SUPPLEMENTARY MATERIAL

A Durability Index for Atopic Dermatitis: Indirect Comparison of Lebrikizumab, Dupilumab, and Tralokinumab in Maintaining Efficacy Under Variable Treatment Adherence

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Supplementary Methods

Estimands

The outcomes of interest are EASI 75 and IGA 0/1. For each of these we have the following estimand: The proportion of patients administered active treatment in the induction phase who achieve the outcome at week 16 *and* maintain the same outcome at week 52, depending on maintenance treatment allocation (i.e., continued treatment or treatment withdrawal).

Baseline population assumption

As the objective is to conduct population-adjusted indirect comparison for the Durability Index (DI) between lebrikizumab (ADvocate1&2), dupilumab (SOLO 1&2 + SOLO CONTINUE), and tralokinumab (ECZTRA 1&2), the comparable baseline characteristics must be available from all three sets of trials.

For dupilumab, reporting on the SOLO CONTINUE trial provides week-16 baseline characteristics for re-randomized participants and reporting on the SOLO trials provide week-0 baseline for the induction treatment arms. Week-0 baseline characteristics are not reported for re-randomized participants. For tralokinumab, a limited subset of week-0 characteristics is reported for re-randomized study participants, in addition to week-0 baseline characteristics for the induction treatment arms.

Consequently, the only trial populations for which comparable baseline characteristics are available both for dupilumab and tralokinumab apply to the week-0 induction populations.

The active induction treatment arms in the three sets of trials are suited to provide population-adjusted estimates of week-16 response. However, as participants were re-randomization at week 16 conditional on treatment response, it is likely that re-randomized participants deviate from the induction treatment arms in terms of their distributions of baseline characteristics. To allow adjustments using information on the distributions of week-0 baseline characteristics in the estimation of maintenance of response at week 52 depending on

maintenance treatment allocation, we employed hypothetical re-randomization of non-responders to the maintenance treatment arms to recreate the expected distribution of characteristics at week 0.

We have baseline characteristics for the active treatment arms which are suited for the estimation of response at week 16. However, for the week 52 maintenance of response, we need to compare the re-randomized treatment and withdrawal arms, for whom the baseline distribution cannot be assumed.

To ensure that the re-randomized groups are unbiased estimates of the initial population in terms of the baseline characteristics, we add non-responders with assigned weights equivalent to the re-randomization probabilities.

The recreation of the underlying characteristic distributions can be shown as follows. Let *P* be a population with baseline *f* denoting the distribution of characteristics. Let *S* and *S'* be subsets of *P*, such that *P* = *S* ∪ *S'*

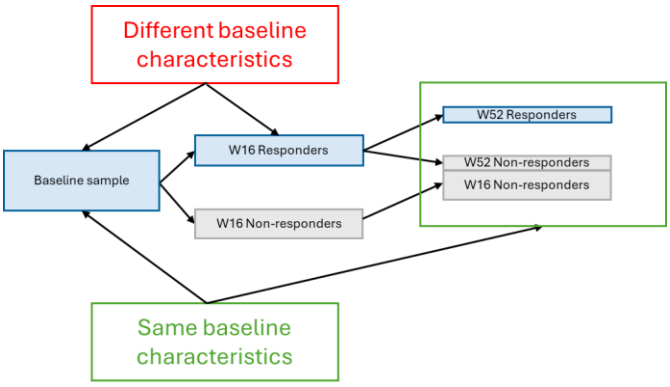
1. A random subsample *S* of a population *P* is an unbiased estimate of the distribution of any characteristics of *P.* (We will not prove this in this context, as it is an axiomatic requirement for RCTs, etc.)
2. If all participants in *P* have the same probability of ending up in *S*, *S* is an unbiased estimate of *P.*
3. Patients in *P* can become responders (*R*) or non-responders (*R'*). $f_R \neq f'_R \; and \; f_R \neq f_p$
4. Patients in *R* are randomized to A, B and C using probabilities $P_A + P_b + P_c = 1$. A, B, and C are now unbiased subsamples of *R*, but not of *P*
5. Let non-responders in *R'* be re-randomized according to the same sampling probabilities, such that *A', B',* and *C'* are unbiased subsamples of *R*'
6. Let us now create populations $A_t = A \cup A'$, $B_t = B \cup B'$ and $C_t = C \cup C'$

7. Participants in *P* can now either become responders, after which they have probability P_A of becoming members of A_t, or they can become non-responders after which they have probability P_A of becoming members of A_t. Regardless of the selection process resulting in participants becoming members of *R* or *R',* they have the same probability of becoming members of the merged re-randomized populations.
8. A_t, B_t, and C_t are unbiased subsamples of *P.*

In the logic above, non-responders were re-randomized. However, if we accept that weighted reassignment using weight equal to the resampling probabilities will produce random subsamples of the population from which the patients derive, i.e. *R',* it follows that randomization of *R* merged with weighted reassignment of *R'* produces unbiased subsamples of *P*, with less stochasticity.

Please note that while this recreation procedure of baseline distributions will hold generally, the resulting pseudo-re-randomized groups will only be meaningful for analysis under the condition that the outcome of interest is binary and that all non-responders at week 16 be handled as failures for week 52.

Using this procedure, we get the following, where the boxes on the right-hand side reflect the pseudo-re-randomized populations that are unbiased estimates of the distributions from the active induction populations.



The pseudo-re-randomization procedure

Simulated Treatment Comparison (STC)

Outcome estimates from the Advocate individual patient data (IPD) were transported to alternative populations defined by mean values along the selected covariates by way of simulated treatment comparison (STC), in line with the procedures described in NICE DSU TSD 18 on population-adjusted indirect comparisons [1, 2].

Simulated treatment comparison employs logistic (or relative risk) regression with a set of covariates assumed to function as effect modifiers and/or prognostic factors. The objective is to adjust estimates to the corresponding mean values reported for the same covariates in the comparator population.

Let *x* be a matrix of covariates assumed to function as prognostic factors, and x_{em} be a corresponding matrix of the subset of *x* assumed to function as effect modifiers. Let x_c be a vector of the corresponding reported mean values for the covariates of interest in the comparison population. We calculate a centered matrix x'

$$x' = x - x_c$$

A general STC regression model would be on the form

$$logit(Y) = \alpha + t \cdot \beta_t + x' \cdot \beta_x + tx_{em}{}' \cdot \beta_{tx_{em}} + \varepsilon$$

Please note that the estimated coefficients β_x and $\beta_{tx_{em}}$ will be the same regardless of the population we adjust to, as centering x' and x_{em}' on a different population will effectively introduce a different linear offset, which would only impact α and β_t

Setting x' to 0, $\alpha + \beta_t$ will take an estimate of the log-odds given t=1 at $x = x_c$, i.e., the estimated response rate given treatment transported to a hypothetical population described by x_c, i.e., no deviation from the covariate means reported for the comparator population.

α alone will take an estimate of the log-odds given t=0 $x = x_c$, i.e., the estimated response rate given no treatment (withdrawal) transported to the population described by x_c.

Uncertainty for the estimates is represented in the form of the estimated standard error (SE) for α and βt.

Maintaining natural population distribution in STC

We applied a non-parametric bootstrap procedure to account for uncertainty, taking the following steps:

For each bootstrap iteration, we randomly sampled with replacement from the active induction treatment pooled ADvocate population. Each sample had the same size as the original population. Using the sampled population, we estimated the STC models for week 52.

To retain the empirical distribution of covariates, we produced transported absolute outcomes by taking model predictions in the empirical ADvocate population offset such that the mean covariate distribution matched the target population covariate means of interest.

As before, let *x* be the matrix of covariates for matching in the ADvocate population and x_c be the corresponding reported mean values for the covariates of interest in the comparison population. Now, let

$$\bar{x} = \frac{\sum_{i=1}^{n} x_i}{n}$$

The STC linear model is fitted on the centered matrix x'

$$x' = x - x_c$$

Given the STC regression model

$$logit(Y) = \alpha + t \cdot \beta_t + x' \cdot \beta_x + t{x_{em}}' \cdot \beta_{tx_{em}} + \varepsilon$$

Using the resulting model, we predicted values for empirical population offset such that the mean covariate distribution matched x_c, i.e., $x_0 = x' - (\bar{x} - x_c)$.

Here, x_0 is the centered matrix of covariates offset by the the mean difference between the covariates in the index population and the reported means for the target population. As such x_0 has a mean of 0 for each covariate, and a distribution equivalent to the original population.

With x_0, we took, for each bootstrap subsample, the predicted outcomes at week 52.

Handling correlations between covariates

The procedure used to provide transported estimates for comparator populations relies on simulations based on reported marginal statistics for baseline characteristics and reported number of participants and responders. However, the published information on distributions of baseline characteristics from the ECZTRA and SOLO trials does not include the correlations between said variables. While such correlations are not expected to greatly influence transported estimates, some impact can be expected. In the absence of information on the observed correlations in the external trials, we made use of the observed correlations in the ADvocate adult subsample. This was included alongside the reported marginal distribution statistics in the simulation approach by way of copulas, thereby producing simulated data with expected correlations equivalent to those from the ADvocate trial. Parametric bootstrap by way of Copula-based resampling was used to account for uncertainty in the modelling of ECZTRA and SOLO data.

Prognostic factors and effect modifiers

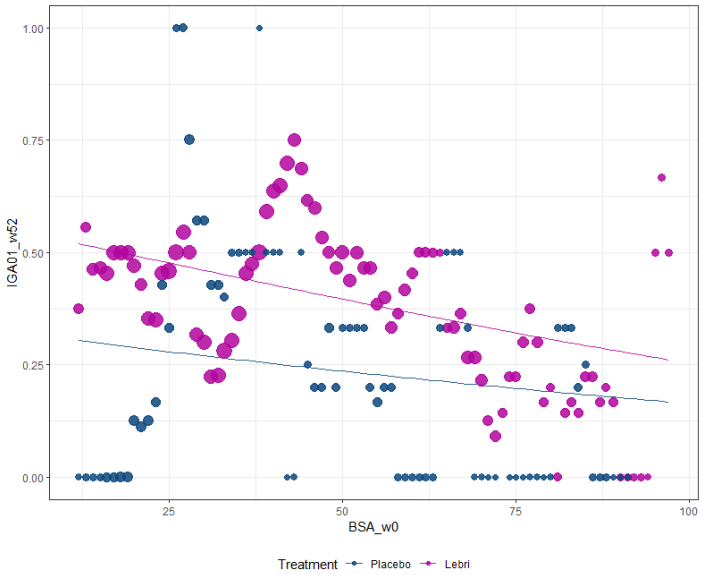
STC relies on adjusting for relevant baseline characteristics. In this study, we utilized a form of unanchored comparison.. Consequently, we relied on covariates functioning both as prognostic factors (PF) and effect modifiers (EM). The subset of variables available as potential candidates for weighting will by necessity be limited by what is reported in terms of aggregate data for the ECZTRA 1&2, the SOLO 1&2 / SOLO CONTINUE, as well as corresponding available IPD from ADvocate trials.

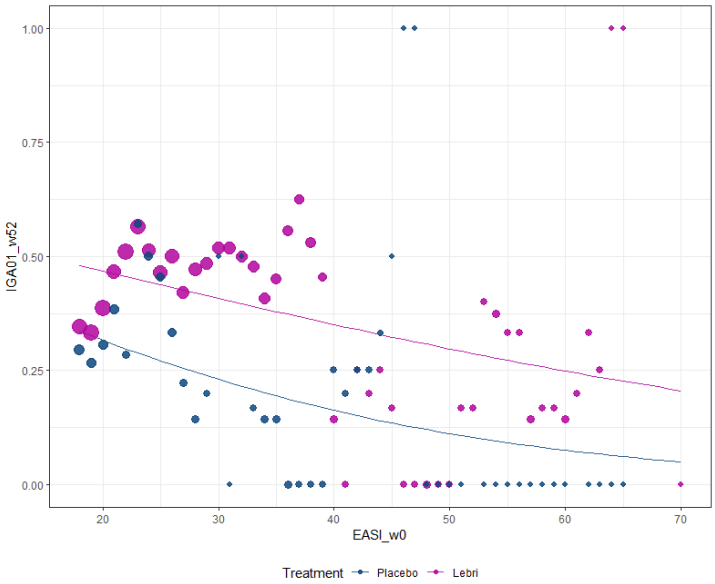
We used empirical analysis of IPD from the ADvocate trials to inform inclusion of effect modifiers. We employed IPD from the ADvocate trials to investigate candidate variables as prognostic factors or effect modifies for end points of interest at weeks 16 and 52.

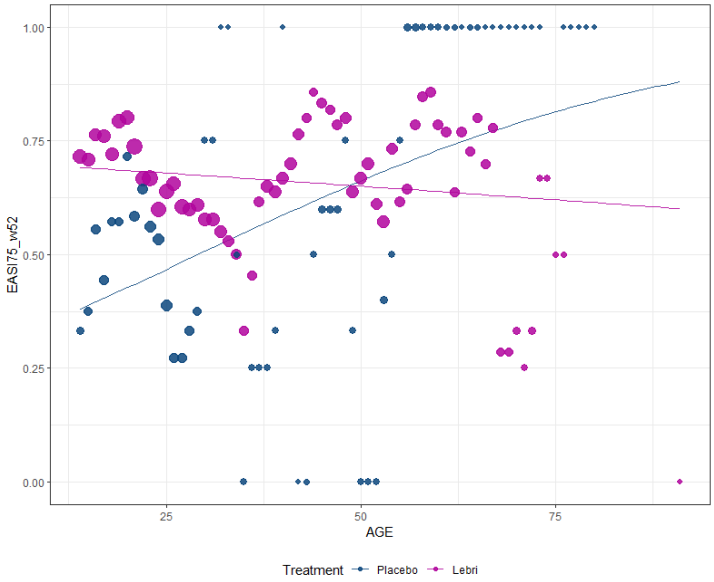
The analyses for which either the predictor coefficient or the predictor × treatment interaction was statistically significant (p-values in bold) are shown in the table below. The empirical and modelled associations between the different statistically significant combinations of outcomes and predictors are shown in the figure below. Based on these analyses, the only apparent effect modifier for week-52 outcomes was patient age, while other covariates functioned as prognostic factors. Consequently, only age was included in the STC models as a maintenance treatment interaction variable, while the other covariates were included only as main effect predictors.

Table: Effect Modifiers and Prognostic Factors.

Outcome	Predictor	Prognostic factors		Effect modifier	
		Coefficient	p-value	Coefficient	p-value
EASI 75 at week 52	Age	0.003	0.732	-0.037	**0.051**
	Male	-0.651	**0.009**	-0.539	0.369
	White	1.16	**<0.001**	-0.08	0.897
	BSA (week 0)	-0.007	0.221	-0.007	0.579
	EASI (week 0)	-0.011	0.312	0.006	0.822
	DURAD	0	0.97	-0.009	0.669
IGA 0/1 at week 52	Age	-0.003	0.727	-0.016	0.409
	Male	-0.381	0.127	-0.001	0.998
	White	1.141	**<0.001**	0.62	0.383
	BSA (week 0)	-0.012	**0.034**	-0.004	0.791
	EASI (week 0)	-0.028	**0.016**	0.019	0.584
	DURAD	0.003	0.737	0.005	0.81







Effect Modifiers and Prognostic Factors

The plots display the empirical (dots) and modeled (lines) associations between the different statistically significant combinations of outcomes and predictors. The dots represent moving averages for scores of 5 on the BSA and EASI baseline. The predictive lines for each treatment group show the directional trends between predictors and outcomes, while the distribution and size of data points indicated the density of the underlying data. Differences in elevation between the lines indicate treatment effect, the overall angle indicates prognostic effect, while difference in angle indicates interaction, i.e. effect modification.

References

1. Phillippo D, Ades T, Dias S, et al. NICE DSU technical support document 18: methods for population-adjusted indirect comparisons in submissions to NICE. 2016.

2. Phillippo DM, Ades AE, Dias S, et al. Methods for population-adjusted indirect comparisons in health technology appraisal. Medical decision making. 2018;38(2):200-11.

Supplementary Results

Table S1: Week-52 ORs for lebrikizumab vs dupilumab at maintenance treatment adherence rates from 100% to 0% at 5-percentage-point intervals

	IGA 0/1			EASI 75		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	1.2	0.8	2.0	1.0	0.7	1.4
98%				1.0	0.7	1.4
95%	1.3	0.8	2.0	1.0	0.7	1.5
90%	1.4	0.9	2.1	1.1	0.8	1.5
85%	1.4	0.9	2.2	1.1	0.8	1.6
80%	1.5	1.0	2.4	1.2	0.9	1.7
78%	**1.5**	**1.0**	**2.5**			
75%	1.6	1.0	2.5	1.3	0.9	1.8
70%	1.7	1.1	2.7	1.3	0.9	1.8
65%	1.8	1.1	3.0	1.4	1.0	2.0
63%				**1.4**	**1.0**	**2.0**
60%	1.8	1.1	3.3	1.5	1.0	2.1
55%	1.9	1.2	3.6	1.5	1.1	2.2
50%	2.0	1.2	3.9	1.6	0.1	2.4
45%	2.1	1.2	4.3	1.7	1.1	2.5
40%	2.2	1.2	4.8	1.8	1.2	2.7
35%	2.4	1.3	5.3	1.9	1.2	2.9
30%	2.5	1.3	5.9	2.0	1.2	3.1
25%	2.6	1.3	6.6	2.1	1.3	3.4
20%	2.7	1.3	7.3	2.2	1.3	3.7
15%	2.9	1.3	8.1	2.3	1.3	3.9
10%	3.0	1.3	9.1	2.4	1.4	4.3
5%	3.2	1.3	10.1	2.5	1.4	4.6
0%	3.4	1.3	11.3	2.6	1.4	5.0

Adherence rates corresponding to changes in statistical significance (**bold**) or numeric difference are shown in red.

Abbreviations: EASI 75, 75% reduction from baseline with the Eczema Area and Severity Index; IGA, Investigator's Global Assessment; LB, lower bound of the 95% confidence interval; OR, odds ratio; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; UB, upper bound of the 95% confidence interval

Table S2: Week-52 RDs for lebrikizumab vs dupilumab at maintenance treatment adherence rates from 100% to 0% at 5-percentage-point intervals

	IGA 0/1			EASI 75		
Adherence	**RD**	**95% LB**	**95% UB**	**RD**	**95% LB**	**95% UB**
100%	3.1%	-4.0%	10.3%	-0.4%	-8.7%	7.9%
98%				0.0%	-8.1%	8.1%
95%	3.8%	-2.9%	10.4%	0.7%	-7.2%	8.5%
90%	4.4%	-1.9%	10.6%	1.7%	-5.8%	9.2%
85%	4.9%	-1.0%	10.9%	2.7%	-4.5%	9.9%
80%	5.4%	-0.3%	11.2%	3.7%	-3.3%	10.7%
78%	**5.6%**	**0.0%**	**11.3%**			
75%	5.8%	0.3%	11.5%	4.7%	-2.2%	11.5%
70%	6.2%	0.8%	11.8%	5.6%	-1.2%	12.3%
65%	6.5%	1.2%	12.1%	6.5%	-0.3%	13.2%
63%				**6.8%**	**0.0%**	**13.5%**
60%	6.8%	1.4%	12.4%	7.3%	0.5%	14.1%
55%	7.1%	1.6%	12.7%	8.1%	1.2%	15.0%
50%	7.3%	1.8%	12.9%	8.9%	1.9%	15.9%
45%	7.5%	1.9%	13.2%	9.6%	2.4%	16.8%
40%	7.7%	1.9%	13.4%	10.3%	2.9%	17.7%
35%	7.8%	2.0%	13.6%	11.0%	3.3%	18.5%
30%	7.9%	2.0%	13.8%	11.6%	3.7%	19.4%
25%	8.0%	2.0%	14.0%	12.2%	4.0%	20.2%
20%	8.0%	2.0%	14.2%	12.8%	4.3%	21.0%
15%	8.0%	1.9%	14.4%	13.3%	4.6%	21.8%
10%	8.0%	1.9%	14.5%	13.8%	4.8%	22.5%
5%	8.0%	1.8%	14.7%	14.2%	5.0%	23.2%
0%	8.0%	1.7%	14.8%	14.7%	5.2%	23.9%

Adherence rates corresponding to changes in statistical significance (**bold**) or numeric difference are shown in red.

Abbreviations: EASI 75, 75% reduction from baseline with the Eczema Area and Severity Index; IGA, Investigator's Global Assessment; LB, lower bound of the 95% confidence interval; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; RD, risk difference; UB, upper bound of the 95% confidence interval

Table S3: Week-52 ORs for lebrikizumab vs tralokinumab at maintenance treatment adherence rates from 100% to 0% at 5-percentage-point intervals

	IGA 0/1			EASI 75		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	2.6	1.6	4.2	3.2	2.2	4.8
95%	2.6	1.7	4.1	3.3	2.3	4.8
90%	2.6	1.7	4.1	3.4	2.3	4.9
85%	2.6	1.7	4.0	3.5	2.4	5.0
80%	2.6	1.7	4.0	3.5	2.5	5.1
75%	2.6	1.7	4.0	3.6	2.6	5.2
70%	2.6	1.7	4.0	3.7	2.6	5.3
65%	2.6	1.7	4.0	3.8	2.7	5.5
60%	2.6	1.7	4.1	3.9	2.7	5.7
55%	2.6	1.6	4.2	4.0	2.8	5.9
50%	2.6	1.6	4.2	4.1	2.8	6.2
45%	2.6	1.5	4.3	4.2	2.8	6.5
40%	2.6	1.5	4.5	4.3	2.8	6.8
35%	2.6	1.5	4.6	4.4	2.9	7.1
30%	2.6	1.4	4.8	4.5	2.9	7.5
25%	2.5	1.4	4.9	4.7	2.9	7.9
20%	2.5	1.3	5.1	4.8	2.9	8.3
15%	2.5	1.3	5.3	4.9	2.9	8.8
10%	2.5	1.2	5.5	5.0	2.8	9.3
5%	2.5	1.2	5.7	5.1	2.8	9.8
0%	2.5	1.1	5.9	5.3	2.8	10.4

Abbreviations: EASI 75, 75% reduction from baseline with the Eczema Area and Severity Index; IGA, Investigator's Global Assessment; LB, lower bound of the 95% confidence interval; OR, odds ratio; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; UB, upper bound of the 95% confidence interval

Table S4: Week-52 RDs for lebrikizumab vs tralokinumab at maintenance treatment adherence rates from 100% to 0% at 5-percentage-point intervals

	IGA 0/1			EASI 75		
Adherence	**RD**	**95% LB**	**95% UB**	**RD**	**95% LB**	**95% UB**
100%	11.5%	5.6%	17.6%	19.5%	12.7%	26.3%
95%	11.3%	5.6%	16.9%	19.7%	13.2%	26.1%
90%	11.0%	5.7%	16.3%	19.8%	13.6%	26.0%
85%	10.7%	5.7%	15.8%	19.9%	14.0%	25.9%
80%	10.4%	5.6%	15.4%	20.0%	14.2%	25.8%
75%	10.2%	5.5%	15.0%	20.1%	14.5%	25.8%
70%	9.9%	5.3%	14.7%	20.2%	14.6%	25.8%
65%	9.7%	5.0%	14.4%	20.3%	14.7%	25.9%
60%	9.4%	4.8%	14.2%	20.3%	14.7%	25.9%
55%	9.2%	4.4%	14.0%	20.4%	14.7%	26.1%
50%	8.9%	4.1%	13.9%	20.4%	14.6%	26.3%
45%	8.7%	3.7%	13.7%	20.5%	14.4%	26.5%
40%	8.5%	3.3%	13.6%	20.5%	14.3%	26.7%
35%	8.3%	3.0%	13.6%	20.5%	14.1%	26.9%
30%	8.0%	2.6%	13.5%	20.6%	13.8%	27.2%
25%	7.8%	2.3%	13.5%	20.6%	13.6%	27.5%
20%	7.6%	1.9%	13.5%	20.6%	13.3%	27.7%
15%	7.4%	1.6%	13.5%	20.6%	13.0%	28.0%
10%	7.2%	1.3%	13.5%	20.6%	12.7%	28.3%
5%	7.0%	1.0%	13.6%	20.5%	12.4%	28.6%
0%	6.8%	0.7%	13.6%	20.5%	12.0%	28.9%

Abbreviations: EASI 75, 75% reduction from baseline with the Eczema Area and Severity Index; IGA, Investigator's Global Assessment; LB, lower bound of the 95% confidence interval; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; RD, risk difference; UB, upper bound of the 95% confidence interval

Table S5: Week-52 ORs for dupilumab vs tralokinumab at maintenance treatment adherence rates from 100% to 0% at 5-percentage-point intervals

	IGA 0/1			EASI 75		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	2.1	1.4	3.3	3.3	2.3	4.7
95%	2.0	1.3	3.1	3.2	2.3	4.6
90%	1.9	1.3	2.9	3.1	2.2	4.4
85%	1.8	1.2	2.7	3.0	2.2	4.2
80%	1.7	1.2	2.6	3.0	2.2	4.1
75%	1.6	1.1	2.4	2.9	2.1	4.0
70%	1.6	1.0	2.3	2.8	2.1	3.9
69%	**1.5**	**1.0**	**2.3**			
65%	1.5	0.9	2.2	2.8	2.0	3.8
60%	1.4	0.9	2.1	2.7	2.0	3.7
55%	1.3	0.8	2.0	2.6	1.9	3.7
50%	1.3	0.7	2.0	2.6	1.8	3.6
45%	1.2	0.7	1.9	2.5	1.8	3.6
40%	1.1	0.6	1.8	2.4	1.7	3.5
35%	1.1	0.6	1.8	2.4	1.6	3.5
30%	1.0	0.5	1.7	2.3	1.6	3.5
28%	1.0	0.5	1.7			
25%	1.0	0.5	1.7	2.3	1.5	3.5
20%	0.9	0.4	1.7	2.2	1.4	3.5
15%	0.9	0.4	1.6	2.2	1.4	3.5
10%	0.8	0.3	1.6	2.1	1.3	3.5
5%	0.8	0.3	1.6	2.1	1.2	3.5
0%	0.7	0.3	1.5	2.0	1.2	3.5

Adherence rates corresponding to changes in statistical significance (**bold**) or numeric difference are shown in red.

Abbreviations: EASI 75, 75% reduction from baseline with the Eczema Area and Severity Index; IGA, Investigator's Global Assessment; LB, lower bound of the 95% confidence interval; OR, odds ratio; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; UB, upper bound of the 95% confidence interval

Table S6: Week-52 RDs for dupilumab vs tralokinumab at maintenance treatment adherence rates from 100% to 0% at 5-percentage-point intervals

	IGA 0/1			EASI 75		
Adherence	**RD**	**95% LB**	**95% UB**	**RD**	**95% LB**	**95% UB**
100%	8.4%	3.5%	13.5%	19.9%	13.7%	26.1%
95%	7.4%	3.0%	12.1%	19.0%	13.2%	24.8%
90%	6.6%	2.4%	11.0%	18.1%	12.6%	23.5%
85%	5.8%	1.8%	9.9%	17.2%	12.0%	22.4%
80%	5.0%	1.3%	8.9%	16.3%	11.4%	21.2%
75%	4.3%	0.7%	8.0%	15.4%	10.8%	20.2%
70%	3.7%	0.1%	7.3%	14.6%	10.1%	19.2%
69%	**3.6%**	**0.0%**	**7.1%**			
65%	3.1%	-0.4%	6.6%	13.8%	9.4%	18.3%
60%	2.6%	-0.9%	6.0%	13.0%	8.6%	17.5%
55%	2.1%	-1.3%	5.4%	12.3%	7.9%	16.7%
50%	1.6%	-1.7%	4.9%	11.6%	7.2%	16.0%
45%	1.2%	-2.1%	4.5%	10.9%	6.5%	15.3%
40%	0.8%	-2.4%	4.1%	10.2%	5.8%	14.7%
35%	0.5%	-2.8%	3.7%	9.6%	5.1%	14.1%
30%	0.1%	-3.0%	3.4%	9.0%	4.5%	13.6%
28%	0.0%	-3.2%	3.3%			
25%	-0.1%	-3.3%	3.1%	8.4%	3.8%	13.1%
20%	-0.4%	-3.5%	2.8%	7.8%	3.3%	12.6%
15%	-0.6%	-3.7%	2.6%	7.3%	2.7%	12.1%
10%	-0.8%	-3.9%	2.4%	6.8%	2.2%	11.6%
5%	-1.0%	-4.1%	2.2%	6.3%	1.7%	11.2%
0%	-1.2%	-4.3%	2.0%	5.8%	1.3%	10.8%

Adherence rates corresponding to changes in statistical significance (**bold**) or numeric difference are shown in red.

Abbreviations: EASI 75, 75% reduction from baseline with the Eczema Area and Severity Index; IGA, Investigator's Global Assessment; LB, lower bound of the 95% confidence interval; OR, odds ratio; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; UB, upper bound of the 95% confidence interval

Table S7: Week-52 outcomes of sensitivity analyses when adjusting the target population to match the SOLO trials only for maintenance treatment adherence rates from 100% to 0% at 25-percentage-point intervals

Lebrikizumab vs dupilumab						
	IGA 0/1			**EASI 75**		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	1.2	0.8	2.0	1.0	0.7	1.4
75%	1.6	1.0	2.5	1.3	0.9	1.8
50%	2.0	1.2	3.9	1.6	1.1	2.4
25%	2.6	1.3	6.4	2.1	1.3	3.4
0%	3.4	1.3	11.1	2.6	1.4	5.0
Lebrikizumab vs tralokinumab						
	IGA 0/1			**EASI 75**		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	2.6	1.6	4.2	3.2	2.2	4.8
75%	2.6	1.7	4.0	3.6	2.6	5.2
50%	2.6	1.6	4.2	4.1	2.8	6.2
25%	2.6	1.3	4.9	4.7	2.9	7.9
0%	2.5	1.1	5.9	5.3	2.8	10.4
Dupilumab vs tralokinumab						
	IGA 0/1			**EASI 75**		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	2.1	1.4	3.3	3.3	2.3	4.7
75%	1.6	1.1	2.4	2.9	2.1	4.0
50%	1.3	0.7	2.0	2.6	1.8	3.6
25%	1.0	0.5	1.7	2.3	1.5	3.5
0%	0.8	0.3	1.6	2.0	1.2	3.5

EASI 75 75% reduction from baseline with the Eczema Area and Severity Index, IGA Investigator's Global Assessment, LB lower bound of the 95% confidence interval, OR odds ratio, QW, every week, Q2W every 2 weeks, Q4W every 4 weeks, UB upper bound of the 95% confidence interval

Table S8: Week-52 outcomes of sensitivity analyses when adjusting the target population to match the ECZTRA trials only for maintenance treatment adherence rates from 100% to 0% at 25-percentage-point intervals

Lebrikizumab vs dupilumab						
	IGA 0/1			**EASI 75**		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	1.2	0.8	2.0	1.0	0.7	1.4
75%	1.6	1.0	2.5	1.3	0.9	1.8
50%	2.0	1.2	3.9	1.6	1.1	2.4
25%	2.6	1.3	6.5	2.1	1.3	3.4
0%	3.3	1.3	11.1	2.6	1.4	5.0
Lebrikizumab vs tralokinumab						
	IGA 0/1			**EASI 75**		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	2.6	1.6	4.2	3.2	2.2	4.8
75%	2.6	1.7	4.0	3.6	2.6	5.2
50%	2.6	1.6	4.3	4.1	2.8	6.2
25%	2.6	1.3	4.9	4.7	2.9	7.9
0%	2.5	1.1	5.9	5.3	2.8	10.4
Dupilumab vs tralokinumab						
	IGA 0/1			**EASI 75**		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	2.1	1.4	3.3	3.3	2.3	4.7
75%	1.6	1.1	2.4	2.9	2.1	4.0
50%	1.3	0.7	2.0	2.6	1.8	3.6
25%	1.0	0.5	1.7	2.3	1.5	3.5
0%	0.8	0.3	1.6	2.0	1.2	3.5

EASI 75 75% reduction from baseline with the Eczema Area and Severity Index, IGA Investigator's Global Assessment, LB lower bound of the 95% confidence interval, OR odds ratio, QW every week, Q2W every 2 weeks, Q4W every 4 weeks, UB upper bound of the 95% confidence interval

Table S9: Week-52 outcomes of naïve analyses with no adjustment for covariates for maintenance treatment adherence rates from 100% to 0% at 25-percentage-point intervals

Lebrikizumab vs dupilumab						
	IGA 0/1			**EASI 75**		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	1.1	0.7	1.6	1.0	0.7	1.4
75%	1.4	0.9	2.0	1.2	0.9	1.7
50%	1.7	1.0	2.9	1.5	1.1	2.2
25%	2.1	1.0	4.5	1.9	1.2	3.1
0%	2.6	1.0	7.2	2.4	1.3	4.4
Lebrikizumab vs tralokinumab						
	IGA 0/1			**EASI 75**		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	2.2	1.4	3.4	3.0	2.0	4.3
75%	2.2	1.5	3.2	3.3	2.4	4.6
50%	2.1	1.3	3.4	3.7	2.6	5.5
25%	2.1	1.1	3.8	4.2	2.6	6.9
0%	2.1	0.9	4.5	4.7	2.6	9.0
Dupilumab vs tralokinumab						
	IGA 0/1			**EASI 75**		
Adherence	**OR**	**95% LB**	**95% UB**	**OR**	**95% LB**	**95% UB**
100%	2.1	1.4	3.0	3.0	2.2	4.2
75%	1.6	1.1	2.3	2.7	2.1	3.6
50%	1.3	0.8	1.9	2.4	1.8	3.3
25%	1.0	0.5	1.7	2.2	1.5	3.2
0%	0.8	0.3	1.5	2.0	1.2	3.3

EASI 75 75% reduction from baseline with the Eczema Area and Severity Index, IGA Investigator's Global Assessment, LB lower bound of the 95% confidence interval, OR odds ratio, QW every week, Q2W every 2 weeks, Q4W every 4 weeks, UB upper bound of the 95% confidence interval

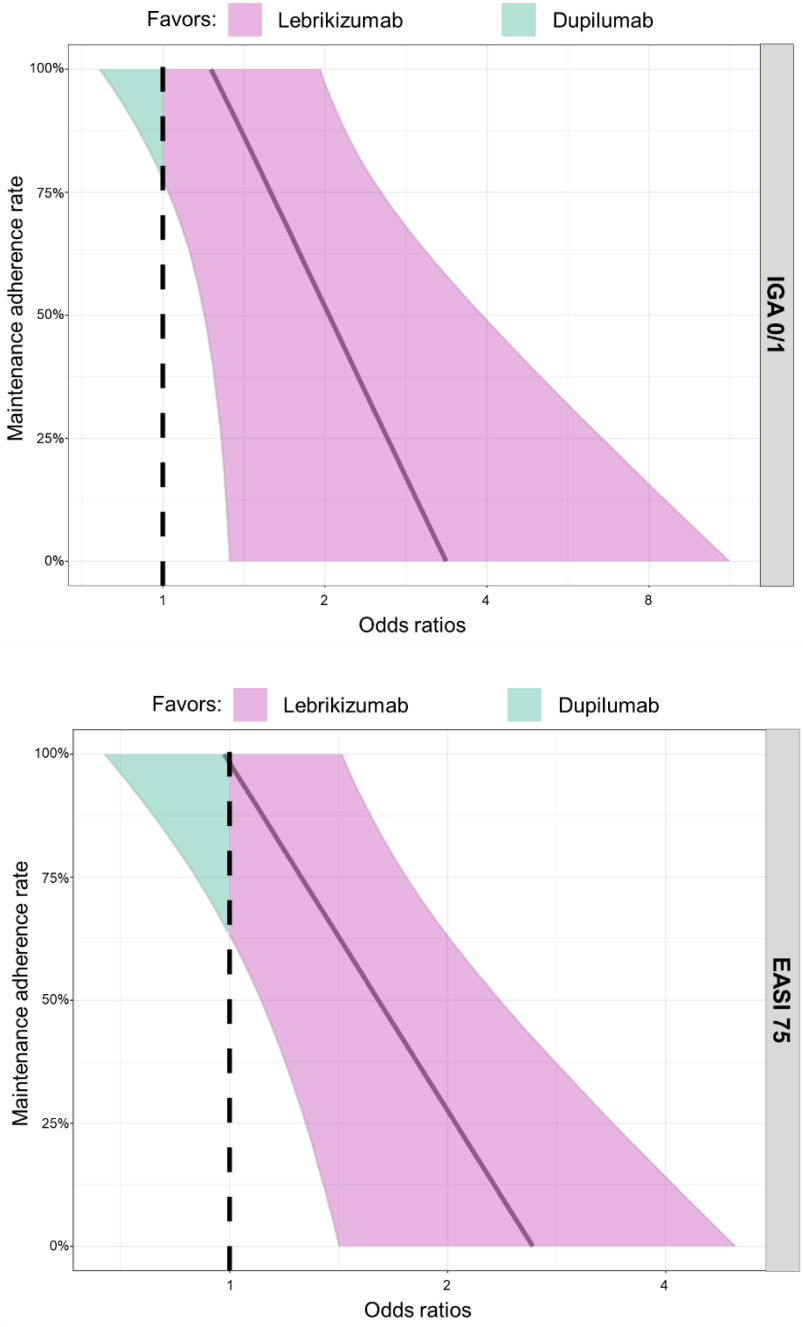


Figure S1: Week-52 outcomes for IGA 0/1 and EASI 75 comparing lebrikizumab vs dupilumab

Ribbon plots display ORs (95% CIs) for week-52 DI estimates of IGA 0/1 and EASI 75, comparing lebrikizumab vs dupilumab across maintenance treatment adherence rates from 100% to 0%. Week-52 maintenance response probabilities were estimated from the 100% adherence (treatment continuation) and 0% adherence (withdrawal) arms; response probabilities at intermediate adherence levels were derived by linear interpolation on the log-odds scale between the response probabilities estimated for these two maintenance arms. ORs were then calculated at each adherence level and displayed as a continuous curve. The solid middle line represents the point estimate for the OR. The left and right lines represent 95% CIs. The vertical dashed line represents the point of equivalence (i.e., no difference between drugs).

Abbreviations: CI, confidence interval; DI, durability index; DUPI, dupilumab QW/Q2W; IGA 0/1, Investigator's Global Assessment; EASI 75, 75% reduction from baseline with the Eczema Area and Severity Index; LEBRI, lebrikizumab Q4W; OR, odds ratio; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks

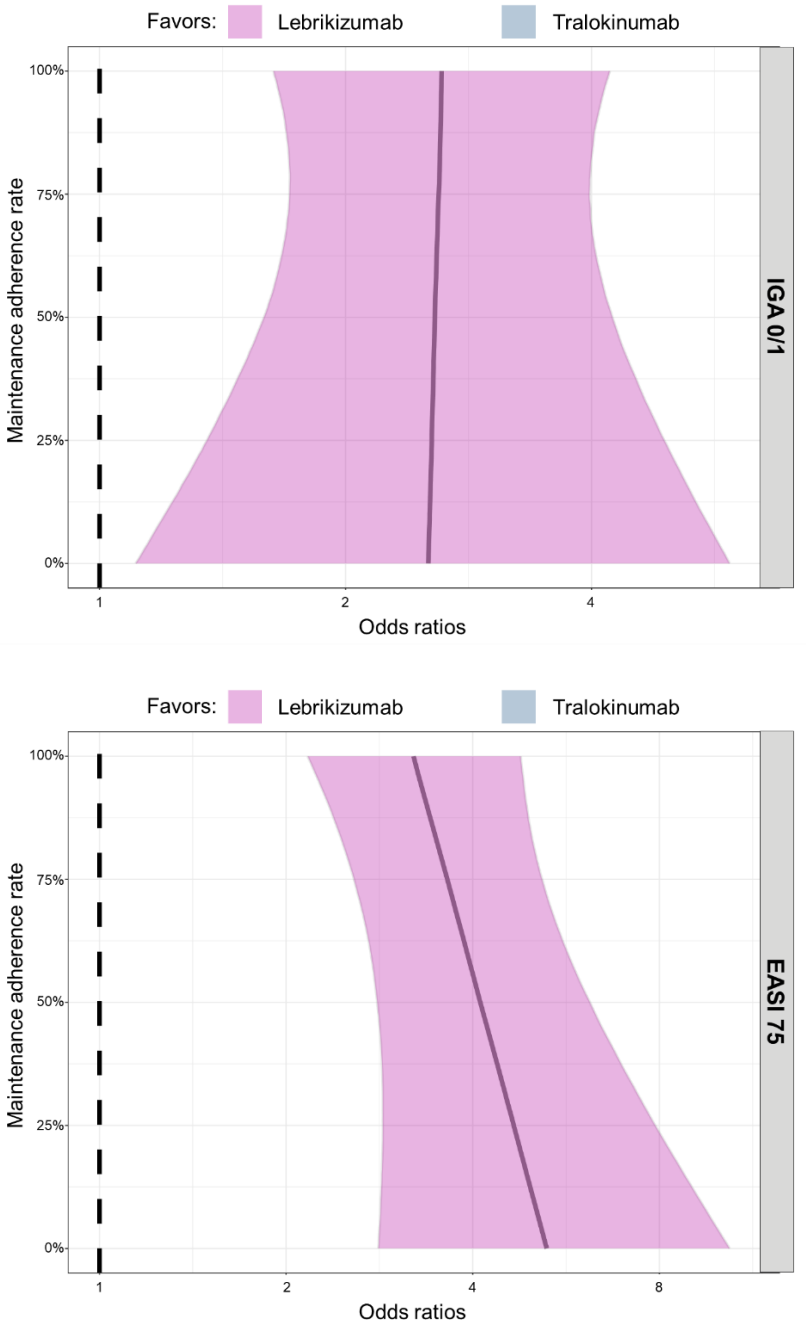


Figure S2: Week-52 outcomes for IGA 0/1 and EASI 75 comparing lebrikizumab vs tralokinumab

Ribbon plots display ORs (95% CIs) for week-52 DI estimates of IGA 0/1 and EASI 75, comparing lebrikizumab vs tralokinumab across maintenance treatment adherence rates from 100% to 0%. Week-52 maintenance response probabilities were estimated from the 100% adherence (treatment continuation) and 0% adherence (withdrawal) arms; response probabilities at intermediate adherence levels were derived by linear interpolation on the log-odds scale between the response probabilities estimated for these two maintenance arms. ORs were then calculated at each adherence level and displayed as a continuous curve. The solid middle line represents the point estimate for the OR. The left and right lines represent 95% CIs. The vertical dashed line represents the point of equivalence (i.e., no difference between drugs).

Abbreviations: CI, confidence interval; DI, durability index; IGA 0/1, Investigator's Global Assessment; EASI 75, 75% reduction from baseline with the Eczema Area and Severity Index; LEBRI, lebrikizumab Q4W; OR, odds ratio; Q2W, every 2 weeks; Q4W, every 4 weeks; TRALO, tralokinumab Q2W

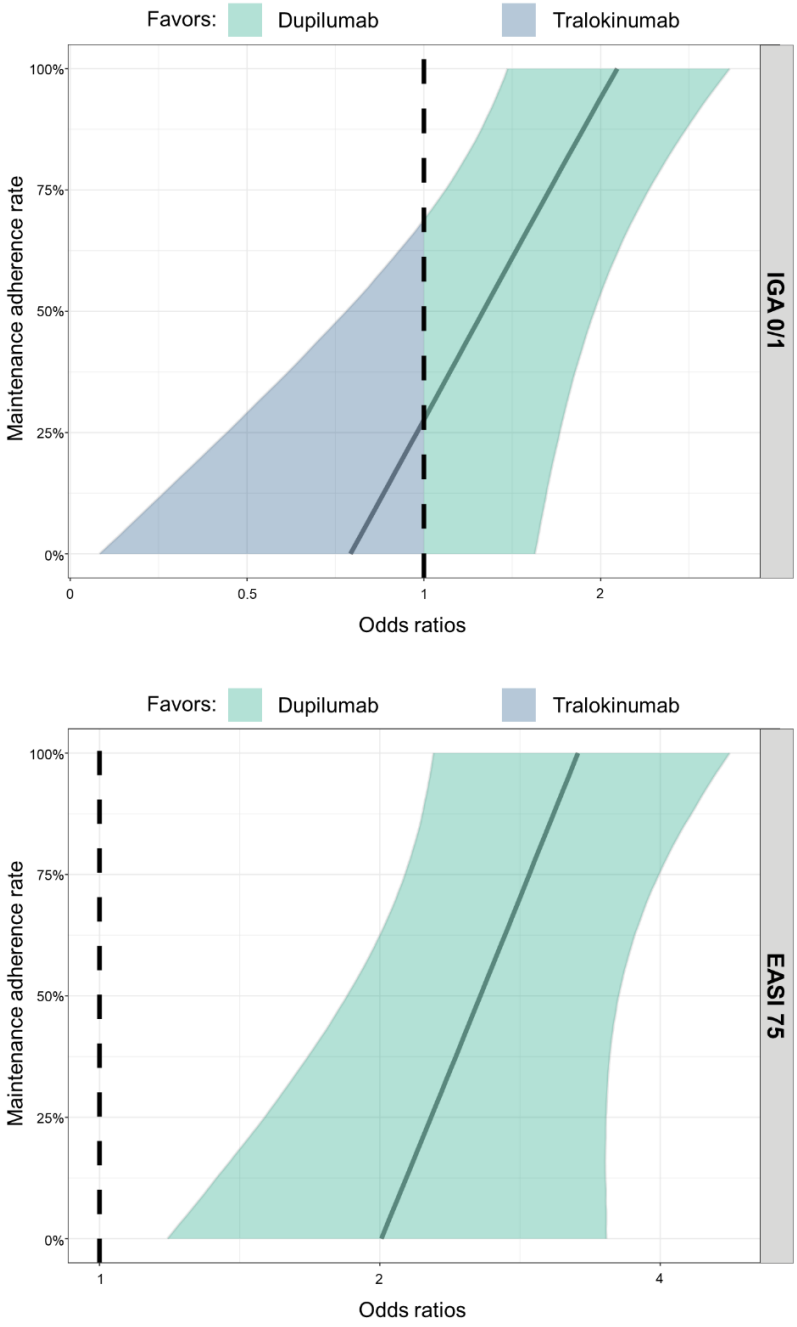


Figure S3: Week-52 outcomes for IGA 0/1 and EASI 75 comparing dupilumab vs tralokinumab

Ribbon plots display ORs (95% CIs) for week-52 DI estimates of IGA 0/1 and EASI 75, comparing dupilumab vs tralokinumab across maintenance treatment adherence rates from 100% to 0%. Week-52 maintenance response probabilities were estimated from the 100% adherence (treatment continuation) and 0% adherence (withdrawal) arms; response probabilities at intermediate adherence levels were derived by linear interpolation on the log-odds scale between the response probabilities estimated for these two maintenance arms. ORs were then calculated at each adherence level and displayed as a continuous curve. The solid middle line represents the point estimate for the OR. The left and right lines represent 95% CIs. The vertical dashed line represents the point of equivalence (i.e., no difference between drugs).

Abbreviations: CI, confidence interval; DI, durability index; DUPI, dupilumab QW/Q2W; IGA 0/1, Investigator's Global Assessment; EASI 75, 75% reduction from baseline with the Eczema Area and Severity Index; OR, odds ratio; QW, every week; Q2W, every 2 weeks; Q4W, every 4 weeks; TRALO, tralokinumab Q2W