Supplemental Online Content

Paller AS, Flohr C, Cork M, et al. Efficacy and safety of tralokinumab in adolescents with moderate to severe atopic dermatitis: the phase 3 ECZTRA 6 randomized clinical trial. *JAMA Dermatol*. Published online April 19, 2023. doi:10.1001/jamadermatol.2023.0627

This supplemental material has been provided by the authors to give readers additional information about their work.

eAppendix 1. Study investigators/institutions

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eAppendix 2. Additional methods

Study Design

A 2–6 week screening period (washout length was prior medication-dependent) was followed by an initial treatment period of 16 weeks. All patients were mandated to use an emollient twice daily (or more if needed) for ≥14 days before randomization and for the duration of the trial. Patients were randomized (and re-randomized where relevant) using a central interactive response system; this assigned the required kit number to each patient at each dispensing visit. The patients, investigators, and staff were blinded to the treatment received. The packaging and labeling of the investigational medicinal products (IMPs) were identical, with non-sequential kit numbers to ensure unblinding did not occur during shipment and handling. As tralokinumab and placebo were not matched for viscosity, IMP was handled and administered by qualified unblinded healthcare professionals, who were not involved in managing the patients or in performing assessments. Each trial site had a plan detailing the process of IMP administration to maintain blinding according to the record of which staff members were blinded/unblinded. A safety follow-up period was carried out from Week 52 to Week 66 to assess safety, pharmacokinetics, and immunogenicity; patients could forego the safety follow-up if entering the ECZTEND extension trial after completing Week 52. Safety data were reviewed regularly by an independent data monitoring committee and by the study sponsor throughout the entire study. Nine patients from two sites with multiple Good Clinical Practice (GCP) non-compliance issues were excluded from all analyses. This is in alignment with considerations regarding exclusion of randomized patients per International Council for Harmonization E9, Section 5.2.1. Sensitivity analyses for primary endpoints, including the two sites, were performed and are presented in eTable 8. Exclusion of these patients did not affect the study findings.

Patients

A full list of inclusion and exclusion criteria can be found in the online protocol (available at: https://clinicaltrials.gov/ProvidedDocs/61/NCT03526861/Prot_000.pdf).

Additional Outcomes

Eczema Area and Severity Index percentage change from baseline to Week 4 and 52 was assessed as a post-hoc analysis.

Safety

Adverse events of special interest were eczema herpeticum, malignancies, skin infections requiring systemic treatment, and the eye disorders conjunctivitis, keratoconjunctivitis, and keratitis. Biochemical and hematologic laboratory parameters were also evaluated.

Statistical Analyses

All significance tests were two-sided using 5% significance, all p values outside the testing hierarchy were nominal and 95% confidence intervals are presented. The full analysis set was defined as all patients randomized to initial treatment who were exposed to IMP (excluding those enrolled at two sites with GCP non-compliance) and was used in all Week 16 efficacy analyses (primary and secondary endpoints). The maintenance analysis set included those patients receiving tralokinumab in the initial period who were re-randomized to maintenance treatment (excluding those enrolled at two sites with GCP non-compliance) and who received at least one dose of maintenance treatment. The open-label efficacy analyses included patients who transferred to the open-label phase at Week 16 and received ≥1 dose of treatment. The open-label safety analysis set included those patients who entered the open-label period at any time and received ≥1 dose of treatment. The safety analysis set was identical to the full analysis set. Further details can be found in the online statistical analysis plan (available at https://clinicaltrials.gov/ProvidedDocs/61/NCT03526861/SAP_001.pdf).

Estimand Framework

The estimand framework incorporated two main types of intercurrent events (initiation of rescue medication after Week 2 and permanent discontinuation of IMP) that could influence the treatment effect estimates. An overview of the estimand framework including both primary and sensitivity analyses that considered different assumptions for missing data and handling of intercurrent events are presented in **Table A** and **Table B**. For confirmatory endpoints, all three estimands were used. For all other endpoints, the primary analysis of the primary estimand was used if no other analysis was stated.

For binary endpoints **Table A**, the differences in response rates between treatment arms were analyzed using the Cochran–Mantel–Haenszel test (single imputation analyses) or with combined inference from multiple Mantel-Haenszel risk differences and associated standard errors using Rubin's rule (multiple imputation analyses), stratified by region and baseline disease severity (Investigator's Global Assessment [IGA] of 3 or 4).

For continuous endpoints **Table B**, the primary analysis of the primary estimand utilized a linear mixed-effect model for repeated measurements with data collected after use of rescue medication or permanent discontinuation of tralokinumab treated as missing (Panel 2). Mean changes from baseline were analyzed using a restricted maximum likelihood-based repeated-measures approach in combination with the Newton-Raphson algorithm.

The model included fixed categorical effects of treatment, baseline disease severity, region and treatment-by-week interaction, and continuous fixed effects of baseline value and baseline-by-week interaction. An unstructured covariance matrix was used to model within-patient errors. Denominator degrees of freedom were estimated using Kenward-Roger approximation. Primary treatment comparisons were the contrast between treatments at the endpoint week.

For other analyses of continuous endpoints, 100 data sets were created by using multiple imputations. For each imputed data set, change from baseline in outcome was analyzed using an analysis of covariance (ANCOVA) model with effects of treatment, region, baseline disease severity (IGA score of 3 or 4) and baseline outcome value. The estimated difference at Week 16 and the associated standard errors were pooled using Rubin's rule to combined inference.

Table A. Estimand framework for binary endpoints

Estimand	Rationale	Intercurrent events	Handling of missing data
Composite (primary)	Treatment difference after 16 weeks was achieved without rescue medication, regardless of treatment discontinuation	All analyses: patients who received rescue medication between Week 2 and 16 were considered non-responders	Primary analysis: missing data imputed as non-response Sensitivity analysis 1: missing data imputed as non-response Sensitivity analysis 2: missing data for patients who withdrew due to an adverse event or lack of efficacy imputed as non-response; otherwise last observation carried forward was used Sensitivity analysis 3: tipping point analysis using multiple imputation assessing the robustness of results of the primary analysis regarding the assumption related to missing Week 16 data among patients not using any rescue medication. Patients in the tralokinumab arms not attending Week 16 were considered non-responders. For patients in the placebo arm who did not use rescue between Week 2 and 16, missing Week 16 data (i.e., response yes =1/no=0) were imputed from a Bernoulli distribution with parameter p (range: from 0 to 1). One hundred data sets were generated and the difference in response rates were analyzed as per the primary analysis. Estimates and standard errors from the 100 analyses were combined using Rubin's rule to form a unique point estimate and standard error. The tipping point was defined as the value of p, which changed the conclusion of the primary analysis (i.e. from significant to non-significant)
	Reflects a treatment effect attributable to the randomized treatment where initiation of rescue medication reflects lack of response	Primary, sensitivity analysis 2 and 3: data retrieved at Week 16 after patients who permanent discontinuation tralokinumab were included	
		Sensitivity analysis 1: patients who have permanently discontinued tralokinumab prior to Week 16 were considered non-responders	
Hypothetical (secondary)	Treatment difference after 16 weeks if all patients adhered (i.e. did not discontinue tralokinumab permanently and rescue medication was not available)	Data collected after initiation of rescue medication at Week 2 or later or permanent discontinuation of tralokinumab were not included	Primary analysis: missing data were imputed using multiple imputation, assuming missing at random within arms Sensitivity analysis: missing data for tralokinumab and placebo were imputed from observed data for placebo using multiple imputation. The underlying assumption was that the effect of tralokinumab following rescue medication or permanent treatment discontinuation was similar to that of placebo; assumption was very conservative in favour of placebo as it tended to minimize the differences between arms

	Reflects a treatment effect in a situation in which intercurrent events would not occur		
Treatment policy (tertiary)	Treatment difference after 16 weeks regardless of rescue medication and treatment discontinuation Reflects a treatment effect regardless of what additional rescue was actually received, which may mimic the real-life clinical setting	Intercurrent events were irrelevant; all data were used as observed	Primary analysis: missing data were imputed using multiple imputation assuming missing at random within arms. Four groups defined according to randomized treatment arm and whether or not patients had permanently discontinued tralokinumab prior to Week 16 Sensitivity analysis: missing data were imputed as non-response, reflecting the fact that discontinued patients without retrieved data at Week 16 were more likely to be non-responders

Table B. Estimand framework for continuous endpoints

Estimand	Rationale	Intercurrent events	Handling of missing data
Hypothetical (primary)	Treatment difference after 16 weeks if all patients adhered i.e. did not permanently discontinue tralokinumab and rescue medication was not available Reflects a treatment effect in a situation in which intercurrent events would not occur	Data collected after initiation of rescue medication at Week 2 or later or permanent discontinuation of tralokinumab were not included	Primary analysis: repeated measurements model (assuming missing at random within treatment arms) Sensitivity analysis: missing data for tralokinumab as well as for placebo were imputed from observed data for placebo using multiple imputation (assessing robustness of the missing at random assumption in the primary analysis)
Treatment policy (secondary)	Treatment difference after 16 weeks, regardless of rescue medication and treatment discontinuation	Intercurrent events are irrelevant; all data used as observed	Primary analysis: missing data were imputed using multiple imputation, assuming missing at random within four groups defined according to randomized treatment arm and whether or not patients have discontinued treatment prior to Week 16

	Reflects a treatment effect, regardless of rescue actually used (may mimic the real-life clinical setting)		Sensitivity analysis: missing data for patients in tralokinumab as well as for placebo arms who have (or have not) discontinued treatment prior to Week 16 were imputed from observed data from patients from placebo who have (or have not) discontinued treatment prior to Week 16 using multiple imputation (assessing robustness of the missing at random assumption in the primary analysis)
Composite (tertiary)	Treatment difference after 16 weeks achieved without rescue medication, regardless of treatment discontinuation Reflects a treatment effect attributable to the randomized treatment in which initiation of rescue medication reflects lack of response	Patients who received rescue medication between Week 2 and 16 were considered non-responders by using worst observation carried forward (including baseline value). Data retrieved at Week 16 after patients who permanently discontinued tralokinumab were included	Primary analysis: missing data were imputed using multiple imputation assuming missing at random within arms Sensitivity analysis: the tipping point analysis assessing how severe the departure from the missing at random assumption in the primary analysis in tralokinumab arm had to be to impact the results. Missing at random-imputed data from the primary analysis were used. For each imputed dataset, Δ was added to the imputed values for patients in the tralokinumab (Δ = 0 implied missing at random) and ANCOVA analysis was performed. A unique point estimate and standard error were obtained using Rubin's rule. The tipping point was found as the value of Δ, which changed the conclusion (of the primary analysis) from significant to non-significant

eTable 1. Primary and secondary efficacy outcomes for the initial treatment period, full analysis set

	Placebo (n=94)	Tralokinumab 150 mg Q2W (n=98)		Tralokinumab 300 mg Q2W (n=97)	
			Diff vs placebo (95% CI)		Diff vs placebo (95% CI)
Primary endpoints, responders n/N (%)					
IGA 0/1 at Week 16	4/94 (4.3)	21/98 (21.4)	17.5 (8.4–26.6), *P<0.001*	17/97 (17.5)	13.8 (5.3–22.3), *P=0.002*
EASI 75 at Week 16	6/94 (6.4)	28/98 (28.6)	22.5 (12.4–32.6), *P<0.001*	27/97 (27.8)	22.0 (12.0–32.0), *P<0.001*
Key secondary endpoints,					
Reduction in Adolescent Worst Pruritus NRS ≥4 from baseline to Week 16, n/N (%)	3/90 (3.3)	22/95 (23.2)	19.9 (10.6–29.2), *P<0.001*	24/96 (25.0)	21.7 (12.3–31.1), *P<0.001*
SCORAD adjusted mean change from baseline to Week 16 (SE)	–9.5 (3.0)	–27.5 (2.4)	–18.0 (–25.6, –10.4), *P<0.001*	–29.1 (2.4)	–19.7 (–27.1, –12.2), *P<0.001*
CDLQI adjusted mean change from baseline to Week 16 (SE)*	–4.1 (0.7)	–6.1 (0.6)	–2.0 (–3.9, –0.1), *P=0.04*	–6.7 (0.6)	–2.6 (–4.5, –0.7), *P=0.007*
Additional secondary endpoints, n/N (%)					
EASI 50 at Week 16	13/94 (13.8)	45/98 (45.9)	32.4 (20.6–44.1), *P<0.001*	50/97 (51.5)	38.5 (26.8–50.2), *P<0.001*
EASI 90 at Week 16	4/94 (4.3)	19/98 (19.4)	15.3 (6.5–24.1), *P<0.001*	17/97 (17.5)	13.7 (5.2–22.2), *P=0.002*

For binary endpoints, patients who received rescue medication after Week 2 were considered non-responders and those with missing values at Week 16 were imputed as non-responders. For continuous endpoints, data collected after permanent discontinuation of tralokinumab or initiation of rescue medication after Week 2 were not included. In case of no post-baseline assessments, the Week 2 change was imputed as 0.

*N=89 for placebo, 95 for tralokinumab 150 mg Q2W, and 94 for tralokinumab 300 mg Q2W
CDLQI, Children's Dermatology Life Quality Index; CI, confidence interval; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; NRS, Numeric Rating Scale; Q2W, every 2 weeks; SCORAD, SCORing Atopic Dermatitis; SE, standard error

eTable 2. IGA 0/1 by visit (initial treatment period; observed data, full analysis set)

	All observed data			Excluding data after rescue medication		
Week IGA, No. (%)	**Placebo (n=94)**	**Tralokinumab 150 mg Q2W (n=98)**	**Tralokinumab 300 mg Q2W (n=97)**	**Placebo (n=94)**	**Tralokinumab 150 mg Q2W (n=98)**	**Tralokinumab 300 mg Q2W (n=97)**
Baseline						
N	94	98	97	94	98	97
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Week 2						
N	93	98	96	93	98	96
0	1 (1.1)	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	0 (0.0)
1	1 (1.1)	2 (2.0)	2 (2.1)	1 (1.1)	2 (2.0)	2 (2.1)
Week 4						
N	90	96	96	69	85	87
0	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	3 (3.3)	4 (4.2)	4 (4.2)	1 (1.4)	4 (4.7)	4 (4.6)
Week 6						
N	91	94	94	66	75	81

0	1 (1.1)	0 (0.0)	2 (2.1)	0 (0.0)	0 (0.0)	2 (2.5)
1	2 (2.2)	11 (11.7)	6 (6.4)	1 (1.5)	11 (14.7)	6 (7.4)
Week 8						
N	88	95	95	53	72	77
0	2 (2.3)	3 (3.2)	2 (2.1)	1 (1.9)	3 (4.2)	1 (1.3)
1	2 (2.3)	13 (13.7)	8 (8.4)	0 (0.0)	11 (15.3)	5 (6.5)
Week 10						
N	86	93	93	47	69	71
0	1 (1.2)	2 (2.2)	2 (2.2)	1 (2.1)	2 (2.9)	2 (2.8)
1	6 (7.0)	15 (16.1)	13 (14.0)	3 (6.4)	14 (20.3)	12 (16.9)
Week 12						
N	90	89	93	44	65	71
0	0 (0.0)	2 (2.2)	2 (2.2)	0 (0.0)	2 (3.1)	2 (2.8)
1	9 (10.0)	19 (21.3)	16 (17.2)	5 (11.4)	15 (23.1)	12 (16.9)
Week 14						
N	83	92	95	34	62	67
0	0 (0.0)	2 (2.2)	5 (5.3)	0 (0.0)	2 (3.2)	4 (6.0)
1	8 (9.6)	21 (22.8)	17 (17.9)	6 (17.6)	17 (27.4)	14 (20.9)

Week 16						
N	87	92	95	36	61	66
0	1 (1.1)	3 (3.3)	5 (5.3)	1 (2.8)	3 (4.9)	5 (7.6)
1	4 (4.6)	20 (21.7)	15 (15.8)	3 (8.3)	18 (29.5)	12 (18.2)
Week 16 without data collected after permanent discontinuation of IMP						
N	85	92	94	35	61	66
0	1 (1.2)	3 (3.3)	5 (5.3)	1 (2.9)	3 (4.9)	5 (7.6)
1	4 (4.7)	20 (21.7)	15 (16.0)	3 (8.6)	18 (29.5)	12 (18.2)

IGA, Investigator's Global Assessment; IMP, investigational medicinal product; Q2W, every 2 weeks

eTable 3. Percentage change from baseline in EASI by visit (initial treatment period; observed data, full analysis set)

	All observed data			Excluding data after rescue medication		
Week EASI change from baseline (%)	**Placebo (n=94)**	**Tralokinumab 150 mg Q2W (n=98)**	**Tralokinumab 300 mg Q2W (n=97)**	**Placebo (n=94)**	**Tralokinumab 150 mg Q2W (n=98)**	**Tralokinumab 300 mg Q2W (n=97)**
Week 2						
N	93	98	96	93	98	96
Mean (SD)	-6.36 (10.09)	-8.60 (10.18)	-9.48 (9.85)	-6.36 (10.09)	-8.60 (10.18)	-9.48 (9.85)
Median	-6.00	-8.15	-8.90	-6.00	-8.15	-8.90
(Q1;Q3)	(-10.60;0.00)	(-13.50;-2.30)	(-15.30;-1.38)	(-10.60;0.00)	(-13.50;-2.30)	(-15.30;-1.38)
Min;max	-44.0;19.2	-40.0;17.1	-40.8;15.9	-44.0;19.2	-40.0;17.1	-40.8;15.9
Week 4						
N	90	96	96	69	85	87
Mean (SD)	-7.88 (12.13)	-13.90 (11.26)	-13.51 (11.34)	-7.90 (10.70)	-14.06 (11.36)	-12.53 (10.94)
Median	-7.88	-12.60	-12.60	-7.25	-12.60	-11.80
(Q1;Q3)	(–14.90;-0.55)	(-21.85;-6.90)	(–19.88;-6.30)	(-13.50;-0.70)	(-21.60;-7.40)	(-19.80;-5.40)
Min;max	-43.4;19.5	-50.0;15.5	-56.4;13.6	-40.9;16.8	-50.0;15.5	-56.4;13.6
Week 6						
N	91	95	94	66	76	81

Mean (SD)	-9.88 (11.90)	-16.98 (10.97)	-15.71 (13.62)	-9.07 (11.01)	-17.87 (10.43)	-14.64 (12.55)
Median	-10.15	-15.30	-13.60	-9.23	-15.53	-13.50
(Q1;Q3)	(-16.90;-0.90)	(-24.10;-9.40)	(-23.30;-7.40)	(-16.00;-0.10)	(-24.05;-9.70)	(-22.70;-7.30)
Min;max	-43.6;28.9	-58.9;14.6	-56.6;19.1	-43.6;14.8	-58.9;1.0	-50.9;19.1
Week 8						
N	88	95	95	53	72	77
Mean (SD)	-10.82 (12.19)	-17.45 (12.26)	-18.19 (12.35)	-9.10 (11.69)	-18.01 (12.48)	-16.78 (11.58)
Median	-9.90	-16.65	-16.80	-8.10	-17.20	-16.60
(Q1;Q3)	(-17.55;-2.65)	(-24.80;-10.30)	(-25.50;-11.10)	(-16.40;-0.60)	(-24.90;-12.50)	(-24.20;-9.70)
Min;max	-50.9;18.4	-60.6;17.9	-50.6;7.0	-44.0;18.4	-60.6;17.9	-47.4;7.0
Week 10						
N	86	93	93	47	69	71
Mean (SD)	-11.07 (12.85)	-17.85 (11.90)	-18.82 (12.82)	-9.06 (13.04)	-18.86 (12.45)	-18.66 (12.80)
Median	-10.40	-17.00	-17.70	-8.95	-17.60	-17.30
(Q1;Q3)	(-17.90;-3.50)	(-24.65;-11.80)	(-27.20;-9.00)	(-16.60;-0.20)	(-25.90;-13.70)	(-27.20;-9.70)
Min;max	-45.0;20.3	-56.3;19.5	-60.7;6.7	-44.0;20.3	-56.3;19.5	-60.7;6.7
Week 12						
N	90	89	93	44	65	71
Mean (SD)	-11.81 (14.49)	-19.55 (11.69)	-18.97 (14.14)	-7.94 (14.71)	-20.40 (12.12)	-18.83 (14.02)

Median	-10.85	-18.70	-16.90	-7.50	-19.20	-17.30
(Q1;Q3)	(-21.10;-2.40)	(-25.95;-14.40)	(-27.10;-10.80)	(-16.95;-0.48)	(-27.40;-14.75)	(-27.10;-11.05)
Min;max	-50.3;23.1	-52.4;16.8	-62.2;16.1	-43.7;23.1	-52.4;16.8	-62.2;16.1
Week 14						
N	83	92	95	34	62	67
Mean (SD)	-12.52 (14.00)	-20.72 (11.76)	-19.24 (13.78)	-11.18 (14.95)	-20.94 (11.48)	-19.81 (12.47)
Median	-12.10	-20.25	-17.30	-9.60	-20.20	-20.80
(Q1;Q3)	(-19.95;-5.65)	(-27.25;-15.25)	(-27.10;-9.90)	(-19.20;-4.80)	(-28.20;-16.40)	(-27.10;-11.90)
Min;max	-60.8;17.5	-49.2;12.8	-63.2;9.4	-60.8;17.5	-45.8;12.8	-63.2;9.0
Week 16						
N	87	92	95	36	61	66
Mean (SD)	-11.67 (12.88)	-18.88 (12.65)	-18.72 (13.43)	-9.48 (12.94)	-18.99 (11.73)	-19.47 (12.04)
Median	-10.00	-18.08	-17.30	-8.20	-18.90	-19.35
(Q1;Q3)	(-18.80;-2.70)	(-25.60;-11.55)	(-27.75;-10.00)	(-15.25;-2.35)	(-25.30;-15.00)	(-27.50;-11.20)
Min;max	-45.2;17.7	-61.0;14.1	-65.8;9.2	-44.9;17.7	-45.4;14.1	-65.8;9.0
Week 16 without data collected after permanent discontinuation of IMP						
N	85	92	94	35	61	66
Mean (SD)	-11.42 (12.88)	-18.88 (12.65)	-18.95 (13.32)	-9.34 (13.10)	-18.99 (11.73)	-19.47 (12.04)
Median	-10.00	-18.08	-17.98	-7.50	-18.90	-19.35

(Q1;Q3)	(-18.00;-2.70)	(–25.60;-11.55)	(-27.75;-10.20)	(-16.00;-1.80)	(-25.30;-15.00)	(-27.50;-11.20)
Min;max	-45.2;17.7	-61.0;14.1	-65.8;9.2	-44.9;17.7	-45.4;14.1	-65.8;9.0

EASI, Eczema Area and Severity Index; IMP, investigational medicinal product; Q1/3, quartile 1/3; Q2W, every 2 weeks; SD, standard deviation

eTable 4. Rescue medications used in the (A) initial and (B) maintenance treatment periods, and concomitant AD medications in the (C) open-label treatment period, by type

A

Initial treatment period, n (%)	Placebo (n=94)	Tralokinumab 150 mg Q2W (n=98)	Tralokinumab 300 mg Q2W (n=97)
Any rescue medication	53 (56.4)	33 (33.7)	29 (29.9)
Topical			
Corticosteroids (any strength)	51 (54.3)	33 (33.7)	29 (29.9)
Other*	8 (8.5)	3 (3.1)	5 (5.2)
Systemic			
Corticosteroids	5 (5.3)	1 (1.0)	1 (1.0)
Immunosuppressants†	1 (1.1)	0	1 (1.0)

B

Maintenance treatment period, n (%)	Week 16 placebo responders	Week 16 tralokinumab 150 mg Q2W responders		Week 16 tralokinumab 300 mg Q2W responders	
	Placebo (n=6)	Tralokinumab 150 mg Q2W (n=12)	Tralokinumab 150 mg Q4W (n=14)	Tralokinumab 300 mg Q2W (n=11)	Tralokinumab 300 mg Q4W (n=13)
Any rescue medication‖	1 (16.7)	3 (25.0)	3 (21.4)	2 (18.2)	1 (7.7)
Topical					
Corticosteroids (any strength)	0	3 (25.0)	3 (21.4)	2 (18.2)	1 (7.7)
Other*	1 (16.7)	0	0	0	1 (7.7)

C

Open-label treatment period, n (%)	Tralokinumab 300 mg Q2W + optional TCS (n=234)
Concomitant AD medication	122 (52.1)
Topical	
Corticosteroids (any strength)	115 (49.1)
High potency‡	13 (5.6)
Other	29 (12.4)
Crisaborole	3 (1.3)
Systemic	
Corticosteroids	2 (0.9)

Dupilumab	1 (0.4)

*Initial phase: pimecrolimus (n=2), tacrolimus (n=14); maintenance phase: tacrolimus (n=2); †Initial phase: cyclosporine (n=2); ‖No patients used additional systemic rescue medication (systemic corticosteroids, methotrexate, cyclosporine, azathioprine, or mycophenolate) in the maintenance phase; ‡Aligned with the Anatomical Therapeutic Chemical Classification ATC D07AD

AD, atopic dermatitis; Q2/4W, every 2/4 weeks; TCS, topical corticosteroids

eTable 5. Primary efficacy analyses for confirmatory endpoints using different estimand approaches

	Placebo (n=94)	Tralokinumab 150 mg Q2W (n=98)		Tralokinumab 300 mg Q2W (n=97)	
	Responders*	**Responders***	**Diff vs placebo** (95% CI), *P******	**Responders***	**Diff vs placebo** (95% CI), *P******
IGA 0/1 at Week 16, n (%)					
Primary estimand: composite‖					
Primary analysis†	4 (4.3)	21 (21.4)	17.5 (8.4–26.6), *P<0.001*	17 (17.5)	13.8 (5.3–22.3), *P=0.002*
Sensitivity analysis 1††	4 (4.3)	21 (21.4)	17.5 (8.4–26.6), *P<0.001*	17 (17.5)	13.8 (5.3–22.3), *P=0.002*
Sensitivity analysis 2†††	5 (5.3)	21 (21.4)	16.4 (7.2–25.7), *P<0.001*	17 (17.5)	12.8 (4.1–21.4), *P=0.005*
Sensitivity analysis 3		Tipping point not met		Tipping point met at 63%††††	
Secondary estimand: hypothetical‡					
Primary analysis‡‡	18.4 (19.6)	31.0 (31.6)	12.5 (–3.5, 28.4), *P=0.13*	25.4 (26.2)	7.2 (–9.0, 23.4), *P=0.38*
Sensitivity analysis‡‡‡	18.6 (19.8)	30.5 (31.1)	11.8 (–2.7, 26.2), *P=0.11*	25.2 (25.9)	6.6 (–7.7, 21.0), *P=0.36*
Tertiary estimand: treatment policy#					
Sensitivity analysis##	5 (5.3)	23 (23.5)	18.5 (9.0–28.0), *P<0.001*	20 (20.6)	15.5 (6.4–24.6), *P=0.001*
EASI 75 at Week 16, n (%)					
Primary estimand: composite‖					
Primary analysis†	6 (6.4)	28 (28.6)	22.5 (12.4–32.6), *P<0.001*	27 (27.8)	22.0 (12.0–32.0), *P<0.001*

Sensitivity analysis 1[††]	5 (5.3)	28 (28.6)	23.5 (13.6–33.5), *P<0.001*	27 (27.8)	23.0 (13.1–32.9), *P<0.001*
Sensitivity analysis 2[†††]	7 (7.4)	28 (28.6)	21.4 (11.2–31.6), *P<0.001*	27 (27.8)	21.0 (10.8–31.1), *P<0.001*
Sensitivity analysis 3		Tipping point not met		Tipping point not met	
Secondary estimand: hypothetical[‡]					
Primary analysis[‡‡]	13.8 (14.7)	37.9 (38.7)	24.5 (9.8–39.1), *P=0.001*	34.6 (35.6)	21.6 (7.6–35.6), *P=0.002*
Sensitivity analysis[‡‡‡]	14.0 (14.9)	35.0 (35.7)	21.2 (7.5–34.9), *P=0.002*	32.7 (33.7)	19.3 (5.7–33.0), *P=0.006*
Tertiary estimand: treatment policy[#]					
Sensitivity analysis[##]	19 (20.2)	39 (39.8)	20.5 (8.3–32.7), *P=0.002*	36 (37.1)	17.3 (5.2–29.4), *P=0.007*
Reduction in adolescent pruritus NRS ≥4, n/N (%)					
Primary estimand: composite[‖]					
Primary analysis[†]	3/90 (3.3)	22/95 (23.2)	19.9 (10.6–29.2), *P<0.001*	24/96 (25.0)	21.7 (12.3–31.1), *P<0.001*
Sensitivity analysis 1[††]	3/90 (3.3)	22/95 (23.2)	19.9 (10.6–29.2), *P<0.001*	24/96 (25.0)	21.7 (12.3–31.1), *P<0.001*
Sensitivity analysis 2[†††]	3/90 (3.3)	25/95 (26.3)	23.0 (13.4–32.7), *P<0.001*	28/96 (29.2)	25.9 (16.1–35.7), *P<0.001*
Sensitivity analysis 3		Tipping point met at 89%[††††]		Tipping point met at 100%[††††]	
Secondary estimand: hypothetical[‡]					
Primary analysis[‡‡]	14.1/90 (15.7)	32.3/95 (34.0)	18.6 (3.7–33.5), *P=0.01*	37.1/96 (38.6)	23.1 (8.0–38.2), *P=0.003*

Sensitivity analysis‡‡‡	14.0/90 (15.6)	31.1/95 (32.7)	17.4 (3.2–31.7), *P=0.02*	33.7/96 (35.1)	19.7 (5.8–33.5), *P=0.005*
Tertiary estimand: treatment policy#					
Sensitivity analysis##	16/90 (17.8)	30/95 (31.6)	14.3 (2.0–26.7), *P=0.02*	32/96 (33.3)	15.7 (3.4–27.9), *P=0.01*
SCORAD adjusted mean change from baseline to Week 16 (SE)					
Primary estimand: hypothetical Primary analysis¶	–9.5 (3.0)	–27.5 (2.4)	–18.0 (–25.6, –10.4), *P<0.001*	–29.1 (2.4)	–19.7 (–27.1, –12.2), *P<0.001*
Sensitivity analysis¶¶	–9.7 (3.3)	–23.5 (2.7)	–13.8 (–21.2, –6.4), *P<0.001*	–26.0 (2.5)	–16.3 (–23.9, –8.7), *P<0.001*
Secondary estimand: treatment policy Sensitivity analysis¶¶¶	–16.6 (2.4)	–28.0 (2.3)	–11.4 (–17.5, –5.2), *P<0.001*	–29.8 (2.1)	–13.2 (–19.5, –7.0), *P<0.001*
Tertiary estimand: composite Primary analysis¶¶¶¶	–2.7 (2.2)	–18.9 (2.2)	–16.3 (–22.4, –10.1), *P<0.001*	–21.7 (2.2)	–19.1 (–25.2, –12.9), *P<0.001*
Sensitivity analysis		Tipping point not met		Tipping point not met	
CDLQI adjusted mean change from baseline to Week 16 (SE)					
Primary estimand: hypothetical‡ Primary analysis¶	–4.1 (0.7)	–6.1 (0.6)	–2.0 (–3.9, –0.1), *P=0.04*	–6.7 (0.6)	–2.6 (–4.5, –0.7), *P=0.007*
Sensitivity analysis¶¶	–3.8 (0.9)	–5.5 (0.7)	–1.7 (–3.5, 0.2), *P=0.08*	–6.2 (0.7)	–2.4 (–4.4, –0.4), *P=0.02*
Secondary estimand: treatment policy Sensitivity analysis¶¶¶	–4.8 (0.6)	–6.3 (0.6)	–1.6 (–3.2, 0.0), *P=0.05*	–7.1 (0.6)	–2.3 (–3.9, –0.7), *P=0.005*
Tertiary estimand: composite Primary analysis¶¶¶¶	–0.8 (0.6)	–3.9 (0.6)	–3.1 (–4.8, –1.4), *P<0.001*	–5.0 (0.6)	–4.2 (–5.9, –2.5), *P<0.001*
Sensitivity analysis 3		Tipping point met at delta=27††††		Tipping point not met	

*Mean across multiple imputations where applicable; **Mantel-Haenszel risk difference compared to placebo, stratified by region and baseline IGA; ***Single imputation analyses: Cochran-Mantel-Haenszel test, stratified by region and baseline IGA; multiple imputation analyses: combined inference from multiple Mantel-Haenszel risk differences and associated standard errors; ‖Patients who initiated rescue medication after Week 2 were considered non-responders; †Missing values at Week 16 imputed as non-responders; ††Patients who permanently discontinued IMP prior to Week 16

considered non-responders; †††Missing data at Week 16 imputed using LOCF for patients who did not receive rescue medication and did not withdraw due to an AE or lack of efficacy; ††††The tipping point was reached at high imputation in Placebo treatment group which is considered clinically implausible. Primary analysis results are considered robust; †††††The tipping point was reached at high delta which is considered clinically implausible. Primary analysis results are considered robust; ‡Data collected after permanent discontinuation of IMP or initiation of rescue medication after Week 2 not included; multiple imputation of missing values at Week 16. ‡‡Multiple imputations within treatment arm. ‡‡‡Placebo based imputation of missing values in active treatment group; #Primary analysis was not performed due to sparse data; ##All data used as observed. Missing values at Week 16 imputed as non-responders; ¶Repeated measurements model: "change = treatment*week+baseline*week+region+baseline IGA", in case of no baseline assessments, Week 2 change was imputed as 0; ¶¶ANCOVA model: "change=treatment+baseline+region+baseline IGA", multiple imputation of missing values at Week 16 based on data from placebo group; ¶¶¶ANCOVA model: "change=treatment+baseline+region+baseline IGA", imputation of missing values for patients who have not discontinued IMP before Week 16 based on data from placebo group who have not discontinued treatment prior to Week 16, imputation of missing values for patients who have discontinued IMP before Week 16 based on data from patients with observed data at Week 16 who have discontinued treatment prior to Week 16;¶¶¶¶Worst observation carried forward for all patients who received rescue medication after Week 2, multiple imputation of missing values for patients who did not use rescue medication after Week 2.

AE, adverse event; ANCOVA, analysis of covariance; CDLQI, Children's Dermatology Life Quality Index; CI, confidence interval; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; IMP, investigational medicinal product; LOCF, last observation carried forward; NRS, Numeric Rating Scale; Q2W, every 2 weeks; SCORAD, SCoring Atopic Dermatitis; SE, standard error

eTable 6. Safety outcomes in the maintenance treatment phase

n (%)	Week 16 placebo Q2W responders	Week 16 tralokinumab 150 mg Q2W responders		Week 16 tralokinumab 300 mg Q2W responders	
	Placebo Q2W (n=6)	Tralo 150 mg Q2W (n=12)	Tralo 150 mg Q4W (n=14)	Tralo 300 mg Q2W (n=11)	Tralo 300 mg Q4W (n=13)
AEs (patients with ≥1)	4 (66.7)	7 (58.3)	8 (57.1)	7 (63.6)	6 (46.2)
SAEs (patients with ≥1)	0	0	0	0	0
Severity					
Mild	1 (16.7)	4 (33.3)	5 (35.7)	4 (36.4)	3 (23.1)
Moderate	3 (50.0)	6 (50.0)	4 (28.6)	6 (54.5)	3 (23.1)
Severe	0	0	0	1 (9.1)	0
Related to IMP	1 (16.7)	3 (25.0)	3 (21.4)	2 (18.2)	2 (15.4)
Leading to withdrawal	0	0	0	0	0
Adverse events (≥5% in any group)					
Viral URTI	0	1 (8.3)	1 (7.1)	2 (18.2)	1 (7.7)
URTI	0	1 (8.3)	1 (7.1)	2 (18.2)	0
Dermatitis atopic	1 (16.7)	1 (8.3)	2 (14.3)	0	0
Acne	0	1 (8.3)	1 (7.1)	0	0
Fatigue	0	0	0	1 (9.1)	0
Conjunctivitis allergic	0	1 (8.3)	1 (7.1)	0	0
AESI: eye disorders					
Conjunctivitis allergic	0	1 (8.3)	1 (7.1)	0	0
Conjunctivitis	0	0	0	0	1 (7.7)
Keratitis	0	0	0	0	0
AESI: eczema herpeticum	0	0	0	0	0

AESI: malignancies	0	0	0	0	0
AESI: skin infections requiring systemic treatment	1 (16.7)	0	0	0	0
Injection site reactions*	0	0	0	0	1 (7.7)

*Includes injection site pain, swelling, and other injection site reactions

AE, adverse event; AESI, adverse event of special interest; IMP, investigational medicinal product; Q2/4W, every 2/4 weeks; SAE, serious adverse event; URTI, upper respiratory tract infection

eTable 7. Safety outcomes in the open-label treatment phase

n (%)	Tralokinumab 300 mg Q2W (n=234)
Adverse events (patients with ≥1)	158 (67.5)
Serious adverse events* (patients with ≥1)	7 (3.0)
Severity	
Mild	122 (52.1)
Moderate	82 (35.0)
Severe	4 (1.7)
Related to IMP	65 (27.8)
Leading to withdrawal	2 (0.9)
Adverse events (≥5%)	
Viral URTI	44 (18.8)
URTI	25 (10.7)
Dermatitis atopic	19 (8.1)
Headache	12 (5.1)
AESI: eye disorders	
Conjunctivitis bacterial	3 (1.3)
Conjunctivitis allergic	4 (1.7)
Conjunctivitis	4 (1.7)
Keratitis	1 (0.4)
AESI: eczema herpeticum	0
AESI: malignancies	0
AESI: skin infections requiring systemic treatment	7 (3.0)
Injection site reactions†	15 (6.4)

*Serious adverse events were anorexia nervosa (n=1), obsessive-compulsive disorder (n=1), suicidal ideation (n=1), gastritis (n=1), anaphylactic reaction (n=1), appendicitis perforated (n=1), and concussion (n=1); †Includes injection site pain, swelling, and other injection site reactions

AESI, adverse event of special interest; IMP, investigational medicinal product; Q2W, every 2 weeks; URTI, upper respiratory tract infection

eTable 8. Primary endpoint at Week 16 in all dosed patients, including nine patients from two sites with GCP non-compliance

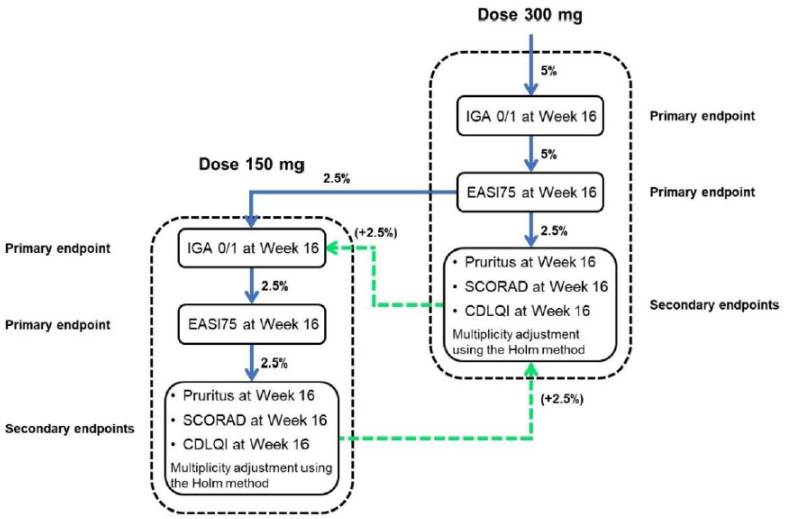
	Placebo (n=99)	Tralokinumab 150 mg Q2W (n=99)		Tralokinumab 300 mg Q2W (n=100)	
			Diff vs placebo** (95% CI)		Diff vs placebo** (95% CI)
Primary endpoints, responders* n (%)					
IGA 0/1 at Week 16	4 (4.0)	21 (21.2)	17.4 (8.5–26.4), *P<0.001*	20 (20.0)	16.4 (7.8–25.1), *P<0.001*
EASI 75 at Week 16	7 (7.1)	28 (28.3)	21.5 (11.5–31.6), *P<0.001*	30 (30.0)	23.5 (13.4–33.5), *P<0.001*

*Patients who received rescue medication after Week 2 were considered non-responders; patients with missing data were imputed as non-responders; **Mantel-Haenszel risk difference compared to placebo, stratified by region and baseline IGA; p values calculated by Cochran-Mantel-Haenszel test, stratified by region and baseline IGA

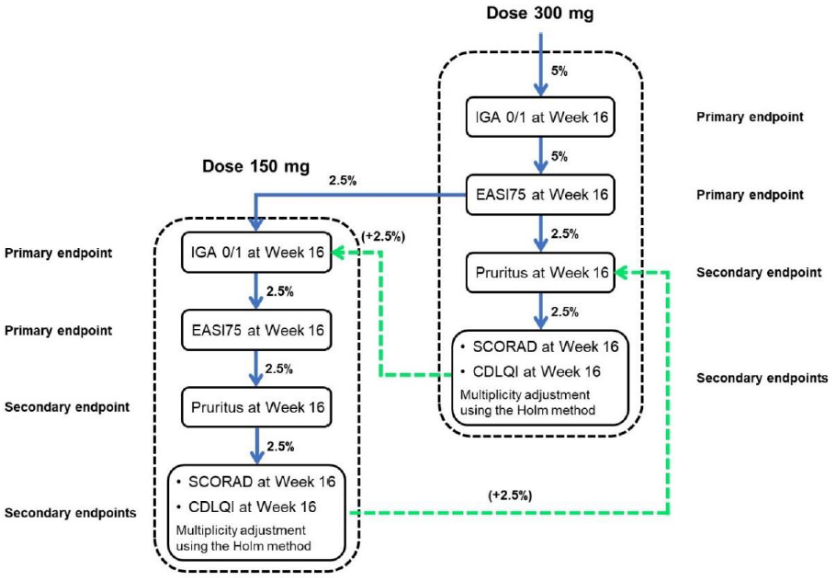
CI, confidence interval; EASI, Eczema Area and Severity Index; GCP, Good Clinical Practice; IGA, Investigator's Global Assessment; Q2W, every 2 weeks

eFigure 1. Testing hierarchy used for the primary and secondary endpoints

Global (non-US; according to protocol)



US (modified)

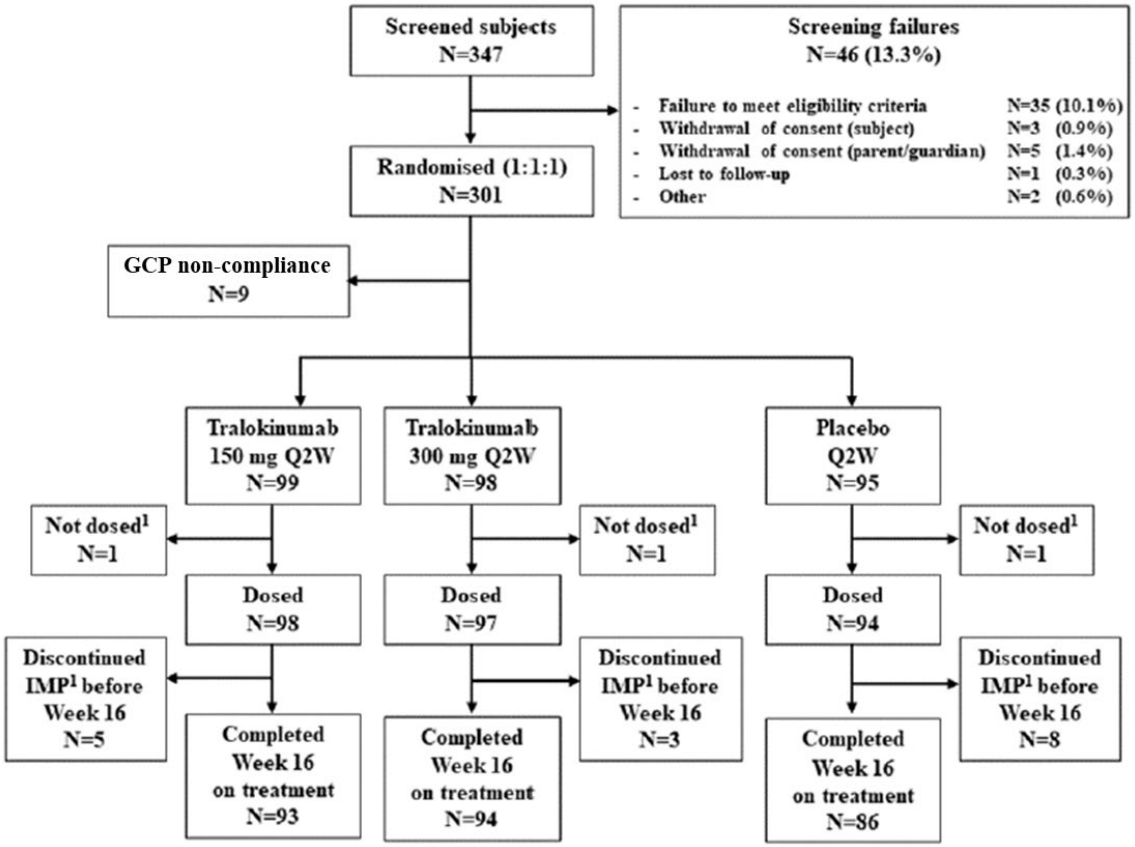


To control the overall type 1 error rate, the primary analysis of the primary estimands (primary and confirmatory secondary endpoints) followed the global testing procedures indicated in the global testing hierarchy (a separate US testing hierarchy was introduced after a request from the FDA); the hypothesis relating to a specific endpoint could not be rejected unless all hypotheses relating to earlier endpoints in the hierarchy were also rejected (numbers in parentheses indicate significance levels that have been passed on from rejected hypotheses for the other tralokinumab dose level). In the global testing procedure, IGA 0/1 at Week 16 (tralokinumab 300 mg vs placebo) was evaluated at 5% significance; if statistically significant, EASI 75 at Week 16 was evaluated at 5% significance. If both primary endpoints were statistically significant, the significance level was split evenly (i.e., 2.5% significance each) between (1) the analyses of the three secondary endpoints (tralokinumab 300 mg vs placebo) and (2) IGA 0/1 at Week 16 for tralokinumab 150 mg vs placebo. If IGA 0/1 at Week 16 (tralokinumab 150 mg vs placebo) was statistically significant, EASI 75 at Week 16 was also evaluated at 2.5% significance. If both primary endpoints were statistically significant, then three secondary endpoints were evaluated at 2.5% significance. The evaluation of the three secondary endpoints (both tralokinumab doses) used the Holm-Bonferroni method for three ordered p-values at 2.5% significance to adjust for multiplicity. If the tests were statistically significant for all three secondary endpoints (300 mg dose), 2.5% significance could be passed on to testing of IGA 0/1 and all subsequent endpoints for the 150 mg dose. Similarly, if all tests were statistically significant at 2.5% for 150 mg dose, 2.5% significance could be passed on for testing of the secondary endpoints for the 300 mg dose. For the US testing hierarchy, this was as per the global testing hierarchy except that for both tralokinumab doses, Adolescent Worst Pruritus at Week 16 was tested independently from the other secondary endpoints, then subsequent testing carried out as indicated.

CDLQI, Children's Dermatology Life Quality Index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; SCORAD, SCORing Atopic Dermatitis

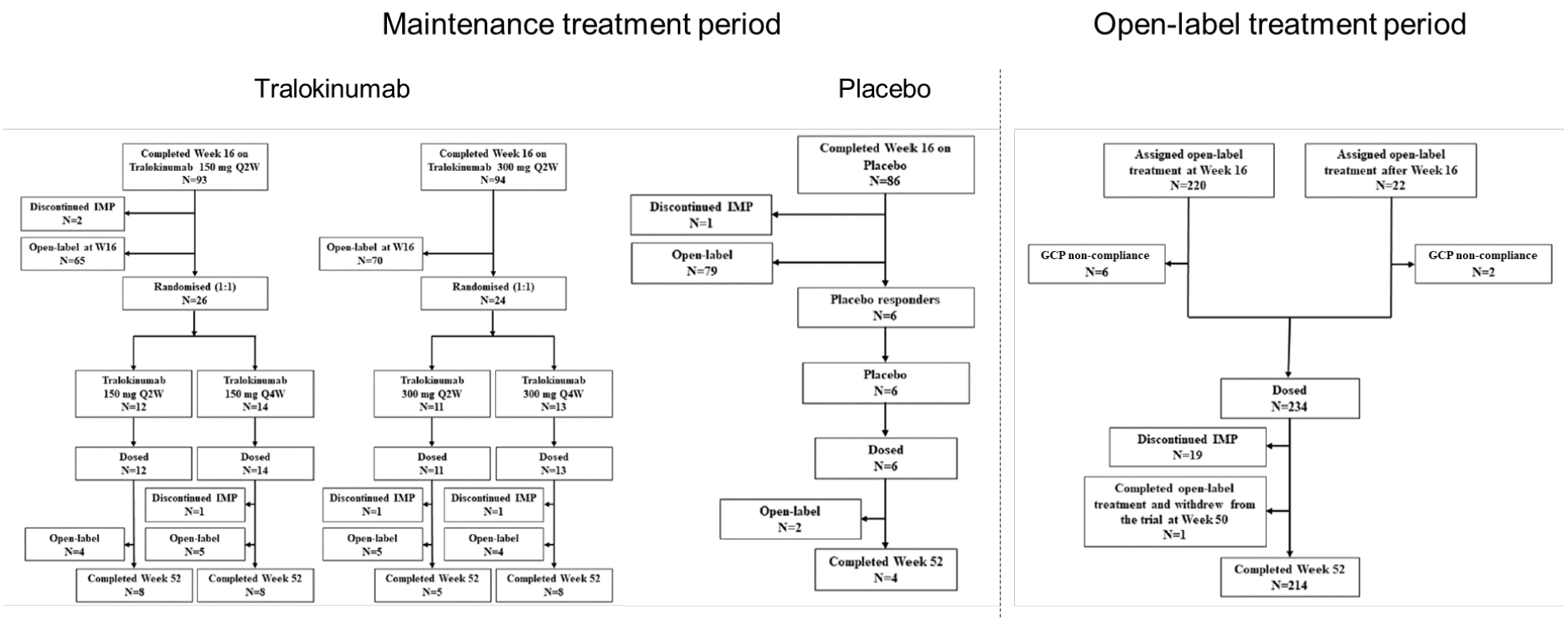
eFigure 2. Patient disposition

(A)



1) Withdrew from the trial prior to first dosing

(B)

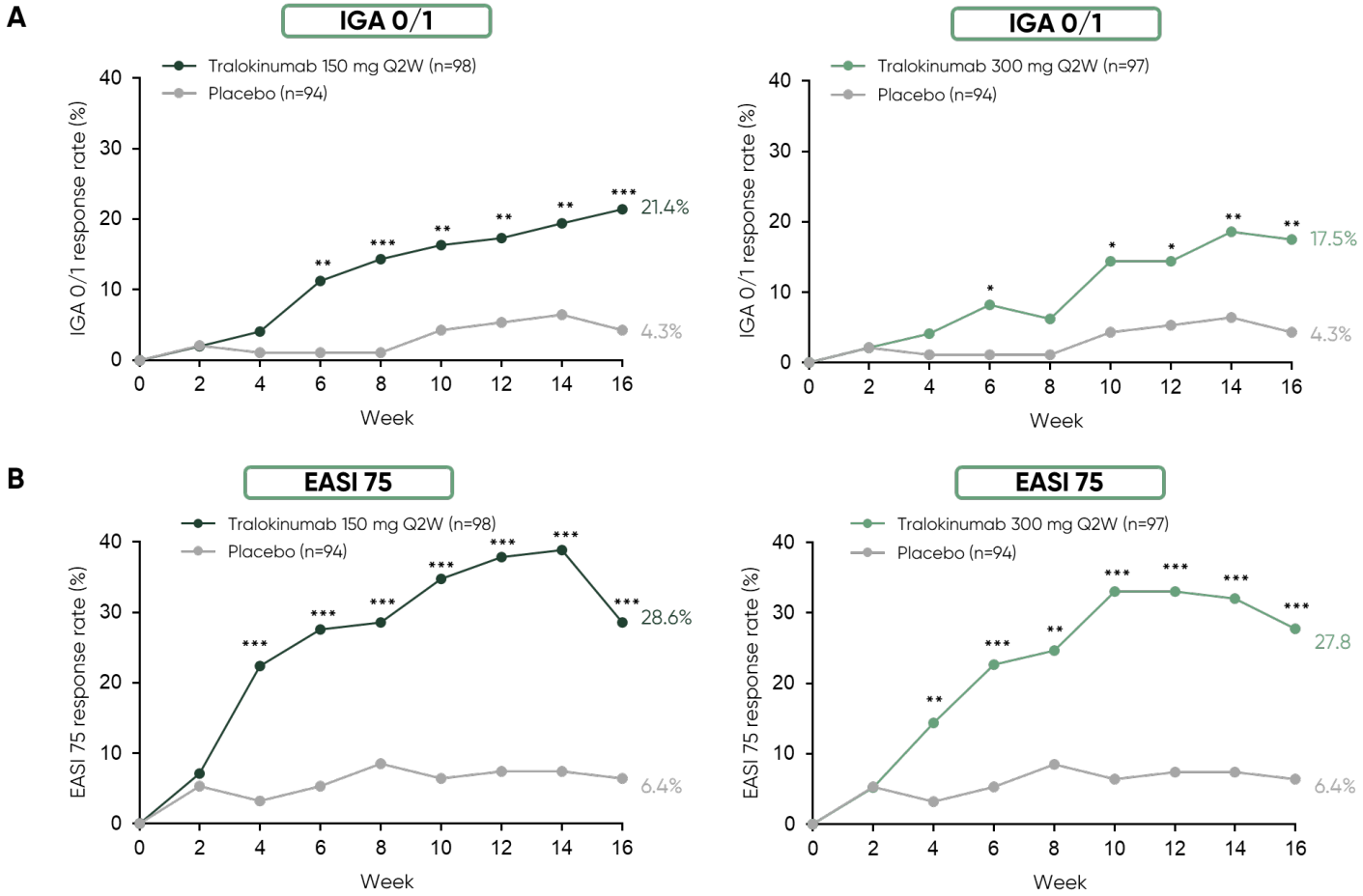


(A) Patient disposition in the initial treatment period and (B) the maintenance and open-label treatment periods

Patients at two sites were excluded from the FAS due to GCP non-compliance reasons. Reasons for permanent discontinuation (initial treatment period) were: tralokinumab 150 mg Q2W, AEs (n=2), withdrawal by patient (n=2), withdrawal by parent/guardian (n=1); tralokinumab 300 mg Q2W, withdrawal by parent/guardian (n=2), other (n=1); placebo, lost to follow-up (n=2), withdrawal by parent/guardian (n=3), lack of efficacy (n=1), other (n=2). Reasons for permanent discontinuation (maintenance treatment period) were: tralokinumab 150 mg Q4W; withdrawal by parent/guardian (n=1); tralokinumab 300 mg Q2W, withdrawal by patient (n=1). Reasons for permanent discontinuation (open-label treatment period) were: AEs (n=2), lost to follow-up (n=1), withdrawal by patient (n=6), withdrawal by parent/guardian (n=1), lack of efficacy (n=8), and other reason (n=1).

AE; adverse event; FAS, full analysis set; GCP, Good Clinical Practice; IMP, investigational medicinal product; Q2/4W, every 2/4 weeks

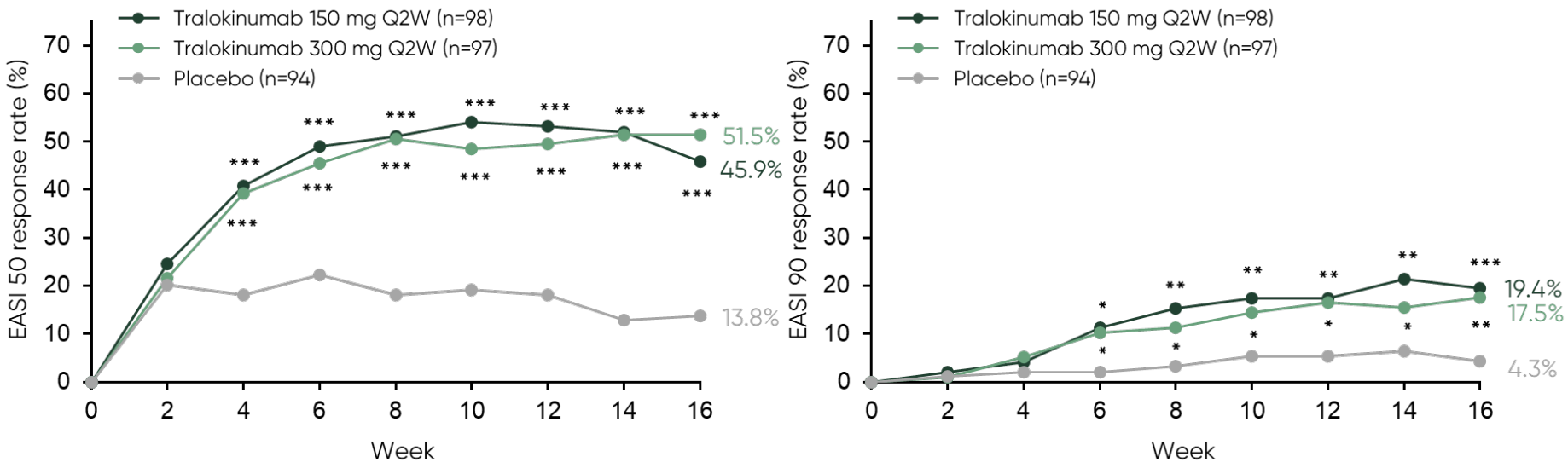
eFigure 3. IGA0/1 and EASI 75 up to Week 16 by individual tralokinumab arm (150 or 300 mg Q2W) vs placebo



(A) IGA 0/1 response rate and (B) EASI 75 by visit up to Week 16 of the initial treatment period in the full analysis set (primary endpoints), by individual tralokinumab dose vs placebo. Patients who received rescue medication after Week 2 were considered non-responders. Patients with missing data were imputed as non-responders *P<0.05 vs placebo; ** P<0.01 vs placebo; *** P<0.001 vs placebo

EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; Q2W, every 2 weeks

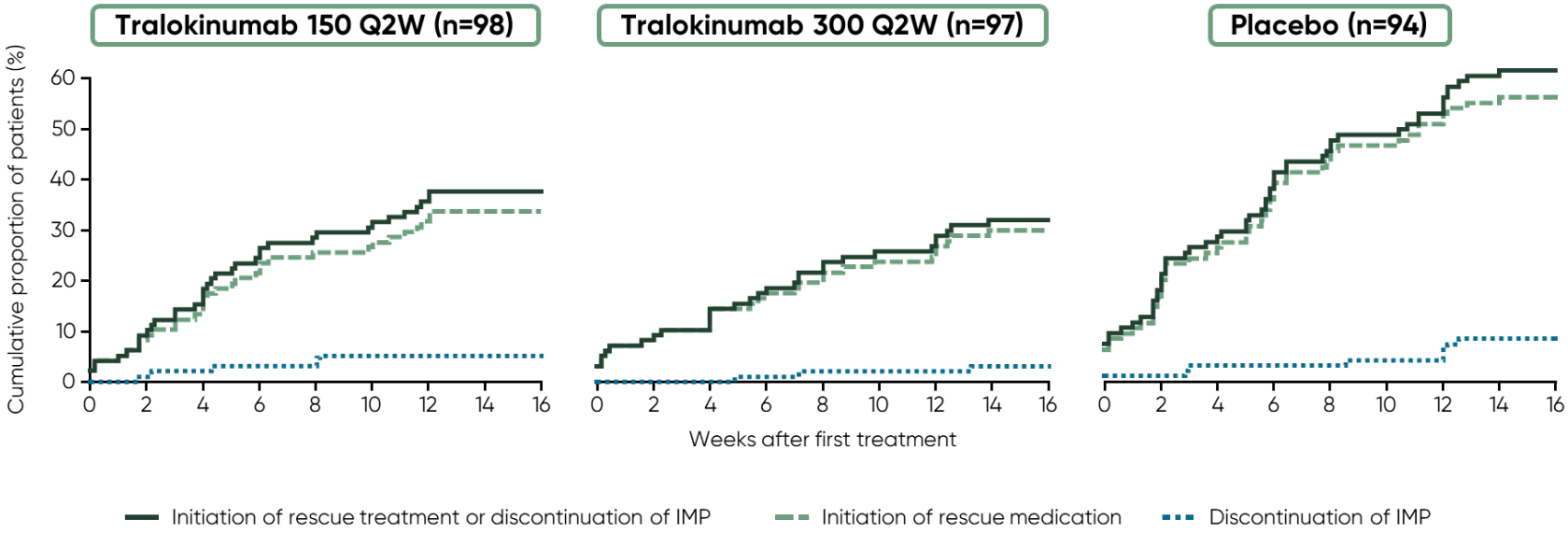
eFigure 4. Achievement of EASI 50 or EASI 90 up to Week 16 (initial treatment period), full analysis set



(A) EASI 50 and (B) EASI 90 response rate by visit up to Week 16 of the initial treatment period in the full analysis set. Patients who received rescue medication after Week 2 were considered non-responders. Patients with missing data were imputed as non-responders. EASI 50 and EASI 90 are defined as patients with ≥50% or ≥90% improvement in EASI, respectively. * *P*<0.05 vs placebo; ** *P*<0.01 vs placebo; *** *P*<0.001 vs placebo.

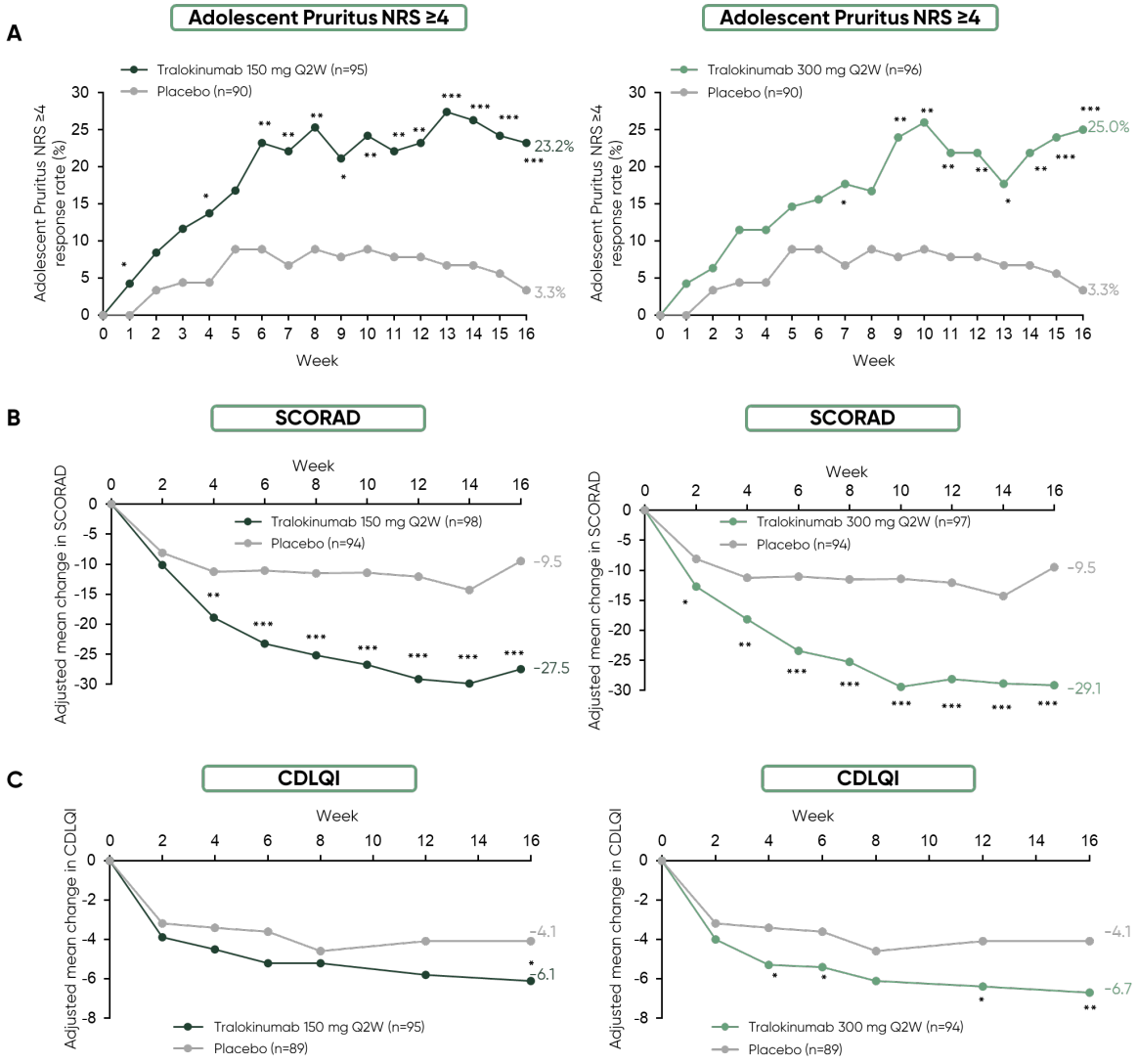
EASI, Eczema Area and Severity Index; Q2W, every 2 weeks

eFigure 5. Initiation of rescue medication and permanent discontinuation of IMP before or at Week 16, full analysis set



IMP, investigational medicinal product; Q2W, every 2 weeks

eFigure 6. Reduction in Adolescent Worst Pruritus NRS ≥4, change in SCORAD, and change in CDLQI from baseline to Week 16 by individual tralokinumab arm (150 or 300 mg Q2W) vs placebo

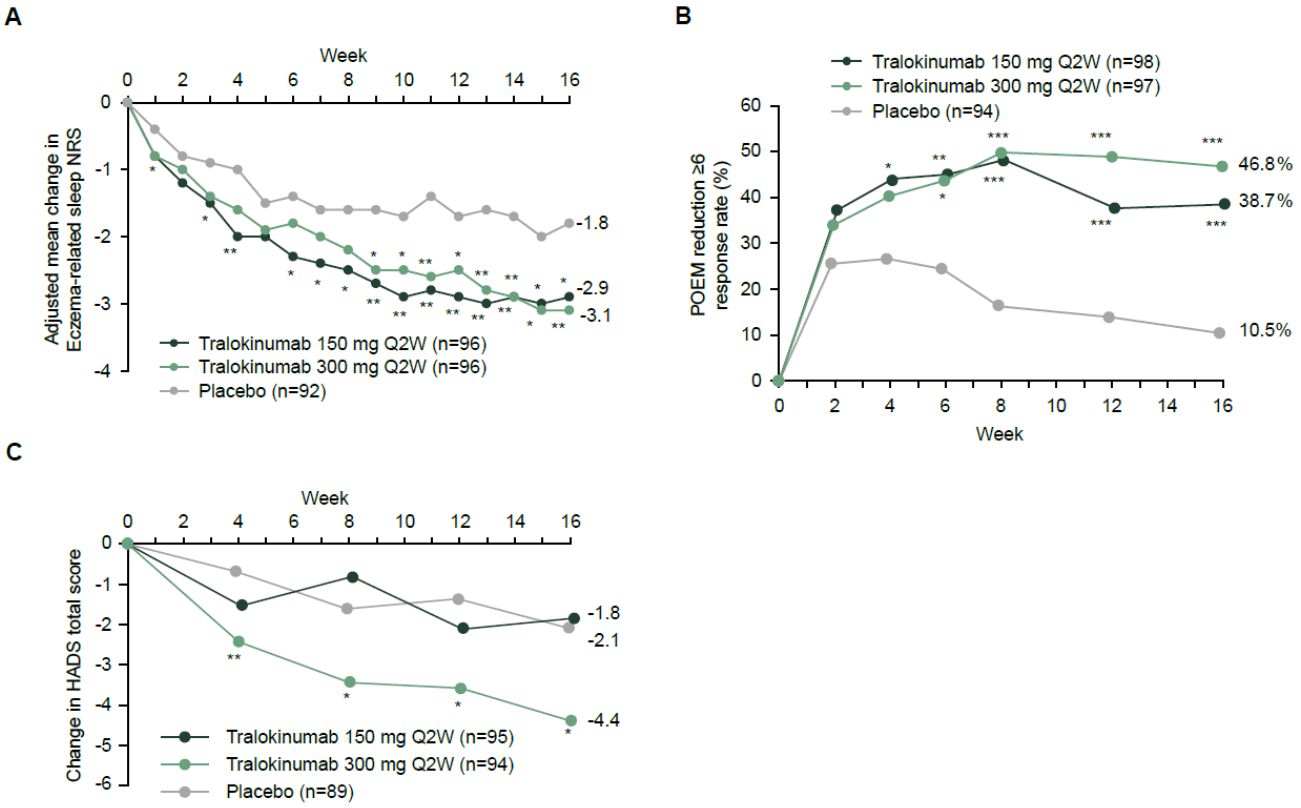


(A) Reduction from baseline in weekly average of worst daily pruritus NRS ≥4 by visit; (B) Change from baseline in SCORAD by visit; and (C) Change from baseline in CDLQI by visit in the initial treatment period up to Week 16 by individual tralokinumab dose vs placebo. For binary endpoints, patients who received rescue medication after Week 2 were considered non-responders and those with missing values at Week 16 were imputed as non-responders. For continuous endpoints, data collected after permanent discontinuation of tralokinumab or initiation of rescue medication after Week 2 were not included. In case of no post-baseline assessments, the Week 2 change was imputed as 0.

*P<0.05 vs placebo; ** P<0.01 vs placebo; ***P<0.001 vs placebo

CDLQI, Children's Dermatology Life Quality Index; NRS, Numeric Rating Scale; Q2W, every 2 weeks; SCORAD, SCORing Atopic Dermatitis

eFigure 7. Tralokinumab efficacy vs placebo across additional patient-reported outcomes up to Week 16 (initial treatment period), full analysis set

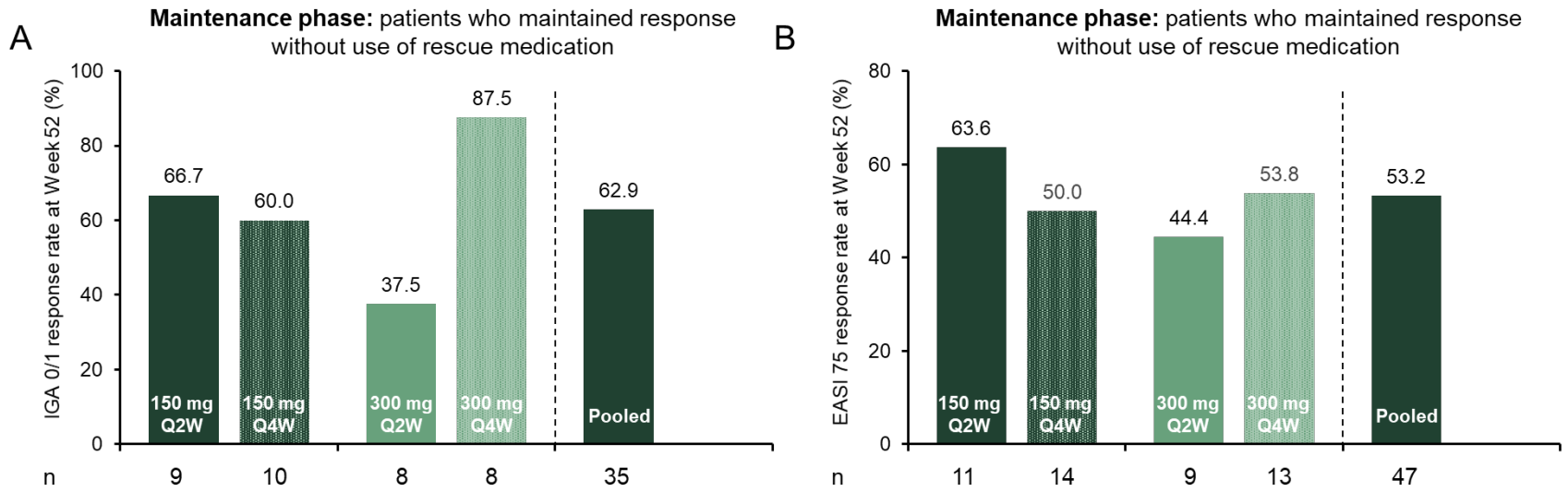


(A) Eczema-related sleep NRS change from baseline; (B) Proportion of patients with a ≥6-point reduction in POEM from baseline; and (C) HADS change from baseline. For binary endpoints, patients who received rescue medication after Week 2 were considered non-responders and those with missing values at Week 16 were imputed as non-responders. For continuous endpoints, data collected after permanent discontinuation of tralokinumab or initiation of rescue medication after Week 2 were not included.

*P<0.05 vs placebo; **P<0.01 vs placebo; ***P<0.001 vs placebo

HADS, Hospital Anxiety and Depression Scale; POEM, Patient-Oriented Eczema Measure; NRS, Numeric Rating Scale; Q2W, every 2 weeks

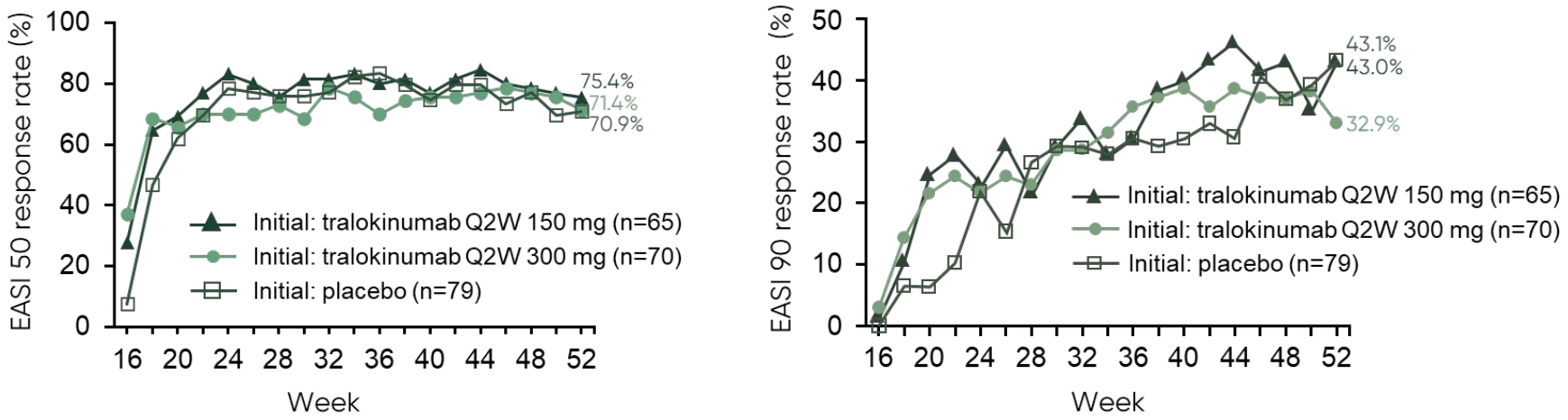
eFigure 8. Tralokinumab efficacy at Week 52 of the maintenance phase



Patients initially treated with tralokinumab who achieved (A) IGA 0/1 and (B) EASI 75 at Week 16 without rescue medication (maintenance analysis set). In the maintenance phase, patients who received rescue medication after Week 2 and/or were permanently discontinued from treatment/transferred to open-label treatment were considered non-responders. Patients receiving Q4W maintenance could not be switched to Q2W maintenance. Twenty patients from the maintenance phase were considered non-responders at Week 52 and were transferred to open-label; they were not included in the open-label analyses.

EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; Q2/4W, every 2/4 weeks

eFigure 9. Achievement of EASI 50 or EASI 90 by Week 52 of the open-label treatment period, open-label analysis set

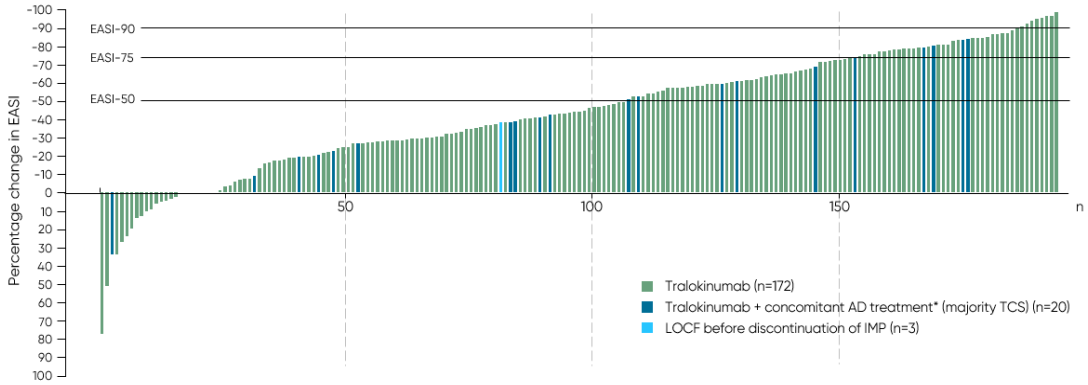


(A) EASI 50 and (B) EASI 90 at Week 16 through Week 52 in the open-label treatment period. Patients in the open-label treatment arm could use weak to moderate strength TCS and/or TCI as needed on lesional skin at the investigator's discretion. Patients who received high potency TCS or systemic treatment during the open-label phase were considered non-responders. Patients with missing data were imputed as non-responders. EASI 50 and EASI 90 are defined as patients with ≥50% or ≥90% improvement in EASI, respectively.

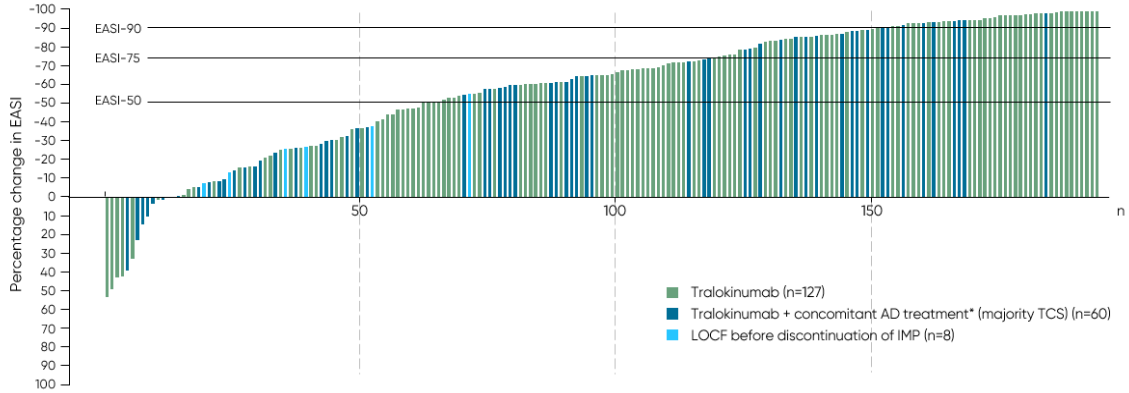
EASI, Eczema Area and Severity Index; Q2W, every 2 weeks; TCI, topical calcineurin inhibitor; TCS, topical corticosteroids

eFigure 10. Individual patient change from baseline in EASI over time (Week 4, 16, and 52)

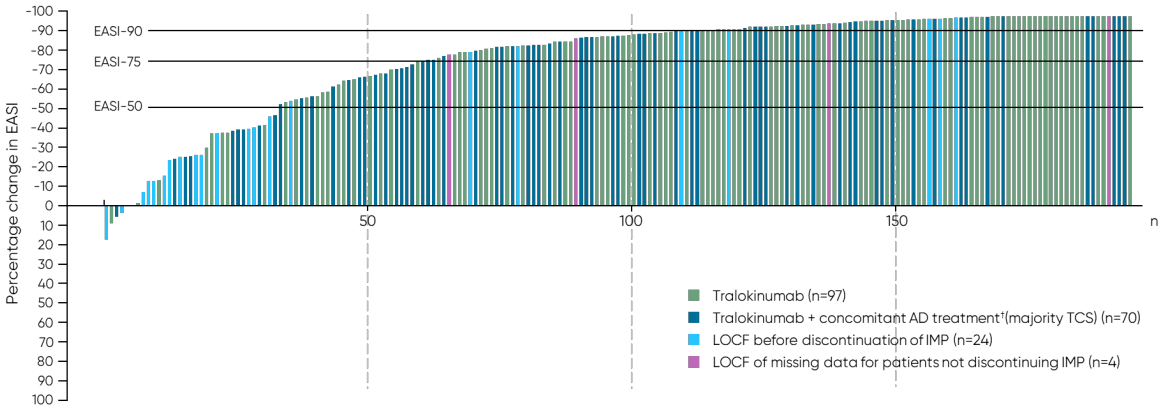
(A)



(B)



(C)



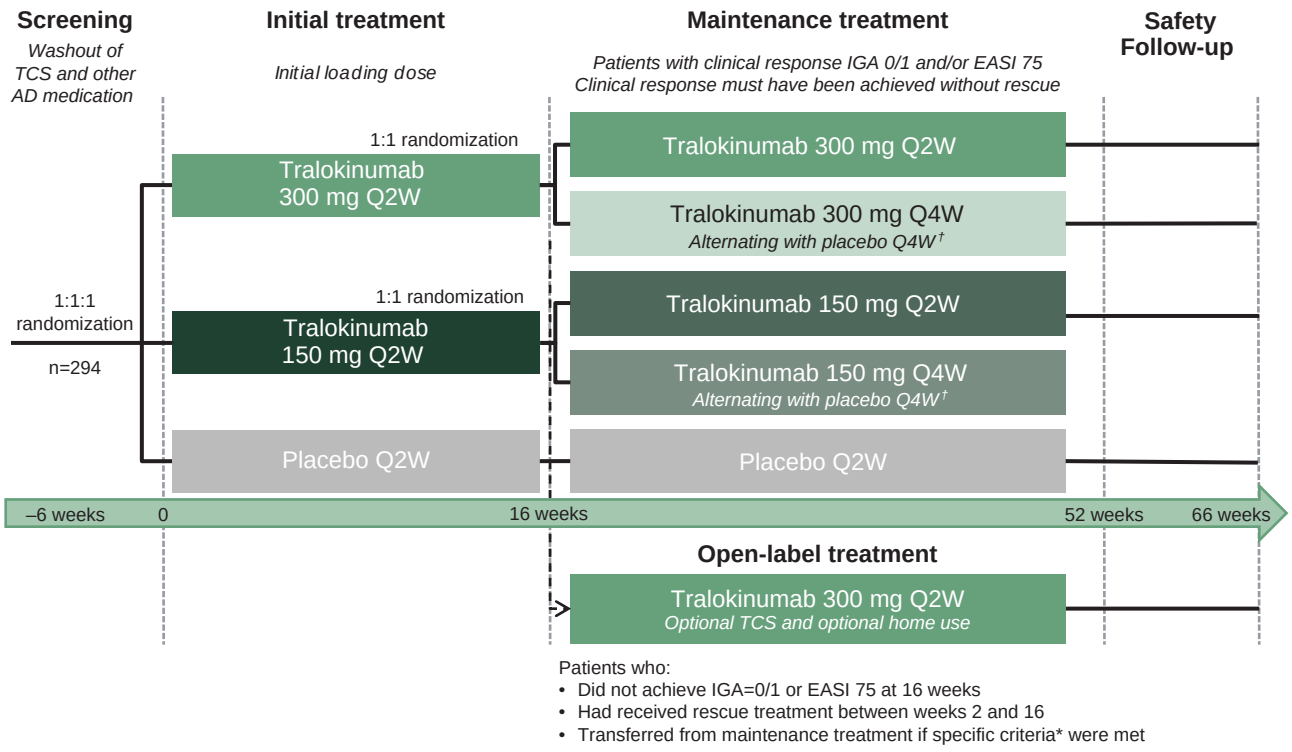
Percent change in EASI from baseline per patient initially treated with tralokinumab 150 mg or 300 mg Q2W (n=195) at (A) Week 4*, (B) Week 16*, and (C) Week 52†.

*Concomitant AD treatments included TCI, TCS, or systemic treatment (>80% was TCS in the initial period). LOCF used for patients discontinuing IMP in initial period. Some patients used concomitant AD treatment before discontinuation. Percentage change = 0 is shown for patients without post-baseline EASI values before discontinuation of IMP.

[†]Concomitant AD treatments included TCI, TCS, or systemic treatment and were defined as rescue treatments in initial and maintenance phases (>70% used were TCS in the maintenance and open-label periods). Concomitant AD treatment use stopped in the initial treatment period was ignored (i.e. concomitant AD treatment use in the initial period did not affect Week 52 response). LOCF used for patients discontinuing IMP. Some patients used concomitant AD treatment before discontinuation. LOCF from initial period was used if patient did not enter maintenance or open-label period. Percentage change = 0 is shown for patients without post-baseline EASI values before discontinuation of IMP.

AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IMP, investigational medicinal product; LOCF, last observation carried forward; Q2W, every 2 weeks; TCI, topical calcineurin inhibitors; TCS, topical corticosteroids

eFigure 11. Study design



*Transfer criteria were: patients with IGA = 0 at Week 16 who over three consecutive visits had IGA≥2 and did not achieve EASI 75; patients with IGA = 1 at Week 16 who over three consecutive visits had IGA≥3 and did not achieve EASI 75; patients with IGA>1 at Week 16 who over three consecutive visits did not achieve EASI 75; and patients who received rescue treatment during the maintenance phase. †To maintain blinding, patients re-randomized to tralokinumab Q4W also received Q4W placebo, such that alternating doses of tralokinumab and placebo were administered every two weeks.

AD, atopic dermatitis; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment. Q2/4W, once every 2/4 weeks; TCS, topical corticosteroids.