# Matching-adjusted indirect comparison of the efficacy of tralokinumab and dupilumab in the treatment of moderate-to-severe atopic dermatitis beyond week 16

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## Objective

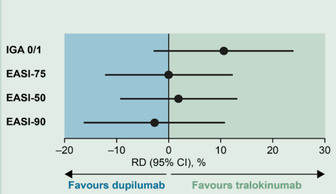
- To indirectly compare tralokinumab and dupilumab, both in combination with TCS, for the treatment of moderate-to-severe AD in adult patients, as determined by clinical endpoints and PROs beyond week 16

## Results

### Clinical outcomes at Week 32

- Tralokinumab and dupilumab showed comparable efficacy across clinical response endpoints at week 32 (**Figure 1**)
- The matched proportion of patients achieving IGA 0/1 was numerically higher for tralokinumab (49.9%), compared with dupilumab (39.3%; matched difference, 10.6%; 95% CI, −2.9%, 24.0%; *P*=0.12)
- For EASI-75, the proportion of responders was equivalent for tralokinumab and dupilumab (both 71.9%; difference 0%; 95% CI, −12.2%, 12.3%; *P*=1.00)
- The proportion of patients with an EASI-50 response was numerically favourable for tralokinumab (79.5%), compared with dupilumab (77.5%; difference 1.9%; 95% CI, −9.3, 13.2; *P*=0.73)
- For EASI-90, the proportion of responders was numerically favourable for dupilumab (56.2%) compared with tralokinumab (53.5%; difference −2.7%; 95% CI, −16.3,10.8; *P*=0.69)

**Figure 1.** Risk difference for achieving clinical responses for tralokinumab vs dupilumab at week 32




| | Response rate, % | | | |
|---|---|---|---|---|
| | Tralokinumab | Dupilumab | RD (95% CI), % | p value |
| IGA 0/1 | 49.9 | 39.3 | 10.6 (−2.9, 24.0) | 0.12 |
| EASI-75 | 71.9 | 71.9 | 0.0 (−12.2, 12.3) | 1.00 |
| EASI-50 | 79.5 | 77.5 | 1.9 (−9.3, 13.2) | 0.73 |
| EASI-90 | 53.5 | 56.2 | −2.7 (−16.3, 10.8) | 0.69 |

*P* −values have not been corrected for multiple comparisons.

### Clinical outcomes at Week 32 vs dupilumab data at Week 52

- More patients receiving tralokinumab achieved IGA 0/1 at week 32 (49.9%), compared with dupilumab at week 52 (36.0%; matched difference, 13.9%; 95% CI, 0.6%, 27.3%; *P*=0.04) (**Figure 2A**)
- The proportion of EASI-75 responders was numerically higher for tralokinumab at week 32 (71.9%), compared with dupilumab at week 52 (65.2%) (**Figure 2A**)
- Tralokinumab and dupilumab showed comparable efficacy based on EASI-50 and EASI-90 response rates, and in the mean change in EASI or SCORAD (**Figure 2B**)

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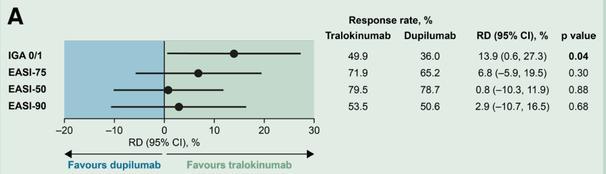
**Figure 2.** (**A**) Risk difference for achieving clinical responses and (**B**) Mean differences in clinical endpoints for tralokinumab at week 32 vs dupilumab at week 52




| | Response rate, % | | | |
|---|---|---|---|---|
| | Tralokinumab | Dupilumab | RD (95% CI), % | p value |
| IGA 0/1 | 49.9 | 36.0 | 13.9 (0.6, 27.3) | **0.04** |
| EASI-75 | 71.9 | 65.2 | 6.8 (−5.9, 19.5) | 0.30 |
| EASI-50 | 79.5 | 78.7 | 0.8 (−10.3, 11.9) | 0.88 |
| EASI-90 | 53.5 | 50.6 | 2.9 (−10.7, 16.5) | 0.68 |

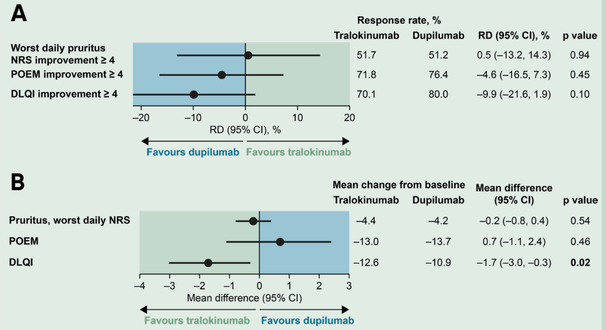
| | Mean % change from baseline | | Mean difference | |
|---|---|---|---|---|
| | Tralokinumab | Dupilumab | (95% CI), % | p value |
| EASI | −83.3 | −78.3 | −5.0 (−14.5, 4.5) | 0.30 |
| SCORAD | −69.3 | −66.2 | −3.1 (−10.0, 3.7) | 0.37 |

*P* −values have not been corrected for multiple comparisons.

### Patient-reported outcomes at week 32 vs dupilumab data at week 52

- PRO results were generally similar for tralokinumab and dupilumab
- Rates of patients experiencing a ≥ 4-point improvement in worst daily pruritus NRS or POEM were similar for both tralokinumab and dupilumab (**Figure 3A**), as were mean changes from baseline in these measures (**Figure 3B**)
- Comparable proportions of tralokinumab and dupilumab patients experienced a ≥ 4-point improvement in DLQI (**Figure 3A**)
- The mean change in DLQI was greater in the tralokinumab arm than in the dupilumab arm (mean difference, −1.7; 95% CI, −3.0, −0.3; *P*=0.02) (**Figure 3B**)

**Figure 3.** (**A**) Risk difference for achieving PRO responses and (**B**) Mean differences in PROs for tralokinumab at week 32 vs dupilumab at week 52




| | Response rate, % | | | |
|---|---|---|---|---|
| | Tralokinumab | Dupilumab | RD (95% CI), % | p value |
| Worst daily pruritus NRS improvement ≥ 4 | 51.7 | 51.2 | 0.5 (−13.2, 14.3) | 0.94 |
| POEM improvement ≥ 4 | 71.8 | 76.4 | −4.6 (−16.5, 7.3) | 0.45 |
| DLQI improvement ≥ 4 | 70.1 | 80.0 | −9.9 (−21.6, 1.9) | 0.10 |

| | Mean change from baseline | | Mean difference | |
|---|---|---|---|---|
| | Tralokinumab | Dupilumab | (95% CI) | p value |
| Pruritus, worst daily NRS | −4.4 | −4.2 | −0.2 (−0.8, 0.4) | 0.54 |
| POEM | −13.0 | −13.7 | 0.7 (−1.1, 2.4) | 0.46 |
| DLQI | −12.6 | −10.9 | −1.7 (−3.0, −0.3) | **0.02** |

*P* −values have not been corrected for multiple comparisons.

## Background

- Tralokinumab and dupilumab are both licensed for the treatment of moderate-to-severe AD in adult patients who are candidates for systemic treatment[1,2,3]
  - However, to date no head-to-head studies or indirect comparisons of their efficacy beyond week 16 have been conducted
  - In the absence of head-to-head data, indirect comparison methods adjusting for cross-trial differences can be used to compare therapies[4]
- In this study, we use a MAIC approach to compare tralokinumab and dupilumab, both used in combination with TCS, beyond 16 weeks of treatment
  - Data were taken from the ECZTRA 3 tralokinumab trial[5] and the LIBERTY AD CHRONOS dupilumab trial[6]

## Matching-Adjusted Indirect Comparison Methods

- An unanchored MAIC analysis[7,8] was conducted using IPD from patients randomized to tralokinumab Q2W, or Q4W from week 16, in the ECZTRA 3 trial[5] and aggregate data from patients treated with dupilumab Q2W in the LIBERTY AD CHRONOS trial[6]
- Tralokinumab IPD were selected by applying the inclusion criteria from LIBERTY AD CHRONOS, then weighted to match the mean baseline characteristics of dupilumab patients
  - The baseline characteristics matched were age, sex, race, BMI, disease duration, DLQI, EASI, IGA and SCORAD
- Outcomes assessed in the MAIC were:
  - Clinical – the proportions of patients achieving an IGA score of 0 or 1 (IGA 0/1) or a 50%, 75% or 90% improvement in EASI (EASI-50, -75 or -90), mean change from baseline in EASI and mean change from baseline in SCORAD
  - PROs – worst daily pruritus NRS, DLQI and POEM, all assessed as mean change from baseline and as the proportion of patients with a ≥ 4-point improvement
- Indirect comparisons for EASI and IGA outcomes were performed at week 32, the duration of ECZTRA 3
  - In addition, MAIC analyses were also conducted across all clinical outcomes and PROs, comparing outcomes reported at week 32 for tralokinumab and week 52 for dupilumab

## Conclusions

- This study used a MAIC approach to compare the efficacy of tralokinumab Q2W, and Q4W after week 16, with that of dupilumab Q2W, both in combination with TCS, beyond 16 weeks
- The results were broadly comparable across treatments in terms of both clinical and PRO endpoints
- The results of this analysis confirm similar efficacy for tralokinumab and dupilumab in the treatment of moderate-to-severe AD beyond 16 weeks of therapy

## Population Matching

- A total of 250 patients treated with tralokinumab in ECZTRA 3 were compared with 106 patients treated with dupilumab
  - After matching, the effective sample size was 49.4% of the original tralokinumab population
  - Unweighted and weighted patient baseline characteristics are presented in **Table 1**

**Table 1.** Population matching

| | Dupilumab | Tralokinumab | |
|---|---|---|---|
| | **Baseline characteristics N = 106** | **Unweighted N = 250** | **Weighted $N_{eff}$ = 123.4** |
| Age, years | 39.6 (14.0) | 39.8 (15.3) | 39.6 (16.0) |
| Sex, % male | 58.5 | 49.2 | 58.5 |
| BMI, kg/m$^2$ | 25.5 (5.8) | 27.6 (6.7) | 25.5 (5.6) |
| Disease duration, years | 30.1 (15.5) | 27.9 (16.4) | 30.1 (17.6) |
| Race, % white | 69.8 | 80.4 | 69.8 |
| EASI score | 33.6 (13.3) | 28.7 (11.8) | 33.6 (13.9) |
| IGA score | 3.5 (0.5) | 3.5 (0.5) | 3.5 (0.5) |
| DLQI score | 14.5 (7.3) | 17.6 (7.1) | 14.5 (6.6) |
| SCORAD score | 69.3 (15.2) | 67.0 (13.2) | 69.3 (14.3) |

## Study Limitations

- For PRO endpoints, the difference in time points may introduce some bias to the analysis
- Results reported after week 16 do not reflect all participants who were randomized to dupilumab Q2W – consequently, the matched tralokinumab population may not be completely representative of the dupilumab population for which outcomes are reported
- Due to differences in the treatment of patients receiving placebo in the two trials, an anchored analysis could not be performed
- As with all indirect comparisons, bias due to observed and unobserved differences across the trials cannot be ruled out

## Abbreviations

AD, atopic dermatitis; BMI, body mass index; CI, confidence interval; DLQI, Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; EASI-75, 75% improvement in EASI; IGA, Investigator's Global Assessment; IPD, individual patient data; MAIC, matching-adjusted indirect comparison; NRS, numerical rating scale; POEM, Patient-Oriented Eczema Measure; PRO, patient-reported outcome; QW, weekly; Q2W, every 2 weeks; Q4W, every 4 weeks; RD, risk difference; SCORAD, SCORing Atopic Dermatitis; SD, standard deviation; SmPC, summary of product characteristics; TCS, topical corticosteroids.

## References

**1.** Wollenberg A et al. *J Eur Acad Dermatol Venereol* 2022;36:1409–1431. **2.** Tralokinumab SmPC. **3.** Dupilumab SmPC. **4.** Phillippo DM et al. *Med Decis Making* 2018;38:200–211. **5.** Silverberg JI et al. *Br J Dermatol* 2021;184:450–463. **6.** Blauvelt A et al. *Lancet* 2017;389:2287–2303. **7.** Signorovitch JE et al. Value Health 2012;15:940–7. **8.** Signorovitch JE et al. Pharmacoeconomics 2010;28:935–45.

## Disclosures

**TT** has received consultancy and/or speaker's honoraria from and/or participated in clinical trials sponsored by AbbVie, Amgen, Almirall, Arena Pharmaceuticals, Biocad, Biogen, Boehringer Ingelheim, Bristol Myers Squibb, Celgene, Fresenius-Kabi, Janssen, LEO Pharma, Eli Lilly, MSD, Mylan, Novartis, Pfizer, Samsung-Bioepis, Sanofi-Genzyme, Sandoz, and UCB. **ASP, AMR and CMT** are employees of LEO Pharma A/S. **JMC** has participated as PI/SI and/or invited speaker and/or advisor for LEO Pharma, Sanofi, Pfizer, Almirall, Lilly, Abbvie, AMGEN, and Galderma.

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