Safety of tralokinumab for the treatment of atopic dermatitis in patients with up to 4.5 years of treatment: an updated integrated analysis of eight clinical trials

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Introduction/Background: Clinical trials of up to 52 weeks showed that tralokinumab, a monoclonal antibody that specifically neutralizes interleukin-13, was efficacious and well-tolerated as monotherapy and combination with TCS.

Objectives: Here, we evaluate the long-term safety of tralokinumab in an integrated analysis of seven phase 3 parent trials (PTs) (NCT03131648, NCT03160885, NCT03363854, NCT03562377, NCT03526861, NCT03761537, NCT04587453), and the ongoing, up to 5-year extension study (ECZTEND; NCT03587805).

Methods: Two datasets were analyzed: placebo-controlled (initial 16-week period of the PTs), and all-tralokinumab combining PTs with ECZTEND including patients from first
dose until end of tralokinumab exposure or data cut-off (April 30th, 2022). In the all-tralokinumab dataset, periods on placebo were disregarded. Treatment-emergent adverse events (AEs) were recorded. AEs of special interest (AESIs) were predefined. Proportions of patients with events and incidence rates (IR) per 100 patient-years of exposure (PYE) were calculated. PYE was defined as time until first event or exposure end, whichever came first, and incidence was defined as first event.

**Results:** 2693 patients (≥12 years) received tralokinumab for up to 238.5 weeks (≈4.5 years) with a median exposure time of 76.5 weeks in the all-tralokinumab dataset. Median age at baseline was 33.0 years (min-max; 12-92). 10.4% of patients were 12-17 years. 2307 patients experienced an AE (IR=202.0), most (97.3%) of which were mild-to-moderate. Serious AEs (SAEs) were reported in 226 patients (IR=4.5); SAEs were considered possibly or probably related by the investigator in 50 patients (IR=0.9). No preferred term level SAEs were reported with an IR≥0.1. Discontinuation of treatment due to AEs was low (IR=2.8). AEs leading to drug withdrawal with an IR>0.1 were dermatitis atopic (IR=0.5) and injection site reaction (ISR) (IR=0.2). Frequently reported AEs in the all-tralokinumab dataset were consistent with the placebo-controlled dataset, including nasopharyngitis (IR=18.4), upper respiratory tract infection (IR=6.9), conjunctivitis (IR=5.0), ISR (IR=3.6), conjunctivitis allergic (IR=2.7), and injection site pain (IR=1.5). AESIs, including eye disorders, skin infections requiring systemic treatment, eczema herpeticum, and malignancies, were observed in the all-tralokinumab dataset at rates similar to or lower than the placebo-controlled dataset.
**Conclusion:** Long-term use of tralokinumab, for up to 4.5 years, was well-tolerated, and the pattern of AEs was consistent with the initial placebo-controlled treatment period with no new safety signals identified.

**Keywords:** atopic dermatitis, tralokinumab, IL-13, safety

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