Tralokinumab monotherapy in adult patients with moderate-to-severe atopic dermatitis: regional differences in baseline disease characteristics and prior treatment in the ECZTRA 1 and ECZTRA 2 trials

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Introduction

- Atopic dermatitis (AD) is a chronic inflammatory skin disease affecting 2.1–4.9% of adults across North America, Europe, and Japan[1]
- AD is characterized by excessive dryness, intense itching, inflamed skin, and open sores or oozing[2,3] and has a significant impact on quality of life due to itch, sleep interference, and psychological distress[4]
- Tralokinumab is a fully human monoclonal antibody which neutralizes interleukin-13, a key driver of the chronic inflammation underlying moderate-to-severe AD[5–9]
- Primary analysis of the Phase 3 trials (ECZTRA 1 [NCT03131648] and ECZTRA 2 [NCT03160885]) demonstrated superiority of tralokinumab 300 mg every 2 weeks compared with placebo in all primary and secondary endpoints of the initial 16-week treatment period. Superiority of tralokinumab for the primary endpoint of Investigator's Global Assessment (IGA) 0/1 was more pronounced in ECZTRA 2 than in ECZTRA 1
- ECZTRA 1 and ECZTRA 2 followed an identical design, but recruited patients from different countries across Europe, North America, Asia, and Oceania. The randomization procedure stratified patients by geographical region and baseline IGA score (moderate or severe). Hence, an imbalance in baseline characteristics may be present within countries

Objective

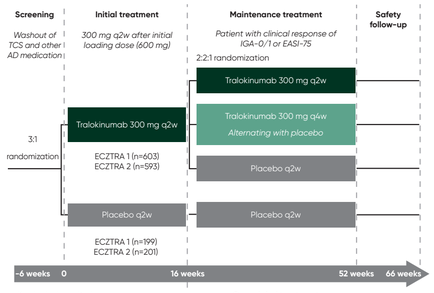
- The objective of this post hoc analysis was to evaluate whether there were meaningful regional differences in baseline characteristics and prior AD treatment in the large cohort of patients with moderate-to-severe AD from the Phase 3 tralokinumab studies (ECZTRA 1 and ECZTRA 2)

Methods

Study design and patients

- ECZTRA 1 and ECZTRA 2 were identically designed, multinational, double-blind, randomized, placebo-controlled, 52-week clinical trials of tralokinumab monotherapy in patients with moderate-to-severe AD
  - In ECZTRA 1, patients were enrolled from Europe (Germany, France, Spain), North America (USA), and Asia (Japan)
  - In ECZTRA 2, patients were enrolled from Europe (UK, Italy, Denmark, Poland, and Russia), North America (USA and Canada), Asia (Korea), and Australia
- Based on the inclusion criteria, eligible patients were ⩾18 years of age, with a confirmed diagnosis of AD for >1 year, Eczema Area and Severity Index (EASI) score of ⩾16, IGA ⩾3, pruritus Numeric Rating Scale (NRS) ⩾4, and were candidates for systemic therapy due to a recent (within 1 year) history of inadequate response or intolerance to topical treatment
- Before treatment, patients underwent a washout period of 2 weeks for topical treatments including topical corticosteroids (TCS), 4 weeks for systemic medications, and 6 weeks for phototherapy **(Figure 1)**

Figure 1. ECZTRA 1 and ECZTRA 2 trial design



Post hoc analysis

- This analysis compared patient demographics, disease characteristics, and prior use of AD treatments in all randomized patients by region in the ECZTRA 1 and ECZTRA 2 trials

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Results

Patient demographics and AD severity at baseline

- In total, 802 and 794 patients were randomized in ECZTRA 1 and 2, respectively. Overall the demographic and disease characteristics at baseline were similar across the trials **(Table 1)**
- Patients had a long mean duration of AD (28.3/28.1 years) and high body surface area (BSA) involvement (53.1/52.7%)

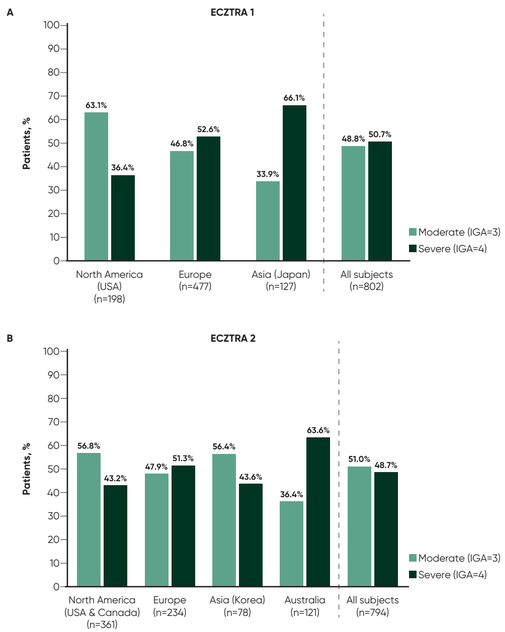
Table 1. Demographics and baseline characteristics of all randomized patients

Characteristic	ECZTRA 1 (n=802)	ECZTRA 2 (n=794)
Mean age, years (SD)	38.8 (14.1)	36.7 (14.6)
Male, %	59.1	59.6
Severe disease (IGA–4), %	50.7	48.7
Mean EASI (SD)	32.4 (13.8)	32.2 (14.2)
Mean SCORAD (SD)	70.6 (12.9)	70.1 (13.1)
Mean DLQI (SD)	16.9 (7.0)	17.7 (7.1)
Mean weekly average worst daily pruritus NRS (SD)	7.7 (1.4)	7.9 (1.4)
Mean duration of AD, years (SD)	28.3 (14.7)	28.1 (15.6)
Mean BSA involvement with AD, % (SD)	53.1 (24.5)	52.7 (25.4)

DLQI, Dermatology Life Quality Index.

- The proportion of patients with severe AD (IGA–4) was 50.7% and 48.7% for the overall study populations in ECZTRA 1 and 2, respectively. Japan (66.1%) and Australia (63.6%) had the highest proportions of patients with severe AD (IGA–4) compared with Europe (52.6/51.3%), North America (36.4/43.2%), and Korea (43.6%) **(Figure 2)**

Figure 2. Proportion of patients with severe (baseline IGA=4) and moderate (IGA=3) AD by region in (A) ECZTRA 1 and (B) ECZTRA 2



- Of the patients with severe AD (IGA–4) at baseline, higher mean baseline EASI was observed in Japan (46.3 and Australia (48.0), compared with Europe (37.9/40.9), North America (37.6/34.9), and Korea (42.3) **(Figure 3)**

Figure 3. Mean baseline EASI scores of patients by region and baseline IGA in (A) ECZTRA 1 and (B) ECZTRA 2

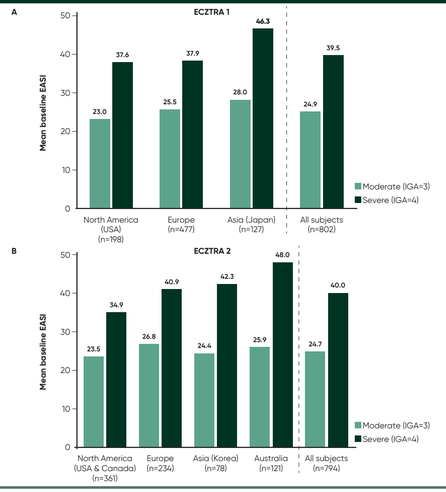
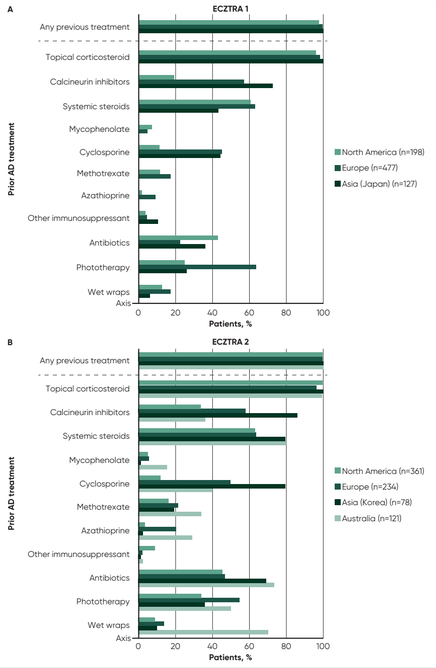


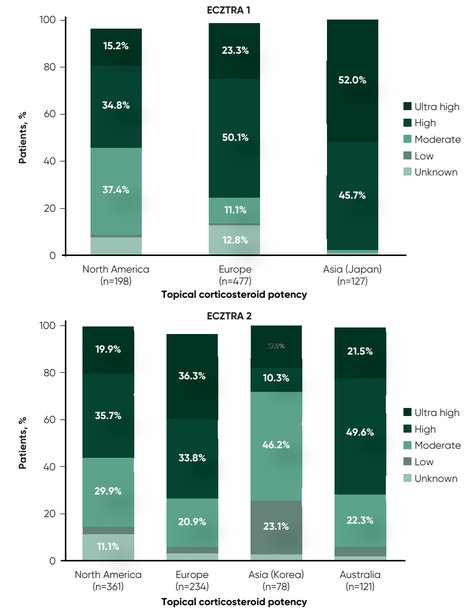
Figure 4. Prior AD treatments in all randomized patients by region in (A) ECZTRA 1 and (B) ECZTRA 2



Prior treatment for AD

- The trial population was heavily pretreated for AD. Almost all patients across all regions had received prior TCS (96–100%) **(Figure 4)**
  - The proportion of patients who had received ultra-high potency TCS was highest in Japan, whereas in Korea the majority of TCS used was of low and moderate potency **(Figure 5)**
- Prior systemic steroid treatment was highest in Australia (80.2%) and Korea (79.5%)
- There was high variability in prior use of systemic immunosuppressants. Cyclosporine was the most commonly used systemic immunosuppressant, used by ⩾40% of patients in Japan, Europe, Korea, and Australia. Use of mycophenolate, methotrexate, and azathioprine was less common, in <22% of patients, except in Australia where methotrexate and azathioprine were used by 33.9% and 28.9%, respectively
- More patients in Europe and Australia had received phototherapy for AD compared with Asia and North America, and use of wet wraps was also higher in Australia compared with other regions

Figure 5. Potency of prior TCS used in all randomized patients in (A) ECZTRA 1 and (B) ECZTRA 2



Conclusions

- In this post hoc analysis of the ECZTRA 1 and ECZTRA 2 studies, regional differences were observed in disease severity and prior AD treatment, despite identical inclusion criteria
- Japan and Australia enrolled a similarly high proportion of patients with severe AD (IGA–4); however, Australia had the highest levels of prior medication use, compared with low use of medications (including systemic immunosuppressants) in Japan, most likely due to regional differences in AD treatment guidelines
- Regional differences in standard of care, in addition to differential assessment of study outcomes may, in part, explain the differences in therapeutic responses observed between ECZTRA 1 and ECZTRA 2. These analyses highlight the importance of stratification by region in the randomization procedure as performed in these trials

References

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Disclosures

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