

Title page

Title

Dupilumab Improves Health-Related Quality of Life in Omalizumab-Naïve Patients with
Chronic Spontaneous Urticaria

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Supplementary material

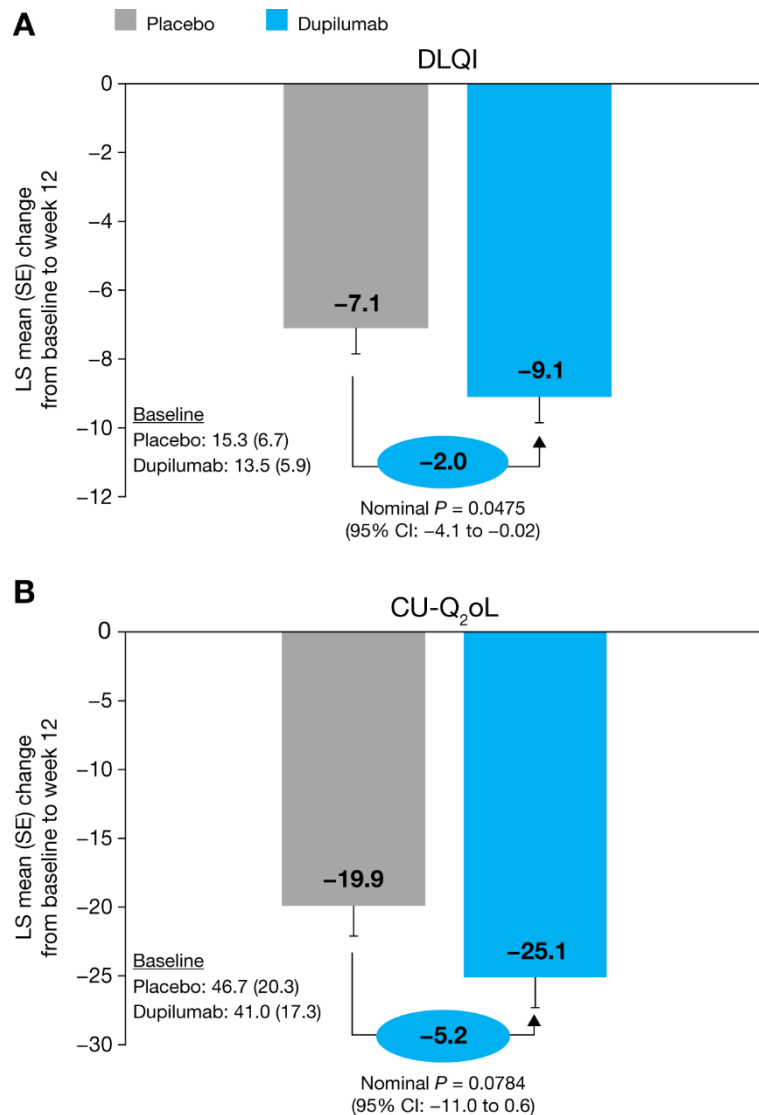


Figure S1. Change from baseline in **a** DLQI and **b** CU-Q_{2oL} total scores at week 12 – ITT population. Baseline data are presented as mean (SD), and error bars display SE values. **a** DLQI, range 0–30, with higher scores indicating greater HRQoL impairment. **b** CU-Q_{2oL}, range 0–100, with higher scores indicating greater HRQoL impairment. *CI* confidence interval, *CU-Q_{2oL}* Chronic Urticaria Quality of Life Questionnaire, *DLQI* Dermatology Life Quality Index, *HRQoL* health-related quality of life, *ITT* intention-to-treat, *LS* least squares, *SD* standard deviation, *SE* standard error

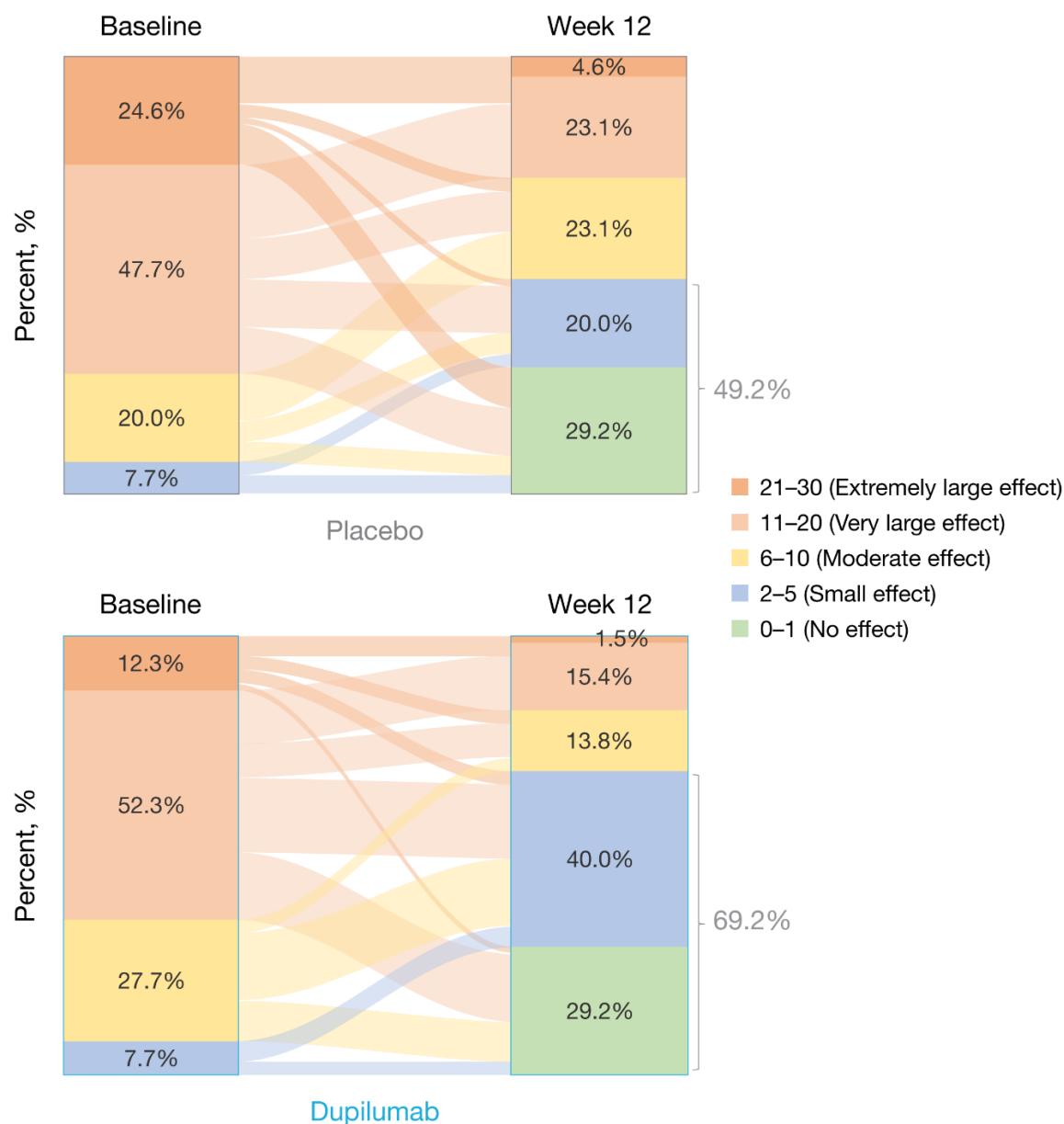


Figure S2. Impact of the skin disease on the HRQoL as measured by DLQI at baseline and week 12 – ITT population. DLQI, range 0–30, with higher scores indicating greater HRQoL impairment. This Sankey plot visualizes the flow of responses by patients from baseline to week 12, following treatment with placebo and dupilumab. Only patients with a value at baseline and week 12 are included. *DLQI* Dermatology Life Quality Index, *HRQoL* health-related quality of life, *ITT* intention-to-treat

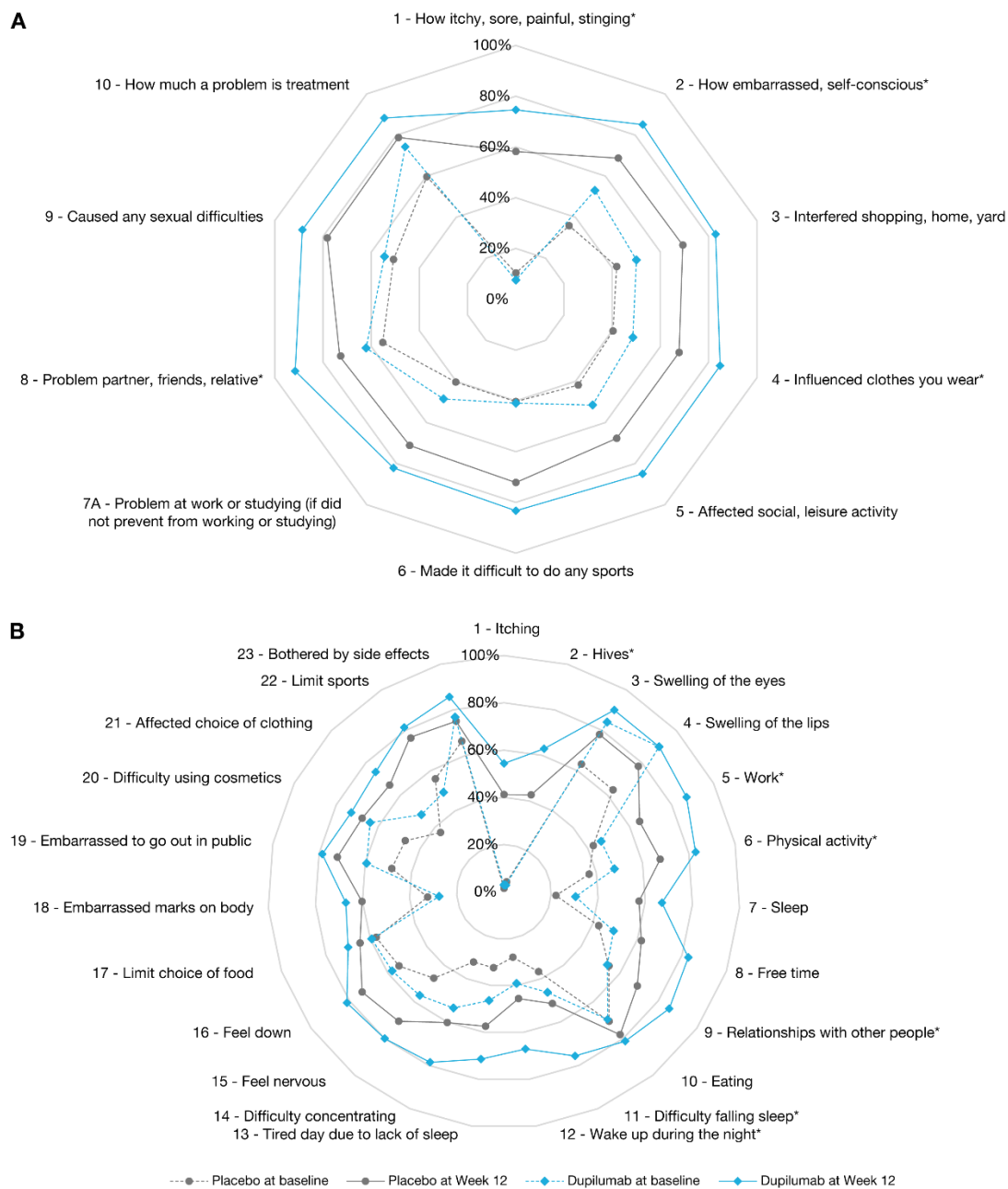


Figure S3. Percentage of patients who reported scores of “not at all/a little” effect for individual items of **a** DLQI and **b** CU-Q_{2o}L at week 12 – ITT population. DLQI, 10 items, range 0–30, with higher scores indicating greater HRQoL impairment. **b** CU-Q_{2o}L, 23 items, range 0–100, with higher scores indicating greater HRQoL impairment. *CU-Q_{2o}L* Chronic Urticaria Quality of Life Questionnaire, *DLQI* Dermatology Life Quality Index, *ITT* intention-to-treat, *HRQoL* health-related quality of life. **P*-value < 0.05

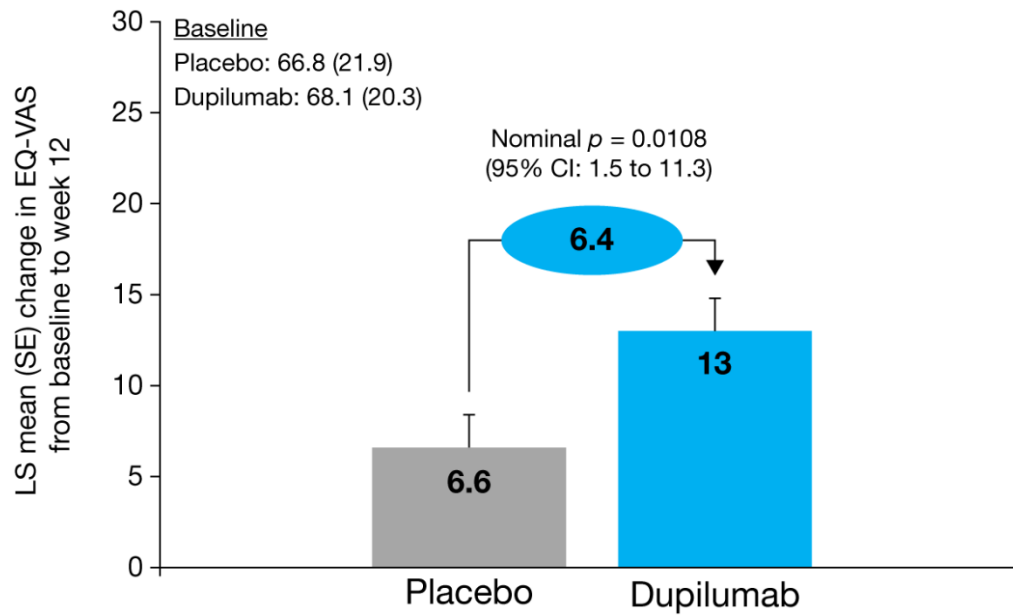


Figure S4. Change from baseline in EQ-VAS scores at week 12 – ITT population. EQ-5D (range 0–100) is rated on a scale from 0 (“The worst health you can imagine”) to 100 (“The best health you can imagine”), with higher scores representing better health. *CI* confidence interval, *CSU* chronic spontaneous urticaria, *EQ-5D* EuroQol 5-Dimension Questionnaire Visual Analog Scale, *EQ-VAS* EuroQol-Visual Analog Scale, *ITT* intention-to-treat, *LS* least squares, *SE* standard error

Table S1 Baseline demographics and disease characteristics – ITT population

	Placebo (n = 68)	Dupilumab (n = 70)	Overall (N = 138)
Age, mean (SD)	41.9 (14.8)	40.7 (16.2)	41.3 (15.5)
≥ 16 years, n (%)	67 (98.5)	67 (95.7)	134 (97.1)
≥ 18 years, n (%)	66 (97.1)	66 (94.3)	132 (95.7)
≥ 12 to < 18 years, n (%)	2 (2.9)	2 (2.9)	4 (2.9)
≥ 6 to < 12 years n (%)	0	2 (2.9)	2 (1.4)
Female, n (%)	50 (73.5)	41 (58.6)	91 (65.9)
Race, n (%)			
White	48 (70.6)	47 (67.1)	95 (68.8)
Black or African American	2 (2.9)	1 (1.4)	3 (2.2)
Asian	16 (23.5)	19 (27.1)	35 (25.4)
Other	2 (2.9)	3 (4.3)	5 (3.6)
Weight, kg, mean (SD)	75.8 (18.4)	77.2 (21.5)	76.5 (20.0)
BMI, kg/m ² , mean (SD)	27.9 (6.2)	27.4 (6.8)	27.7 (6.5)
Age at onset of CSU, years, mean (SD)	36.7 (16.0)	35.5 (16.6)	36.1 (16.2)
Time since first diagnosis of CSU, years, mean (SD)	5.7 (7.7)	5.8 (9.3)	5.7 (8.5)
Baseline ISS7 score, mean (SD)	15.7 (4.1)	16.1 (4.0)	15.9 (4.0)
Baseline UAS7 score, mean (SD)	30.8 (8.2)	31.9 (7.2)	31.3 (7.7)
Baseline UAS7 score ≥ 28, n (%)	44 (64.7)	53 (75.7)	97 (70.3)
Baseline HSS7 score, mean (SD)	15.0 (4.8)	15.8 (3.8)	15.4 (4.3)
Presence of angioedema at baseline, n (%) ^a	34 (50.0)	28 (40.0)	62 (44.9)
Baseline AAS7 score for participants with angioedema, mean (SD)	35.3 (27.4)	32.1 (23.2)	33.9 (25.4)
Baseline UCT score, mean (SD)	3.6 (2.3)	3.8 (2.3)	3.7 (2.3)
Baseline DLQI score ^b mean (SD)	15.3 (6.7)	13.5 (5.9)	14.4 (6.4)
DLQI score severity categories ^b n (%)			
0–1 (No effect)	0	0	0
2–5 (Small effect)	5 (7.5)	5 (6.7)	10 (7.5)
6–10 (Moderate effect)	13 (19.4)	18 (27.3)	31 (23.3)
11–20 (Very large effect)	33 (49.3)	35 (53.0)	68 (51.1)
21–30 (Extremely large effect)	16 (23.9)	8 (12.1)	24 (18.0)
Baseline EQ-VAS score, mean (SD)	66.8 (21.9)	68.1 (20.3)	67.4 (21.1)
Baseline CU-Q2oL score, mean (SD)	46.7 (20.3)	41.0 (17.3)	43.9 (19.0)
Baseline total IgE, IU/mL, median (IQR)	96.5 (27.9; 221.0)	109.4 (49.2; 381.0)	101.0 (38.9; 274.0)
Baseline H1-AH, n (%)			
Standard dose ^c	41 (60.3)	31 (44.3)	72 (52.2)
2–3-fold standard dose ^c	16 (23.5)	27 (38.6)	43 (31.2)
4-fold standard dose ^c	11 (16.2)	12 (17.1)	23 (16.7)

Unless otherwise indicated, data are presented for all participants in the ITT population, which included all randomized participants. Higher scores indicate worse disease activity/outcomes, except for the UCT, where lower scores reflect higher disease activity/worse disease control.

AAS7 Angioedema Activity Score over 7 days (0–105), BMI body mass index, CSU chronic spontaneous urticaria, CU-Q2oL Chronic Urticaria Quality of Life Questionnaire, DLQI/CDLQI

Dermatology Life Quality Index/Children's Dermatology Life Quality Index (0–30), *EQ-VAS* EuroQol Visual Analog Scale, *H1-AH* H1-antihistamines, *HSS7* Hives Severity Score over 7 days (0–21), *IgE* immunoglobulin E, *IQR* interquartile range, *ISS7* Itch Severity Score over 7 days (0–21), *ITT* intention-to-treat, *n* (%), number and percentage of participants, *SD* standard deviation, *UAS7* Urticaria Activity Score over 7 days (0–42), *UCT* Urticaria Control Test (0–16)

^aParticipants with an AAS7 baseline score > 0.

^bPatients were aged ≥ 16 years (i.e., exclude adolescents/children who completed the CDLQI) and exclude one adult who incorrectly completed the CDLQI and one child who incorrectly completed the DLQI.

^cStandard dose is the locally approved dose of H1-AH.

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102 **Table S2** Proportion of participants with DLQI item score of 0 or 1 (not at all/a little) at baseline, week 12, and week 24

DLQI items, n/N (%) ^a	Baseline		Week 12		Week 24					
	Placebo	Dupilumab	Placebo	Dupilumab	OR (95% CI) ^b	Nominal p-value ^c	Placebo	Dupilumab	OR (95% CI) ^b	Nominal p-value ^c
1 – How itchy, sore, painful, stinging	7/67 (10.4)	5/66 (7.6)	39/67 (58.2)	50/67 (74.6)	2.340 (1.063 to 5.152)	0.0299	32/67 (47.8)	50/67 (74.6)	2.969 (1.343 to 6.564)	0.0061
2 – How embarrassed, self-conscious	24/67 (35.8)	35/66 (53.0)	46/67 (68.7)	57/67 (85.1)	3.237 (1.157 to 9.060)	0.0228	40/67 (59.7)	55/67 (82.1)	3.225 (1.236 to 8.413)	0.0161
3 – Interfered shopping, home, yard	28/67 (41.8)	33/66 (50.0)	45/65 (69.2)	48/58 (82.8)	1.982 (0.831 to 4.727)	0.1154	39/51 (63.9)	44/54 (81.5)	2.624 (1.072 to 6.425)	0.0346
4 – Influenced clothes you wear	27/67 (40.3)	32/66 (48.5)	44/65 (67.7)	50/59 (84.7)	2.571 (1.039 to 6.365)	0.0327	37/65 (56.9)	44/58 (75.9)	2.197 (0.949 to 5.086)	0.0704
5 – Affected social, leisure activity	28/67 (41.8)	34/66 (51.5)	44/65 (67.7)	51/60 (85.0)	2.309 (0.931 to 5.728)	0.0685	42/66 (63.6)	51/60 (85.0)	2.850 (1.163 to 6.982)	0.0207
6 – Made it difficult to do any sports	27/67 (40.3)	27/66 (40.9)	39/54 (72.2)	45/54 (83.3)	2.939 (0.896 to 9.636)	0.0671	34/57 (59.6)	42/53 (79.2)	4.225 (1.362 to 13.110)	0.0117
7A – Problem at work or studying (if did not prevent from working or studying) ^d	27/67 (40.3)	32/66 (48.5)	42/59 (71.2)	46/56 (82.1)	1.635 (0.583 to 4.582)	0.3601	36/63 (57.1)	45/53 (84.9)	3.655 (1.343 to 9.943)	0.0091
8 – Problem partner, friends, relative	37/67 (55.2)	41/66 (62.1)	46/63 (73.0)	54/59 (91.5)	4.164 (1.316 to 13.176)	0.0082	45/66 (68.2)	50/57 (87.7)	5.862 (1.782 to 19.283)	0.0018
9 – Caused any sexual difficulties	34/67 (50.7)	36/66 (54.5)	43/55 (78.2)	46/52 (88.5)	1.910 (0.475 to 7.678)	0.3794	38/57 (66.7)	43/50 (86.0)	2.996 (0.902 to 9.944)	0.0658
10 – How much a problem is treatment	40/67 (59.7)	49/66 (74.2)	52/66 (78.8)	53/60 (88.3)	1.746 (0.575 to 5.304)	0.3251	43/66 (65.2)	54/62 (87.1)	3.097 (1.169 to 8.202)	0.0149

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116 *P*-values < 0.05 are bold.

117 One adult patient in the dupilumab arm incorrectly completed the Children's Dermatology Life Quality Index at baseline. This patient was excluded from the
118 baseline analyses but was included in the analyses at week 12 and week 24. Patients who received selected prohibited medications and/or rescue medications
119 before week 24 were considered non-responders, missing data were considered non-responders; patients with a not relevant item at the visit were excluded from
120 the analyses. Patients whose skin prevented them from studying or working were considered non-responders.

121 *CI* confidence interval, *DLQI* Dermatology Life Quality Index, *OR* odds ratio

122 ^an: number of patients who responded with “not at all/a little”; N: number of patients who were included in the analysis (Patients who responded “Not relevant” at
123 week 24 were excluded. At item 7A, “N” indicates number of patients whose disease did not prevent from working or studying).

124 ^bOR is derived from the Mantel-Haenszel estimator.

125 ^cCochran–Mantel–Haenszel test was performed on the association between the responder status and intervention group, adjusted by baseline disease severity
126 (UAS7 < 28, ≥ 28), baseline endpoint, presence of angioedema at baseline, and region.

127 ^dFor item 7A at baseline, the denominator corresponds to the number of patients who replied to question 7.

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129 **Table S3** Proportion of participants with CU-Q2oL item score of 1 or 2 (not at all/a little) at baseline, week 12, and week 24

CU-Q2oL items, <i>n</i> (%)	Baseline		Week 12		OR ^a (95% CI)	Nominal <i>p</i> -value ^b	Week 24		OR ^a (95% CI)	Nominal <i>p</i> -value ^b
	Placebo (<i>N</i> = 68)	Dupilumab (<i>N</i> = 69)	Placebo (<i>N</i> = 68)	Dupilumab (<i>N</i> = 70)			Placebo (<i>N</i> = 68)	Dupilumab (<i>N</i> = 70)		
1 – Itching	1 (1.5)	2 (2.9)	28 (41.2)	38 (54.3)	1.886 (0.915 to 3.887)	0.0909	25 (36.8)	42 (60.0)	2.395 (1.144 to 5.014)	0.0195
2 – Hives	3 (4.4)	2 (2.9)	29 (42.6)	44 (62.9)	2.210 (1.074 to 4.548)	0.0271	25 (36.8)	48 (68.6)	4.010 (1.827 to 8.800)	0.0004
3 – Swelling of the eyes	43 (63.2)	58 (84.1)	53 (77.9)	63 (90.0)	1.949 (0.679 to 5.594)	0.1782	43 (63.2)	59 (84.3)	2.936 (1.230 to 7.006)	0.0078
4 – Swelling of the lips	43 (63.2)	62 (89.9)	53 (77.9)	63 (90.0)	1.153 (0.357 to 3.728)	0.8079	46 (67.6)	62 (88.6)	2.256 (0.898 to 5.671)	0.0475
5 – Work	29 (42.6)	32 (46.4)	44 (64.7)	61 (87.1)	3.330 (1.267 to 8.750)	0.0107	41 (60.3)	59 (84.3)	2.524 (1.068 to 5.968)	0.0227
6 – Physical activity	25 (36.8)	33 (47.8)	46 (67.6)	58 (82.9)	2.575 (1.016 to 6.529)	0.0390	42 (61.8)	60 (85.7)	4.242 (1.617 to 11.128)	0.0017
7 – Sleep	15 (22.1)	21 (30.4)	39 (57.4)	47 (67.1)	1.518 (0.718 to 3.209)	0.2567	33 (48.5)	54 (77.1)	4.151 (1.701 to 10.130)	0.0008
8 – Free time	29 (42.6)	34 (49.3)	42 (61.8)	58 (82.9)	2.152 (0.901 to 5.137)	0.0723	41 (60.3)	57 (81.4)	2.155 (0.954 to 4.870)	0.0519
9 – Relationships with other people	37 (54.4)	37 (53.6)	47 (69.1)	60 (85.7)	3.258 (1.180 to 8.997)	0.0168	44 (64.7)	58 (82.9)	4.358 (1.639 to 11.591)	0.0022
10 – Eating	48 (70.6)	48 (69.6)	53 (77.9)	57 (81.4)	1.662 (0.608 to 4.543)	0.3118	43 (63.2)	56 (80.0)	2.762 (1.186 to 6.432)	0.0099
11 – Difficulty falling sleep	25 (36.8)	32 (46.4)	35 (51.5)	53 (75.7)	2.890 (1.331 to 6.276)	0.0043	34 (50.0)	53 (75.7)	3.527 (1.517 to 8.204)	0.0029
12 – Wake up during the night	19 (27.9)	27 (39.1)	31 (45.6)	47 (67.1)	2.362 (1.052 to 5.305)	0.0354	33 (48.5)	52 (74.3)	3.370 (1.479 to 7.678)	0.0022
13 – Tired day due to lack of sleep	22 (32.4)	32 (46.4)	39 (57.4)	50 (71.4)	1.583 (0.711 to 3.522)	0.2752	30 (44.1)	53 (75.7)	3.405 (1.549 to 7.484)	0.0016
14 – Difficulty concentrating	22 (32.4)	37 (53.6)	41 (60.3)	55 (78.6)	1.566 (0.637 to 3.850)	0.3431	37 (54.4)	52 (74.3)	1.604 (0.713 to 3.608)	0.2551
15 – Feel nervous	32 (47.1)	39 (56.5)	48 (70.6)	56 (80.0)	1.596 (0.637 to 4.003)	0.3240	40 (58.8)	55 (78.6)	2.269 (1.004 to 5.130)	0.0328

16 – Feel down	37 (54.4)	40 (58.0)	50 (73.5)	57 (81.4)	1.701 (0.658 to 4.398)	0.2654	41 (60.3)	56 (80.0)	2.273 (1.027 to 5.028)	0.0254
17 – Limit choice of food	39 (57.4)	41 (59.4)	44 (64.7)	49 (70.0)	1.828 (0.771 to 4.338)	0.1844	40 (58.8)	54 (77.1)	2.901 (1.274 to 6.604)	0.0085
18 – Embarrassed marks on body	22 (32.4)	19 (27.5)	41 (60.3)	47 (67.1)	1.656 (0.764 to 3.588)	0.1984	31 (45.6)	48 (68.6)	3.788 (1.598 to 8.979)	0.0024
19 – Embarrassed to go out in public	33 (48.5)	41 (59.4)	49 (72.1)	55 (78.6)	1.373 (0.598 to 3.149)	0.4264	41 (60.3)	59 (84.3)	3.520 (1.492 to 8.305)	0.0017
20 – Difficulty using cosmetics	32 (47.1)	44 (63.8)	46 (67.6)	51 (72.9)	1.511 (0.688 to 3.319)	0.2998	40 (58.8)	57 (81.4)	3.327 (1.376 to 8.047)	0.0022
21 – Affected choice of clothing	25 (36.8)	33 (47.8)	45 (66.2)	52 (74.3)	1.654 (0.730 to 3.744)	0.2104	40 (58.8)	56 (80.0)	3.200 (1.385 to 7.392)	0.0040
22 – Limit sports	38 (55.9)	34 (49.3)	52 (76.5)	57 (81.4)	1.762 (0.702 to 4.422)	0.2216	41 (60.3)	58 (82.9)	3.747 (1.548 to 9.072)	0.0023
23 – Bothered by side effects	45 (66.2)	53 (76.8)	51 (75.0)	60 (85.7)	1.822 (0.726 to 4.576)	0.1620	43 (63.2)	60 (85.7)	2.800 (1.180 to 6.646)	0.0055

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131 *P*-values < 0.05 are bold.132 *CI* confidence interval, *CU-Q2oL* Chronic Urticaria Quality of Life Questionnaire, *OR* odds ratio, *UAS7* Urticaria Activity Score over 7 days (0–42).133 ^aOR is derived from the Mantel–Haenszel estimator.134 ^bCochran–Mantel–Haenszel test was performed on the association between the responder status and intervention group, adjusted by baseline disease severity.

135 (UAS7 < 28, ≥ 28), baseline endpoint, presence of angioedema at baseline, and region.