Association Between Early Clinical Responses and Long-Term Outcomes With Ruxolitinib Cream Treatment in Mild to Moderate Atopic Dermatitis

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Introduction
- Atopic dermatitis (AD) is a chronic, heterogeneous, high pruritic, relapsing inflammatory skin disease.
- Ruxolitinib cream is a topical formulation of ruxolitinib, a selective Janus kinase (JAK) 1/2 inhibitor.2–3
- In two phase 3 randomized studies of identical TRuE-AD1 [NCT03745638] and TRuE-AD2 [NCT03745615], 1.5% ruxolitinib cream demonstrated anti-inflammatory and antipruritic effects and was well tolerated during the 8-week vehicle-controlled period in patients with AD:
  - During the 44-week long-term safety (LTS) period, 1.5% ruxolitinib cream was well tolerated and demonstrated effective disease control with as-needed use, with 43.9% of time off treatment due to lesion clearance and patients achieving an Investigator’s Global Assessment (IGA) score of 0/1 (clear or almost clear skin) at a mean of 73.5% of visits (among patients with ≥2 study visits).4–5
  - With each consecutive study visit every 4 weeks, the majority of patients maintained IGA 0/1.
  - 80%–90% of patients maintained or improved their response between subsequent visits.

Objectives
- A post hoc analysis of adolescent and adult patients with AD in phase 2 and 3 studies evaluating:
  - The association of responder status at Week 8 with outcomes in the LTS periods.
  - The association of previous therapies with outcomes in the LTS periods.

Methods
Patients and Study Design
- TRuE-AD1 and TRuE-AD2 had identical study designs (Figure 1): see http://clinicaltrials.gov/ct2/ct2 Details/NCT03745638 and http://clinicaltrials.gov/ct2/ct2 Details/NCT03745615 for additional inclusion/exclusion criteria.
- Patients recorded all applications of assigned study treatment via diary cards, which were collected at each study visit.

Figure 1. Study Design

Endpoints
- At Weeks 2, 4, and 8, patients were assessed for IGA–Treatement Success (IGA-TS; score of 0 or 1 with ≥2-grade improvement from baseline), ≥75% improvement from baseline in Eczema Area and Severity Index (EASI-75), and achievement of ICH numerical rating scale (NRS) scores of 0 or 1.
- At each visit (every 4 weeks) during the LTS period, patients were assessed for achievement of IGA score of 0/1 (control disease) and for percent of visits with IGA 0/1 and reported for patients with ≥2 visits.
- Patients who achieved IGA-TS, EASI-75, and ICH NRS 0/1 at Week 8 were reported previously and are similar to those in the overall study population.7

Statistical Analyses
- Data were analyzed using descriptive statistics, reported as observed.
- Patients who applied ≥1 dose of 1.5% ruxolitinib cream since Day 1 were included in the analysis.
- Of 446 patients originally randomized to 1.5% ruxolitinib cream since Day 1 who continued into the LTS, 18 patients from 1 study site were excluded for quality issues.4–5

Results
- Of 1249 randomized patients, 1072 (85.8%) continued into the LTS period; 428 (34.3%) who applied 1.5% ruxolitinib cream since Day 1 were evaluated for disease control in the LTS period.
- Baseline demographics and clinical characteristics for patients who applied 1.5% ruxolitinib cream since Day 1 and continued into the LTS period were reported previously and are similar to those in the overall study population.7

Efficacy at Week 8
- At Week 8, of the LTS-eligible patients applying 1.5% ruxolitinib cream, 57.0% (244/428) achieved IGA-75, 66.5% (285/428) achieved EASI-75, and 45.8% (196/428) achieved ICH NRS 0/1.

Association of Responder Status at Week 8 With Disease Control in the LTS Period
- Mean percentages of visits with IGA 0/1 were numerically higher among patients who achieved IGA-TS, EASI-75, and ICH NRS 0/1 at Week 8 than among those who did not achieve these efficacy thresholds at Week 8 (Figure 2).

Figure 2. Mean (%I50) Percentage of Visits* With IGA 0/1 Among Patients Who Achieved or Did Not Achieve IGA-TS, EASI-75, and ICH NRS 0/1 at Week 8

Time Off Treatment in the LTS Period
- Patients who achieved IGA-TS, EASI-75, and ICH NRS 0/1 at Week 8 experienced a numerically greater number of mean cumulative treatment-free days in the LTS period than patients who did not achieve these efficacy thresholds at Week 8 (Figure 4).

Figure 4. Mean (%I50) Treatment-Free Days in the LTS Period Among Patients Who Achieved or Did Not Achieve IGA-TS, EASI-75, and ICH NRS 0/1 at Week 8

- Mean percentages of treatment-free days due to lesion clearance between study visits increased throughout the LTS period for patients who achieved IGA-TS, EASI-75, and ICH NRS 0/1 at Week 8 and completed 52 weeks of treatment (Figure 5).
- Continued treatment in patients who did not achieve these efficacy thresholds at Week 8 led to increased mean percentages of treatment-free days between study visits approaching levels observed in patients who achieved them at Week 8.

- Percentages of visits with IGA 0/1 and mean cumulative treatment-free days were similar between numbers of prior lines of therapy (Figure 6).

Figure 5. Mean Percentage of Treatment-Free Days Between Study Visits for Patients Who Did or Did Not Achieve (A) IGA-TS, (B) EASI-75, or (C) ICH NRS 0/1 at Week 8 and Completed 52 Weeks of Treatment

Conclusions
- Efficacy responses after 8 weeks of 1.5% ruxolitinib cream treatment were associated with greater disease control in the LTS period; however, Week 8 responders did not achieve equivalent levels of disease control with continued treatment.
- As-needed ruxolitinib cream monotherapy demonstrated substantial long-term disease control regardless of time to first-response achievement or number of prior lines of therapy.

Disclosures
- P.L. is a consultant, speaker, and/or investigator for or has received grants from AbbVie, Amgen, Anaptys, Aprelipta Therapeutics, Arzulea, Arcutis, Arena, Avanos, Bausch Health, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cidara, Cymbaltek, Daiichi Sankyo, Daiichi Sankyo, Galderma, Genzyme, Gilead Sciences, GlaxoSmithKline, {}; and received honoraria for presentation of scientific results and/or as a clinical trial steering committee member from AbbVie, Almirall, Amgen, Anaptys, Aprelipta Therapeutics, Arzulea, Arcutis, Arena, Avanos, Bausch Health, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cidara, Cymbaltek, Daiichi Sankyo, Daiichi Sankyo, Galderma, Genzyme, Gilead Sciences, GlaxoSmithKline, {}; and received honoraria for presentation of scientific results and/or as a clinical trial steering committee member from AbbVie, Almirall, Amgen, Anaptys, Aprelipta Therapeutics, Arzulea, Arcutis, Arena, Avanos, Bausch Health, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cidara, Cymbaltek, Daiichi Sankyo, Daiichi Sankyo, Galderma, Genzyme, Gilead Sciences, GlaxoSmithKline, {}. HR and DS are employees and investigators of supporting organizations.

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References

Figure 6. (A) Mean (%I50) Percentage of Visits* With IGA 0/1 and (B) Mean (%I50) Cumulative Treatment-Free Days in the LTS Period According to Number of Prior Lines of Therapy

Notes
IA = Investigator’s Assessment; O = Onset; NRS = Numerical Rating Scale; B = Baseline; A = Achieved response; I = ICH NRS; R = Recurrence; M = Median; HR = Honorable mention; DS = Distinguished Service; L = Lower.

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- P.L. is a consultant, speaker, and investigator for or has received grants from or has served as a speaker or advisory board member for AbbVie, Amgen, Anaptys, Aprelipta Therapeutics, Arzulea, Arcutis, Arena, Avanos, Bausch Health, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cidara, Cymbaltek, Daiichi Sankyo, Daiichi Sankyo, Galderma, Genzyme, Gilead Sciences, GlaxoSmithKline, {}; and received honoraria for presentation of scientific results and/or as a clinical trial steering committee member from AbbVie, Almirall, Amgen, Anaptys, Aprelipta Therapeutics, Arzulea, Arcutis, Arena, Avanos, Bausch Health, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cidara, Cymbaltek, Daiichi Sankyo, Daiichi Sankyo, Galderma, Genzyme, Gilead Sciences, GlaxoSmithKline, {}; and received honoraria for presentation of scientific results and/or as a clinical trial steering committee member from AbbVie, Almirall, Amgen, Anaptys, Aprelipta Therapeutics, Arzulea, Arcutis, Arena, Avanos, Bausch Health, Baxter, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Cidara, Cymbaltek, Daiichi Sankyo, Daiichi Sankyo, Galderma, Genzyme, Gilead Sciences, GlaxoSmithKline, {}.