

Supplementary Material

Lebrikizumab Provides Stable and Deep Long-Term Response with No or Minimal Fluctuations for Up To 3 Years in Patients with Moderate-To-Severe Atopic Dermatitis

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Table S1. Summary of Concomitant Rescue Therapy Use by Week 16 EASI 75 Responders^a from Weeks 16 to 152

Rescue Therapy Use	LEB Q4W (N = 99)	LEB Q2W (N = 82)
Any rescue medication ^b	29 (29.3)	17 (20.7)
Topical therapy ^c	20 (20.2)	14 (17.1)
TCI	5 (5.1)	5 (6.1)
TCS	17 (17.2)	13 (15.9)
Low-potency	2 (2.0)	3 (3.7)
Moderate-potency	10 (10.1)	3 (3.7)
High-potency	10 (10.1)	8 (9.8)
Systemic therapy	11 (11.1)	4 (4.9)

^a The analysis was comprised of the modified Intent-to-Treat population of patients coming from Week 16 responders (patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of lebrikizumab Q2W treatment without use of rescue therapy) of parent studies ADvocate1 and ADvocate2 who were Week 16 EASI 75 responders; re-randomized to lebrikizumab Q2W or Q4W in the maintenance period and then enrolled in the ADjoin study in the same lebrikizumab treatment regimen. Patients who transferred to the escape arm during the maintenance period (Week 16 to Week 52) were excluded.

^b Any use of topical or systemic treatments for AD is considered rescue medication.

^c Topical AD treatment (including TCS, TCI, and crisaborole); systemic AD treatment (including systemic corticosteroids, immunosuppressants, biologics, and phototherapy or photochemotherapy) were defined as rescue medications.

Note: Data are n (%). The differences in potency for the same preferred term are driven by concentration and/or formulation.

AD = atopic dermatitis; EASI = Eczema Area and Severity Index; EASI 75 = greater than or equal to 75% Improvement in EASI score from baseline; IGA = Investigator's Global Assessment; IGA (0,1) = Investigator's Global Assessment score of 0 or 1; LEB = lebrikizumab; Q2W = every 2 weeks; Q4W = every 4 weeks; TCI = topical calcineurin inhibitor; TCS = topical corticosteroid.

Table S2. Summary of Week 152 Efficacy Outcomes Achieved by Week 16 Lebrikizumab Responders

Endpoint	LEB Q4W				LEB Q2W			
	N	Nx	n	%	N	Nx	n	%
EASI 75	96	68	64	94.1	81	63	57	90.5
EASI 90	61	44	39	88.6	53	40	32	80.0
EASI 100	19	14	9	64.3	22	16	11	68.8
EASI ≤7	96	68	66	97.1	81	63	56	88.9
EASI ≤1	96	68	49	72.1	81	63	36	57.1
IGA (0,1)	67	50	42	84.0	55	41	34	82.9
IGA 0	67	50	25	50.0	55	41	26	63.4
POEM (0,1)	99	55	18	32.7	82	50	12	24.0
Pruritus NRS (0,1) ^a	35	25	21	84.0	28	19	16	84.2
POEM itch (0,1)	99	55	38	69.1	82	50	33	66.0

^a Pruritus NRS diary capture halted after Week 104.

Note: Data are as observed, reported as n (%). Overall, the analysis population comprised the modified Intent-to-Treat population of patients coming from Week 16 responders (patients who achieved either EASI 75 or IGA (0,1) following 16 weeks of lebrikizumab Q2W treatment without use of rescue therapy) of parent studies ADvocate1 and ADvocate2; re-randomized to LEB Q2W or Q4W in the maintenance period and then enrolled in the ADjoin study in the same lebrikizumab treatment regimen. Patients who transferred to the escape arm during the maintenance period (Week 16 to Week 52) were excluded. Not all patients completing ADvocate1 & 2 were enrolled to ADjoin; Week 52 data are from ADvocate1 & 2 parent studies.

For EASI 75, EASI ≤ 7 , and EASI ≤ 1 , the analysis used a subgroup of the overall analysis population described above, who achieved EASI 75 at Week 16.

For EASI 90 the analysis used a subgroup of the overall analysis population described above, who achieved EASI 90 at Week 16.

For EASI 100 the analysis used a subgroup of the overall analysis population described above who achieved EASI 100 at Week 16.

For IGA (0) and IGA (0,1), the analysis used a subgroup of the overall analysis population described above who achieved IGA (0,1) at Week 16.

For POEM (0,1) and POEM itch (0,1) the analysis used the overall analysis population described above.

For Pruritus NRS (0,1), the analysis is from a subgroup of the overall analysis population described above who achieved Pruritus (0,1) at Week 16. Baseline weekly Pruritus NRS were calculated by averaging the daily scores up to 7 days before the first injections with at least 4 non-missing values. Post-baseline weekly Pruritus NRS were calculated by averaging the daily scores from the previous 7 days with at least 1 non-missing values.

EASI = Eczema Area and Severity Index; EASI 75 = greater than or equal to 75% improvement in EASI score from baseline; EASI 90 = greater than or equal to 90% improvement in EASI score from baseline; EASI 100 = 100% improvement in EASI score from baseline; EASI ≤ 1 = Eczema Area and Severity Index score of less than or equal to 1; EASI ≤ 7 = Eczema Area and Severity Index score of less than or equal to 7;

IGA = Investigator Global Assessment; IGA (0,1) = Investigator's Global Assessment score 0 (clear) or 1 (almost clear); IGA(0) = Investigator Global Assessment score 0 (clear); LEB = Lebrikizumab; N = number of patients in the analysis population; n = number of patients in the specified category; NRS = Numerical Rating Scale; Nx = number of patients with non-missing values; POEM = Patient-Oriented Eczema Measure; POEM (0,1) = POEM total score 0 or 1; POEM itch (0,1) = POEM Skin Itchy Because of Your Eczema Parameter score 0 or 1; Pruritus NRS (0,1) = Pruritus Numerical Rating Scale score of 0 or 1; Q2W = every 2 weeks; Q4W = every 4 weeks.

Table S3. Summary of Lebrikizumab Responders Maintaining Stable Response from Weeks 16 to 152

Endpoint	≥80% visits	
	LEB Q4W	LEB Q2W
EASI 75, N	99	82
Maintained, n (%)	92 (92.9)	76 (92.7)
EASI 90, N	63	53
Maintained, n (%)	49 (77.8)	43 (81.1)
EASI 100, N	19	22
Maintained, n (%)	11 (57.9)	14 (63.6)
EASI ≤7, N	93	75
Maintained, n (%)	90 (96.8)	73 (97.3)
EASI ≤1, N	37	38
Maintained, n (%)	26 (70.3)	28 (73.7)
Pruritus NRS (0,1)^a, N	37	29
Maintained, n (%)	26 (70.3)	20 (69.0)
SLSS (0,1)^a, N	84	67
Maintained, n (%)	77 (91.7)	65 (97.0)

^a Pruritus NRS (0,1) and SLSS (0,1) were collected through Week 104.

Note: Data are n (%) unless specified otherwise, from the observed data. Overall, the analysis population consisted of patients treated with lebrikizumab in the pooled modified Maintenance Primary Population of ADvocate1 & ADvocate2 who were responders at Week 16 and who subsequently enrolled into ADjoin with the same lebrikizumab treatment regimen. Stability of response was defined as patients'

maintenance of response in at least 80% of attended visits. Patients who transferred to the escape arm during the maintenance period (Week 16 to Week 52) were excluded. Not all patients completing ADvocate1 and ADvocate2 were enrolled to ADjoin; Week 52 data are from ADvocate1 & ADvocate2 parent studies.

For EASI 75, the analysis used a subgroup of the overall analysis population described above who were EASI 75 responders at Week 16. Stability of response was defined as patients' maintenance of EASI 75 response in at least 80% of attended visits.

For EASI 90, the analysis used a subgroup of the overall analysis population described above who were EASI 90 responders at Week 16. Stability of response was defined as patients' maintenance of EASI 90 response in at least 80% of attended visits.

For EASI 100, the analysis used a subgroup of the overall analysis population described above who were EASI 100 responders at Week 16. Stability of response was defined as patients' maintenance of EASI 100 response in at least 80% of attended visits.

For EASI ≤ 1 , the analysis used a subgroup of the overall analysis population described above who were EASI ≤ 1 responders at Week 16. Stability of response was defined as patients' maintenance of EASI ≤ 1 response in at least 80% of attended visits.

For EASI ≤ 7 , the analysis used a subgroup of the overall analysis population described above who were EASI ≤ 7 responders at Week 16. Stability of response was defined as patients' maintenance of EASI ≤ 7 response in at least 80% of attended visits.

For Pruritus NRS (0,1), the analysis used a subgroup of the overall analysis population described above who were Pruritus NRS (0,1) responders at Week 16. Stability of

response was defined as patients' maintenance of Pruritus NRS (0,1) response in at least 80% of attended visits.

For SLSS (0,1), the analysis used a subgroup of the overall analysis population described above who were SLSS (0,1) responders at Week 16. Stability of response was defined as patients' maintenance of SLSS (0,1) response in at least 80% of attended visits.

EASI = Eczema Area and Severity Index; EASI 75 = greater than or equal to 75% improvement in EASI score from baseline; EASI 90 = greater than or equal to 90% improvement in EASI score from baseline; EASI 100 = 100% improvement in EASI score from baseline; EASI ≤ 1 = Eczema Area and Severity Index score of less than or equal to 1; EASI ≤ 7 = Eczema Area and Severity Index score of less than or equal to 7; LEB = Lebrikizumab; N = number of patients in the analysis population; n = number of patients in the specified category; NRS = Numerical Rating Scale; Nx = number of patients with non-missing values; Pruritus NRS (0,1) = Pruritus Numerical Rating Scale score of 0 or 1; Q2W = every 2 weeks; Q4W = every 4 weeks; SLSS = Sleep Loss score; SLSS (0,1) = Sleep Loss score of 0 or 1.

Table S4. Summary of Lebrikizumab Responders of Diverse Backgrounds Maintaining Stable Response from Weeks 16 to 152

Endpoint	SOC		non-SOC	
	LEB Q4W	LEB Q2W	LEB Q4W	LEB Q2W
EASI 75, N	24	23	75	59
Maintained, n (%)	19 (79.2)	19 (82.6)	73 (97.3)	57 (96.6)
Pruritus NRS $\geq$ 4-point improvement, N	14	12	44	35
Maintained, n (%)	12 (85.7)	8 (66.7)	39 (88.6)	33 (94.3)

Stable maintenance of EASI 75 and Pruritus NRS $\geq$ 4-point improvement responses by diverse patients (skin of color [SOC] vs non-SOC) among those who achieved the respective response at Week 16, reported in at least 80% of attended visits.

Note: Data are reported as observed, n (%) unless specified otherwise. Patients who transferred to the escape arm during the maintenance period (Week 16 to Week 52) were excluded. Not all patients completing ADvocate1 and ADvocate2 were enrolled to ADjoin; Week 52 data are from ADvocate1 & ADvocate2 parent studies.

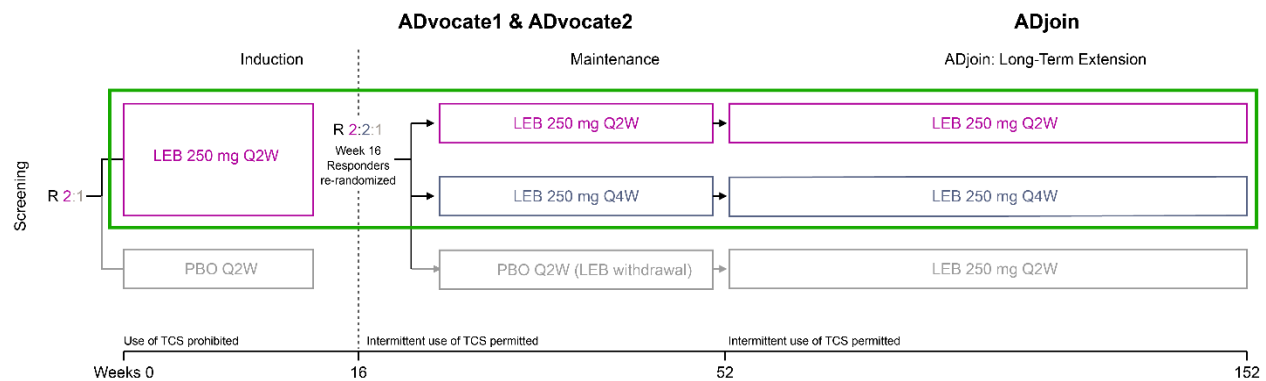
For EASI 75, the analysis population consisted of patients treated with lebrikizumab in the pooled modified Maintenance Primary Population of ADvocate1 & ADvocate2 who were EASI 75 responders at Week 16 and who subsequently enrolled into ADjoin with the same lebrikizumab treatment regimen. Stability of response was defined as patients' maintenance of EASI 75 response in at least 80% of attended visits.

For Pruritus NRS $\geq$ 4-point improvement, the analysis population consisted of patients treated with lebrikizumab in the pooled modified Maintenance Primary Population of ADvocate1 & ADvocate2 who were Pruritus NRS $\geq$ 4-point improvement responders at

Week 16 with baseline score ≥ 4 in ADvocate1 & ADvocate2 and who subsequently enrolled into ADjoin with the same lebrikizumab treatment regimen. Stability of response was defined as patients' maintenance of Pruritus NRS ≥ 4 -point improvement response in at least 80% of attended visits.

EASI = Eczema Area and Severity Index; EASI 75 = greater than or equal to 75% improvement in EASI score from baseline; LEB = lebrikizumab; NRS = Numeric Rating Scale; Q2W = every 2 weeks; Q4W = every 4 weeks; SOC = skin of color.

Figure S1. ADjoin Study Design



Study design of ADvocate1 and ADvocate2 and the ADjoin long-term extension.

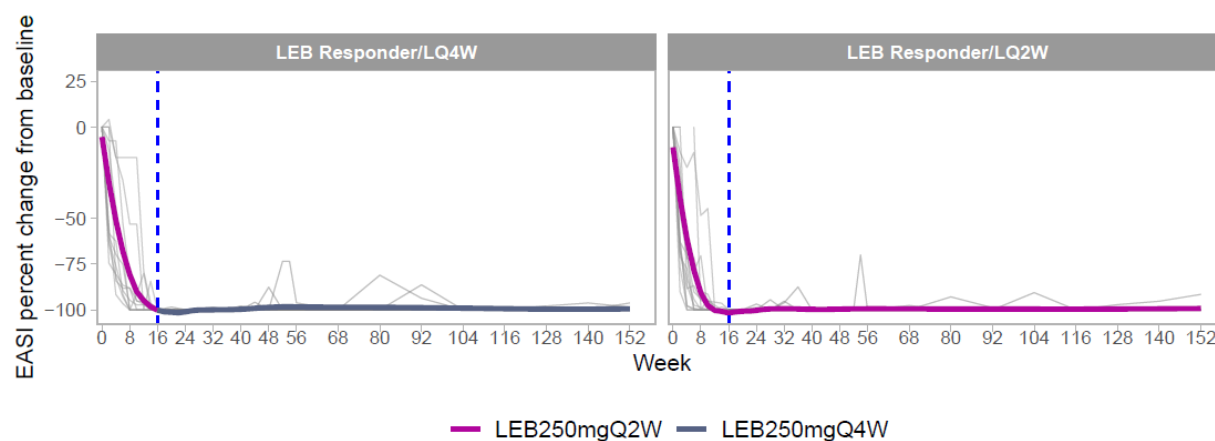
Following screening, patients were randomized 2:1 to lebrikizumab 250 mg Q2W^a or placebo during the 16-week induction period. At Week 16, lebrikizumab responders^b were re-randomized 2:2:1 to lebrikizumab 250 mg Q2W, lebrikizumab 250 mg Q4W, or PBO (lebrikizumab withdrawal) for the maintenance period through Week 52. Eligible patients could then enter ADjoin, the long-term extension, through Week 152. Topical therapy use was prohibited during induction and permitted intermittently during maintenance and the long-term extension. The patients who received continuous lebrikizumab treatment through 152 weeks are the subject of this analysis (outlined in green). The PBO induction arm and the lebrikizumab withdrawal (LEB→PBO) arms are shown for completeness but are excluded from this analysis (shaded in gray).

^a Lebrikizumab was administered as a 500 mg loading dose (two 250-mg subcutaneous injections) at baseline and at Week 2, followed by 250 mg Q2W starting at Week 4.

^b Week 16 responders were defined as patients who achieved IGA (0,1) or EASI 75 at Week 16 without use of rescue medication.

EASI = Eczema Area and Severity Index; EASI 75 = greater than or equal to 75% Improvement in EASI score from baseline; IGA = Investigator Global Assessment; IGA (0,1) = Investigator's Global Assessment score 0 (clear) or 1 (almost clear); LEB = lebrikizumab; PBO = placebo; Q2W = every 2 weeks; Q4W = every 4 weeks; R = randomization; TCS = topical corticosteroids.

Figure S2. Individual Patient Trajectories of Lebrikizumab EASI 100 Responders at Week 16 of ADvocate1 and ADvocate2 Maintaining Stable EASI 100 Response in Attended Visits through Week 152



Individual patient trajectories of absolute EASI total score in stable EASI 100 responders. Each line represents data of an individual patient who achieved a stable EASI 100 response over time between Week 16 and Week 152 with lebrikizumab Q4W (left) and lebrikizumab Q2W (right).

Note: The analysis population is the patients who were Week 16 EASI 100 responders in ADvocate1 & 2, re-randomized to lebrikizumab Q2W or Q4W in the maintenance period and then enrolled in the ADjoin study. Patients who transferred to the escape arm during the maintenance period (Week 16 to 52) were excluded. EASI percent change from baseline is based on the observed data. The smoothing lines are fitted by LOESS.

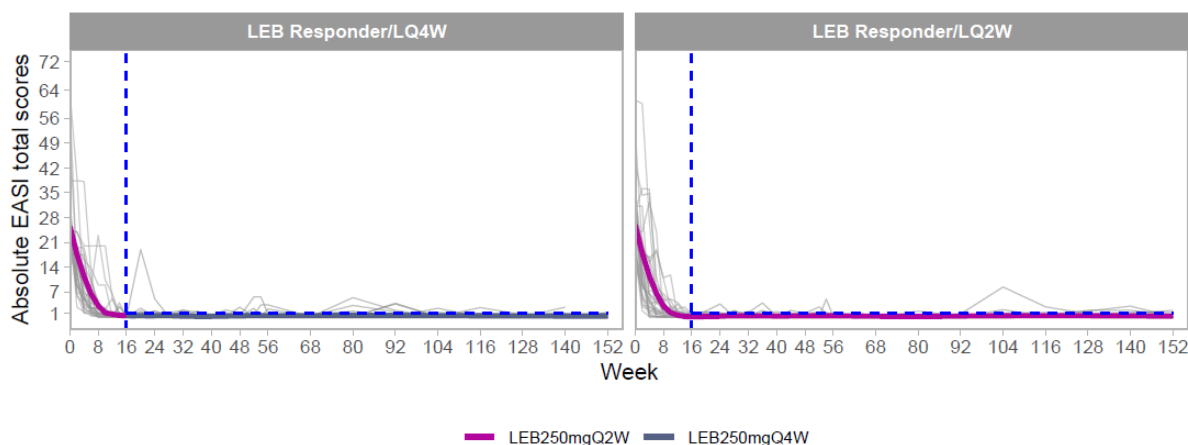
EASI = Eczema Area and Severity Index; EASI75 = greater than or equal to 75%

Improvement in EASI score from baseline; EASI 100 = 100% Improvement in EASI

score from baseline; LEB250Q2W = Lebrikizumab 250mg every 2 weeks; LEB250Q4W

= Lebrikizumab 250mg every 4 weeks; LOESS = locally estimated scatterplot smoothing.

Figure S3. Individual Patient Trajectories of Lebrikizumab Responders at Week 16 of ADvocate1 and ADvocate2 Maintaining Stable Absolute EASI ≤ 1 Response in Attended Visits through Week 152

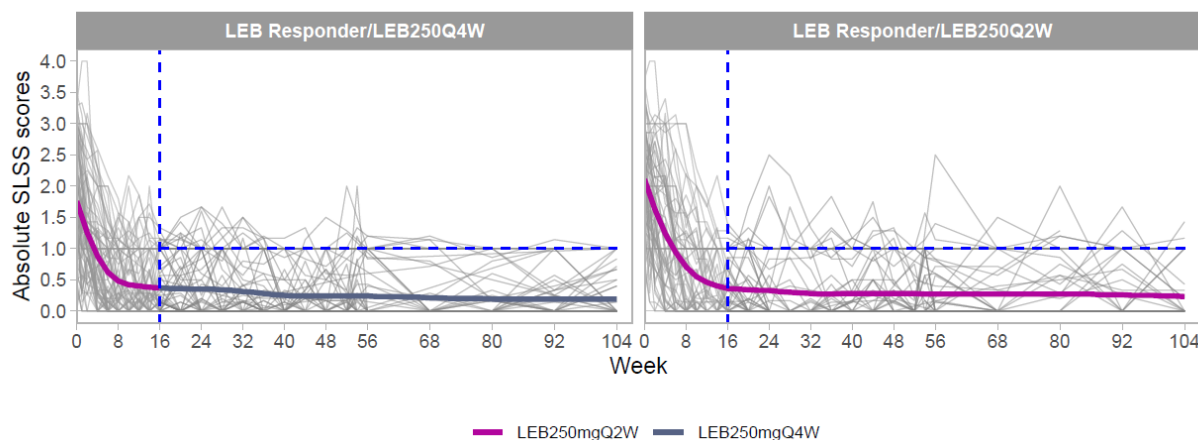


Individual patient trajectories of absolute EASI total score in stable EASI ≤ 1 responders. Each line represents data of an individual patient who achieved a stable EASI ≤ 1 response over time between Week 16 and Week 152 with lebrikizumab Q4W (left) and lebrikizumab Q2W (right).

Note: The analysis population is the patients who were Week 16 EASI ≤ 1 responders in ADvocate1 & 2, re-randomized to lebrikizumab Q2W or Q4W in the maintenance period and then enrolled in the ADjoin study. Patients who transferred to the escape arm during the maintenance period (Week 16 to 52) were excluded. EASI absolute total score is based on the observed data. The smoothing lines are fitted by LOESS.

EASI = Eczema Area and Severity Index; EASI ≤ 1 = absolute EASI total scores less than or equal to 1; LEB250Q2W = Lebrikizumab 250mg every 2 weeks; LEB250Q4W = Lebrikizumab 250mg every 4 weeks; LOESS = locally estimated scatterplot smoothing.

Figure S4. Individual Patient Trajectories of Lebrikizumab SLSS (0,1) Responders at Week 16 of ADvocate1 and ADvocate2 Maintaining Stable SLSS (0,1) Response in Attended Visits through Week 104

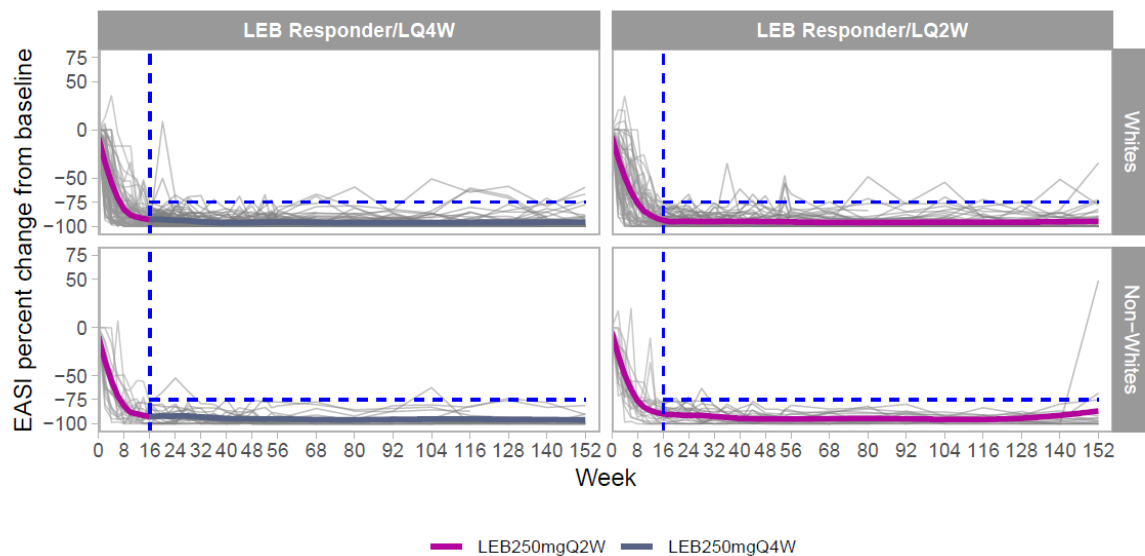


Individual patient trajectories of SLSS absolute scores in stable SLSS (0,1) responders. Each line represents data of an individual patient who achieved a stable SLSS (0,1) response over time between Week 16 and Week 104 with lebrikizumab Q4W (left) and lebrikizumab Q2W (right).

Note: The analysis population is the patients who were Week 16 SLSS (0,1) responders in ADvocate1 & 2, re-randomized to lebrikizumab Q2W or Q4W in the maintenance period and then enrolled in the ADjoin study. Patients who transferred to the escape arm during the maintenance period (Week 16 to 52) were excluded. Not all patients completing ADvocate1 and ADvocate2 were enrolled to ADjoin; Week 52 data are from ADvocate1 & ADvocate2 parent studies. Absolute SLSS score is based on the observed data. The smoothing lines are fitted by LOESS.

LEB = lebrikizumab; LOESS = locally estimated scatterplot smoothing; mMPP = modified Maintenance Primary Population; N = number of patients; SLSS = Sleep Loss score; SLSS (0,1) = Sleep Loss score of 0 or 1; Q2W = every 2 weeks; Q4W = every 4 weeks.

Figure S5. Individual Patient Trajectories of Lebrikizumab EASI 75 Responders of Diverse Backgrounds at Week 16 of ADvocate1 and ADvocate2 Maintaining Stable EASI 75 Response in Attended Visits through Week 152



Individual patient trajectories of EASI percent change in stable EASI 75 responders of diverse backgrounds. Each line represents data of an individual patient who achieved a stable EASI 75 response over time between Week 16 and Week 152 with lebrikizumab Q4W (left) and lebrikizumab Q2W (right).

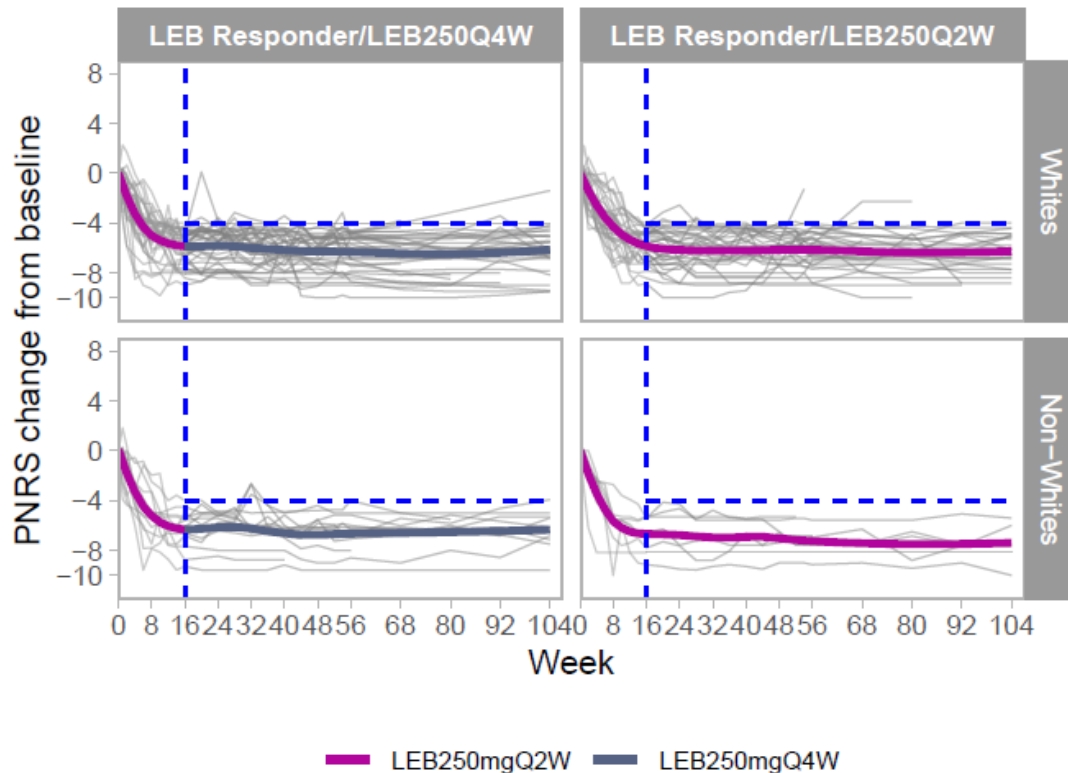
Note: The analysis population consisted of patients treated with lebrikizumab in the pooled modified Maintenance Primary Population of ADvocate1 & ADvocate2 who were EASI 75 responders at Week 16 and who subsequently enrolled into ADjoin with the same lebrikizumab treatment regimen. Stability of response was defined as patients' maintenance of EASI 75 response in at least 80% of attended visits. Patients who transferred to the escape arm during the maintenance period (Week 16 to Week 52) were excluded. Not all patients completing ADvocate1 and ADvocate2 were enrolled to ADjoin; Week 52 data are from ADvocate1 & ADvocate2 parent studies. EASI percent

change from baseline is based on the observed data. The smoothing lines are fitted by LOESS.

EASI = Eczema Area and Severity Index; EASI 75 = greater than or equal to 75%

Improvement in EASI score from baseline; LEB250Q2W = Lebrikizumab 250mg every 2 weeks; LEB250Q4W = Lebrikizumab 250mg every 4 weeks; LOESS = locally estimated scatterplot smoothing.

Figure S6. Individual Patient Trajectories of Lebrikizumab Pruritus NRS ≥ 4 -Point Improvement Responders of Diverse Backgrounds at Week 16 of ADvocate1 and ADvocate2 Maintaining Stable Pruritus NRS ≥ 4 -Point Improvement Response in Attended Visits Through Week 104



Individual patient trajectories of Pruritus NRS change from baseline in stable responders of diverse backgrounds. Each line represents data of an individual patient over time; between Week 16 and Week 104, lines represent patients who achieved a stable Pruritus NRS ≥ 4 -point improvement, response among Pruritus NRS ≥ 4 -point improvement responders at Week 16 with baseline score ≥ 4 for lebrikizumab Q4W (left) and lebrikizumab Q2W (right).

Note: For Pruritus NRS ≥ 4 -point improvement, the analysis population consisted of patients treated with lebrikizumab in the pooled modified Maintenance Primary Population of ADvocate1 & ADvocate2 who were Pruritus NRS ≥ 4 -point improvement responders at Week 16 with baseline score ≥ 4 in ADvocate1 & ADvocate2 and who subsequently enrolled into ADjoin with the same lebrikizumab treatment regimen. Stability of response was defined as patients' maintenance of Pruritus NRS ≥ 4 -point improvement response in at least 80% of attended visits. Pruritus NRS change from baseline is based on the observed data. Baseline weekly Pruritus NRS were calculated by averaging the daily scores up to 7 days before the first injection with at least 4 non-missing values. Post-baseline weekly Pruritus NRS were calculated by averaging the daily scores from the previous 7 days with at least 1 non-missing values. The smoothing lines are fitted by LOESS.

LEB250Q2W = Lebrikizumab 250mg every 2 weeks; LEB250Q4W = Lebrikizumab 250mg every 4 weeks; LOESS = locally estimated scatterplot smoothing; PNRS = Pruritus Numeric Rating Scale; PNRS4 = greater than or equal to 4-point Improvement in Pruritus NRS from baseline.