

Nemolizumab Improves Patient-Reported Symptoms of Atopic Dermatitis With Pruritus: Post Hoc Analysis of a Japanese Phase III Randomized Controlled Trial

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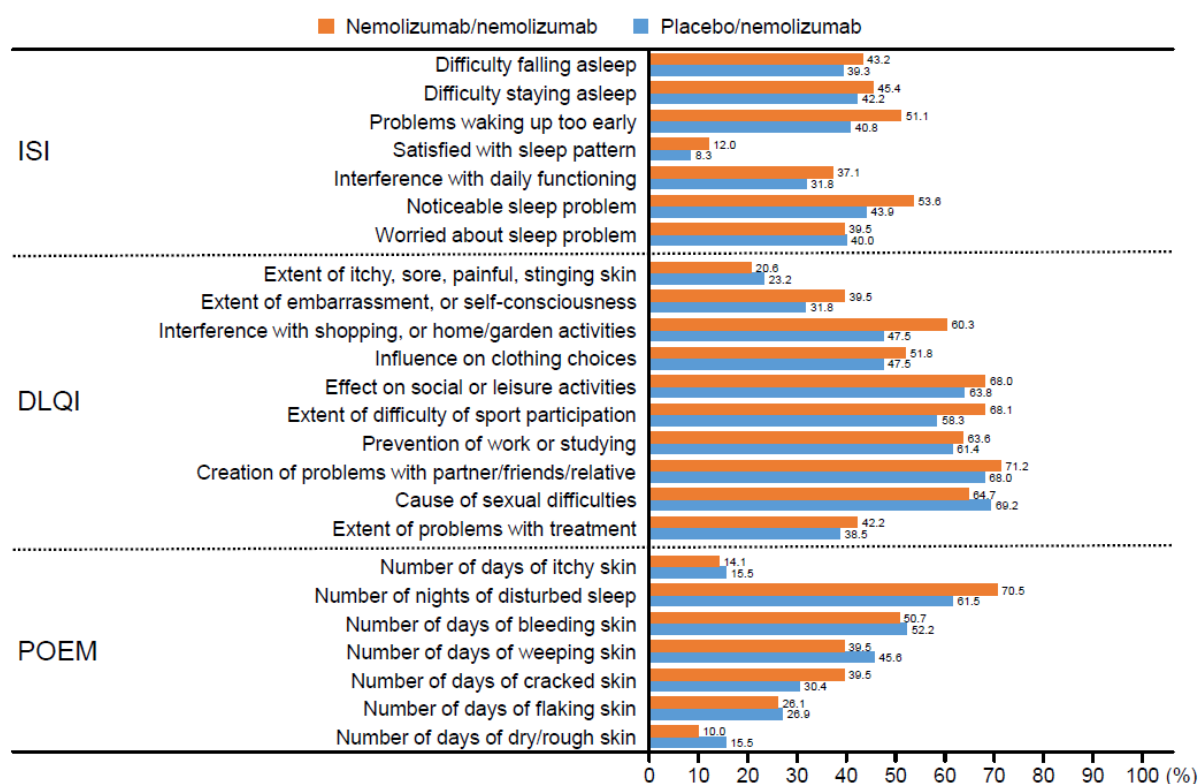
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Supplementary Text S1. Summary of inclusion and exclusion criteria for the phase III study.

Inclusion criteria: age ≥ 13 years; body weight 30.0–120.0 kg; confirmed diagnosis of atopic dermatitis (AD) with pruritus; inadequate pruritic response to ≥ 4 weeks of stable-dose medium-potency topical corticosteroids or topical calcineurin inhibitors and to ≥ 2 weeks of stable-dose oral antihistamines, or an inability to receive such therapies (with inadequate pruritic response defined as a score of ≥ 3 on a five-level itch scale); a Visual Analog Scale score for pruritus of ≥ 50 and an Eczema Area and Severity Index score of ≥ 10 on the day of randomization.

Exclusion criteria: presence of any serious disease of the heart, liver, kidney, lung, or blood; congestive heart failure; malignancy within the past 5 years; use of systemic therapy for uncontrolled asthma; use of systemic therapies within 7 days prior to randomization for infections (including skin infections); positivity for infections including hepatitis B or C, human immunodeficiency virus, or tuberculosis; confirmed immune deficiency; known hypersensitivity to nemolizumab or participation in prior nemolizumab clinical trials; recent use of any antibody drugs for AD, live vaccines, or any other prohibited concomitant therapy; pregnancy, lactation or unwillingness to use contraception during the trial period; any abnormal laboratory test value; or any other medical condition which could confound the trial outcome or endanger the patient.

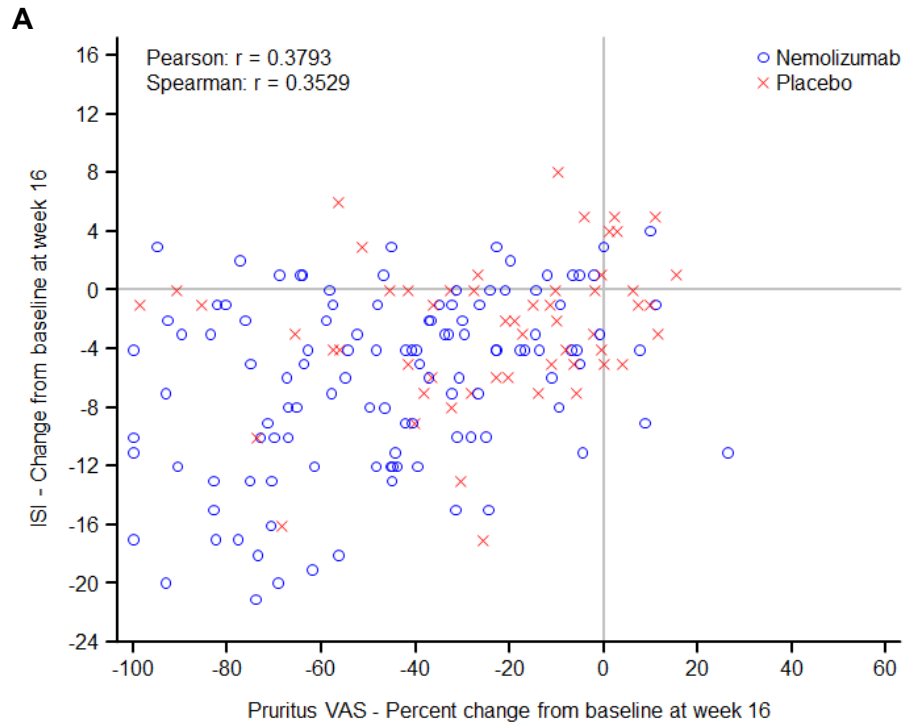
Supplementary Fig. S1 Proportions of patients reporting 0 for each symptom at week 68 (modified intention-to-treat population^a).

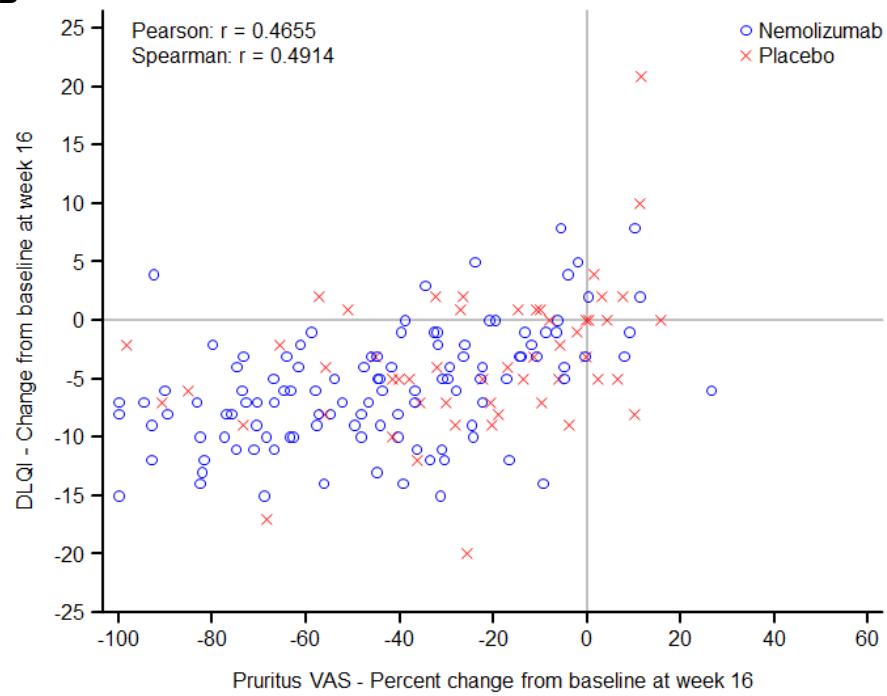
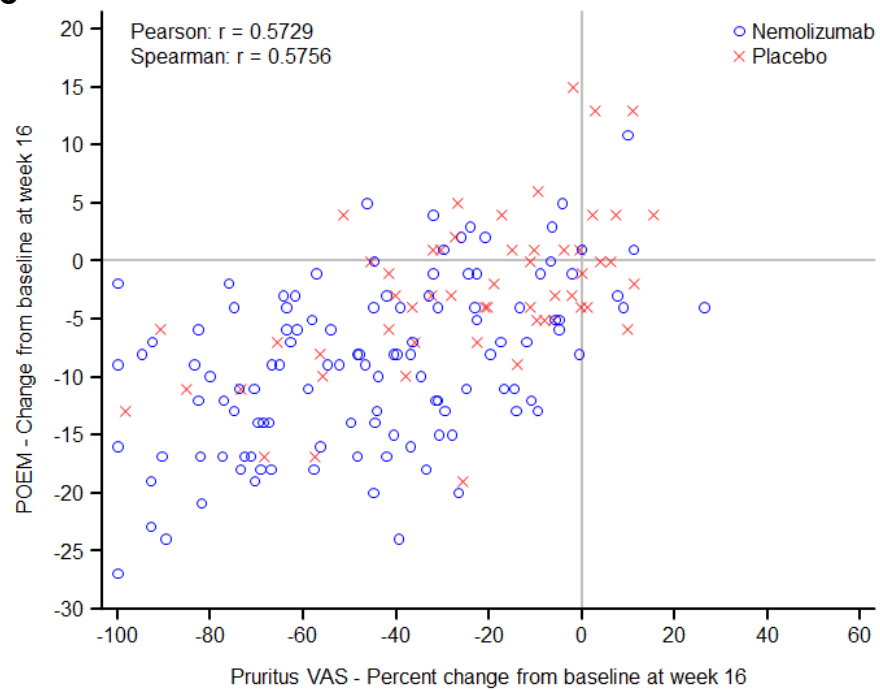


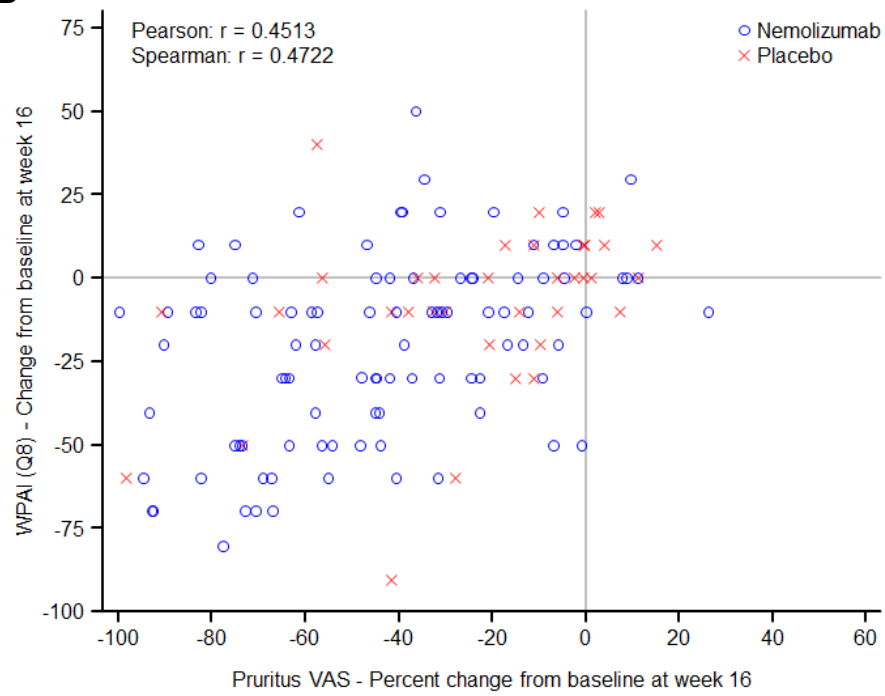
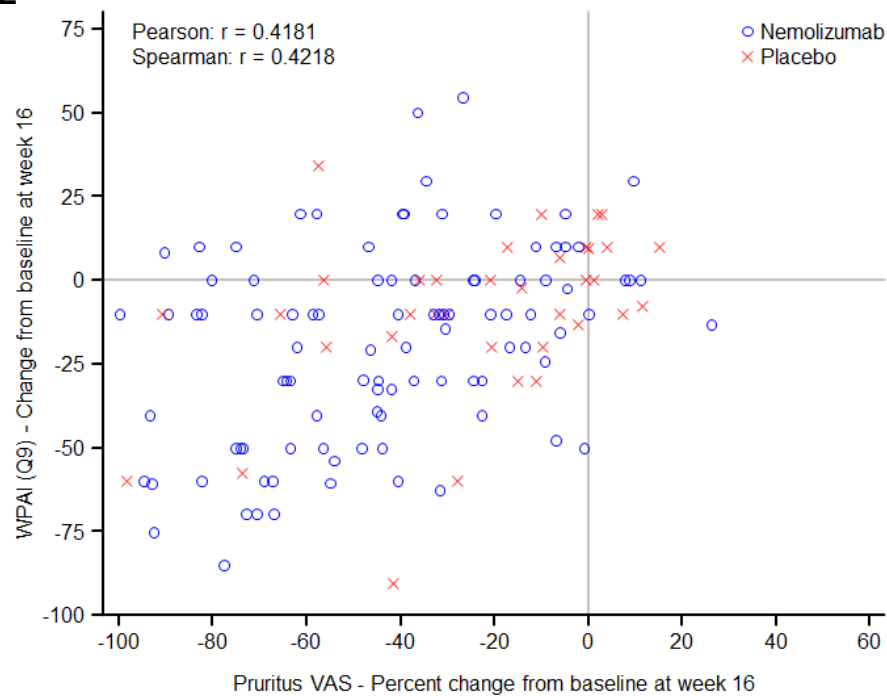
DLQI Dermatology Life Quality Index, *ISI* Insomnia Severity Index, *POEM* Patient-Oriented Eczema Measure

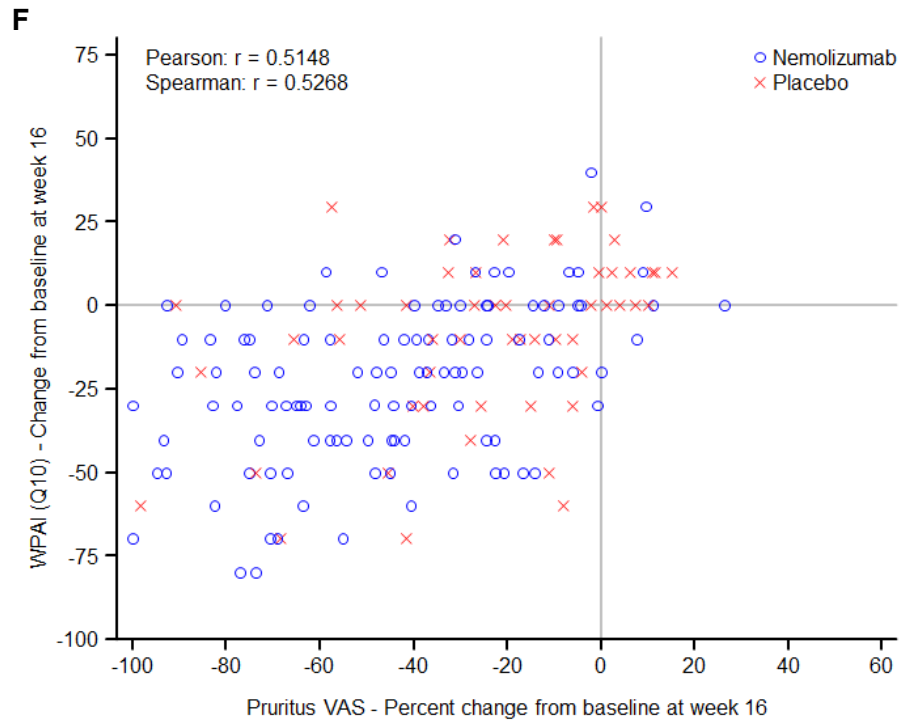
^aAnalysis was conducted only for patients with a score of 1 or more for the selected symptom at baseline

Supplementary Fig. S2 Scatter plots showing correlations between pruritus VAS and scores at week 16 for **A** ISI, **B** DLQI, **C** POEM, **D** WPAI-AD question 8, **E** WPAI-AD question 9, and **F** WPAI-AD question 10.



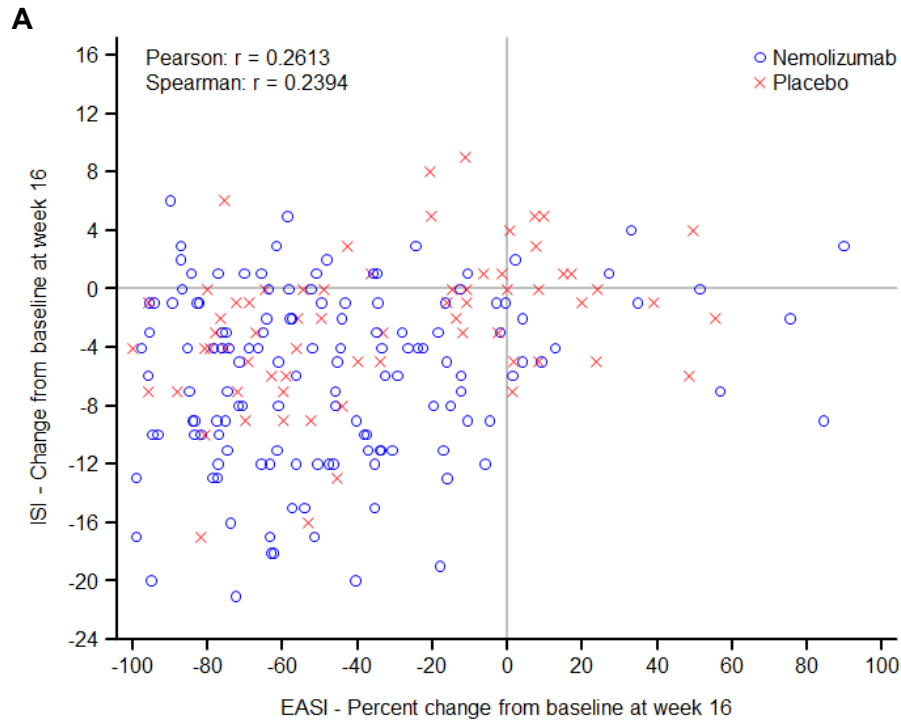
B**C**

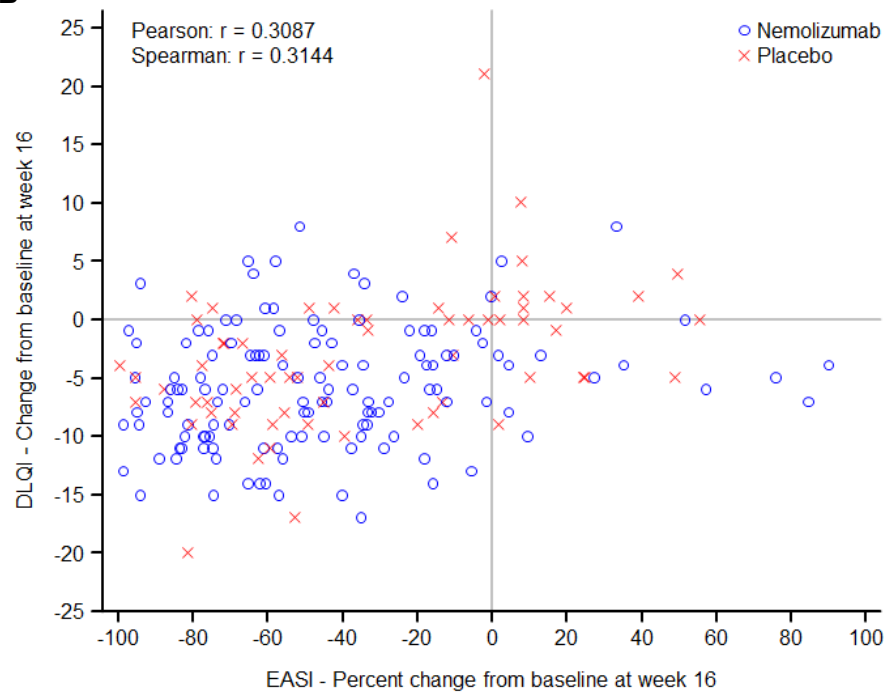
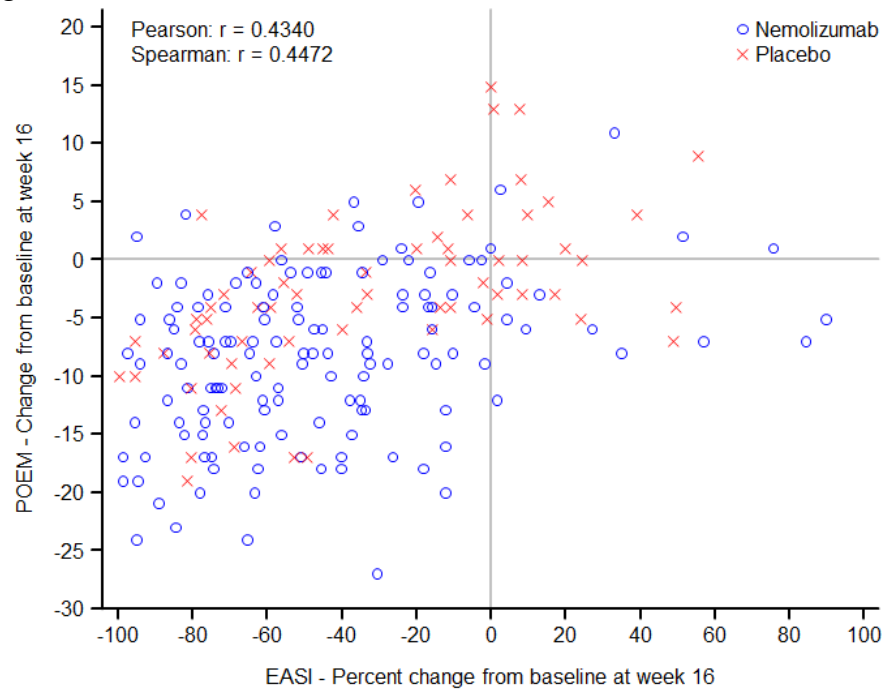
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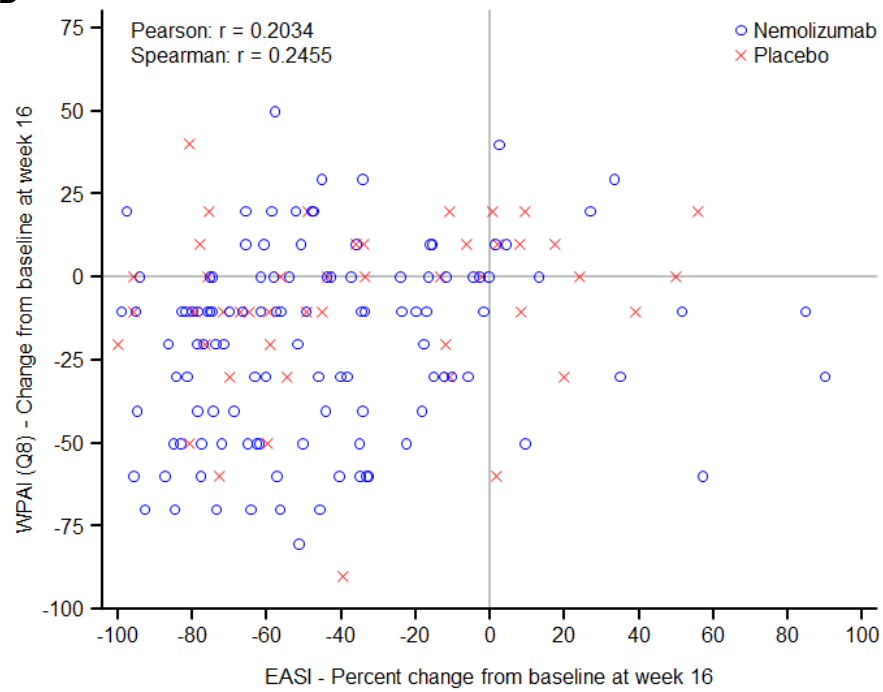
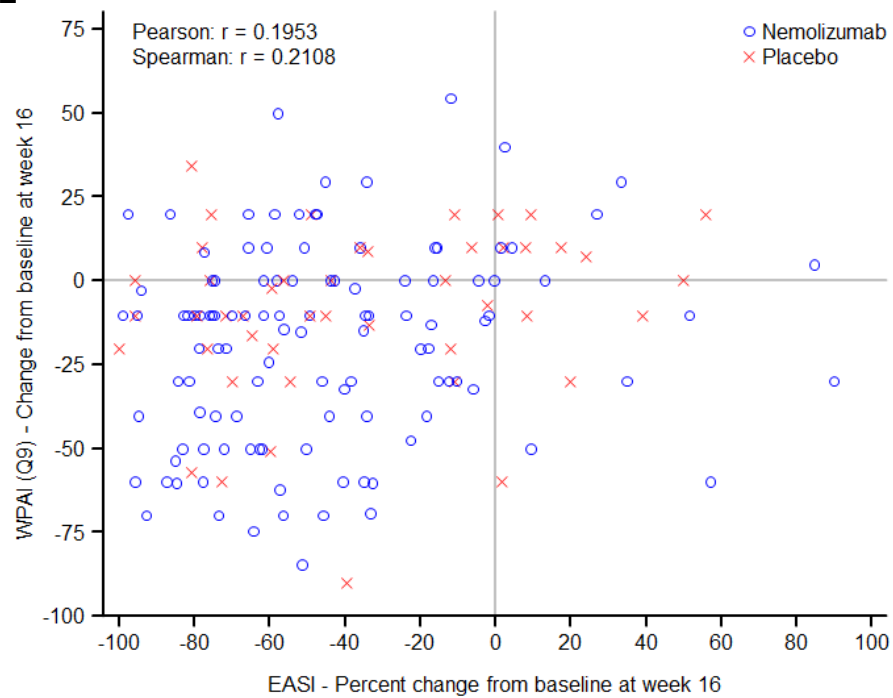


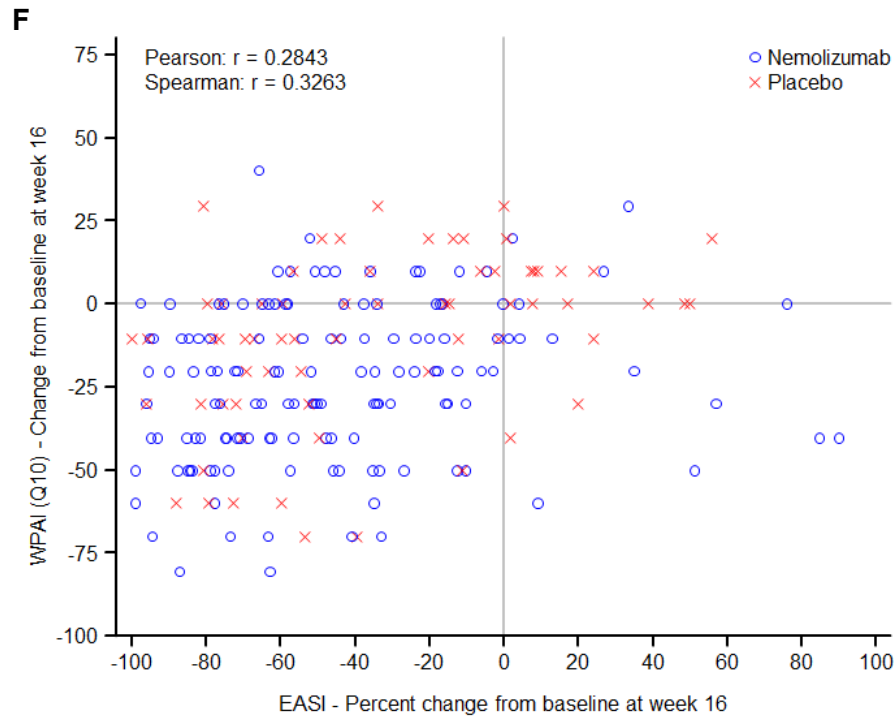
A value of 1 represents perfect correlation; thus, values closer to 1 indicate stronger correlations. *DLQI* Dermatology Life Quality Index, *ISI* Insomnia Severity Index, *POEM* Patient-Oriented Eczema Measure, VAS visual analog scale, *WPAI-AD* Work Productivity and Activity Impairment: Atopic Dermatitis questionnaire

Supplementary Fig. S3 Scatter plots showing correlations between EASI and scores at week 16 for **A** ISI, **B** DLQI, **C** POEM, **D** WPAI-AD question 8, **E** WPAI-AD question 9, and **F** WPAI-AD question 10.



B**C**

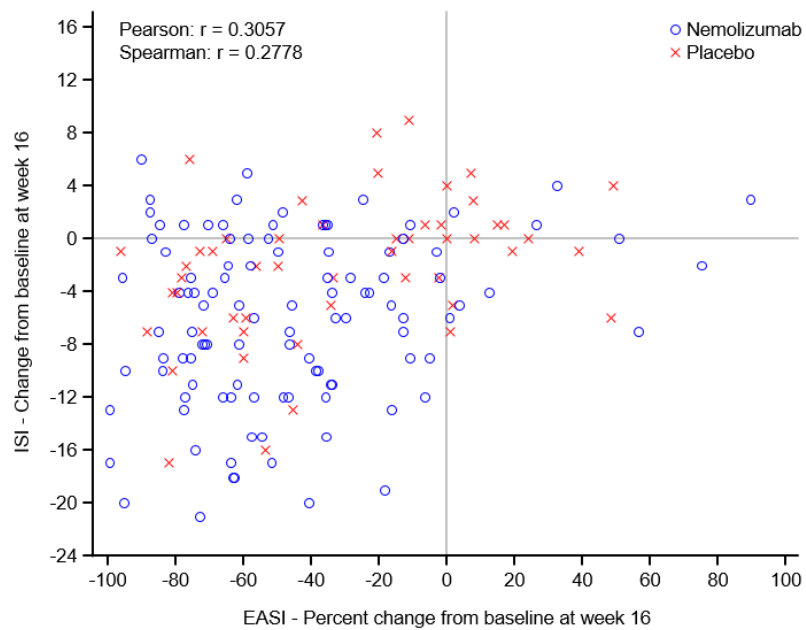
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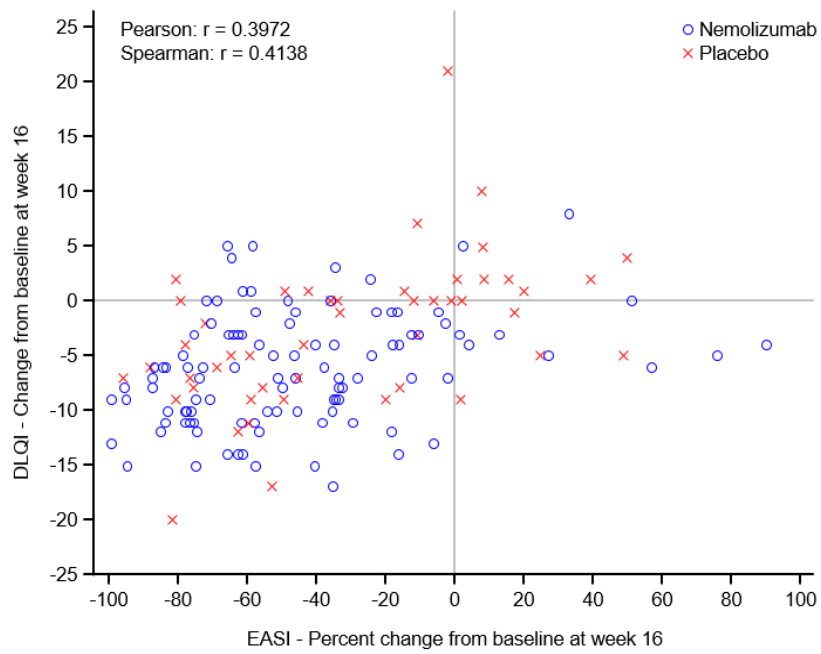
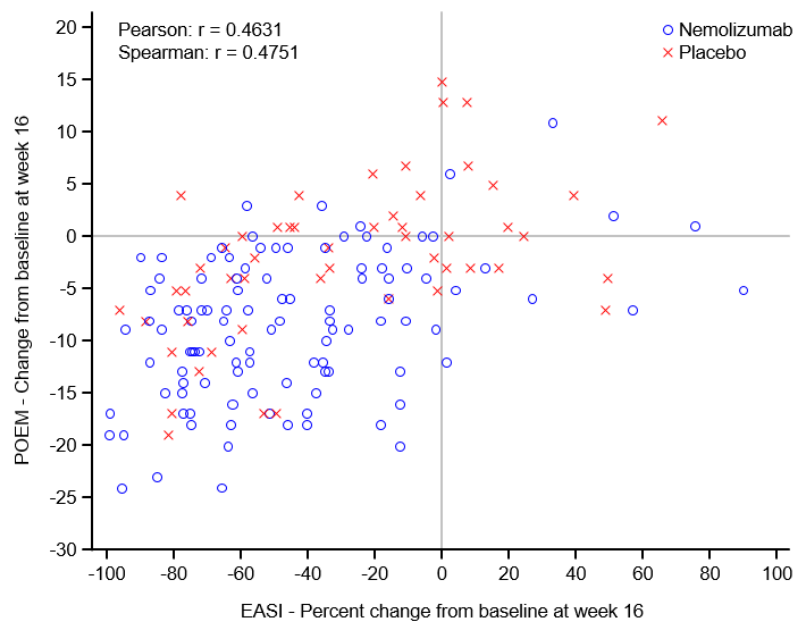


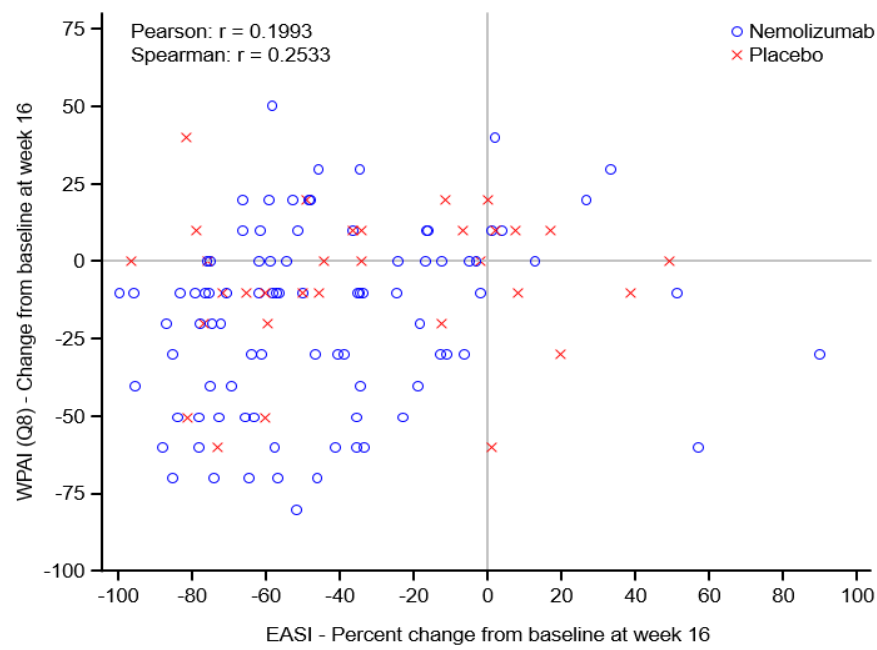
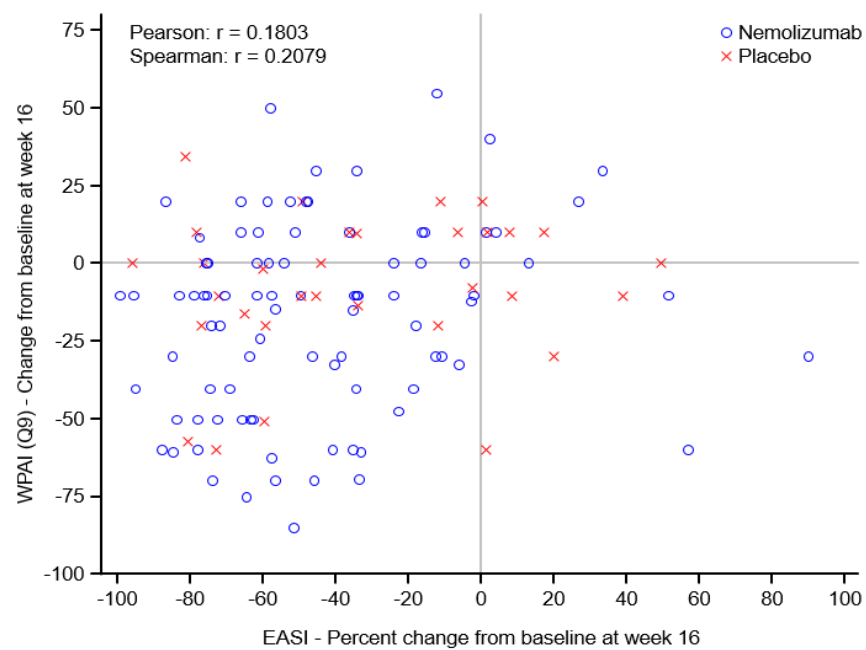
A value of 1 represents perfect correlation; thus, values closer to 1 indicate stronger correlations. *DLQI* Dermatology Life Quality Index, *EASI* Eczema Area and Severity Index, *ISI* Insomnia Severity Index, *POEM* Patient-Oriented Eczema Measure, *WPAI-AD* Work Productivity and Activity Impairment: Atopic Dermatitis questionnaire

Supplementary Fig. S4 Scatter plots in patients with more severe EASI scores (≥ 16) at baseline showing correlations between EASI and scores at week 16 for **A** ISI, **B** DLQI, **C** POEM, **D** WPAI-AD question 8, **E** WPAI-AD question 9, and **F** WPAI-AD question 10.

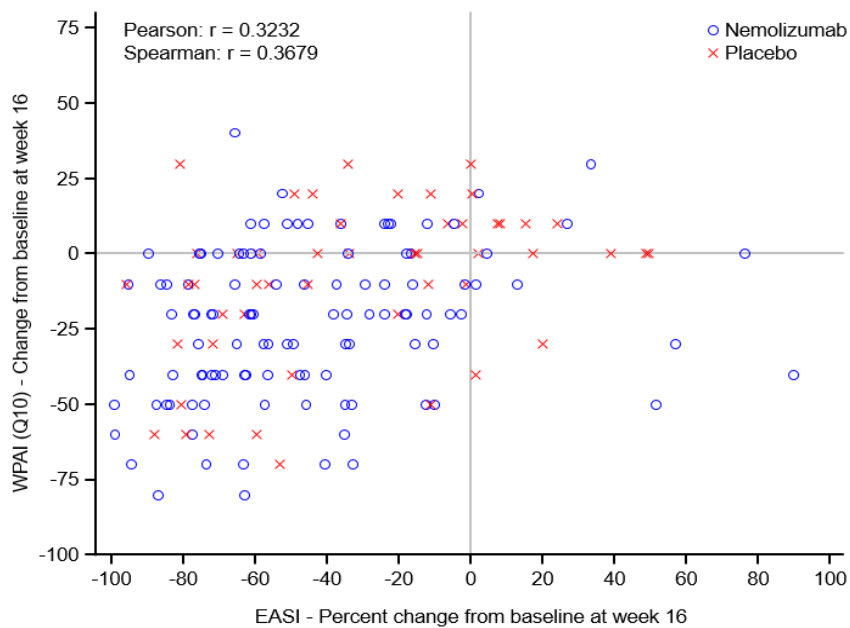
A



B**C**

D**E**

F



A value of 1 represents perfect correlation; thus, values closer to 1 indicate stronger correlations. *DLQI* Dermatology Life Quality Index, *EASI* Eczema Area and Severity Index, *ISI* Insomnia Severity Index, *POEM* Patient-Oriented Eczema Measure, *WPAI-AD* Work Productivity and Activity Impairment: Atopic Dermatitis questionnaire

Supplementary Table S1 Summary statistics for the pruritus VAS, EASI, ISI, DLQI, POEM, and WPAI-AD assessments up to week 16 (modified intention-to-treat population)

Scores ^a	Baseline	Week 1	Week 2	Week 4	Week 8	Week 12	Week 16
Nemolizumab/nemolizumab (<i>n</i> = 143)							
Pruritus VAS ^b , <i>n</i>	143	143	142	136	126	117	116
Total score	74.9 (0.9)	60.7 (1.3)	53.7 (1.6)	49.9 (1.8)	45.4 (2.0)	42.7 (1.9)	39.9 (2.0)
Percent change from baseline	-	-18.8 (1.5)	-28.1 (2.0)	-33.3 (2.2)	-38.7 (2.6)	-42.0 (2.6)	-45.6 (2.7)
EASI, <i>n</i>	143	143	142	142	142	140	140
Total score	27.6 (1.1)	21.0 (1.1)	19.0 (1.1)	17.7 (1.1)	17.9 (1.1)	16.3 (1.1)	14.7 (1.0)
Percent change from baseline	-	-24.9 (1.9)	-33.1 (2.2)	-37.5 (2.6)	-34.3 (3.5)	-40.7 (3.5)	-46.0 (3.2)
ISI, <i>n</i>	142	-	143	142	142	140	140
Total score	12.4 (0.5)	-	8.8 (0.4)	7.9 (0.5)	7.3 (0.5)	6.9 (0.4)	6.4 (0.4)
Change from baseline	-	-	-3.7 (0.4)**	-4.5 (0.4)**	-5.1 (0.5)**	-5.5 (0.5)**	-6.0 (0.5)**
Range, <i>n</i> (%)							
0–7: no clinically significant insomnia	34 (23.9)	-	64 (44.8)	78 (54.9)	78 (54.9)	82 (58.6)	91 (65.0)
8–14: subthreshold insomnia	57 (40.1)	-	60 (42.0)	47 (33.1)	48 (33.8)	43 (30.7)	37 (26.4)
15–21: clinical insomnia (moderate)	44 (31.0)	-	16 (11.2)	14 (9.9)	12 (8.5)	13 (9.3)	10 (7.1)
22–28: clinical insomnia (severe)	7 (4.9)	-	3 (2.1)	3 (2.1)	4 (2.8)	2 (1.4)	2 (1.4)

Scores ^a	Baseline	Week 1	Week 2	Week 4	Week 8	Week 12	Week 16
DLQI, <i>n</i>	136	137	137	137	137	135	135
Total score	12.4 (0.5)	7.5 (0.4)	7.1 (0.4)	7.4 (0.5)	7.5 (0.5)	6.9 (0.4)	6.6 (0.4)
Change from baseline	-	-4.9 (0.4)**	-5.3 (0.4)**	-5.0 (0.4)**	-4.8 (0.4)**	-5.4 (0.4)**	-5.7 (0.4)**
Range, <i>n</i> (%)							
0–1: No effect at all on patient's life	0	5 (3.6)	11 (8.0)	17 (12.4)	17 (12.4)	15 (11.1)	19 (14.1)
2–5: Small effect on patient's life	10 (7.4)	50 (36.5)	45 (32.8)	40 (29.2)	38 (27.7)	40 (29.6)	49 (36.3)
6–10: Moderate effect on patient's life	46 (33.8)	56 (40.9)	55 (40.1)	51 (37.2)	50 (36.5)	52 (38.5)	39 (28.9)
11–20: Very large effect on patient's life	67 (49.3)	20 (14.6)	23 (16.8)	24 (17.5)	27 (19.7)	28 (20.7)	27 (20.0)
21–30: Extremely large effect on patient's life	13 (9.6)	6 (4.4)	3 (2.2)	5 (3.6)	5 (3.6)	0	1 (0.7)
POEM, <i>n</i>	142	143	142	142	142	140	140
Total score	21.1 (0.5)	14.0 (0.5)	13.2 (0.6)	13.3 (0.6)	13.9 (0.6)	12.9 (0.5)	12.6 (0.6)
Change from baseline	-	-7.1 (0.5)**	-7.8 (0.5)**	-7.8 (0.6)**	-7.1 (0.5)**	-8.1 (0.5)**	-8.4 (0.6)**
Range, <i>n</i> (%)							
0–2: Clear or almost clear	0	2 (1.4)	5 (3.5)	8 (5.6)	11 (7.7)	7 (5.0)	10 (7.1)
3–7: Mild eczema	2 (1.4)	25 (17.5)	27 (19.0)	26 (18.3)	18 (12.7)	25 (17.9)	30 (21.4)
8–16: Moderate eczema	27 (19.0)	65 (45.5)	67 (47.2)	60 (42.3)	62 (43.7)	64 (45.7)	57 (40.7)
17–24: Severe eczema	66 (46.5)	42 (29.4)	37 (26.1)	41 (28.9)	45 (31.7)	37 (26.4)	35 (25.0)
25–28: Very severe eczema	47 (33.1)	9 (6.3)	6 (4.2)	7 (4.9)	6 (4.2)	7 (5.0)	8 (5.7)

Scores ^a	Baseline	Week 1	Week 2	Week 4	Week 8	Week 12	Week 16
WPAI-AD							
Question 7: Percent work time missed, n	122	118	119	120	116	115	115
Score	2.3 (0.7)	3.4 (1.0)	2.7 (0.8)	2.9 (0.9)	4.1 (1.4)	2.8 (0.9)	2.2 (0.8)
Question 8: Percent impairment while working, n	122	118	119	120	114	115	115
Score	46.7 (2.5)	35.4 (2.0)*	30.8 (2.0)**	31.0 (2.1)*	29.8 (2.1)**	27.3 (2.0)**	25.9 (2.0)**
Question 9: Percent overall work impairment, n	122	118	119	120	114	115	115
Score	47.3 (2.5)	37.1 (2.1)	32.4 (2.1)*	32.5 (2.2)*	31.4 (2.1)**	29.1 (2.1)**	27.6 (2.0)**
Question 10: Percent activity impairment, n	142	143	142	142	142	140	140
Score	54.9 (2.1)	41.2 (2.0)*	35.0 (2.0)**	36.7 (2.2)**	34.3 (2.2)**	31.1 (2.0)**	30.9 (2.0)**

Scores ^a	Baseline	Week 1	Week 2	Week 4	Week 8	Week 12	Week 16
Placebo/nemolizumab (<i>n</i> = 72)							
Pruritus VAS ^b , <i>n</i>	72	72	71	69	66	60	55
Total score	75.3 (1.2)	70.3 (1.3)	67.2 (1.6)	64.9 (1.9)	61.1 (2.1)	59.5 (2.6)	56.8 (2.9)
Percent change from baseline	-	-6.5 (1.1)	-10.6 (1.7)	-13.5 (2.1)	-18.5 (2.7)	-20.2 (3.5)	-24.1 (3.7)
EASI, <i>n</i>	72	70	70	69	69	68	68
Total score	25.7 (1.4)	22.4 (1.4)	20.9 (1.4)	19.1 (1.4)	19.0 (1.5)	18.6 (1.7)	18.3 (1.8)
Percent change from baseline	-	-13.6 (2.3)	-21.0 (3.0)	-27.5 (3.7)	-28.3 (4.2)	-30.7 (5.0)	-33.2 (4.9)
ISI, <i>n</i>	72	-	72	69	69	68	68
Total score	12.3 (0.8)	-	11.4 (0.7)	11.2 (0.8)	11.4 (0.7)	11.4 (0.8)	10.1 (0.7)
Change from baseline	-	-	-1.0 (0.5)	-1.3 (0.5)	-1.1 (0.6)	-1.2 (0.6)	-2.5 (0.6)
Range, <i>n</i> (%)							
0–7: No clinically significant insomnia	16 (22.2)	-	19 (26.4)	22 (31.9)	18 (26.1)	22 (32.4)	23 (33.8)
8–14: Subthreshold insomnia	34 (47.2)	-	30 (41.7)	27 (39.1)	30 (43.5)	21 (30.9)	28 (41.2)
15–21: Clinical insomnia (moderate)	15 (20.8)	-	21 (29.2)	17 (24.6)	18 (26.1)	22 (32.4)	15 (22.1)
22–28: Clinical insomnia (severe)	7 (9.7)	-	2 (2.8)	3 (4.3)	3 (4.3)	3 (4.4)	2 (2.9)

Scores ^a	Baseline	Week 1	Week 2	Week 4	Week 8	Week 12	Week 16
DLQI, <i>n</i>	69	67	68	67	67	66	66
Total score	12.1 (0.6)	9.3 (0.6)	9.2 (0.6)	9.6 (0.7)	9.6 (0.7)	9.7 (0.7)	8.9 (0.7)
Change from baseline	-	-2.7 (0.5)	-3.1 (0.6)	-2.5 (0.6)	-2.6 (0.6)	-2.5 (0.7)	-3.2 (0.7)
Range, <i>n</i> (%)							
0–1: No effect at all on patient's life	0	1 (1.5)	2 (2.9)	1 (1.5)	5 (7.5)	5 (7.6)	4 (6.1)
2–5: Small effect on patient's life	5 (7.2)	15 (22.4)	17 (25.0)	19 (28.4)	12 (17.9)	11 (16.7)	14 (21.2)
6–10: Moderate effect on patient's life	23 (33.3)	26 (38.8)	25 (36.8)	23 (34.3)	24 (35.8)	23 (34.8)	30 (45.5)
11–20: Very large effect on patient's life	37 (53.6)	23 (34.3)	22 (32.4)	21 (31.3)	22 (32.8)	24 (36.4)	16 (24.2)
21–30: Extremely large effect on patient's life	4 (5.8)	2 (3.0)	2 (2.9)	3 (4.5)	4 (6.0)	3 (4.5)	2 (3.0)
POEM, <i>n</i>	72	70	70	69	69	68	68
Total score	20.2 (0.7)	17.6 (0.7)	17.7 (0.8)	17.7 (0.8)	18.1 (0.9)	18.0 (0.9)	17.5 (0.9)
Change from baseline	-	-2.4 (0.5)	-2.6 (0.6)	-2.6 (0.6)	-2.1 (0.8)	-2.3 (0.9)	-2.8 (0.9)
Range, <i>n</i> (%)							
0–2: Clear or almost clear	0	0	1 (1.4)	0	2 (2.9)	0	2 (2.9)
3–7: Mild eczema	0	4 (5.7)	4 (5.7)	5 (7.2)	5 (7.2)	3 (4.4)	8 (11.8)
8–16: Moderate eczema	25 (34.7)	25 (35.7)	24 (34.3)	25 (36.2)	20 (29.0)	26 (38.2)	19 (27.9)
17–24: Severe eczema	27 (37.5)	32 (45.7)	27 (38.6)	27 (39.1)	24 (34.8)	24 (35.3)	26 (38.2)
25–28: Very severe eczema	20 (27.8)	9 (12.9)	14 (20.0)	12 (17.4)	18 (26.1)	15 (22.1)	13 (19.1)

Scores ^a	Baseline	Week 1	Week 2	Week 4	Week 8	Week 12	Week 16
WPAI-AD							
Question 7: Percent work time missed, n	51	51	54	54	52	51	51
Score	3.1 (1.3)	3.2 (1.6)	4.4 (2.2)	1.8 (1.0)	5.0 (1.9)	2.9 (1.4)	3.0 (1.7)
Question 8: Percent impairment while working, n	52	51	53	54	53	51	51
Score	47.5 (3.4)	43.5 (3.2)	40.8 (3.1)	40.7 (3.1)	44.0 (3.3)	41.2 (3.7)	40.2 (3.6)
Question 9: Percent overall work impairment, n	51	51	53	54	52	51	51
Score	48.3 (3.5)	44.7 (3.3)	41.7 (3.3)	41.4 (3.2)	46.4 (3.4)	43.0 (3.6)	40.9 (3.7)
Question 10: Percent activity impairment, n	72	70	70	69	69	68	68
Score	54.3 (2.9)	48.9 (2.5)	46.6 (2.8)	45.9 (2.8)	48.7 (3.0)	46.6 (3.2)	44.0 (3.1)

DLQI Dermatology Life Quality Index, *EASI* Eczema Area and Severity Index, *ISI* Insomnia Severity Index, *POEM* Patient-Oriented Eczema Measure, *VAS* visual analog scale, *WPAI-AD* Work Productivity and Activity Impairment: Atopic Dermatitis questionnaire

P-values for nemolizumab vs. placebo were calculated using the t-test. **p* < 0.05; ***p* < 0.01

^aScores are means (standard error) unless otherwise stated. ^bPatient numbers exclude those who had received rescue treatment at each post-baseline time point