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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Introduction

Atopic dermatitis (AD), a common, inflammatory skin disease, characterized by exacerbation-dominant disease activity, affects about 20% of the global population (1). The disease negatively impacts quality of life and lifestyle, and is associated with various comorbidities (2). Current therapeutic strategies are focused on either topical steroids (TCS) or systemic treatment with biologic therapies (e.g., IL-17 and IL-23 antagonists) (3). However, many AD patients are inadequately controlled by these therapies (4).

Objectives

The primary objectives of this study were to assess the long-term efficacy of tralokinumab monotherapy for the treatment of AD in adults with moderate-to-severe disease activity following an initial 16-week treatment period, and to further characterize the overall safety profile of tralokinumab during this long-term maintenance period.

Methods

Study Design and Patients

ECZTRA 1 (NCT03924694) and ECZTRA 2 (NCT03924700) were identical, multicenter, double-blind, randomized, placebo-controlled trials evaluating tralokinumab (300 mg q2w or q4w) as monotherapy for the treatment of AD in adults with moderate-to-severe disease activity following an initial 16-week treatment period (5).

Patients who achieved Investigator’s Global Assessment (IGA) 0/1 and/or EASI-75 response at Week 16 with tralokinumab were eligible for a 36-week maintenance treatment period (ECZTRA 1) or a 52-week maintenance treatment period (ECZTRA 2) with tralokinumab or placebo (6). The maintenance treatment consisted of tralokinumab 300 mg q2w or q4w, or placebo (6).

Patients who did not achieve IGA 0/1 or EASI-75 at Week 16 with tralokinumab were eligible for a 52-week maintenance treatment period with placebo (7).

Results

Analyses

A total of 1596 patients were randomized to tralokinumab 300 mg q2w (1196) or placebo (400) for the initial 16-week treatment period. Of the patients who achieved IGA 0/1 or EASI-75 response at Week 16, 90.8% received tralokinumab q2w and 9.2% received tralokinumab q4w for the maintenance period (8). The maintenance treatment of patients achieving an EASI score of 11 or lower at Week 16 was continued until a Week 52 follow-up visit, if available (9).

A total of 864 patients achieved IGA 0/1 or EASI-75 response at Week 16 (10). Of these patients, 686 (80.3%) were maintained on tralokinumab for the entire maintenance period, 93 (10.8%) were re-randomized to placebo, and 85 (10.0%) did not achieve IGA 0/1 or EASI-75 response at Week 52 with tralokinumab (11). Further details of the AE profile in these populations have been reported previously (12). Patients who did not achieve IGA 0/1 or EASI-75 at Week 16 with tralokinumab were maintained on placebo for the entire maintenance period, without the use of rescue medication including TCS (13).

Safety

A total of 1596 patients were randomized to tralokinumab 300 mg q2w or q4w, or placebo (in the primary analysis, patients who used rescue medication, if any, were included up to the last visit in which rescue was used). In total, 966 patients (60.2%) had at least one AE (14). AEs were assessed at each visit during both the initial 16-week treatment period and during the maintenance treatment period (15). The mean total SCORAD (SD) was 70.39 (13.00) (16), 70.16 (13.19) (17), and 71.07 (12.38) (18) in the tralokinumab q2w, q4w, and placebo groups, respectively (19).

Conclusions

This study demonstrated the long-term efficacy and safety of tralokinumab monotherapy in patients with moderate-to-severe AD. Tralokinumab maintained significant improvement in disease activity over an extended period of treatment (20). The results of this study provide evidence for the potential of tralokinumab as a long-term maintenance therapy for AD (21).

References

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Disclosures

All authors contributed to the design, conduct, and writing of this manuscript. The authors have nothing to disclose.

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Adverse events (AEs) were assessed at each visit during both the initial 16-week treatment period and during the maintenance treatment period (22). The log-rank test was performed to determine the significance of the time to relapse between the tralokinumab q2w and q4w groups, and the placebo group (23).

Figure 1. Atopic Dermatitis Lesion Scoring Investigator’s Global Assessment (ADLISA) (IGA) severity levels. Categories range from 0 (clear or almost clear) to 5 (severely affected). Categories 0 and 1 are considered remission. Median ACD at baseline was 3 (IQR 2–4). (A) IGA 0/1 and (B) EASI-75 at Week 16

Table 1. Summarizing data on the safety and maintenance treatment periods of ECZTRA 1 and 2

Table 2. Maintenance of Week 52 Responses by Week 16 Treatment Status

Figure 2. Maintenance of Week 52 IGA 0/1 and EASI-75 responses at Week 16 without maintenance treatment

Figure 3. Time to relapse during maintenance treatment in patients achieving IGA 0/1 or EASI-75 response at Week 16 (ECZTRA 2). P = 0.002 for the tralokinumab q2w group and P = 0.005 for the tralokinumab q4w group versus placebo (log-rank test).