Treatment with tralokinumab improves health-related quality of life in adult patients with moderate to severe atopic dermatitis: results from a Phase 2b, randomised, double-blind, placebo-controlled study

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Introduction

- Atopic dermatitis (AD) is a chronic, in ammatory skin disease associated with skin barrier disruption and immune-mediated in ammation characterised by increased levels of type 2 cytokines, including interleukin (IL)-13.[1,2]
- Symptoms of AD include intense and debilitating itch, often leading to sleep disruption, anxiety or depression, and reduced health-related quality of life (HRQoL).[3,4]
- The burden of AD may be assessed by dermatology-specific patient-reported outcome measures, including the Dermatology Life Quality Index (DLQI). However, it is also important to assess overall aspects of health and mental well-being in patients with AD and to determine how the burden of AD compares with other non-dermatologic health disorders via the use of generic HRQoL instruments, such as the 36-Item Short Form Health Survey version 2 (SF-36v2). —The SF-36v2 is widely used in health research to assess overall HRQoL.[5,6]
- Tralokinumab, a fully human IgG_4 monoclonal antibody that speci fically binds to, and neutralizes, IL-13,[7] showed improvements in Eczema Area and Severity Index (EASI), Investigator's Global Assessment (IGA), SCORing Atopic Dermatitis (SCORAD) and DLQI in a Phase 2b, randomised, double-blind, placebo-controlled study (NCT02347176) in adults with moderate to severe AD.[8]
- The tralokinumab Phase 2b study also included exploratory assessment of improvement in HRQoL in patients with moderate to severe AD.

Objective

- To analyse HRQoL improvement, as evaluated by the SF-36v2, in patients receiving tralokinumab as treatment for moderate to severe AD in the Phase 2b study.

Methods

Study design

- Patients were randomised (1:1:1:1) to tralokinumab (45 mg, 150 mg or 300 mg) or placebo treatment every 2 weeks for 12 weeks on a background of topical corticosteroids (TCS) [**Figure 1**].
- Eligible patients were aged 18–75 years with physician-con firmed diagnosis of AD for ≥1 year[9] and with 10% body surface area involvement, EASI score of ≥12, SCORAD of ≥25 and IGA score of ≥3.
- Key exclusion criteria included: active dermatological conditions that may confound AD diagnosis, allergic or irritant contact dermatitis and history of anaphylaxis following any biologic therapy.
- Concomitant World Health Organisation (WHO) Class 3 TCS were administered at least once daily during the 2-week run-in and as needed throughout the treatment and follow-up periods.

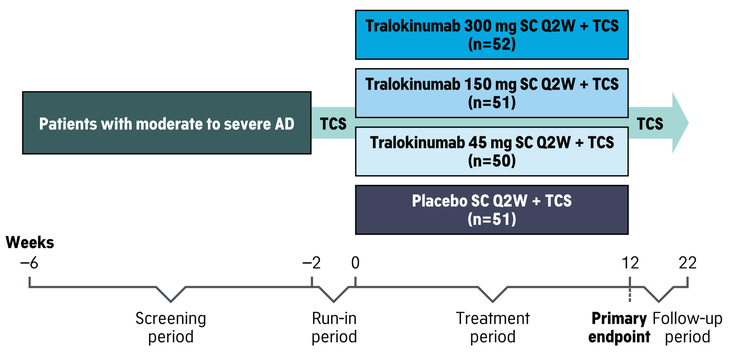
SF-36v2

- The SF-36v2 includes eight scale scores measuring: bodily pain, general health, mental health, role limitations related to physical health problems, role limitations related to personal or emotional problems, social functioning, vitality and physical functioning, plus Physical Component Summary (PCS) and Mental Component Summary (MCS) scores.[5,6] Higher scores indicate better health.[5,6]
- The SF-36v2 was assessed at baseline and at weeks 6, 12 and 22.

Statistical analyses

- SF-36v2 results at each study visit and changes from baseline for each post-baseline visit were reported, with descriptive statistics for each domain and summary score.
- All non-missing data for all patients were included in the analysis, up to the point of prohibited AD therapy being received.
- Mean change from baseline for each domain and summary score was analysed with mixed model with repeated measures, with treatment, visit and treatment-by-visit interaction as categorical factors and baseline SF-36v2 as covariate. Nominal p values for each domain and summary score were derived without adjustment for multiple testing.
- Minimal clinically important difference (MCID) was used to evaluate clinically relevant improvements (adjusted mean difference versus placebo: MCS, 3; PCS, 2; bodily pain, 3; general health, 2; mental health, 3; role-physical, 3; role-emotional, 4; social functioning, 3; vitality, 2; physical functioning, 3).
- Results are presented for the tralokinumab 300-mg treatment and placebo treatment groups at week 12, as the tralokinumab 300-mg dose was chosen for further evaluation in Phase 3 trials.

Figure 1. Study design



AD, atopic dermatitis; Q2W, every 2 weeks; SC, subcutaneous; TCS, topical corticosteroids.

Table 1. Summary of SF-36v2 scores at baseline and adjusted mean change in SF-36v2 from baseline at week 12

		MCS	PCS	Bodily pain	General health	Mental health	Role-physical	Role-emotional	Social functioning	Vitality	Physical functioning
Placebo											
SF-36v2 score at baseline, mean (SD) n=49	Mean (SD)	43.72 (13.23)	47.07 (7.94)	45.10 (10.41)	42.24 (9.31)	45.11 (11.65)	45.32 (11.79)	43.71 (13.36)	45.30 (11.58)	45.37 (11.06)	50.01 (8.36)
Adjusted mean change from baseline in SF-36v2 at week 12,* mean (SE) n=36	**Mean (SE)**	**1.18 (1.222)**	**–0.21 (0.907)**	**–0.43 (1.369)**	**0.00 (1.022)**	**1.03 (1.297)**	**–0.02 (1.109)**	**0.20 (1.278)**	**1.57 (1.271)**	**1.39 (1.208)**	**0.66 (0.883)**
Tralokinumab 300 mg											
SF-36v2 score at baseline, mean (SD) n=52	Mean (SD)	43.02 (12.36)	47.20 (8.17)	44.64 (11.55)	42.47 (10.16)	43.98 (11.18)	45.70 (10.81)	44.83 (13.30)	43.99 (11.64)	44.37 (10.71)	50.22 (8.08)
Adjusted mean change from baseline in SF-36v2 at week 12,* mean (SE) n=46	**Mean (SE)**	**5.41 (1.095)**	**4.05 (0.828)**	**5.63 (1.242)**	**3.43 (0.934)**	**4.12 (1.164)**	**4.80 (1.008)**	**4.95 (1.160)**	**6.81 (1.138)**	**5.47 (1.087)**	**3.26 (0.799)**

*Analysis of SF-36v2 change from baseline with repeated measures, excluding data after prohibited medications.

MCS, Mental Component Summary; PCS, Physical Component Summary; SD, standard deviation; SE, standard error; SF-36v2, 36-Item Short Form Health Survey version 2.

Results

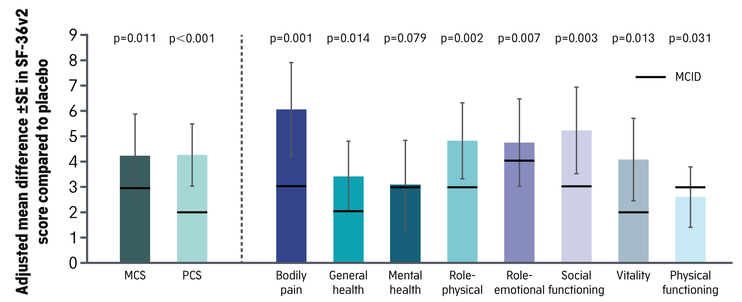
Patient characteristics

- Overall, 204 patients were randomised in the Phase 2b study; of these, 52 patients received tralokinumab 300 mg and 51 patients received placebo.
- Mean (standard deviation [SD]) age at baseline was 39.4 (14.5) years for placebo and 35.7 (14.6) years for tralokinumab 300 mg; 43.1% (n=22) and 63.5% (n=33) of participants were male in the placebo and tralokinumab 300-mg groups, respectively.
- At baseline, mean (SD) EASI scores were 26.4 (12.6) and 27.3 (10.9) for the placebo and tralokinumab 300-mg groups, respectively.

HRQoL

- SF-36v2 data were available at baseline for 49 patients in the placebo group and 52 patients in the tralokinumab 300-mg group.
- At baseline, mean (SD) MCS was 43.72 (13.23) for the placebo group and 43.02 (12.36) for the tralokinumab 300-mg group; mean (SD) PCS was 47.07 (7.94) and 47.20 (8.17), respectively (**Table 1**).
- At week 12, significantly improved SF-36v2 summary scores were seen in patients treated with tralokinumab 300 mg compared to placebo for both MCS (adjusted mean di erence: 4.23; p=0.011) and PCS (adjusted mean difference: 4.26; p 0.001) [**Table 1** and **Figure 2**].
- Significant improvements were also seen in all other domains for the tralokinumab 300-mg group compared to placebo (i.e. bodily pain, general health, role-physical, role-emotional, social functioning, vitality, physical functioning), except for mental health, which showed a numerical increase but did not reach statistical significance.
- MCS and PCS summary scores and all other domains, except for physical functioning, surpassed MCID for the tralokinumab 300-mg group compared to placebo (**Figure 2**)

Figure 2. Adjusted mean difference for the tralokinumab 300-mg group compared to placebo at week 12 for SF-36v2 domains, with MCID indicated for each score



All p values refer to the adjusted mean difference compared to placebo.

MCS, Mental Component Summary; MCID, minimal clinically important difference; PCS, Physical Component Summary; SE, standard error; SF-36v2, 36-Item Short Form Health Survey version 2.

Conclusions

- Treatment with tralokinumab 300 mg on a background of TCS provided significant and clinically relevant improvements over a broad range of HRQoL domains in adult patients with moderate to severe AD compared to placebo in this exploratory analysis of a Phase 2b study.
- Moderate to severe AD was associated with a profoundly negative impact on both mental and physical aspects of patients' lives at baseline.
- Phase 3 trials using the tralokinumab 300-mg dose are underway to further evaluate and confirm the impact that tralokinumab monotherapy (NCT03131648; NCT03160885) or tralokinumab in combination with TCS (NCT03363854) may have on reducing the disease burden of moderate to severe AD.

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