SUPPLEMENTAL MATERIAL

Short-term Efficacy of Lebrikizumab versus Dupilumab in Combination with Topical Corticosteroids in Adults with Moderate-to-Severe Atopic Dermatitis: Matching-Adjusted Indirect Comparison

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Table S1. Baseline characteristics of the ADhere and CHRONOS trial populations

	CHRONOS trial		ADhere trial[a]	
	Placebo (n=315)	**Dupilumab 300 mg Q2W plus TCS (n=106)**	**Placebo (n=52)**	**Lebrikizumab 250 mg Q2W plus TCS (n=113)**
Age in years, mean (SD)	36.6 (13.0)	39.6 (14.0)	42.6 (15.6)	44.0 (17.7)
Sex, %				
Male	61.3	58.5	51.9	51.3
Female	38.7	41.5	48.1	48.7
Race, %				
White	66.0	69.8	55.8	58.4
Asian	26.3	27.4	25.0	13.3
Black or African American	6.0	1.9	15.4	16.8
American Indian/Alaska Native	0.0	0.0	1.9	2.7
Native Hawaiian/Pacific Islander	0.0	0.0	0.0	2.7
Multiple	0.0	0.0	0.0	4.4
Other/Unknown/Unreported	1.6	0.9	1.9	1.8
EASI score, mean (SD)	32.6 (12.9)	33.6 (13.3)	26.2 (11.0	27.6 (11.2)
IGA score, %				
4	47	50	28.8	34.5
3	53	50	71.2	65.5
PNRS score, mean (SD)[b]	7.3 (1.8)	7.4 (1.7)	6.9 (2.0)	7.5 (1.6)

[a] Data for the ADhere trial represents the adult subpopulation used in the analysis.
[b] Nx, number of patients with non-missing data: Placebo: n=50; Lebrikizumab: n=110
Abbreviations: EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; SD, standard deviation; TCS, topical corticosteroids Q2W, every 2 weeks.

Table S2. Baseline characteristics used in study arm-level matching of the ADhere and CHRONOS trial populations

	CHRONOS trial		ADhere trial			
	Target population		Before matching		After matching	
	Placebo	Dupi	Placebo	Lebri	Placebo	Lebri
Age in years, mean (SD)	36.6 (13.0)	39.6 (14.0)	42.6 (15.6)	44.0 (17.7)	36.6 (13.2)	39.6 (14.1)
% male	61	59	52	51	61	59
% white	66	70	56	58	66	70
EASI, mean (SD)	32.6 (12.9)	33.6 (13.3)	26.2 (11.0)	27.6 (11.2)	32.6 (13.1)	33.6 (13.4)
% with IGA=4	47	50	29	35	47	50
N	315	106	52	113	–	–
Effective sample size	–	–	–	–	26	68

Data based on the weights when the whole ADhere adult population was used in the analysis. IGA=4 indicates severe atopic dermatitis. Abbreviations: Dupi, dupilumab; EASI, Eczema Area and Severity Index; IGA, Investigator Global Assessment; Lebri, lebrikizumab; SD, standard deviation.

Table S3. Efficacy at week 16 for lebrikizumab Q2W plus TCS versus dupilumab Q2W plus TCS after matching study arms from the ADhere and CHRONOS trials

	CHRONOS trial		ADhere trial									
	Target population % response		Before matching % response		After matching % response		Odds ratio (95% CI)	p value	Risk ratio (95% CI)	p value	Risk difference (95% CI)	p value
	PBO	Dupi	PBO	Lebri	PBO	Lebri						
EASI 50[a]	38	80	52	77	36	85	1.48 (0.50–4.38)	0.48	1.11 (0.66–1.86)	0.71	0.06 (-0.15–0.27)	0.56
EASI 75[a]	23	69	35	62	23	70	1.06 (0.36–3.08)	0.92	1.02 (0.52–2.02)	0.95	0.01 (-0.19–0.22)	0.92
EASI 90[a]	11	40	17	35	10	40	1.16 (0.31–4.33)	0.83	1.13 (0.37–3.41)	0.83	0.02 (-0.17–0.21)	0.85
IGA0/1[a]	12	39	17	35	10	41	1.40 (0.38–5.20)	0.62	1.31 (0.44–3.92)	0.63	0.05 (-0.14–0.23)	0.62
PNRS ≥4[b]	20	59	30	46	24	49	0.54 (0.18–1.58)	0.26	0.70 (0.33–1.46)	0.34	-0.14 (-0.36–0.08)	0.23
DLQI ≥4[c]	43	81	51	76	44	82	1.04 (0.32–3.33)	0.95	0.99 (0.59–1.66)	0.96	0.0 (-0.25–0.25)	1.0

[a] CHRONOS: N=315 in the placebo group and N=106 in the dupilumab group; ADhere (pre-matching): N=52 in the placebo group and N=113 in the lebrikizumab group; ADhere (post-matching): ESS=26 in the placebo group and ESS=68 in the lebrikizumab group.

[b] CHRONOS: N=299 in the placebo group and N=102 in the dupilumab group; ADhere (pre-matching): N=46 in the placebo group and N=106 in the lebrikizumab group; ADhere (post-matching): ESS=25 in the placebo group and ESS=64 in the lebrikizumab group.

[c] CHRONOS: N=300 in the placebo group and N=100 in the dupilumab group; ADhere (pre-matching): N=47 in the placebo group and N=104 in the lebrikizumab group; ADhere (post-matching): ESS=24 in the placebo group and ESS=66 in the lebrikizumab group.

For [b] and [c], patients with baseline PNRS or DLQI values ≥4 points from the two trials were used in the analysis. This subset of the target CHRONOS population was assumed to have the same baseline characteristics at the arm level as the whole CHRONOS population (i.e., without restricting for baseline values ≥4 points).

Abbreviations: CI, confidence interval; DLQI≥4, Dermatology Life Quality Index score ≥4-point improvement from baseline; dupi, dupilumab; EASI 75, ≥75% improvement in Eczema Area and Severity Index score from baseline; IGA0/1, Investigator Global Assessment score of 0/1; lebri, lebrikizumab; MAIC, matching-adjusted indirect comparison; PBO, placebo Q2W plus TCS; PNRS≥4, Pruritus Numerical Rating Scale score ≥4-point improvement from baseline; Q2W+TCS, every 2 weeks plus topical corticosteroids.

Table S4. Itch efficacy at weeks 2 and 4 for lebrikizumab Q2W plus TCS versus dupilumab Q2W plus TCS after matching the study arms from the ADhere and CHRONOS trials

	CHRONOS trial		ADhere trial									
	Target population % response		Before matching % response		After matching % response		Odds ratio (95% CI)	p value	Risk ratio (95% CI)	p value	Risk difference (95% CI)	p value
	PBO	Dupi	PBO	Lebri	PBO	Lebri						
PNRS ≥4 at week 2[a]	8	18	4	9	2	11	3.37 (0.49–23.05)	0.22	3.40 (0.54–21.30)	0.19	0.00 (-0.12–0.12)	0.99
PNRS ≥4 at week 4[a]	16	37	9	25	3	27	3.92 (0.96–15.96)	0.06	3.95 (1.11–14.11)	0.03	0.03 (-0.13–0.18)	0.73

[a] CHRONOS: N=299 in the placebo group and N=102 in the dupilumab group; ADhere (pre-matching): N=46 in the placebo group and N=106 in the lebrikizumab group; ADhere (post-matching): ESS=25 in the placebo group and ESS=64 in the lebrikizumab group. Patients with baseline PNRS values ≥4 points from the two trials were used in the analysis. This subset of the target CHRONOS population was assumed to have the same baseline characteristics at the study level as the whole CHRONOS population (i.e., without restricting for baseline values ≥4 points).

Abbreviations: CI, confidence interval; dupi, dupilumab Q2W plus TCS; lebri, lebrikizumab Q2W plus TCS; MAIC, matching-adjusted indirect comparison; PBO, placebo Q2W plus TCS; PNRS≥4, Pruritus Numerical Rating Scale score ≥4-point improvement from baseline; Q2W+TCS, every 2 weeks plus topical corticosteroids.

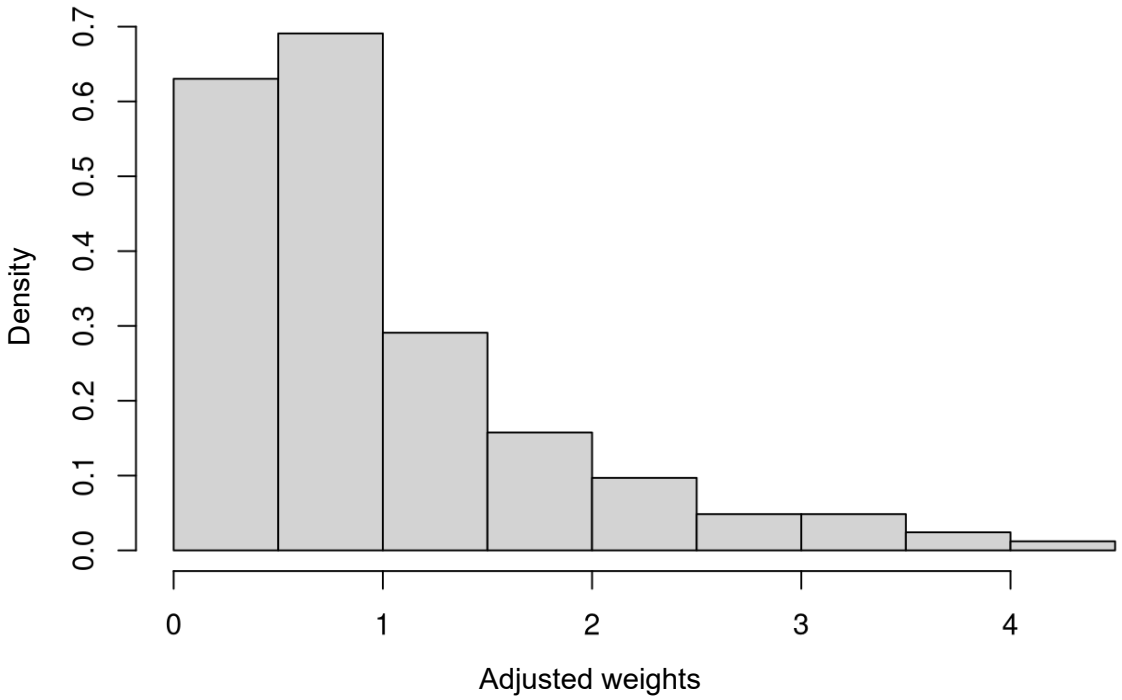


Figure S1. Histogram showing the distribution of weights of individual patient data from the ADhere adult population after matching at the study level.

Patients in the ADhere trial were reweighted to resemble the CHRONOS population based on study-level matching of baseline characteristics. In the original, non-weighted ADhere population, each individual was assigned a weight of 1. After reweighting, individuals were assigned weights based on their similarity to the CHRONOS study. Weights evenly distributed around 1 indicate that the two trial populations are similar. Weights distributed near zero or markedly higher than 1 indicate that the trial populations are different, and extreme weights will result in a small effective sample size and potentially unstable results.

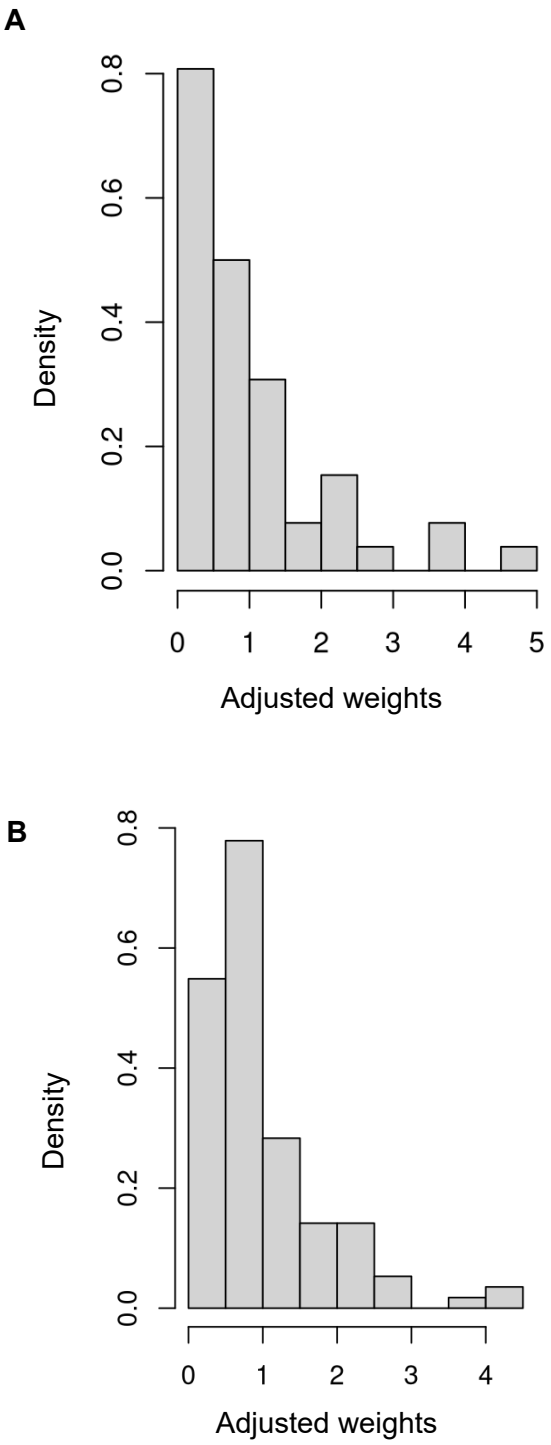
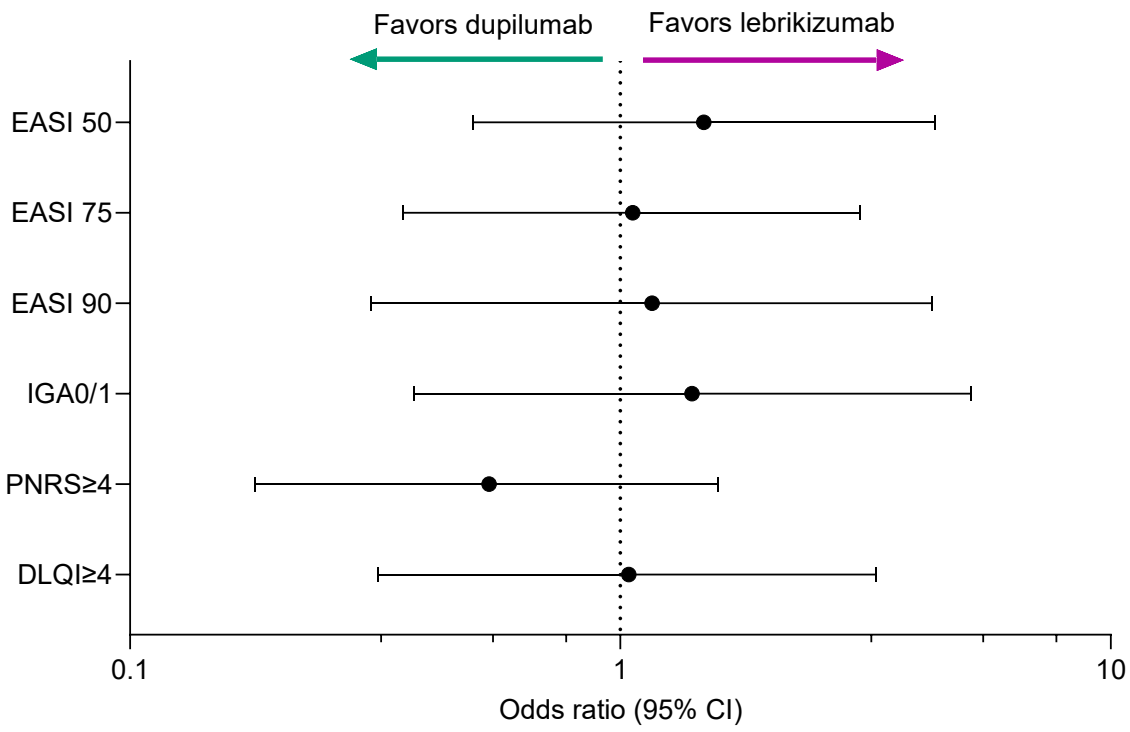


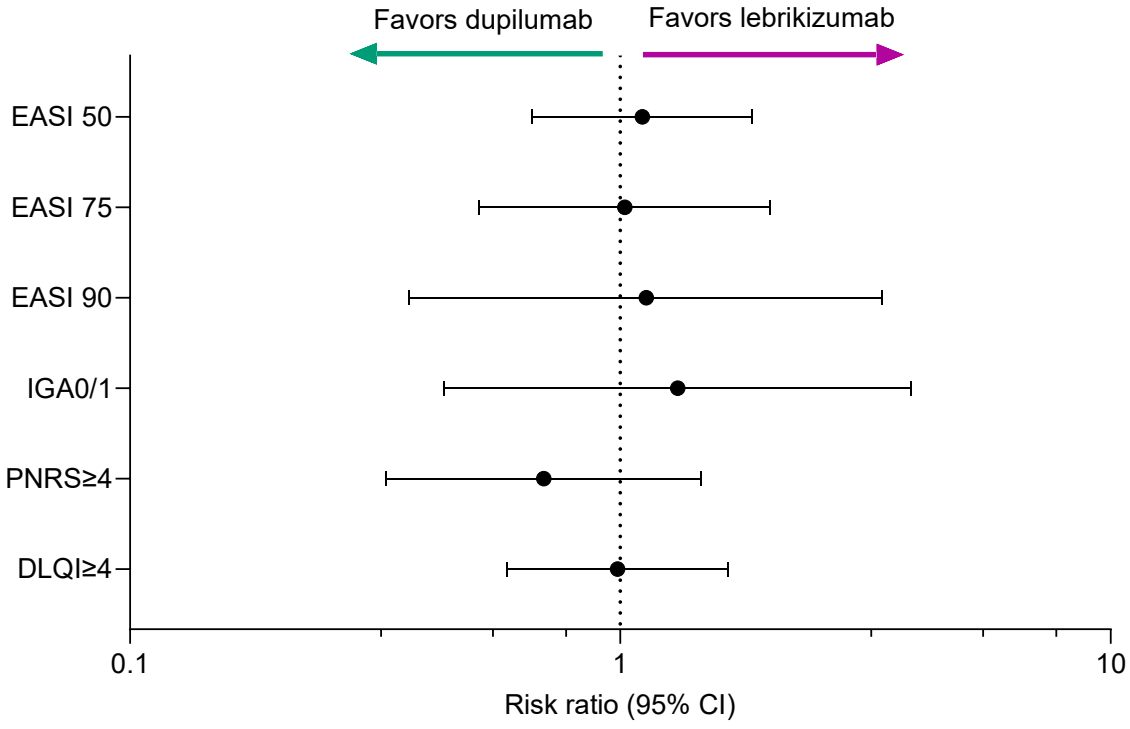
Figure S2. Histogram showing the distribution of weights of individual patient data from the placebo (A) and lebrikizumab (B) arms of the ADhere adult population after matching at the study arm level. Patients in the ADhere trial were reweighted to resemble the CHRONOS population based on study arm-level matching of baseline characteristics. In the original, non-weighted ADhere population, each individual was

assigned a weight of 1. After reweighting, individuals were assigned weights based on their similarity to the arms in the CHRONOS study. Weights evenly distributed around 1 indicate that the two trial populations are similar. Weights distributed near zero or markedly higher than 1 indicate that the trial populations are different, and extreme weights will result in a small effective sample size and potentially unstable results.

A


Favors dupilumab
Favors lebrikizumab
EASI 50
EASI 75
EASI 90
IGA0/1
PNRS≥4
DLQI≥4
0.1
1
10
Odds ratio (95% CI)

B


Favors dupilumab
Favors lebrikizumab
EASI 50
EASI 75
EASI 90
IGA0/1
PNRS≥4
DLQI≥4
0.1
1
10
Risk ratio (95% CI)

C

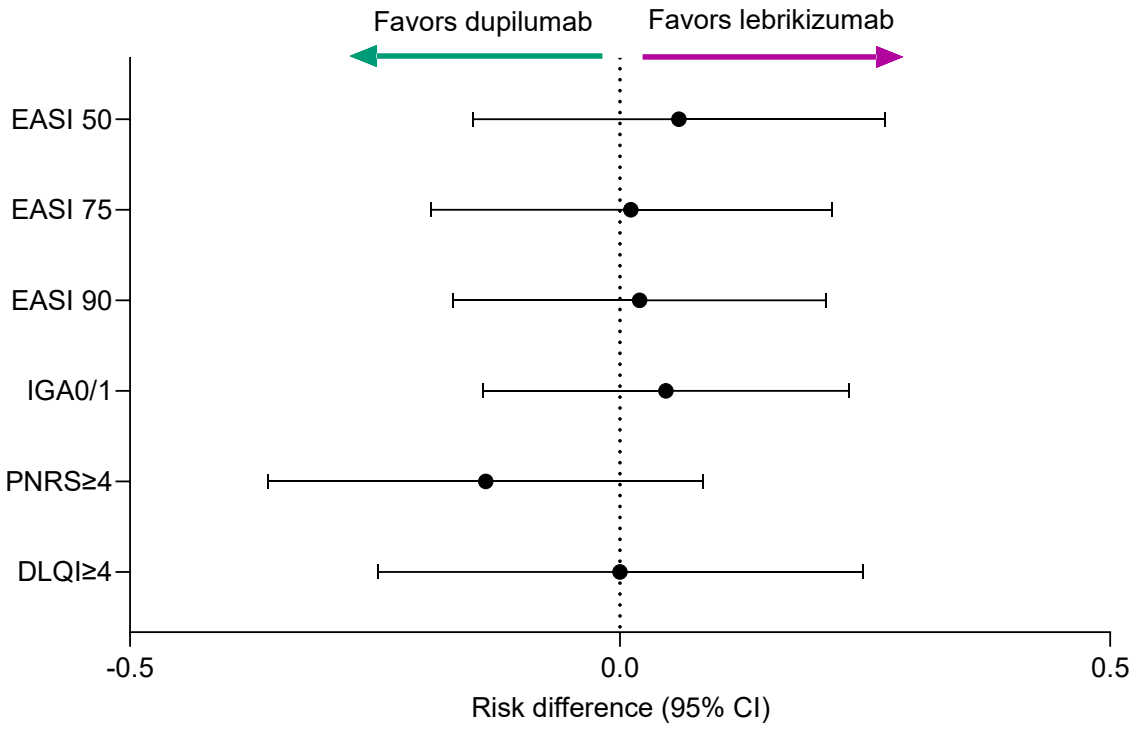
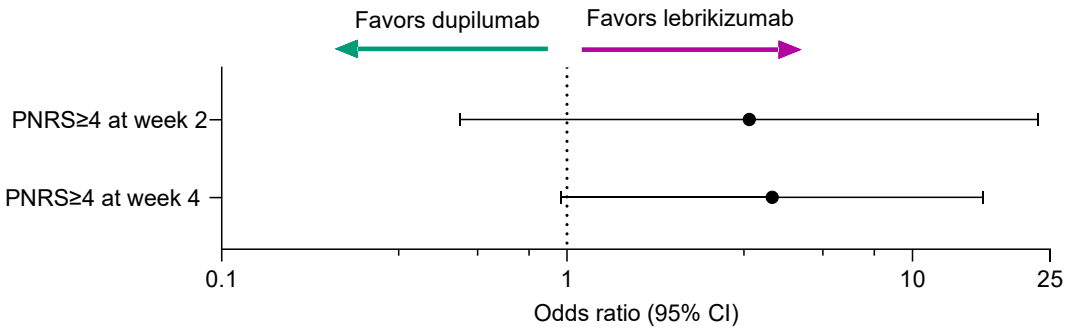


Figure S3. Efficacy at week 16 of lebrikizumab Q2W plus TCS versus dupilumab Q2W plus TCS after matching study arms from the ADhere and CHRONOS trials

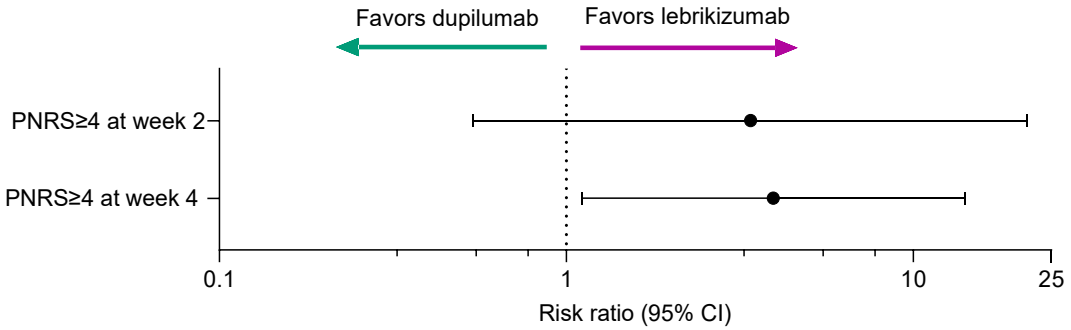
ORs (A), RR, (B), and RD (C) comparing the efficacy of lebrikizumab Q2W plus TCS to dupilumab Q2W plus TCS. Panels A and B use a logarithmic scale; panel C uses a linear scale. Error bars represent 95% confidence intervals. For PNRS4 and DLQI4, available patients with baseline values ≥4 points from the two trials were used in analysis. The analysis population in the target CHRONOS study was assumed to have the same baseline characteristics as the whole CHRONOS population. Differences in baseline characteristics (age, sex, race, mean EASI score, and proportion of patients with an IGA of 4) at the study arm level were adjusted to create comparable populations as described in the Methods.

Abbreviations: CI, confidence interval; DLQI≥4, Dermatology Life Quality Index score ≥4-point improvement from baseline; EASI 75, ≥75% improvement in Eczema Area and Severity Index score from baseline; IGA0/1, Investigator Global Assessment score of 0/1; MAIC, matching-adjusted indirect comparison; PNRS≥4, Pruritus Numerical Rating Scale score ≥4-point improvement from baseline; Q2W plus TCS, every 2 weeks plus topical corticosteroids.

A



B



C

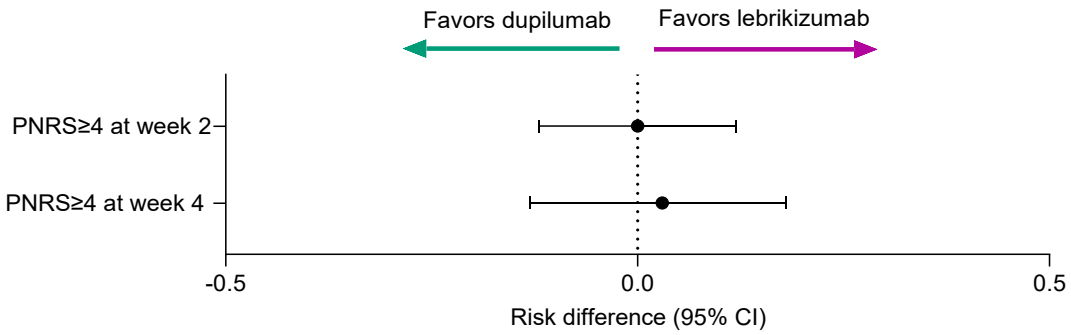


Figure S4. Itch efficacy at weeks 2 and 4 of lebrikizumab Q2W plus TCS versus dupilumab Q2W plus TCS after matching the study arms from the ADhere and CHRONOS trials

ORs (A), RR, (B), and RD (C) comparing itch efficacy of lebrikizumab Q2W plus TCS to dupilumab Q2W plus TCS. Panels A and B use a logarithmic scale; panel C uses a linear scale. Error bars represent 95% confidence intervals. Available patients with baseline values ≥4 points from the two trials were used in analysis. The analysis population in the target CHRONOS study was assumed to have the same baseline characteristics as the whole CHRONOS population. Differences in baseline characteristics (age, sex, race,

mean EASI score, and proportion of patients with an IGA of 4) at the study level were adjusted to create comparable populations as described in the Methods.

Abbreviations: CI, confidence interval; PNRS≥4, Pruritus Numerical Rating Scale score ≥4-point improvement from baseline; Q2W plus TCS, every 2 weeks plus topical corticosteroids.