Progressive and sustained improvements in the extent and severity of atopic dermatitis with tralokinumab in combination with topical corticosteroids as needed in moderate-to-severe atopic dermatitis

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Introduction: Atopic dermatitis is a chronic, inflammatory skin disease characterized by recurrent eczematous skin lesions. Interleukin (IL)-13 is a key driver of the underlying type 2 inflammation and skin barrier dysfunction in atopic dermatitis. Tralokinumab is a fully human monoclonal antibody that specifically binds to IL-13 with high affinity, preventing interaction with the IL-13 receptor and subsequent IL-13 downstream signaling. The pivotal Phase 3 ECZTRA 3 trial (NCT03363854) investigated the efficacy and safety of tralokinumab plus topical corticosteroids (TCS) as needed in adults with moderate-to-severe

atopic dermatitis.[1] The objective of this analysis was to assess the effects of tralokinumab plus TCS as needed on extent and severity over 32 weeks.

Methods: ECZTRA 3 was a double-blind, multicenter, placebo plus TCS-controlled, Phase 3 trial.[1] Adult patients with atopic dermatitis for ≥1 year who were candidates for systemic therapy were randomized 2:1 to subcutaneous tralokinumab 300 mg every 2 weeks (q2w) plus TCS (mometasone furoate 0.1% cream applied once daily to active lesions as needed) or placebo plus TCS for an initial treatment period of 16 weeks. Hereafter, tralokinumab-treated patients continued on either q2w or every 4 weeks (q4w) + TCS for an additional 16-week continuation period. *Post hoc* analyses of week 16–32 data were conducted by pooling all patients who were randomized to tralokinumab in the initial treatment period (week 0–16; n=252) irrespective of what dosing regimen (q2w/q4w) they received beyond week 16. Statistical analyses followed pre-specifications, i.e. Cochran-Mantel-Haenszel stratified by region and baseline Investigator's Global Assessment (IGA) for binary endpoints, and mixed model for repeated measures with fixed effects of planned treatment, region, baseline IGA, and interactions between treatment and visit and baseline value and visit for continuous endpoints. Missing data or data after rescue medication were imputed as non-response for binary endpoints. For continuous endpoints, data after rescue medication or permanent discontinuation of trial treatment was set to missing and a compound symmetric covariance matrix was assumed for repeated measures of a patient.

Results: At week 16, significantly more patients achieved 50% improvement in Eczema Area and Severity Index (EASI-50: 79.4 vs 57.9%; difference of 21.3% [95% confidence interval (CI) 11.3, 31.3]; $P<0.001$), EASI-75 (56.0 vs 35.7%; difference of 20.2% [9.8, 30.6]; $P<0.001$), and EASI-90 (32.9 vs 21.4%; difference of 11.4% [2.1, 20.7]; $P=0.022$) with tralokinumab q2w plus TCS versus placebo plus TCS. The EASI-50 response rate was

sustained through week 32 (81.0%; 204/252); EASI-75 response rate progressively increased to 69.0% (174/252) at week 24 and was sustained through week 32 (70.2%; 177/252); and EASI-90 response rate progressively increased throughout the continuation period to 50.4% (127/252) at week 32. At week 16, least square mean (standard error [SE]) EASI scores were reduced from 29.0 (0.5) at baseline to 8.0 (0.5) with tralokinumab q2w plus TCS versus 13.0 (0.8) with placebo plus TCS (–5.1 [–6.9, –3.2]; $P<0.001$), and mean (SE) SCORing Atopic Dermatitis (SCORAD) was reduced from 67.3 (1.0) at baseline to 29.2 (1.0) with tralokinumab q2w plus TCS and 39.5 (1.5) with placebo plus TCS (–10.3 [–13.8, –6.8]; $P<0.001$). At week 32, further improvements were seen with continued tralokinumab plus TCS in EASI (estimated mean [SE] of 4.6 [0.5]) and SCORAD (estimated mean [SE] of 21.8 [1.0]) corresponding to mean changes from baseline of 84% (EASI) and 68% (SCORAD). The cumulative use of TCS at the end of the initial treatment period (week 16) was lower in the tralokinumab group versus placebo (mean [SE] 134.9g [11.7] vs 193.5g [16.7]; $P=0.004$). At weeks 15–16, tralokinumab-treated patients used approximately 50% less TCS versus placebo-treated patients ($P=0.002$) and 55.3% of tralokinumab treated patients used no or very limited amounts (0–5 g) of TCS.

Conclusion: Tralokinumab plus TCS as needed provided significant improvements in the extent and severity of atopic dermatitis versus placebo plus TCS as needed at week 16 in patients with moderate-to-severe atopic dermatitis. The week 16 response rates progressively improved with continued tralokinumab plus TCS, with 70% of patients achieving EASI-75 at week 32. The extent and severity of atopic dermatitis was reduced from mean EASI and SCORAD scores equivalent to severe disease at baseline to mild at week 32.

1. Silverberg JI, et al. Br J Dermatol 2020. doi:10.1111/bjd.19573.

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Conflicts of interest:

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