Long-term efficacy of dupilumab in adults with moderate-to-severe atopic dermatitis: results from a 5-year open-label extension trial

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INTRODUCTION

- Topical therapies often cannot sufficiently control moderate-to-severe atopic dermatitis (AD), a chronic inflammatory skin disease
- Systemic immunosuppressants are not recommended for the long-term treatment of moderate-to-severe AD due to safety concerns
- Data from an open-label extension study (OLE; NCT01949311) previously demonstrated acceptable safety and sustained efficacy of dupilumab in adult patients up to 204 weeks (approximately 4 years)

OBJECTIVE

- **To assess the long-term efficacy and safety of dupilumab in adult patients with moderate-to-severe AD up to 5 years (the end of this OLE study)**

METHODS

- LIBERTY AD OLE (NCT01949311) was a phase 3, multicenter OLE trial with a duration of up to 5 years administering dupilumab 300 mg weekly (qw) to adults with moderate-to-severe AD who previously participated in dupilumab clinical trials (parent studies)
- 226 patients transitioned to 300 mg every 2 weeks (q2w) to align with approved dosage
- Concomitant treatments for AD were permitted, including topical corticosteroids (TCS) and topical calcineurin inhibitors
- This analysis examined the overall population treated for up to 5 years, at the end of this OLE; data are presented as observed
- Because the OLE trial lacked a control arm, LIBERTY AD CHRONOS (NCT02260986) 52-week safety results for adults with moderate-to-severe AD receiving dupilumab 300 mg qw plus TCS were provided as a comparison

RESULTS

- Baseline demographics and disease characteristics
  - 60.2% of the 2,677 patients were male and 72.3% were White
  - Mean (standard deviation, SD) age of patients was 39.2 (13.4) years and duration of AD was 29.9 (14.8) years

RESULTS (CONT.)

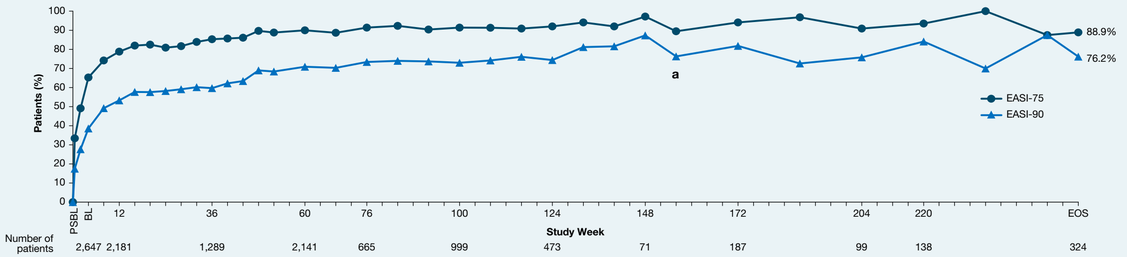
  - At parent study baseline mean (SD) Eczema Area and Severity Index (EASI) and Peak Pruritus Numerical Rating Scale (PP-NRS) scores were 32.8 (13.2) and 7.1 (1.9) respectively
  - OLE baseline mean (SD) EASI and PP-NRS scores were 16.4 (14.6) and 5.0 (2.5) respectively

Table 1. Patient disposition.

	Total N = 2,677 n (%)
Patients who completed up to:	
Week 52	2,207 (82.4)
Week 100	1,065 (39.8)
Week 148	557 (20.8)
Week 172	362 (13.5)
Week 196	353 (13.2)
Week 220	352 (13.1)
Week 244	344 (12.9)
Week 260	334 (12.5)
Patients who completed study	1,297 (48.4)
Patients withdrawn from study	1,380 (51.6)
Study terminated by sponsor[a]	708 (26.4)
Withdrawal by subject[b]	375 (14.0)
Adverse event[c]	107 (4.0)
Lost to follow-up	73 (2.7)
Lack of efficacy	50 (1.9)
Protocol deviation	34 (1.3)
Pregnancy	20 (0.7)
Physician decision	9 (0.3)
Unknown	4 (0.1)

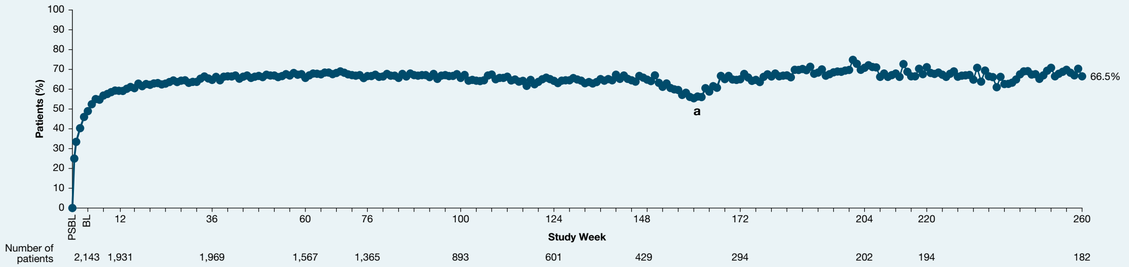
[a]Regulatory approval/commercialization. [b]Includes reasons of relocation, desire for pregnancy, did not want to discontinue treatment for safety follow-up, work/school reasons and personal/not specified reasons. [c]Includes patients receiving treatment at the time of withdrawal and those not receiving treatment during the 12-week safety follow-up period following end of treatment.

Figure 1. Proportion of patients achieving EASI-75/90 from PSBL to end of study



[a]Following protocol amendments in June 2017 and January 2018, 114 and 272 patients re-entered the trial, with 103 and 207 patients having a treatment interruption of > 8 weeks between study Weeks 148 and 164. BL, OLE study baseline; EASI-75/90, ≥ 75%/90% improvement from PSBL in EASI; EOS, end of study: all study Days ≥ 1,794 (Week ≥ 260) are included; study day is calculated relative to the date of first study drug injection. PSBL, parent study baseline.

Figure 2. Proportion of patients achieving ≥ 4-point reduction in Peak Pruritus NRS or a score of 0 from PSBL to Week 260



[a]Following protocol amendments in June 2017 and January 2018, 114 and 272 patients re-entered the trial, with 103 and 207 patients having a treatment interruption of > 8 weeks between study Weeks 148 and 164. NRS, numerical rating score (range 0 [no itch] to 10 [worst itch imaginable]).

Table 2. Safety summary.

	OLE, Final data set Dupilumab 300 mg qw[a] N = 2,677			CHRONOS Week 52, Final data set Placebo + TCS N = 315			CHRONOS Week 52, Final data set Dupilumab 300 mg qw + TCS N = 315		
	No. of events	Patients ≥ 1 event, n (%)	nP/100PY	No. of events	Patients ≥ 1 event, n (%)	nP/100PY	No. of events	Patients ≥ 1 event, n (%)	nP/100PY
TEAE	14,717	2,276 (85.0)	166.0	1,520	268 (85.1)	325.1	1,500	263 (83.5)	322.4
Severe TEAE	391	269 (10.0)	5.0	46	28 (8.9)	10.3	24	17 (5.4)	5.9
SAE	388	283 (10.6)	5.2	24	16 (5.1)	5.8	11	10 (3.2)	3.4
SAE related to treatment	38	33 (1.2)	0.6	3	3 (1.0)	1.1	2	2 (0.6)	0.7
TEAEs leading to discontinuation	122	101 (3.8)	1.7	29	25 (7.9)	9.1	10	9 (2.9)	3.1

[a]Includes the 226 patients who switched from 300 mg qw to 300 mg q2w in Amendment 9 (Nov 2019). nP/100PY, number of patients per 100 patient-years; qw, every week; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- **In this long-term (5 year/260 week) open-label study, dupilumab demonstrated continued efficacy substantiated by sustained improvement of AD signs and symptoms (including skin lesions and pruritus) in adult patients with moderate-to-severe AD**
- **The most common reason for study withdrawals during the OLE was dupilumab approval and commercialization; incidence of discontinuations due to adverse events was low**
- **The safety profile was acceptable and consistent with the known safety profile observed in previous dupilumab placebo-controlled studies**

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