Anchored matching-adjusted indirect comparison of the long-term maintenance of efficacy of tralokinumab and lebrikizumab in patients with moderate-to-severe atopic dermatitis

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Supplemental Figure 1. Unmatched response differences from placebo in achieving efficacy endpoints for tralokinumab vs. lebrikizumab at Week 52 among Week 16 responders re-randomized to Q2W dosing.

	Lebrikizumab vs. Placebo			Tralokinumab vs. Placebo			Tralokinumab vs. Lebrikizumab	
	n	RR, % (lebri vs. placebo)	RD, % (SE)	n	RR, % (tralo vs. placebo)	RD, % (SE)	RD, % (95% CI)	*P*-value*
Q2W								
IGA 0/1 and ≥2-pt improvement	77	58.4 vs. 39.5	18.9 (9.7)	91	56.0 vs. 34.8	21.3 (8.7)	2.4 (-23.3; 28.0)	0.86
EASI-75	112	66.1 vs. 56.1	10.0 (8.0)	122	57.4 vs. 27.1	30.2 (6.9)	20.2 (-0.5; 40.9)	0.055
EASI-90	112	55.4 vs. 36.8	18.6 (7.9)	122	49.2 vs. 21.4	27.8 (6.7)	9.2 (-11.2; 29.5)	0.38
EASI % improvement	112	--	8.1 (3.2)	122	--	12.1 (3.5)	4.0 (-5.4; 13.4)	0.40
Pruritus NRS ≥4-pt improvement	61	59.0 vs. 53.6	5.4 (11.3)	71	57.7 vs. 26.3	31.4 (9.2)	26.0 (-2.6; 54.7)	0.075

CI, confidence interval; EASI, Eczema Area and Severity Index; EASI-75, 75% reduction in EASI; EASI-90, 90% reduction in EASI; IGA, Investigator's Global Assessment; lebri, lebrikizumab; pt, point; MAIC, matching-adjusted indirect comparison; n, number of patients included; NRS, numerical rating scale; Q2W, every 2 weeks; RD, response difference from placebo; RR, response rate; SE, standard error; tralo, tralokinumab.

*A *P*-value of ≤0.05 was considered statistically significant.

P-value is for 2-sided test of zero difference between responder proportions for tralokinumab vs. lebrikizumab. ECZTRA treatment differences (tralokinumab vs. placebo) are unadjusted risk differences with asymptotic standard errors. The indirect comparisons are calculated as ECZTRA treatment differences minus ADvocate treatment differences and are thus anchored in placebo. Standard errors for the indirect comparisons are calculated as the square root of the sum of respective treatment difference variances. Within treatment ECZTRA proportions are estimated by back-transformation from logit models. Prior to analysis, ECZTRA data following rescue medication, discontinuation or transfer to open-label arm as well as missing data have been imputed as non-response.

Supplemental Figure 2. Unmatched response differences from placebo in achieving efficacy endpoints for tralokinumab vs. lebrikizumab at Week 52 among Week 16 responders re-randomized to Q4W dosing.

	Lebrikizumab vs. Placebo			Tralokinumab vs. Placebo			Tralokinumab vs. Lebrikizumab	
	n	RR, % (lebri vs. placebo)	RD, % (SE)	n	RR, % (tralo vs. placebo)	RD, % (SE)	RD, % (95% CI)	*P*-value*
Q4W								
IGA 0/1 and ≥2-pt improvement	77	66.2 vs. 39.5	26.7 (9.6)	81	44.4 vs. 34.8	9.7 (8.9)	-17.0 (-42.7; 8.6)	0.19
EASI-75	115	69.6 vs. 56.1	13.5 (7.8)	127	52.0 vs. 27.1	24.8 (6.9)	11.3 (-9.2; 31.8)	0.28
EASI-90	115	58.3 vs. 36.8	21.5 (7.9)	127	40.2 vs. 21.4	18.7 (6.6)	-2.8 (-22.8; 17.3)	0.79
EASI % improvement	115	--	11.3 (3.2)	127	--	8.0 (3.5)	-3.3 (-12.6; 6.1)	0.50
Pruritus NRS ≥4-pt improvement	65	66.2 vs. 53.6	12.6 (11.1)	72	45.8 vs. 26.3	19.5 (9.2)	6.9 (-21.4; 35.2)	0.63

CI, confidence interval; EASI, Eczema Area and Severity Index; EASI-75, 75% reduction in EASI; EASI-90, 90% reduction in EASI; IGA, Investigator's Global Assessment; lebri, lebrikizumab; pt, point; MAIC, matching-adjusted indirect comparison; n, number of patients included; NRS, numerical rating scale; Q4W, every 4 weeks; RD, response difference from placebo; RR, response rate; SE, standard error; tralo, tralokinumab.
*A *P*-value of ≤0.05 was considered statistically significant.
P-value is for 2-sided test of zero difference between responder proportions for tralokinumab vs. lebrikizumab. ECZTRA treatment differences (tralokinumab vs. placebo) are unadjusted risk differences with asymptotic standard errors. The indirect comparisons are calculated as ECZTRA treatment differences minus ADvocate treatment differences and are thus anchored in placebo. Standard errors for the indirect comparisons are calculated as the square root of the sum of respective treatment difference variances. Within treatment ECZTRA proportions are estimated by back-transformation from logit models. Prior to analysis, ECZTRA data following rescue medication, discontinuation or transfer to open-label arm as well as missing data have been imputed as non-response.

Supplemental Figure 3. Sensitivity analysis using the hybrid estimand for endpoints at Week 52 in Week 16 responders

	Lebrikizumab vs. Placebo			Tralokinumab vs. Placebo			Tralokinumab vs. Lebrikizumab	
	n	RR, % (lebri vs. placebo)	RD, % (SE)	n	RR, % (tralo vs. placebo)	RD, % (SE)	RD % (95% CI)	*P*-value*
Q2W								
IGA 0/1 and ≥2-pt improvement								
Unmatched	77	71.2 vs. 47.9	23.3 (9.6)	91	61.5 vs. 45.6	15.8 (9.4)	-7.5 (-33.9; 19.0)	0.58
Matched	77	71.2 vs. 47.9	23.3 (9.6)	48	64.8 vs. 45.7	19.0 (13.8)	-4.3 (-37.2, 28.6)	0.80
EASI-75								
Unmatched	112	78.4 vs. 66.4	12.0 (7.4)	122	63.4 vs. 40.2	23.2 (7.8)	11.2 (-9.9, 32.2)	0.30
Matched	112	78.4 vs. 66.4	12.0 (7.4)	69	65.7 vs. 43.9	21.8 (11.6)	9.8 (-17.2, 36.8)	0.48
EASI-90								
Unmatched	112	64.0 vs. 41.9	22.1 (8.0)	122	53.0 vs. 29.7	23.3 (7.6)	1.2 (-20.3; 22.8)	0.91
Matched	112	64.0 vs. 41.9	22.1 (8.0)	69	52.4 vs. 38.7	13.6 (11.5)	-8.5 (-35.8, 18.9)	0.54
EASI % improvement								
Unmatched	112	--	18.3 (5.5)	122	--	18.0 (7.1)	-0.3 (-17.9; 17.4)	0.98
Matched	112	--	18.3 (5.5)	69	--	15.9 (7.4)	-2.4 (-20.6, 15.8)	0.80
Pruritus NRS ≥4-pt improvement								
Unmatched	61	84.6 vs. 66.3	18.3 (10.1)	71	71.1 vs. 42.9	28.2 (10.6)	9.9 (-18.8; 38.5)	0.50
Matched	61	84.6 vs. 66.3	18.3 (10.1)	37	69.1 vs. 48.2	20.9 (15.1)	2.6 (-33.0, 38.2)	0.89
Q4W								
IGA 0/1 and ≥2-pt improvement								
Unmatched	77	76.9 vs. 47.9	29.0 (9.4)	81	49.0 vs. 45.6	3.3 (9.8)	-25.7 (-52.3; 1.0)	0.059
Matched	77	76.9 vs. 47.9	29.0 (9.4)	47	50.6 vs. 45.7	4.9 (14.2)	-24.1 (-57.5, 9.2)	0.16
EASI-75								
Unmatched	115	81.7 vs. 66.4	15.3 (7.2)	127	60.0 vs. 40.2	19.7 (8.1)	4.4 (-16.8; 25.6)	0.68
Matched	115	81.7 vs. 66.4	15.3 (7.2)	67	68.8 vs. 43.9	24.8 (12.1)	9.5 (-18.1, 37.0)	0.50
EASI-90								
Unmatched	115	66.4 vs. 41.9	24.5 (7.9)	127	44.5 vs. 29.7	14.8 (7.7)	-9.7 (-31.2; 11.9)	0.38
Matched	115	66.4 vs. 41.9	24.5 (7.9)	67	46.8 vs. 38.7	8.0 (11.9)	-16.5 (-44.4, 11.5)	0.25
EASI % improvement								
Unmatched	115	--	18.4 (5.5)	127	--	15.4 (7.2)	-3.0 (-20.9; 14.9)	0.74
Matched	115	--	18.4 (5.5)	67	--	20.5 (7.7)	2.1 (-16.6, 20.8)	0.83
Pruritus NRS ≥4-pt improvement								
Unmatched	65	84.7 vs. 66.3	18.4 (10.0)	72	61.8 vs. 42.9	18.8 (11.1)	0.4 (-28.8; 29.6)	0.98
Matched	65	84.7 vs. 66.3	18.4 (10.0)	39	66.1 vs. 48.2	17.7 (15.7)	-0.7 (-37.1, 35.8)	0.97

CI, confidence interval; EASI, Eczema Area and Severity Index; EASI-75, 75% reduction in EASI; EASI-90, 90% reduction in EASI; IGA, Investigator's Global Assessment; lebri, lebrikizumab; pt, point; RD, response difference; MAIC, matching-adjusted indirect comparison; n, number of patients included; NRS, numerical rating scale; Q2W, every 2 weeks; Q4W, every 4 weeks; RD, response difference; RR, response rate; SE, standard error; tralo, tralokinumab.

*A *P*-value of ≤0.05 was considered statistically significant.

P-value is for 2-sided test of zero difference between responder proportions for tralokinumab vs. lebrikizumab. ECZTRA treatment differences (tralokinumab vs. placebo) are unadjusted (and weighted) risk differences with asymptotic standard errors. The applied weights are derived so that baseline means for selected variables match comparator data. ADvocate treatment differences (lebrikizumab vs placebo) are derived from published data. The indirect comparisons are calculated as ECZTRA treatment differences minus ADvocate treatment differences and are thus anchored in placebo. Standard errors for the indirect comparisons are calculated as the square root of the sum of respective treatment difference variances. Within treatment ECZTRA proportions are estimated by back-transformation from logit models. Prior to analysis, ECZTRA data have been multiply imputed by trial in a way mimicking the protocol specified multiple imputation approach used in the ADvocate trials. See their protocols for reference [1]. Results are combined using Rubin's rule.