Two-year Maintenance of Response with Tralokinumab in Moderate-to-Severe Atopic Dermatitis: Interim Analysis of the ECZTEND Open-Label Extension Trial

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Introduction. Atopic dermatitis (AD) is a chronic inflammatory skin disease associated with intense itch, sleep disturbance, and impaired quality of life. There is a need for additional long-term treatment options in patients with moderate-to-severe AD. The efficacy and safety of tralokinumab, a fully human monoclonal antibody specifically targeting interleukin-13, were demonstrated in Phase 3 trials up to 52 weeks [Wollenberg A, et al. *Br J Dermatol.* 2021;184:437-449; Silverberg JI, et al. *Br J Dermatol.* 2021;184:450-463]. An ongoing, 5-year, open-label extension trial, ECZTEND (NCT03587805), is evaluating the safety and efficacy of long-term tralokinumab treatment in patients from parent trials with moderate-to-severe AD. We investigated the 2-year efficacy and safety of continued tralokinumab treatment and the ability to regain response after pausing and reinitiating tralokinumab.

Methods. In ECZTEND, patients receive subcutaneous tralokinumab 300 mg every 2 weeks plus optional topical corticosteroids. This analysis included patients who received tralokinumab for the full 52 weeks in the ECZTRA 1 and 2 trials and had been enrolled ≥60 weeks in ECZTEND (as of April 30, 2020). Patients were analyzed in 3 cohorts, defined by the interval between last parent-trial dose and first ECZTEND dose: ≤5 weeks, 6-15 weeks, and >15 weeks. Long-term control at 56 weeks in ECZTEND was assessed as percentage improvement from parent-trial baseline in Eczema Area and Severity Index (EASI) and achievement of ≥50%, 75%, and 90% improvement in EASI (EASI-50, -75, -90). Worst weekly pruritus Numeric Rating Scale (NRS) and weekly eczema-related sleep interference NRS were also assessed.

Results. 345 patients had ≥60 weeks of enrollment at data cut-off. Median age was 42 years, 59% were male, and median AD duration was 30 years at ECZTEND baseline. Median time between last dose in parent trial and first dose in ECZTEND was 63 days. 126, 133, and 86 patients had ≤5 weeks, 6-15 weeks, and >15 weeks between tralokinumab doses, respectively. At 1 year of the parent trials, median (IQR) EASI improvement from baseline was 88.0% (range, 78.4% to 96.1%). At ECZTEND baseline, median EASI improvement from parent-trial baseline was 88.9% (range, 80.5% to 95.3%), 78.8% (range, 55.9% to 91.6%), and 68.6% (range, 37.1% to 82.6%) in patients in the ≤5-week, 6-15 week, and >15-week cohorts, respectively. At Week 56 in ECZTEND (2 years of tralokinumab treatment), median EASI improvement was 92.7% (range, 83.3% to 98.2%), 91.7% (range, 83.3% to 97.8%), and 92.7% (range, 74.9% to 97.9%), respectively. Median EASI improvement equivalent to parent-trial levels was maintained for patients continuing treatment with a ≤5-week interval, and was regained by Week 8 for the 6-15−week cohort and Week 16 for the >15-week cohort. EASI-50, -75, and -90 response rates after 56 weeks were comparable between cohorts (Table). Sensitivity analyses were consistent with efficacy for all observed patients. At Week 56 in ECZTEND, median (IQR) worst weekly pruritus NRS was 3.0 (range, 1.0 to 5.0) for all cohorts (mild itch); median (IQR) weekly eczema-related sleep interference NRS was 1.0 (range, 0.0 to 3.0) in the ≤5-week and 6-15−week cohorts, and 1.5 (range, 0.0 to 3.5) in the >15-week cohort. The adverse event profile was consistent with that in the parent trials and the ECZTEND overall safety population as of April 30, 2020 (n=1174).

Conclusions. Continued tralokinumab treatment (≤5 weeks from last dose in parent trial to first dose in ECZTEND) was associated with consistent long-term control from parent trial through ECZTEND. Among patients with >5 weeks between last dose in parent trial and first dose in ECZTEND, median improvement in EASI scores equivalent to parent trial levels was regained by Week 12. Tralokinumab provided long-term control of AD extent and severity, improved itch and sleep interference irrespective of the interval between doses, and was well tolerated over 2 years.

Responders, %*	Week 16 of ECZTEND	Week 56 of ECZTEND (2 years of tralokinumab treatment)
EASI-50		
≤5 weeks	96.7	92.5
6-15 weeks	91.5	95.5
>15 weeks	92.6	93.2
EASI-75		
≤5 weeks	86.7	84.1
6-15 weeks	80.8	86.5
>15 weeks	75.3	74.0
EASI-90		
≤5 weeks	61.7	65.4
6-15 weeks	62.3	57.7
>15 weeks	46.9	54.8

*Cohorts defined based on time between last dose in parent trials and first dose in ECZTEND. Data are as observed.
EASI, Eczema Area and Severity Index