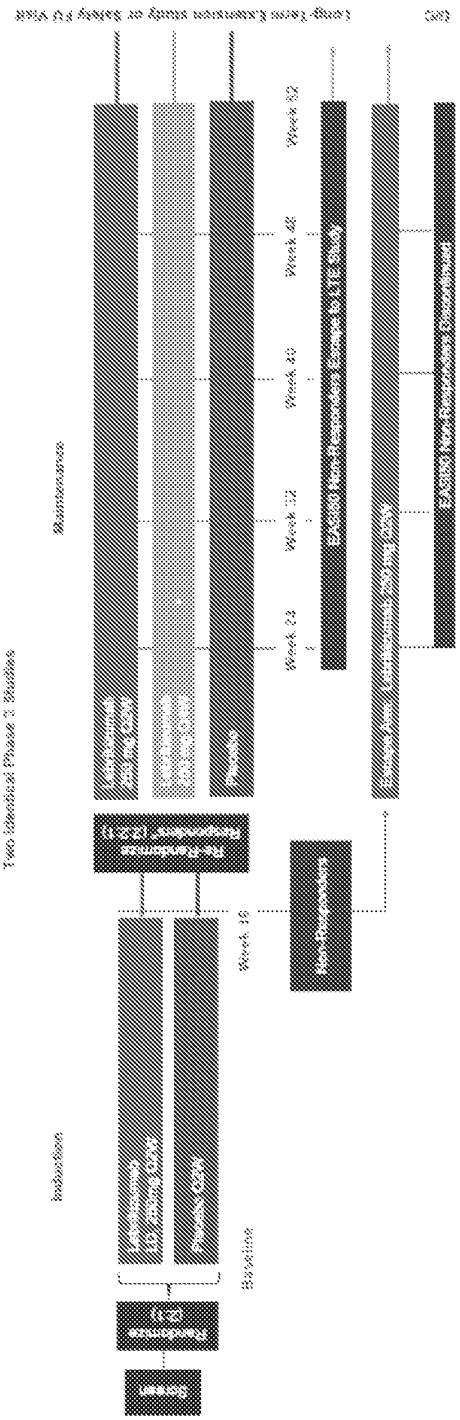


* Responder is defined as having an IGA of 0 or 1 or a 75% reduction in EASI from Baseline to Week 16 (EASI-75)

Figure 1

Figure 2A

	PBO N=141	LEB 250 Q2W N=283
Age (years), mean (SD)	34.2 (16.38)	36.1 (17.79)
Adults (≥18 years), n (%)	123 (87.2)	246 (86.9)
Adolescents (12- <18 years), n (%)	18 (12.8)	37 (13.1)
Female, n (%)	73 (51.8)	141 (49.8)
Race, n (%)		
White	93 (66.0)	196 (69.3)
Black or African American	16 (11.3)	33 (11.7)
Asian	31 (22)	39 (13.8)
Duration since AD onset (years), mean (SD)	23.7 (15.38)	22.0 (14.84)

Figure 2B

	PBO N=141	LEB 250 Q2W N=283
Age (years), mean (SD)	34.2 (16.38)	36.1 (17.79)
Adults (≥18 years), n (%)	123 (87.2)	246 (86.9)
Adolescents (12- <18 years), n (%)	18 (12.8)	37 (13.1)
Female, n (%)	73 (51.8)	141 (49.8)
Race, n (%)		
White	93 (66.0)	196 (69.3)
Black or African American	16 (11.3)	33 (11.7)
Asian	31 (22)	39 (13.8)
Duration since AD onset (years), mean (SD)	23.7 (15.38)	22.0 (14.84)

Figure 2C

	PBO N=141	LEB 250 Q2W N=283
IGA score, n (%)		
3, moderate	83 (58.9)	170 (60.1)
4, severe	58 (41.1)	113 (39.9)
EASI score, median (IQR)	26.70 (21.10-38.20)	25.70 (19.65-34.25)
SCORAD, median (IQR)	65.65 (58.25-75.5)	64.96 (57.5-73.0)
% BSA affected, median (IQR)	43 (28.00-65.00)	42 (28.00-60.00)
Pruritis NRS, median (IQR)	7.23 (6.34-8.46)	7.5 (6.14-8.6)
≥4, n (%)	130 (95.6)	263 (94.9)
Sleep-loss score, median (IQR)	2.37 (1.66-3.00)	2.43 (1.71-3.00)
≥2, n (%)	91 (66.9)	195 (70.7)
POEM, median (IQR)	22 (17.0-25.0)	22 (17.0-26.0)
DLQI[a], median (IQR)	15 (11.0-21.0)	15 (9.0-20.0)

Figure 3A

	PBO N=141 n (%)	LEB 250 Q2W N=282 n (%)
Any TEAE	72 (51.1)	128 (45.4)
Mild	34 (24.1)	78 (27.7)
Moderate	31 (22.0)	44 (15.6)
Severe	7 (5.0)	6 (2.1)
Serious adverse event	1 (0.7)	6 (2.1)
Death	0	0
AEs leading to treatment discontinuation*	1 (0.7)	3 (1.1)

Figure 3B

Preferred Term	PBO N=141 n (%)	LEB 250 Q2W N=282 n (%)
Serious adverse events*	1 (0.7)	6 *(2.1)
Arthralgia	0	1 (0.4)
Synovitis	0	1 (0.4)
Myocardial infarction	0	1 (0.4)
Oedema peripheral	0	1 (0.4)
Cellulitis	1 (0.7)	0
Sepsis	1 (0.7)	0
Accidental overdose**	0	1 (0.4)
Carpal tunnel syndrome	0	1 (0.4)

Figure 3C

Category	PBO N=141 n (%)	LEB 250 Q2W N=282 n (%)
Infections	28 (19.9)	61 (21.6)
Opportunistic and potential opportunistic (narrow)	0	1 (0.4)
Herpes infections	6 (4.3)	9 (3.2)
Parasitic infections	0	0
Skin infections	5 (3.5)	8 (2.8)
Conjunctivitis (narrow search)	5 (3.5)	26 (9.2)
Hypersensitivity (narrow/algorithm search on immediate events[a])	8 (5.7)	6 (2.1)
Anaphylactic reaction	0	0
Hypersensitivity	8 (5.7)	6 (2.1)
Angioedema	0	0
Injection-site reactions	3 (2.1)	3 (1.1)
Malignancies	0	0
Atopic Dermatitis Exacerbation	28 (19.9)	16 (5.7)
Suicide/self-injury	0	0
Eosinophilia and Eosinophil-related disorders	3 (2.1)	1 (0.4)

Figure 3D

Preferred Term	PBO N=141 n (%)	LEB 250 Q2W N=282 n (%)
Any injection site reactions	3 (2.1)	3 (1.1)
Mild	3 (2.1)	2 (0.7)
Moderate	0	1 (0.4)
Severe	0	0
Injection site erythema	0	1 mild
Injection site pain	2 mild	1 mild
Injection site reaction	0	1 moderate
Injection site bruising	1 mild	0

Figure 4A

	Response rate (%)		Significance	
	[redacted]	[redacted]	p-value[a]	Achieved
Primary endpoint				
IGA (0,1) at Week 16 with ≥2-point improvement from BL	12.8	43.0	<.000001	
Major secondary endpoints				
EASI-75 at Week 16	16.4	59.3	<.000001	
EASI-90 at Week 16	9.1	36.2	<.000001	
Pruritis NRS ≥4-point improvement from BL at Week 16[a]	12.7	46.3	<.000001	
IGA (0,1) at Week 16 in adults	11.3	42.2	<.000001	
Pruritis NRS ≥4-point improvement from BL at Week 4[b]	2.4	21.6	0.000003	
Pruritis NRS ≥4-point improvement from BL at Week 2[b]	0.9	6.1	0.016543	
IGA (0,1) at Week 4 with ≥2-point improvement from BL	1	10.2	0.000982	
Sleep-loss ≥2-point improvement from BL at Week 16[c]	5.1	38.7	<.000001	

[a]Nominal p-values are reported. Assessment of statistical significance (achieved or not) is based on prespecified graphical multiple testing scheme with a control of overall Type I error rate at two-sided alpha of 0.05. [b]In patients with Pruritis NRS ≥4 at BL. [c]In patients with Sleep-loss ≥2 at BL.

Figure 4B

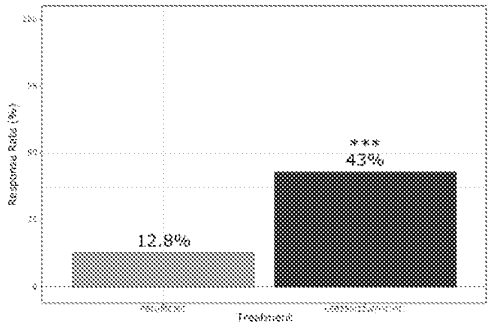


Figure 4C

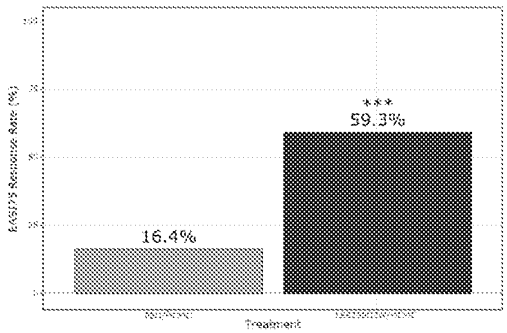


Figure 4D

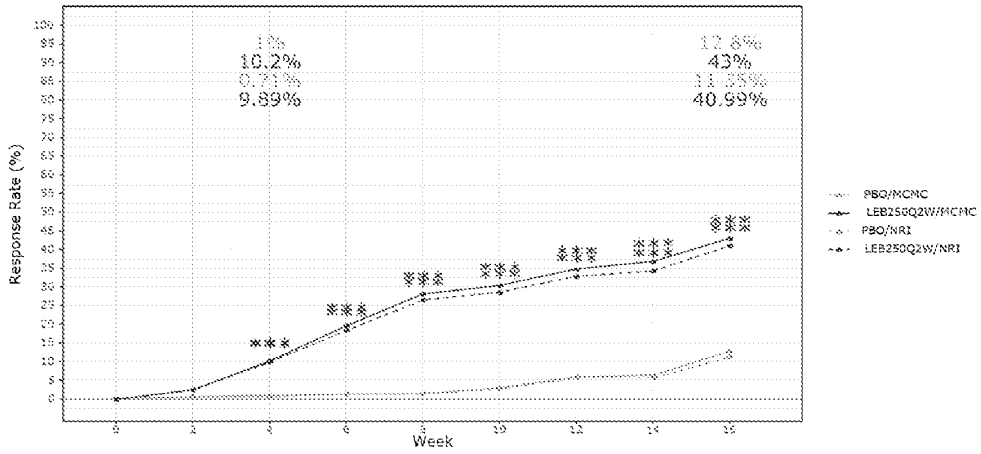


Figure 4E

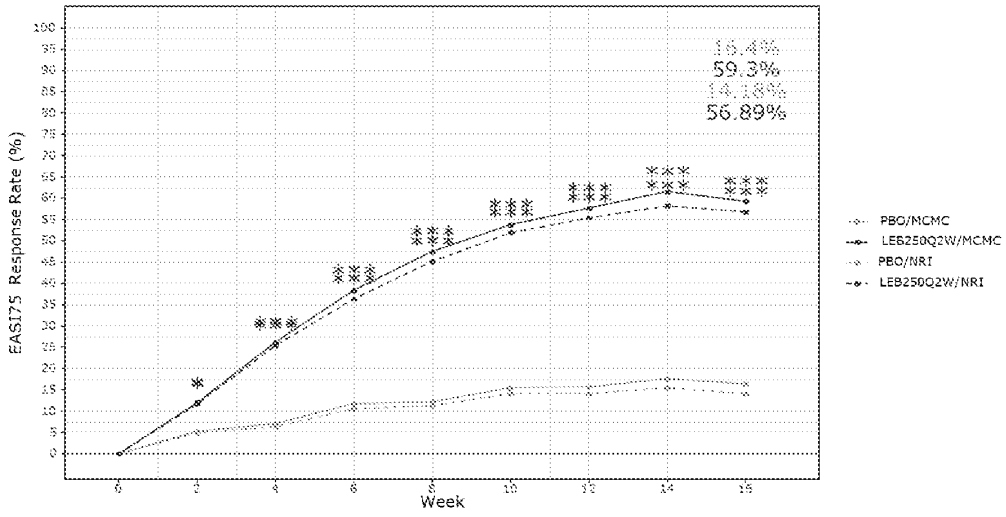


Figure 4F

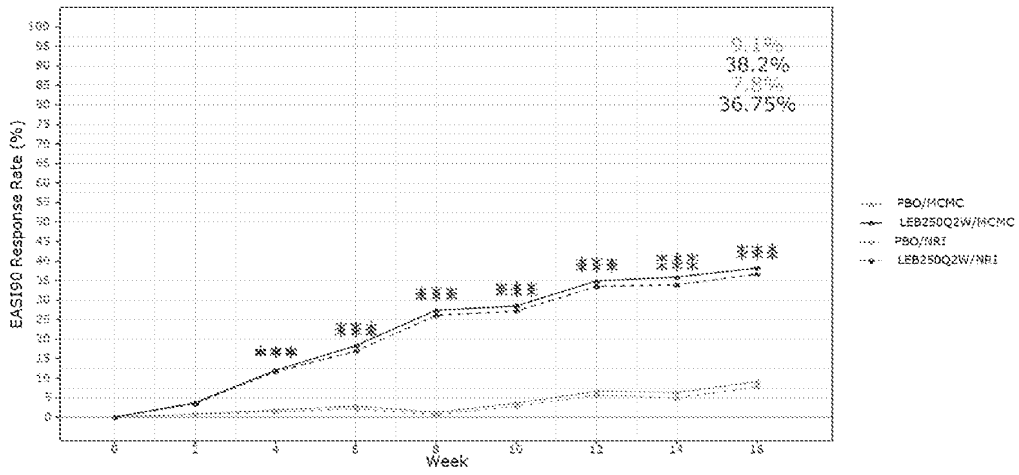


Figure 4G

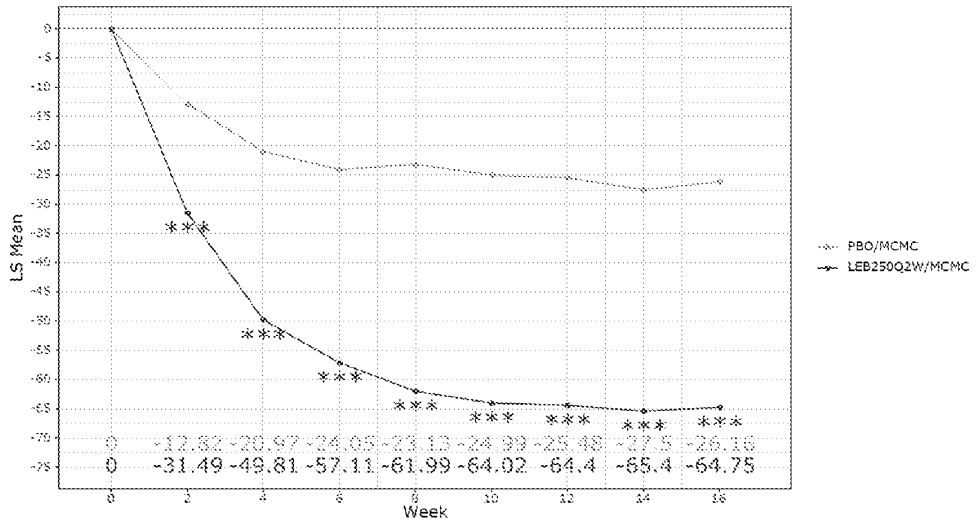


Figure 5A

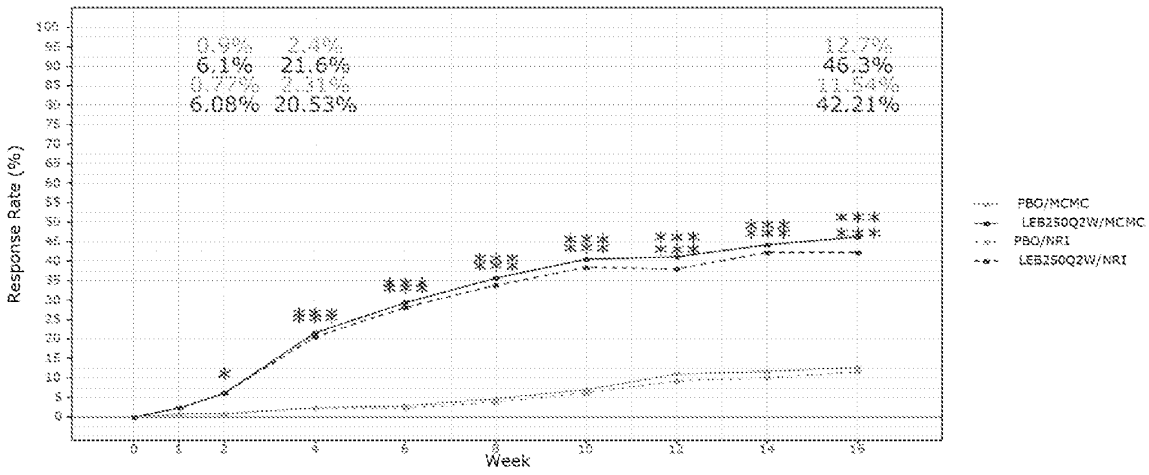


Figure 5B

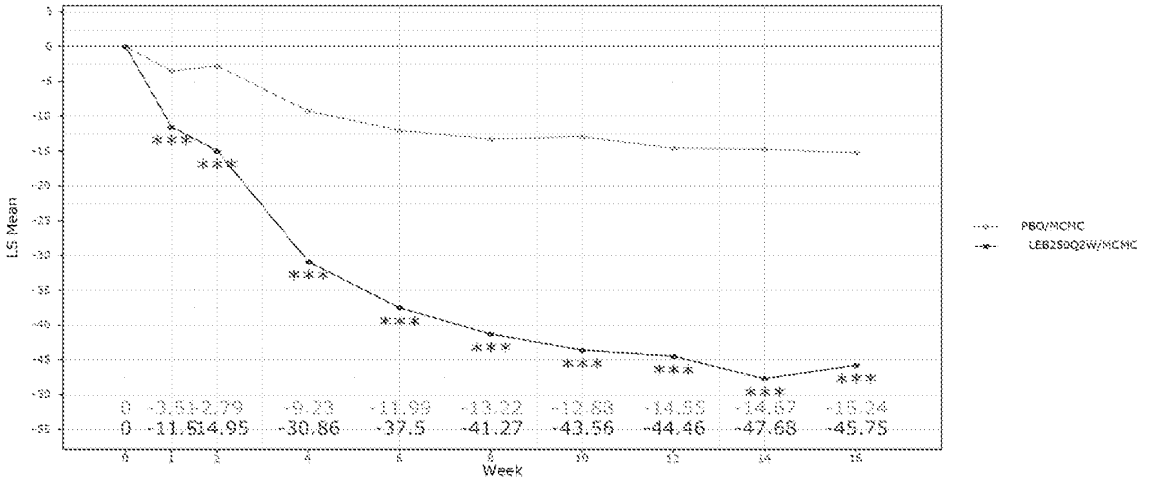


Figure 5C

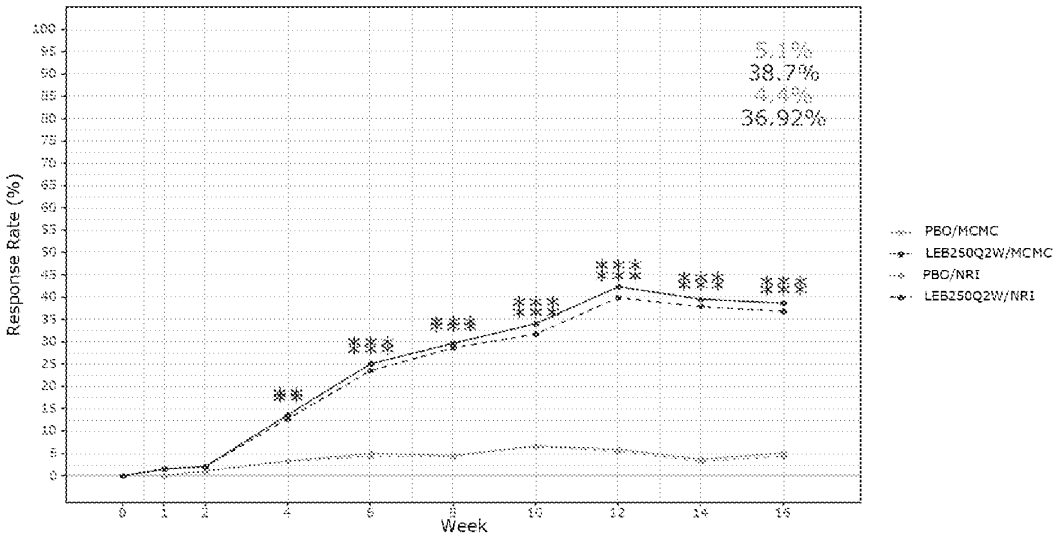
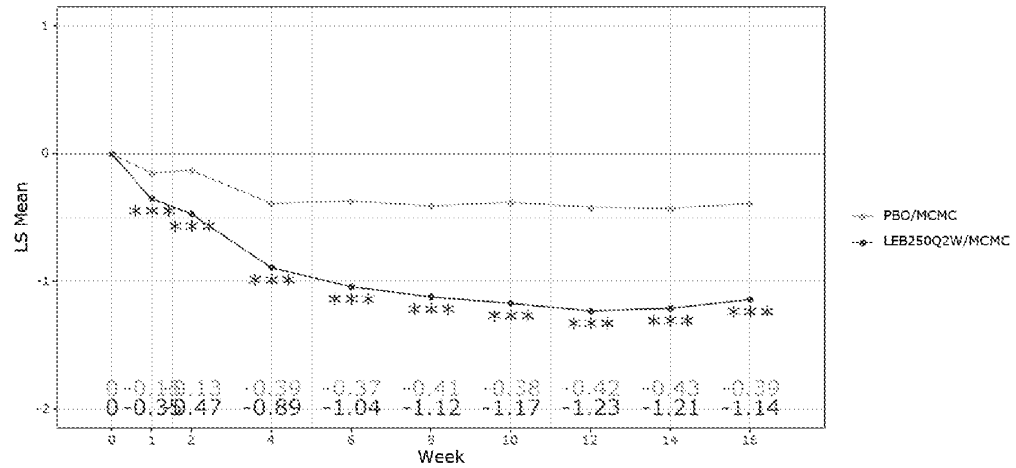
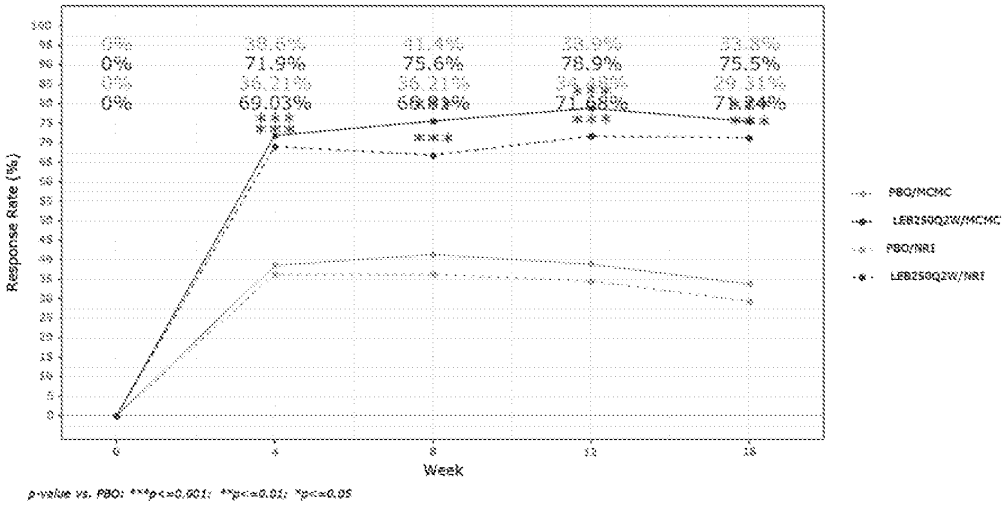


Figure 5D



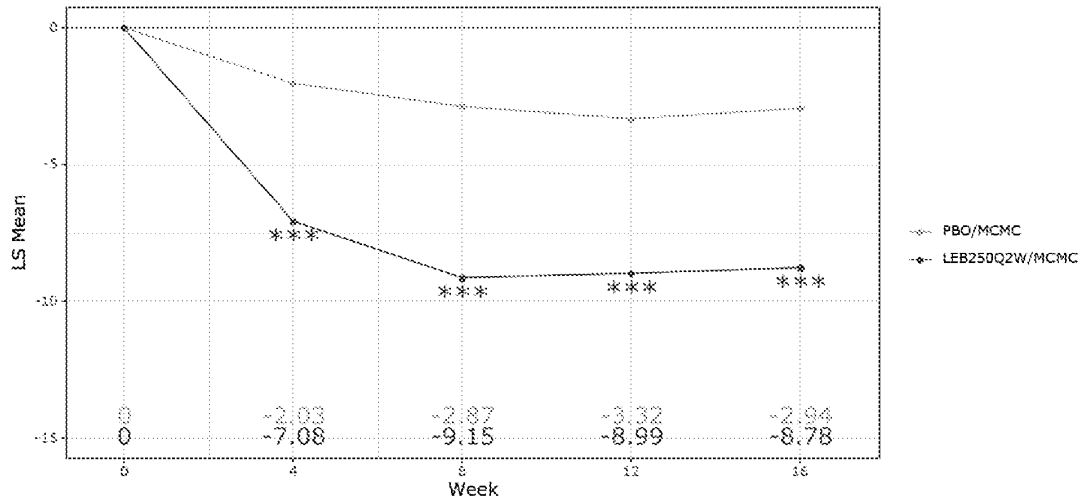
*p-value vs. PBO: ***p<=0.001; **p<=0.01; *p<=0.05*

Figure 5E



p-value vs. PBO: ***p<=0.001; **p<=0.01; *p<=0.05

Figure 5F



p-value vs. PBO: ***p<=0.001; **p<=0.01; *p<=0.05

Figure 6A

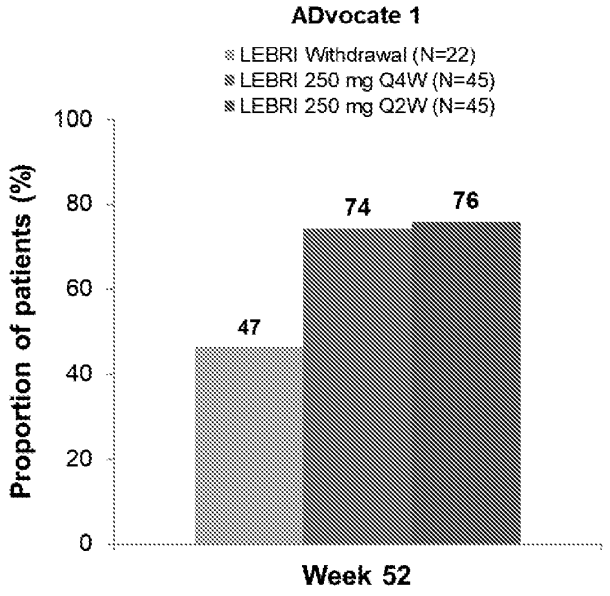


Figure 6B

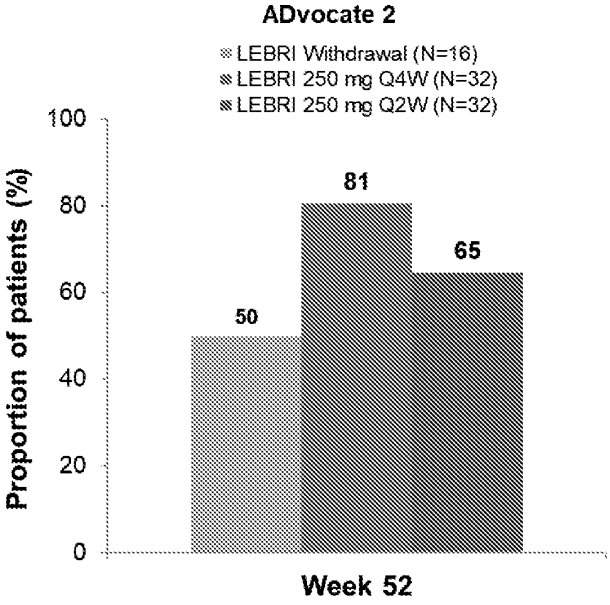


Figure 6C

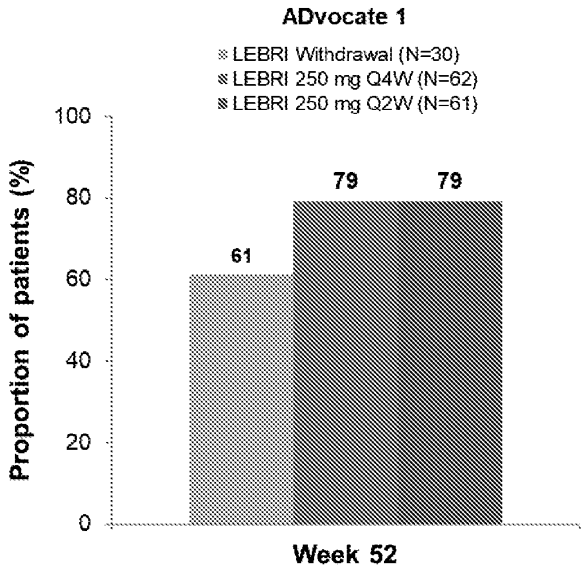


Figure 6D

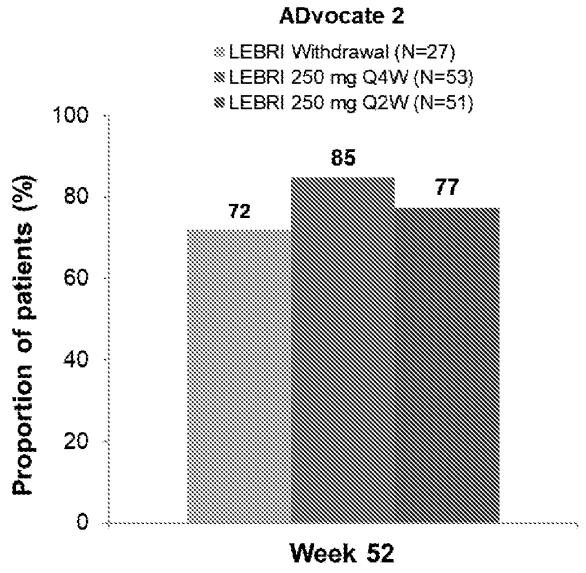


Figure 6E

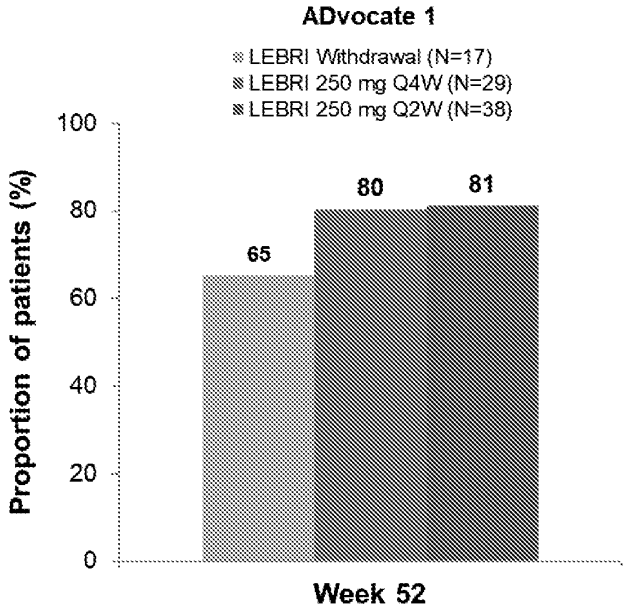


Figure 6F

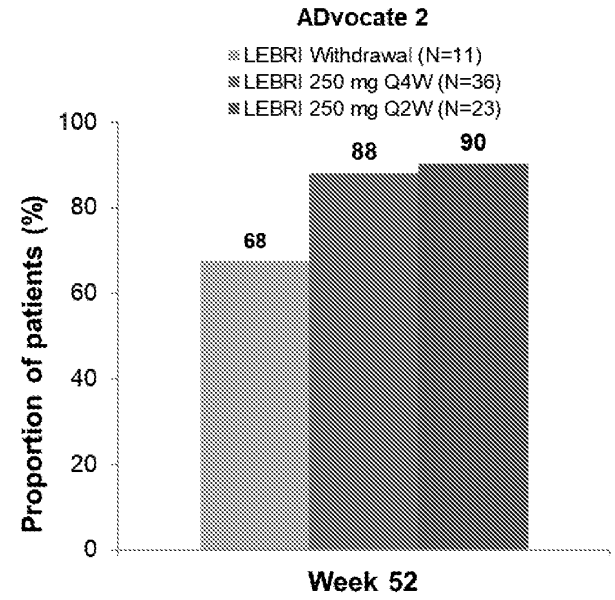


Figure 7

	ADvocate 1			ADvocate 2		
	LEBRI Placebo QW N=32 n (%)	LEBRI 250 mg QWP N=54 n (%)	LEBRI 250 mg Q2W N=62 n (%)	LEBRI Placebo QW N=28 n (%)	LEBRI 250 mg QWP N=55 n (%)	LEBRI 250 mg Q2W N=51 n (%)
Any TEAE	15 (46.9)	33 (52.4)	25 (40.3)	15 (53.6)	28 (50.9)	31 (60.8)
Mild	7 (21.9)	14 (22.2)	18 (29.0)	8 (28.6)	10 (18.2)	17 (33.3)
Moderate	8 (25.0)	15 (23.8)	5 (8.1)	7 (25.0)	16 (29.1)	12 (23.5)
Severe	0 (0.0)	4 (6.3)	2 (3.2)	0 (0.0)	2 (3.6)	2 (3.9)
Serious adverse event	0 (0.0)	2 (3.2)	0 (0.0)	1 (3.6)	0 (0.0)	2 (3.9)
Death						
AEs leading to treatment discontinuation	0 (0.0)	1 (1.6)	1 (1.6)	0 (0.0)	1 (1.8)	0 (0.0)

Figure 8A

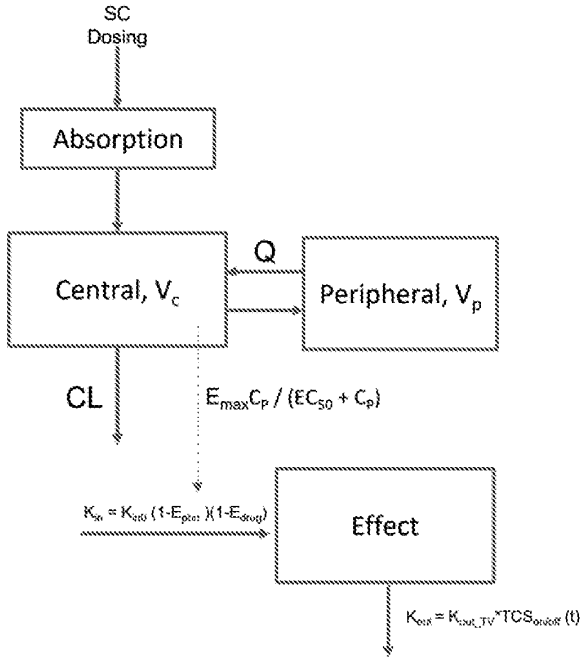


Figure 8B

Param	Alias	Estimate	Relative SE (%)	95% CI
θ_1	Baseline EASI (KGAG)	23.9	3.1	(22.4 - 25.3)
θ_2	Baseline EASI (KGAF,KGAD)	26.8	1.9	(25.8 - 27.8)
θ_3	Kout (1/d)	0.0523	.....	(0.0489 - 0.0559)
θ_4	Placebo Effect (Fixed)	0.702	.....	.....
θ_5	TCS on Kout (unitless multiplier)	1.08	.....	(1.06 - 1.10)
θ_6	sigmaE	0.468	.....	(0.463 - 0.474)
θ_7	Emax	0.831	.....	(0.761 - 0.883)
θ_8	EC50 (ug/mL)	16.5	.....	(9.84 - 27.6)
θ_9	Baseline EASI (KGAB,KGAC)	29.5	0.5	(29.3 - 29.8)
$\omega_{1,1}$	ω^2_{E0}	1.74	8.4	(1.45 - 2.03)
$\omega_{2,1}$	$\omega^2_{E0,Kout}$	-0.0599	82.5	(-0.157 - 0.0370)
$\omega_{2,2}$	ω^2_{kout}	0.340	8.2	(0.285 - 0.395)
$\omega_{3,2}$	$\omega^2_{kout,Epbo}$	0.0860	81.8	(-0.0519 - 0.224)
$\omega_{3,3}$	ω^2_{Epbo}	2.46	7.9	(2.08 - 2.84)
$\omega_{5,5}$	ω^2_{EC50}	4.96	32.2	(1.83 - 8.09)

Parameter values for the final PK-PD model. **EASI:** Eczema Area and Severity Index; **TCS:** topical corticosteroid; **E0:** individual baseline EASI estimate; Epbo: placebo effect; **sigmaE:** individual variability on baseline; ω^2_X: variance of the IIV of parameter X, IIV is derived from variance according to $\sqrt{\omega^2_X} \cdot 100$. $\omega^2_{X,Y}$: covariance of the IIV of parameters X and Y.

Figure 9

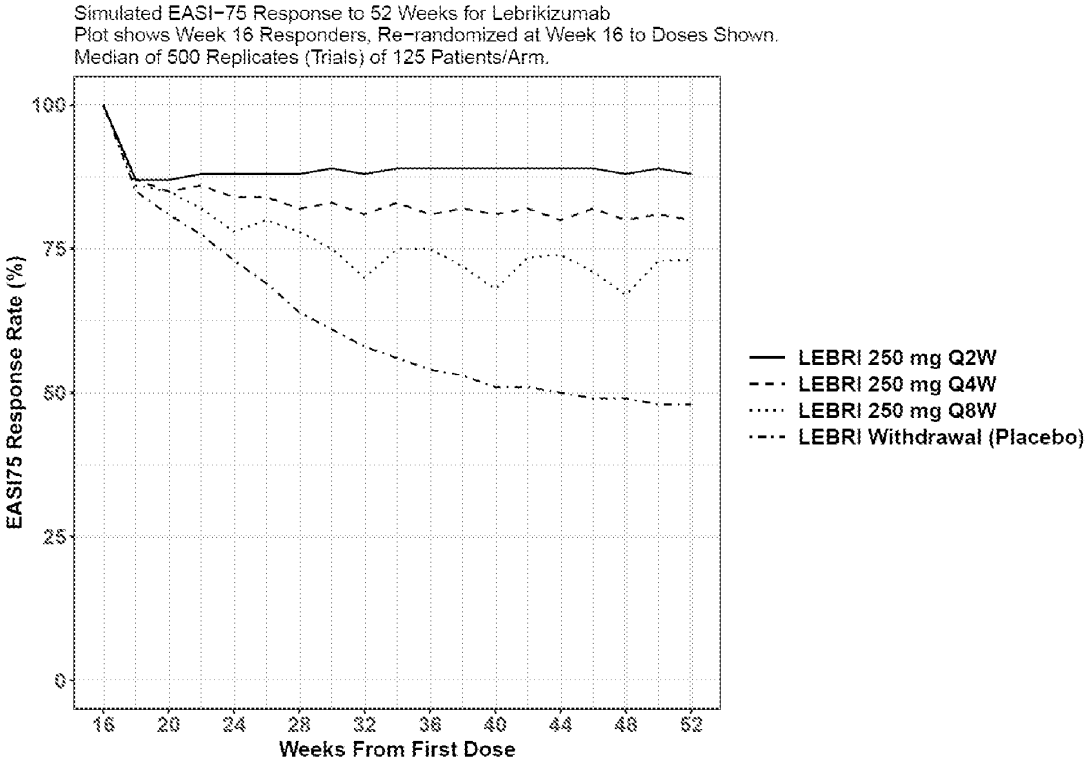

Simulated EASI-75 Response to 52 Weeks for Lebrikizumab
Plot shows Week 16 Responders, Re-randomized at Week 16 to Doses Shown.
Median of 500 Replicates (Trials) of 125 Patients/Arm.
EASI75 Response Rate (%)
100
75
50
25
0
16
20
24
28
32
36
40
44
48
52
Weeks From First Dose
LEBRI 250 mg Q2W
LEBRI 250 mg Q4W
LEBRI 250 mg Q8W
LEBRI Withdrawal (Placebo)

Figure 10

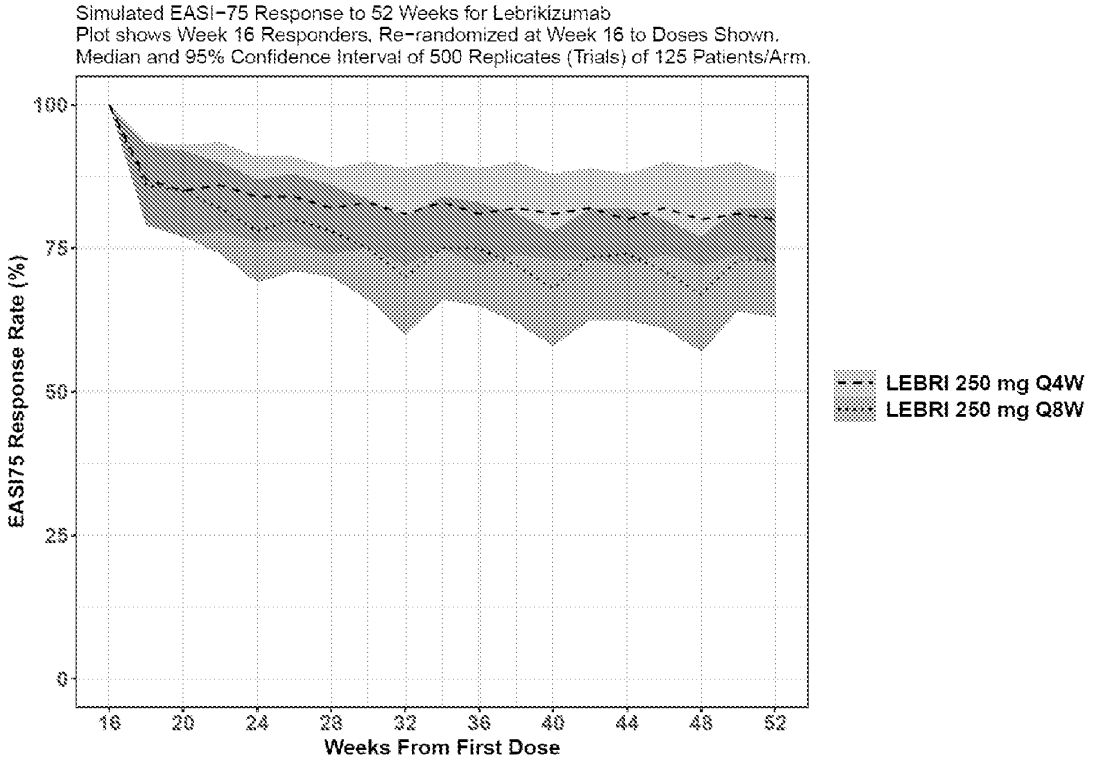

Simulated EASI-75 Response to 52 Weeks for Lebrikizumab
Plot shows Week 16 Responders, Re-randomized at Week 16 to Doses Shown.
Median and 95% Confidence Interval of 500 Replicates (Trials) of 125 Patients/Arm.
EASI75 Response Rate (%)
100
75
50
25
0
16
20
24
28
32
36
40
44
48
52
Weeks From First Dose
LEBRI 250 mg Q4W
LEBRI 250 mg Q8W

Figure 11

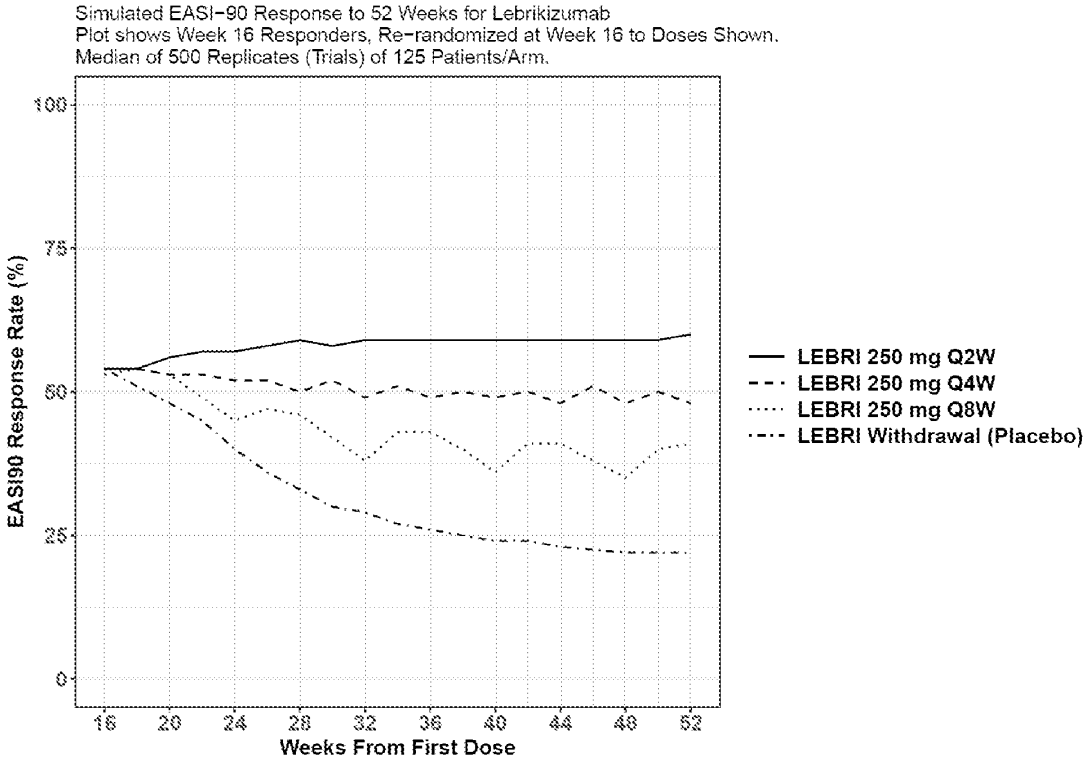
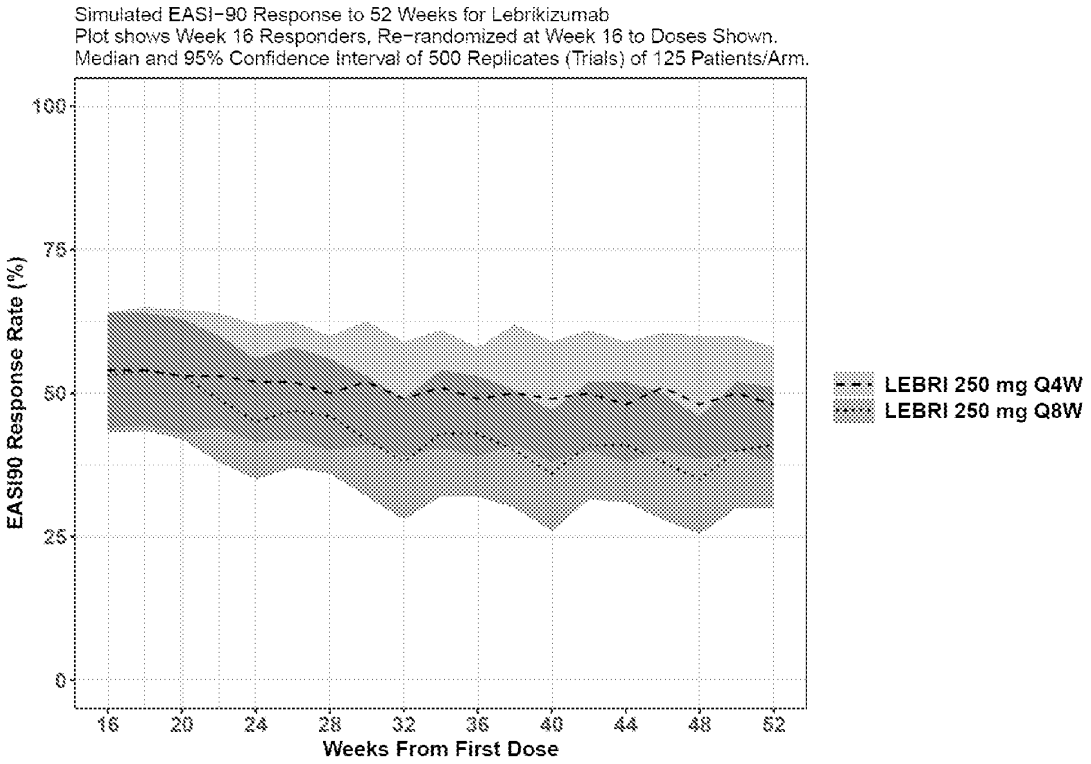

Simulated EASI-90 Response to 52 Weeks for Lebrikizumab
Plot shows Week 16 Responders, Re-randomized at Week 16 to Doses Shown.
Median of 500 Replicates (Trials) of 125 Patients/Arm.
EASi90 Response Rate (%)
100
75
50
25
0
16
20
24
28
32
36
40
44
48
52
Weeks From First Dose
LEBRI 250 mg Q2W
LEBRI 250 mg Q4W
LEBRI 250 mg Q8W
LEBRI Withdrawal (Placebo)

Figure 12


Simulated EASI-90 Response to 52 Weeks for Lebrikizumab
Plot shows Week 16 Responders, Re-randomized at Week 16 to Doses Shown.
Median and 95% Confidence Interval of 500 Replicates (Trials) of 125 Patients/Arm.
EASI90 Response Rate (%)
100
75
50
25
0
16
20
24
28
32
36
40
44
48
52
Weeks From First Dose
LEBRI 250 mg Q4W
LEBRI 250 mg Q8W