Assessing long-term maintenance of efficacy with tralokinumab monotherapy in patients with moderate-to-severe atopic dermatitis: combined results from two Phase 3, randomized, double-blind, placebo-controlled trials (ECZTRA 1 and 2)

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Background: Tralokinumab is a fully human, high-affinity monoclonal antibody that specifically neutralizes interleukin-13, a key driver of skin inflammation and barrier dysfunction in atopic dermatitis (Bieber T, et al. *Allergy*. 2020;75:54-62; Popovic B et al. *J Mol Biol*. 2017;429:208-219). In two phase 3 trials, ECZTRA 1 and 2, tralokinumab monotherapy was superior to placebo for all primary and secondary endpoints at week 16 in adults with moderate-to-severe atopic dermatitis (Wollenberg A, et al. *Br J Dermatol.* 2021;184:437-449). We evaluated the maintenance of efficacy beyond 16 weeks of tralokinumab monotherapy in patients with atopic dermatitis who were initial responders; and assessed whether reduced dosing frequency of tralokinumab from q2w to q4w had an impact on maintenance of efficacy.
Methods: High-responding patients achieving Investigator's Global Assessment (IGA) 0/1 or Eczema Area and Severity Index (EASI)-75 at week 16 on tralokinumab q2w were rerandomized in the maintenance phase 2:2:1 to tralokinumab q2w, q4w, or placebo for 36 weeks. A prespecified, pooled analysis assessed maintenance of response (IGA 0/1 or EASI-75) at week 52. Rescue medication use, including topical corticosteroids, was considered non-response. Post hoc analysis of time to relapse (transfer to open-label period, rescue medication, or treatment discontinuation) was conducted.
Results: A large proportion of high-responding patients (n=337) continuing tralokinumab q2w or q4w maintained response without any rescue medication, including topical corticosteroids, at week 52. With q2w, 56.2% maintained IGA 0/1 or EASI-75 (difference=26.3% vs placebo; $P<0.001$) at week 52. With q4w, 50.0% maintained IGA 0/1 or EASI-75 (difference=20.7% vs placebo; $P=0.003$). Time to relapse based on IGA 0/1 and EASI-75 was prolonged with tralokinumab vs placebo (q2w, $P=0.004$ and q4w, $P=0.14$; q2w, $P=0.002$ and q4w, $P=0.044$, respectively). Overall, adverse event frequency was similar for tralokinumab q2w (73%), q4w (66%), and placebo (70%).
Conclusions: In patients with moderate-to-severe atopic dermatitis treated with tralokinumab monotherapy, the initial response to tralokinumab was maintained at high levels at week 52 without topical corticosteroid use and was well tolerated. Step-down to q4w dosing may be an option for some patients.
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