Table 5-6 Secondary analyses of the primary endpoint (Change in CholUAS7 between treatment groups, CHOLUAS7 from baseline to week 16); positive means indicate improvement, while negative means indicate worsening.

Population	Adjustments	Dupilumab N	Placebo N	Dupilumab Mean (CI95%)	Placebo Mean (CI95%)	Mean difference (CI95%)	P-value
With imputations							
ITT	unadjusted	30	18	0.462 (-0.155, 1.079)	0.392 (-0.405, 1.188)	-0.070 (-1.078, 0.937)	0.889
ITT	baseline CholUAS7 (fixed); study center (random)	30	18	-0.264 (-1.124, 0.596)	-0.360 (-1.357, 0.596)	-0.097 (-1.051, 0.858)	0.840
FAS	baseline CholUAS7 (fixed);	30	18	0.574 (-0.003, 1.150)	0.205 (-0.544, 0.954)	-0.368 (-1.324, 0.587)	0.442
PPP	baseline CholUAS7 (fixed);	17	9	0.216 (-0.606, 1.037)	0.735 (-0.403, 1.874)	0.519 (-0.901, 1.940)	0.457
Without imputations							
ITT	baseline CholUAS7 (fixed);	24	12	0.582 (-0.064, 1.228)	0.372 (-0.54, 1.289)	-0.210 (-1.337, 0.917)	0.707
FAS	baseline CholUAS7 (fixed);	24	12	0.582 (-0.064, 1.228)	0.372 (-0.54, 1.289)	-0.210 (-1.337, 0.917)	0.707
PPP	baseline CholUAS7 (fixed);	17	9	0.216 (-0.606, 1.037)	0.735 (-0.40, 1.874)	0.519 (-0.901, 1.940)	0.457

5.3 Secondary efficacy results

In all secondary analysis we are displaying explorative p-values the standard alpha level of 0.05 does not apply

5.3.1 Efficacy

The mean difference in change from baseline to all study visits between Dupilumab and placebo arms was calculated for the following secondary efficacy endpoints - of CholUAS7, ProvoUAS, IGA, PGA, ISS7, UCT, and the use of rescue medication (per week) using ANCOVA model adjusted for respective baseline value (analogues to the secondary analysis for the primary endpoint, but without imputations). The results are shown in Figure 5-1 and Tables 5-7 to 5-13. Here, comparable rates of improvement and similar use of rescue medication between Dupilumab and placebo can be observed in all analyses.

Figure 5-1. Change in CholUAS7 from baseline over time shows comparable rates of improvement in both treatment groups [negative values indicate an improvement in disease severity]

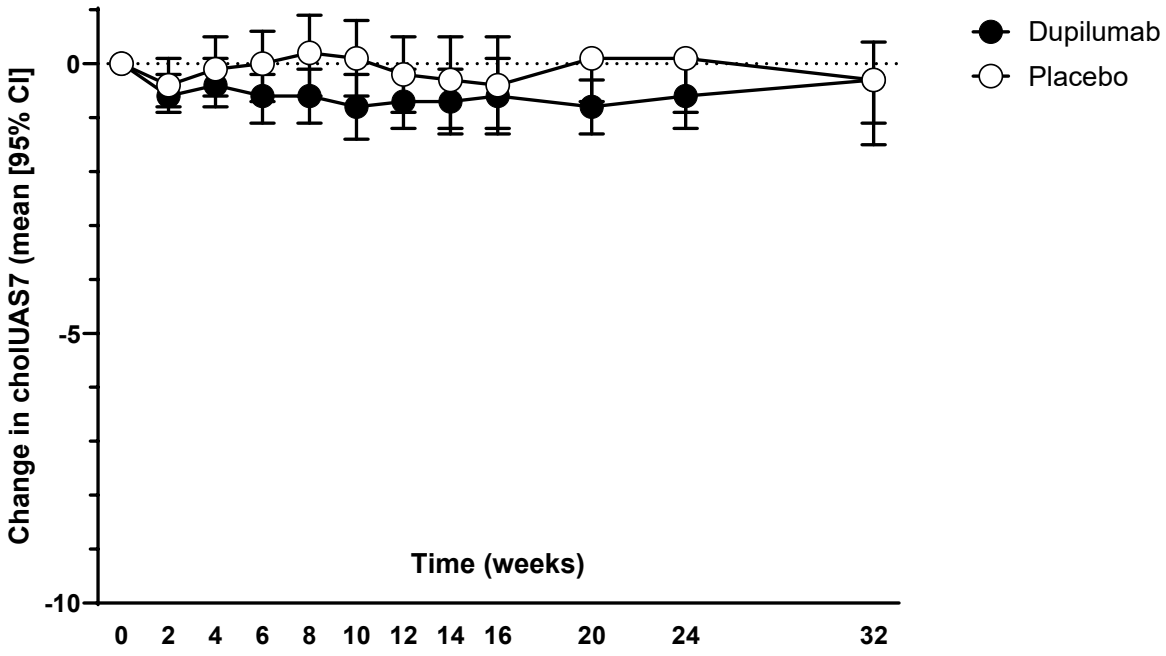

Table 5-7. Change versus baseline over time for CholUAS7 [FAS population]. Change calculated as change from baseline (Week 0) to a given time point (Week 0 minus week X); Here: in the treatment groups higher values indicate an improvement of disease severity as compared to baseline.

Week	N	Dupilumab Adj. Mean [95% CI]	Placebo Adj. Mean [95% CI]	Difference Adj. Mean [95% CI]	p-Value
2	48	0.6 [0.2;0.9]	0.4 [-0.1;0.8]	0.2 [-0.4;0.8]	0.547
4	46	0.4 [-0.1;0.8]	0.1 [-0.5;0.6]	0.3 [-0.4;1.1]	0.403
6	47	0.6 [0.2;1.1]	0.0 [-0.6;0.7]	0.6 [-0.2;1.4]	0.129
8	45	0.6 [0.1;1.1]	-0.2 [-0.9;0.6]	0.8 [-0.2;1.7]	0.106
10	42	0.8 [0.2;1.4]	-0.1 [-0.8;0.6]	0.9 [-0.1;1.8]	0.066
12	40	0.7 [0.1;1.2]	0.2 [-0.5;0.9]	0.5 [-0.4;1.4]	0.287
14	37	0.7 [0.1;1.3]	0.3 [-0.5;1.2]	0.4 [-0.7;1.5]	0.456
16	36	0.6 [-0.1;1.2]	0.4 [-0.5;1.3]	0.2 [-0.9;1.3]	0.707
20	33	0.8 [0.3;1.3]	-0.1 [-0.8;0.7]	0.9 [-0.0;1.8]	0.061
24	32	0.6 [-0.1;1.2]	-0.1 [-1.0;0.9]	0.7 [-0.5;1.8]	0.258
32	24	0.3 [-0.4;1.1]	0.3 [-0.9;1.5]	0.0 [-1.4;1.4]	0.979

Table 5-8. Change versus baseline over time for ProvoUAS [FAS population]. Change calculated as change from baseline (Week 0) to a given time point (Week 0 minus Week X); in the treatment groups higher values indicate an improvement of disease severity as compared to baseline.

Week	N	Dupilumab Adj. Mean [95% CI]	Placebo Adj. Mean [95% CI]	Difference Adj. Mean [95% CI]	p-Value
16	35	3.7 [3.0;4.5]	3.0 [2.1;4.0]	0.7 [-0.5;1.9]	0.248
32	27	3.0 [2.2;3.8]	2.9 [1.6;4.3]	0.1 [-1.5;1.7]	0.914

Table 5-9. Change versus baseline over time for IGA [FAS population]. Change calculated as change from baseline (Week 0) to a given time point (Week 0 minus week X); in the treatment groups the negative values indicate an improvement as compared to baseline

Week	N	Dupilumab Adj. Mean [95% CI]	Placebo Adj. Mean [95% CI]	Difference Adj. Mean [95% CI]	p-Value
2	46	6.5 [-1.5;14.5]	7.3 [-3.2;17.8]	-0.8 [-14.1;12.5]	0.904
4	44	15.4 [6.2;24.5]	1.2 [-12.3;14.7]	14.2 [-2.3;30.6]	0.089
6	42	11.2 [1.3;21.2]	2.2 [-11.1;15.6]	9.0 [-7.7;25.7]	0.281
8	40	21.1 [9.0;33.1]	12.4 [-2.3;27.1]	8.6 [-10.4;27.6]	0.364
10	38	23.1 [12.3;33.9]	5.2 [-9.8;20.3]	17.9 [-0.7;36.5]	0.059
12	40	19.8 [9.6;29.9]	5.3 [-8.6;19.2]	14.4 [-2.9;31.7]	0.099
14	37	23.1 [11.5;34.7]	13.2 [-2.6;29.0]	9.9 [-9.8;29.6]	0.315
16	38	15.4 [1.9;28.9]	11.4 [-5.3;28.2]	4.0 [-17.7;25.6]	0.713
20	34	12.9 [-0.2;26.1]	9.4 [-9.6;28.4]	3.5 [-19.6;26.6]	0.757
24	33	21.7 [9.3;34.1]	4.6 [-14.2;23.5]	17.1 [-5.5;39.7]	0.132
32	33	14.0 [1.1;26.8]	8.0 [-11.5;27.5]	5.9 [-17.4;29.3]	0.608

Table 5-10. Change versus baseline over time for PGA [FAS population]. Change calculated as change from baseline (Week 0) to a given time point (Week 0 minus week X); in the treatment groups higher values indicate an improvement of PGA as compared to baseline.

Week	N	Dupilumab Adj. Mean [95% CI]	Placebo Adj. Mean [95% CI]	Difference Adj. Mean [95% CI]	p-Value
2	46	14.5 [6.9;22.0]	11.9 [2.0;21.8]	2.5 [-10.0;15.0]	0.687
4	46	15.6 [5.8;25.3]	3.5 [-10.0;16.9]	12.1 [-4.6;28.8]	0.152
6	43	14.3 [5.3;23.4]	-0.4 [-12.9;12.0]	14.8 [-0.7;30.3]	0.061
8	43	18.7 [8.9;28.4]	7.3 [-5.3;20.0]	11.3 [-4.8;27.4]	0.163
10	40	20.3 [9.6;30.9]	4.7 [-9.9;19.2]	15.6 [-2.6;33.8]	0.091
12	40	21.1 [9.7;32.4]	14.0 [-1.7;29.6]	7.1 [-12.5;26.8]	0.467
14	38	26.4 [15.1;37.7]	15.9 [0.2;31.6]	10.6 [-8.9;30.0]	0.278
16	38	21.4 [9.3;33.6]	15.3 [0.2;30.4]	6.2 [-13.4;25.7]	0.527
20	34	22.3 [11.9;32.7]	11.4 [-3.7;26.5]	10.9 [-7.5;29.3]	0.235
24	34	25.5 [13.7;37.2]	14.5 [-2.5;31.5]	11.0 [-9.7;31.6]	0.288
32	32	17.1 [5.2;29.1]	10.3 [-7.5;28.1]	6.8 [-14.8;28.3]	0.524

Table 5-11. Change versus baseline over time for ISS7 [FAS population]. Change calculated as change from baseline (Week 0) to a given time point (Week 0 minus week X); in the treatment groups higher values indicate an improvement of IGA as compared to baseline.

Week	N	Dupilumab Adj. Mean [95% CI]	Placebo Adj. Mean [95% CI]	Difference Adj. Mean [95% CI]	p-Value
2	47	2.1 [0.6;3.5]	2.0 [-0.0;3.9]	0.1 [-2.4;2.6]	0.939
4	45	1.7 [-0.0;3.4]	0.5 [-1.8;2.8]	1.2 [-1.7;4.1]	0.407
6	46	2.1 [0.1;4.0]	0.4 [-2.2;3.1]	1.6 [-1.7;5.0]	0.336
8	44	2.3 [0.3;4.4]	-0.0 [-2.9;2.9]	2.3 [-1.3;6.0]	0.203
10	41	2.6 [0.5;4.7]	-0.1 [-2.9;2.7]	2.7 [-0.9;6.2]	0.140
12	39	1.7 [-0.5;3.8]	0.5 [-2.4;3.4]	1.2 [-2.5;4.9]	0.510
14	36	2.3 [0.1;4.5]	0.9 [-2.5;4.3]	1.4 [-2.7;5.4]	0.493
16	35	1.4 [-1.1;3.9]	1.6 [-2.1;5.3]	-0.2 [-4.7;4.3]	0.922
20	31	2.4 [0.6;4.2]	0.2 [-2.8;3.2]	2.2 [-1.3;5.7]	0.201
24	31	1.4 [-0.8;3.5]	0.6 [-2.9;4.0]	0.8 [-3.3;4.9]	0.703
32	23	-0.1 [-2.9;2.6]	1.3 [-3.4;6.0]	-1.4 [-6.9;4.0]	0.586

Table 5-12. Change versus baseline over time for UCT [FAS population]. Change calculated as change from baseline (Week 0) to a given time point (Week 0 minus week X); in the treatment groups higher values indicate an improvement of HSS7 as compared to baseline.

Week	N	Dupilumab Adj. Mean [95% CI]	Placebo Adj. Mean [95% CI]	Difference Adj. Mean [95% CI]	p-Value
2	47	-1.5 [-2.5;-0.4]	-1.3 [-2.6;0.1]	-0.2 [-1.9;1.5]	0.833
4	47	-2.2 [-3.5;-0.9]	-0.9 [-2.6;0.9]	-1.3 [-3.5;0.9]	0.243
6	44	-2.2 [-3.5;-0.8]	-1.2 [-3.1;0.6]	-0.9 [-3.2;1.4]	0.417
8	43	-3.0 [-4.6;-1.4]	-1.5 [-3.6;0.6]	-1.5 [-4.1;1.2]	0.268
10	40	-3.6 [-5.4;-1.9]	-1.3 [-3.7;1.1]	-2.3 [-5.3;0.7]	0.127
12	40	-3.5 [-5.3;-1.7]	-2.6 [-5.1;-0.2]	-0.9 [-3.9;2.2]	0.568
14	38	-3.6 [-5.4;-1.9]	-2.2 [-4.6;0.1]	-1.4 [-4.3;1.6]	0.344
16	38	-2.8 [-4.7;-0.8]	-2.4 [-4.8;0.1]	-0.4 [-3.5;2.7]	0.788
20	34	-3.3 [-5.0;-1.6]	-2.2 [-4.6;0.3]	-1.2 [-4.2;1.8]	0.433
24	34	-3.6 [-5.5;-1.7]	-1.9 [-4.6;0.8]	-1.7 [-5.0;1.7]	0.315
32	32	-2.8 [-4.6;-1.1]	-2.6 [-5.5;0.2]	-0.2 [-3.6;3.1]	0.898

Table 5-13. Use of rescue medication (antihistamines) per week (descriptive analysis [mean±SD]) [FAS population] Change calculated as change from baseline (Week 0) to a given time point (Week 0 minus week X); higher values indicate a decrease in taken rescue medications H1AH as compared to baseline.

Week	N	Dupilumab Adj. Mean [95% CI]	Placebo Adj. Mean [95% CI]	Difference Adj. Mean [95% CI]	p-Value
2	48	-0.5 [-1.4;0.3]	0.3 [-0.8;1.5]	-0.9 [-2.3;0.6]	0.233
4	46	-0.1 [-0.8;0.6]	-0.0 [-1.0;0.9]	-0.1 [-1.3;1.1]	0.892
6	47	-0.3 [-1.3;0.6]	-0.1 [-1.4;1.1]	-0.2 [-1.7;1.4]	0.817

Week	N	Dupilumab Adj. Mean [95% CI]	Placebo Adj. Mean [95% CI]	Difference Adj. Mean [95% CI]	p-Value
8	45	-0.1 [-0.8;0.7]	0.1 [-0.9;1.2]	-0.2 [-1.5;1.1]	0.717
10	42	-0.1 [-0.9;0.7]	0.3 [-0.7;1.3]	-0.4 [-1.7;0.9]	0.544
12	40	0.1 [-0.4;0.6]	-0.0 [-0.7;0.6]	0.2 [-0.7;1.0]	0.724
14	38	-0.4 [-1.0;0.2]	0.7 [-0.1;1.6]	-1.1 [-2.1;-0.0]	0.046
16	36	-0.4 [-1.1;0.3]	0.8 [-0.2;1.8]	-1.2 [-2.4;0.1]	0.061
20	33	-0.4 [-1.1;0.3]	0.1 [-1.0;1.1]	-0.4 [-1.7;0.9]	0.502
24	32	-0.8 [-1.7;0.1]	-0.0 [-1.4;1.3]	-0.8 [-2.4;0.8]	0.339
32	24	-0.9 [-2.1;0.2]	0.3 [-1.6;2.1]	-1.2 [-3.4;1.0]	0.259

5.3.2 Effects on quality of life

Organ- and disease-specific quality of life was assessed using the dermatology life quality index (DLQI) and the cholinergic urticaria quality of life questionnaire (CholU-QoL). ANCOVA analyses adjusted for baseline values showed comparable rates of improvement in quality of life between Dupilumab and placebo can be observed in all analyses (Tables 5-14, 5-15).

Table 5-14. Change versus baseline over time for DLQI [FAS population]. Change calculated as change from baseline (Week 0) to a given time point (Week 0 minus week X); Overall, higher values indicate worse QoL; here: positive values indicate an improvement of QoL as compared to baseline.

Week	N	Dupilumab Adj. Mean [95% CI]	Placebo Adj. Mean [95% CI]	Difference Adj. Mean [95% CI]	p-Value
2	47	4.3 [2.6;6.1]	2.1 [-0.2;4.3]	2.3 [-0.6;5.2]	0.114
4	47	4.5 [2.7;6.3]	1.8 [-0.6;4.1]	2.7 [-0.3;5.7]	0.074
6	44	4.2 [2.2;6.2]	2.4 [-0.2;5.0]	1.8 [-1.6;5.1]	0.290
8	43	5.3 [3.2;7.5]	3.3 [0.4;6.1]	2.1 [-1.5;5.6]	0.248
10	40	4.5 [2.1;6.9]	1.6 [-1.6;4.9]	2.8 [-1.2;6.9]	0.159
12	40	4.6 [2.2;6.9]	3.1 [-0.1;6.4]	1.4 [-2.6;5.5]	0.472
14	38	5.9 [3.6;8.2]	3.8 [0.6;7.0]	2.1 [-1.8;6.1]	0.284
16	38	5.0 [2.5;7.6]	3.7 [0.5;6.8]	1.3 [-2.7;5.4]	0.510
20	34	5.0 [2.5;7.5]	3.2 [-0.5;6.9]	1.8 [-2.7;6.3]	0.420
24	34	5.6 [3.0;8.2]	3.9 [0.2;7.7]	1.6 [-3.0;6.2]	0.475
32	33	5.1 [2.5;7.7]	2.9 [-1.0;6.9]	2.2 [-2.6;6.9]	0.355

Table 5-15. Change versus baseline over time for CholU-QoL [FAS population]. Change calculated as change from baseline (Week 0) to a given time point (Week 0 minus week X); Overall, lower values indicate better QoL; here: positive values indicate an improvement of QoL as compared to baseline.

Week	N	Dupilumab Adj. Mean [95% CI]	Placebo Adj. Mean [95% CI]	Difference Adj. Mean [95% CI]	p-Value
2	47	13.6 [8.3;19.0]	4.4 [-2.4;11.2]	9.3 [0.6;17.9]	0.036
4	47	15.5 [9.8;21.1]	6.4 [-1.2;13.9]	9.1 [-0.4;18.5]	0.059

Week	N	Dupilumab Adj. Mean [95% CI]	Placebo Adj. Mean [95% CI]	Difference Adj. Mean [95% CI]	p-Value
6	44	15.4 [9.2;21.6]	7.1 [-1.1;15.3]	8.3 [-2.0;18.6]	0.111
8	43	18.2 [11.8;24.7]	9.4 [1.0;17.7]	8.9 [-1.7;19.4]	0.097
10	40	18.6 [11.9;25.3]	6.4 [-2.8;15.5]	12.2 [0.9;23.5]	0.035
12	40	17.3 [10.7;23.9]	13.5 [4.5;22.6]	3.7 [-7.4;14.9]	0.502
14	38	21.6 [13.9;29.2]	16.4 [5.8;27.0]	5.2 [-7.9;18.3]	0.426
16	38	19.9 [12.0;27.9]	11.4 [1.5;21.2]	8.5 [-4.1;21.2]	0.180
20	34	19.9 [12.8;27.0]	14.3 [4.0;24.6]	5.5 [-7.0;18.1]	0.374
24	34	22.2 [14.1;30.3]	13.4 [1.7;25.1]	8.8 [-5.4;23.1]	0.215
32	33	19.8 [12.3;27.4]	11.1 [-0.3;22.6]	8.7 [-5.0;22.4]	0.206

5.3.3 Responder analyses

5.3.3.1 Clinical response based on minimal important difference (MID)

Responder analyses have been performed regarding a clinical response in UCT (reduction of 3 points or more [MID]) and ISS7 (reduction of 5 points or more [MID]) (Tables 5-16 to 5-19). Overall, no relevant differences have been observed between the treatment groups.

Table 5-16. Urticaria Control test (UCT) Clinical responders - descriptive analysis, unadjusted (n,%) [FAS population]

Week	N	Outcome	Dupilumab (n=30)	Placebo (n=18)	Total (n=48)
2	47	responder	9 (31.0%)	4 (22.2%)	13 (27.7%)
4	47	responder	14 (46.7%)	4 (23.5%)	18 (38.3%)
6	44	responder	14 (50.0%)	4 (25.0%)	18 (40.9%)
8	43	responder	14 (51.9%)	6 (37.5%)	20 (46.5%)
10	40	responder	14 (53.8%)	5 (35.7%)	19 (47.5%)
12	40	responder	12 (46.2%)	5 (35.7%)	17 (42.5%)
14	38	responder	13 (52.0%)	4 (30.8%)	17 (44.7%)
16	38	responder	10 (43.5%)	5 (33.3%)	15 (39.5%)

Table 5-17. Urticaria Control test (UCT) Clinical responders – proportion of clinical responders – logistic regression adj. for baseline [FAS population]

Week	N	Odds ratio (Dupilumab vs placebo)	95% Confidence interval		p-value
2	47	1.635	0.407	6.567	0.4882
4	47	2.894	0.757	11.069	0.1205
6	44	3.021	0.779	11.724	0.1100
8	43	2.063	0.531	8.013	0.2957
10	40	2.546	0.582	11.142	0.2148
12	40	2.154	0.482	9.624	0.3149
14	38	2.403	0.567	10.189	0.2343
16	38	1.591	0.397	6.370	0.5119

Table 5-18. Weekly Itch Activity score (ISS7) Clinical responders - descriptive analysis, unadjusted (n,%) [FAS population]

Week	N	Total (n=48)	Placebo (n=18)	Dupilumab (n=30)
2	48	12 (25.0%)	6 (33.3%)	6 (20.0%)
4	46	12 (26.1%)	5 (29.4%)	7 (24.1%)
6	47	14 (29.8%)	5 (29.4%)	9 (30.0%)
8	45	15 (33.3%)	3 (18.8%)	12 (41.4%)
10	42	11 (26.2%)	3 (18.8%)	8 (30.8%)
12	40	10 (25.0%)	2 (13.3%)	8 (32.0%)
14	37	12 (32.4%)	3 (25.0%)	9 (36.0%)
16	36	10 (27.8%)	4 (33.3%)	6 (25.0%)

Table 5-19. Weekly Itch Activity score (ISS7) Clinical responders – proportion of clinical responders – logistic regression adj. for baseline [FAS population]

Week	N	Odds ratio (Dupilumab vs placebo)	95% Confidence Interval		p-value
2	47	0.613	0.148	2.542	0.0700
4	45	2.127	0.342	13.235	0.4185
6	46	1.740	0.379	7.993	0.4764
8	44	10.920	1.399	85.227	0.0226
10	41	5.484	0.730	41.200	0.0981
12	39	5.499	0.744	40.648	0.0949
14	36	3.371	0.489	23.245	0.2174
16	35	0.992	0.164	6.019	0.9934

5.3.3.2 Complete response

Responder analyses have been performed regarding a complete response in UCT (UCT of ≥12), weekly itch severity Score (ISS7, Score of 0 or a reduction of ≥ 90%) and CholUAS7 (Score of 0 or reduction of ≥ 90%) compared to baseline (Tables 5-20 to 5-25). Overall, no relevant differences have been observed between the treatment groups. Odds ratios are partially not to be interpreted due to low sample size.

Table 5-20. Urticaria Control test (UCT) Complete responders - descriptive analysis, unadjusted (n,%) [FAS population]

Week	N	Dupilumab (n=30)	Placebo (n=18)	Total (n=48)
2	47	0 (0.0%)	0 (0.0%)	0 (0.0%)
4	47	0 (0.0%)	0 (0.0%)	0 (0.0%)
6	44	0 (0.0%)	1 (6.3%)	1 (2.3%)
8	43	1 (3.7%)	0 (0.0%)	1 (2.3%)
10	40	3 (11.5%)	0 (0.0%)	3 (7.5%)
12	40	2 (7.7%)	1 (7.1%)	3 (7.5%)
14	38	2 (8.0%)	1 (7.7%)	3 (7.9%)

Week	N	Dupilumab (n=30)	Placebo (n=18)	Total (n=48)
16	38	1 (4.3%)	1 (6.7%)	2 (5.3%)

Table 5-21. Urticaria Control test (UCT) Complete responders – proportion of clinical responders – logistic regression adj. for baseline [FAS population]

Week	N	Odds ratio (Dupilumab vs placebo)	95% Confidence Interval		p-value
2	47	-	-	-	-
4	47	-	-	-	-
6	44	<0.001	<0.001	>999.999	0.7206
8	43	>999.999	<0.001	>999.999	0.9622
10	40	>999.999	<0.001	>999.999	0.9525
12	40	3.073	0.163	57.999	0.4539
14	38	2.185	0.112	42.784	0.6066
16	38	1.190	0.050	28.265	0.9141

Table 5-22. Weekly Itch Activity score (ISS7) complete responders - descriptive analysis, unadjusted (n,%) [FAS population]

Week	N	Dupilumab (n=30)	Placebo (n=18)	Total (n=48)
2	48	3 (10.0%)	2 (11.1%)	5 (10.4%)
4	46	4 (13.8%)	1 (5.9%)	5 (10.9%)
6	47	7 (23.3%)	1 (5.9%)	8 (17.0%)
8	45	8 (27.6%)	2 (12.5%)	10 (22.2%)
10	42	6 (23.1%)	2 (12.5%)	8 (19.0%)
12	40	6 (24.0%)	2 (13.3%)	8 (20.0%)
14	37	7 (28.0%)	2 (16.7%)	9 (24.3%)
16	36	5 (20.8%)	4 (33.3%)	9 (25.0%)

Table 5-23. Weekly Itch Activity score (ISS7) complete responders - proportion of complete responders – logistic regression adj. for baseline [FAS population]

Week	N	Odds ratio (Dupilumab vs placebo)	95% Confidence Interval		p-value
2	47	1.100	0.065	18.682	0.9476
4	45	>999.999	<0.001	>999.999	0.9473
6	46	>999.999	<0.001	>999.999	0.9579
8	44	4.125	0.393	43.284	0.2375
10	41	3.157	0.301	33.055	0.3374
12	39	3.484	0.362	33.568	0.2801
14	36	3.332	0.327	33.933	0.3094
16	35	0.633	0.115	3.471	0.5984

Table 5-24. Weekly CholUAS7 - Complete responders - descriptive analysis, unadjusted (n,%) [FAS population]

Week	N	Dupilumab (n=30)	Placebo (n=18)	Total (n=48)
2	48	2 (6.7%)	0 (0.0%)	2 (4.2%)
4	46	1 (3.4%)	0 (0.0%)	1 (2.2%)
6	47	3 (10.0%)	0 (0.0%)	3 (6.4%)
8	45	4 (13.8%)	0 (0.0%)	4 (8.9%)
10	42	4 (15.4%)	0 (0.0%)	4 (9.5%)
12	40	4 (16.0%)	0 (0.0%)	4 (10.0%)
14	37	5 (20.0%)	1 (8.3%)	6 (16.2%)
16	36	4 (16.7%)	3 (25.0%)	7 (19.4%)

Table 5-25. Weekly CholUAS7 complete responders - proportion of complete responders – logistic regression adj. for baseline [FAS population]

Week	N	Odds ratio (Dupilumab vs placebo)	95% Confidence Interval		p-value
2	48	>999.999	<0.001	>999.999	0.9592
4	46	>999.999	<0.001	>999.999	0.9671
6	47	>999.999	<0.001	>999.999	0.9614
8	45	>999.999	<0.001	>999.999	0.9556
10	42	>999.999	<0.001	>999.999	0.9541
12	40	>999.999	<0.001	>999.999	0.9543
14	37	2.445	0.245	24.424	0.4465
16	36	0.597	0.108	3.303	0.5542

5.3.4 Time to response

Time to clinical response was assessed for ISS7 and UCT; time to complete response was assessed for CholUAS7, ISS7, and UCT (Figures 5-2 to 5-6). Hazard ratios (CI 95%) for clinical and complete responders were assessed for all pre-defined responders' categories (Table 5-26). No relevant difference was observed between the treatment groups.

Table 5-26. The hazard ratio for dupilumab vs placebo responders [FAS]

Clinical Responder				
Responder	Hazard Ratio	95% Confidence Limits		p-value
ISS7 Clinical Responder	1.159	0.489	2.746	0.7372
UCT Clinical Responder	1.459	0.704	3.025	0.3096
Complete Responders				

Clinical Responder				
Responder	**Hazard Ratio**	**95% Confidence Limits**		**p-value**
Responder	**Hazard Ratio**	**95% Confidence Limits**		**p-value**
CholUAS7 Complete Responder	1.538	0.402	5.884	0.5294
ISS7 Complete Responder	2.586	0.733	9.120	0.1395
UCT Complete Responder	2.309	0.238	22.418	0.4706

Figure 5-2. Time to clinical response ISS7

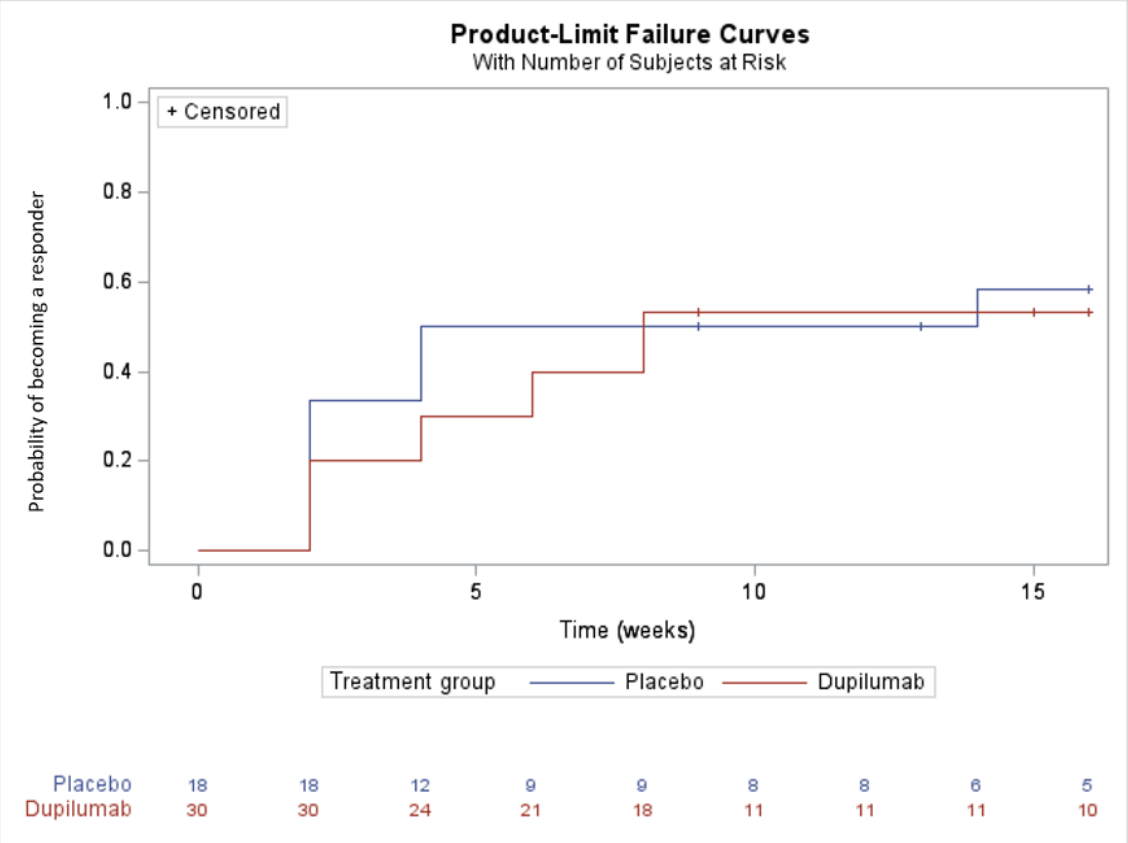

Figure 5-3. Time to clinical response UCT

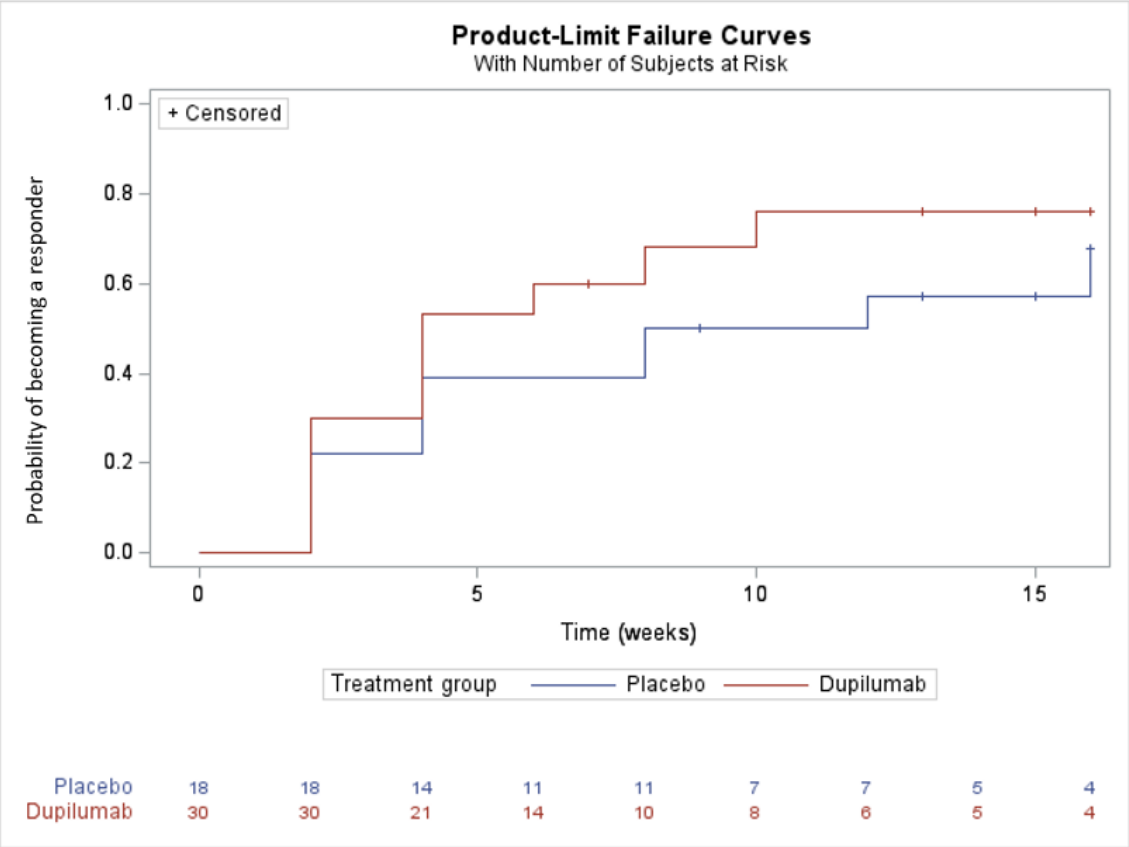

Figure 5-4. Time to complete response CholUAS7

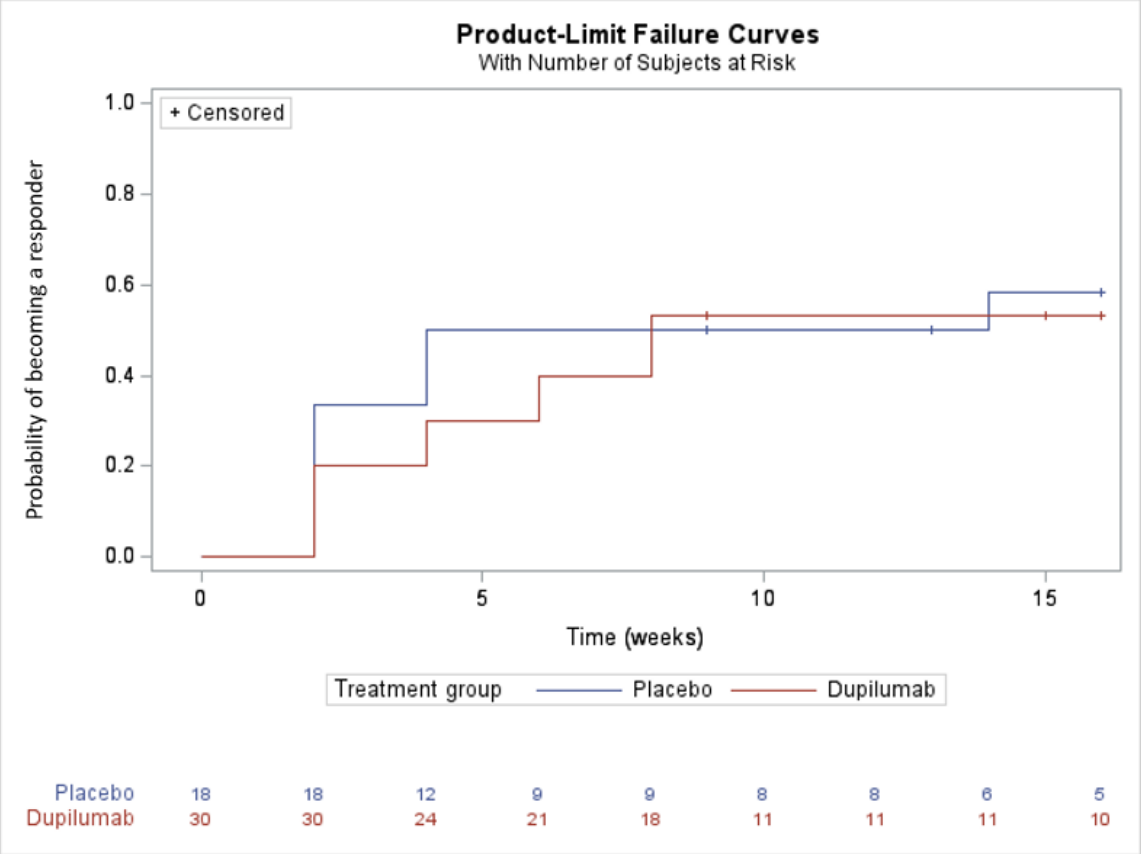

Figure 5-5. Time to complete response ISS7

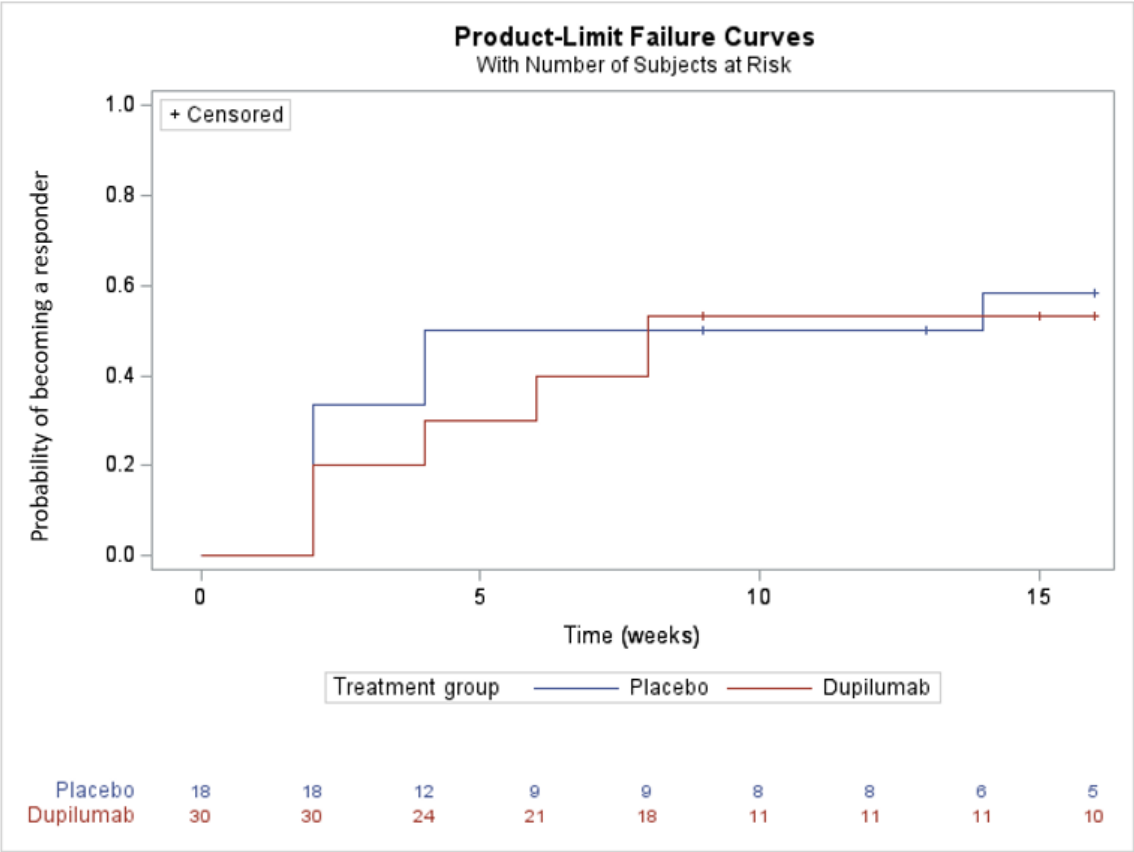

Figure 5-6. Time to complete response UCT