2 to 11 years with extensive, moderate to severe AD, 1.5% ruxolitinib cream was well tolerated under 4 weeks of continuous twice daily and with as-needed use through Week 52
- Continuous-use, maximum-use ruxolitinib cream for 4 weeks led to rapid lesion clearance, which was maintained with as-needed use through Week 52
- Consistent with this, there were early improvements from baseline in PROs, which were sustained through Week 52
- Rapid lesion clearance with twice-daily therapy and longer-term disease control with as-needed use that is associated with lower daily cream usage may address application burden concerns

Table 1. TEAEs From Baseline to Week 52

- Parameter (N=5) 1.5% Ruxolitinib Cream 8-Week Treatment Period (N=5) 52-Week Study Period (N=3) Patients with ≥TEAE 7/5 0/5
- Patients with a treatment-related TEAE 1/5 1/5
- Patients with a severe TEAE 0/5 0/5
- Patients with a grade ≥3 TEAE 0/5 0/5
- Patients with application site reactions 1/5 1/5
- Total exposure to JAK inhibitor 0/5 0/5
- Discontinuation due to TEAE 0/5 0/5
- Stop treatment due to a TEAE 0/5 0/5

Table 2. Summary of PK and Exposure Parameters During the Entire 52-Week Period

- Parameter 1.5% Ruxolitinib Cream (N=5) Maximum-use period (baselines Week 0–4) 98.2 (148) nM Ruxolitinib cream applied per day; mean (SD) Maximum-use baseline (Week 0–4) 6.5 (4.8) 6.5 (4.5) 6.3 (2.9) Baseline–Week 1 (N=3) 1.5 (0.4) 1.5 (0.4) 1.5 (0.4) LT period (Week 8–52) 1.7 (1.1) 1.7 (1.1) 1.7 (1.1)

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References