Dupilumab Provides Long-Term Efficacy for up to 4 Years in an Open-Label Extension Study of Adults With Moderate-to-Severe Atopic Dermatitis

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BACKGROUND

- Atopic dermatitis (AD) is a chronic systemic inflammatory disease requiring long-term management
- Conventional systemic treatments for moderate to severe AD are not recommended for continuous use due to safety concerns and lack of long term efficacy data
- Data from an open-label extension (OLE) study (NCT01949311) have previously demonstrated favorable safety and sustained efficacy in adult patients for up to 172 weeks

OBJECTIVE

- **To evaluate the long-term efficacy of dupilumab up to 4 years in patients with moderate-to-severe AD**

METHODS

Study design

- LIBERTY AD OLE (NCT01949311) is an ongoing, phase 3, multicenter study assessing long-term safety and efficacy of dupilumab 300 mg qw in adults with moderate-to-severe AD who previously participated in dupilumab clinical trials (parent studies), including in the placebo group
- Protocol amendments in June 2017 and January 2018 allowed for patient re-entry and treatment extension for up to 5 years in certain countries
- In 2019, 226 ongoing patients transitioned from 300 mg weekly (qw) to 300 mg every other week (q2w) to align with approved dosage
- Concomitant treatments for AD, including topical corticosteroids (TCS) and topical calcineurin inhibitors, were permitted
- This interim analysis examined the overall population treated for up to 4 years at time of database cutoff in April 2021
- Because the OLE trial lacks a control arm, safety results from the LIBERTY AD CHRONOS 52-week study (NCT02260986) in adults with moderate-to-severe AD receiving dupilumab 300 mg qw plus TCS are provided as a comparison

RESULTS

Table 1. Baseline demographics and disease characteristics

	N = 2677	
Age, mean (SD), years	39.2 (13.4)	
Duration of AD, mean (SD), years	29.9 (14.8)	
Sex, male, n (%)	1611 (60.2)	
Race, n (%)		
White	1936 (72.3)	
Black	147 (5.5)	
Asian	541 (20.2)	
Other/not reported	33 (1.2)	
Not reported	20 (0.7)	
BMI, mean (SD), kg/m^2	26.4 (5.6)	
	Parent study	**Current study**
EASI (0-72), mean (SD)	32.8 (13.2)	16.4 (14.6)
IGA score, mean (SD)	3.49 (0.5)	2.7 (1.0)
IGA score, n (%)		
0/1	0	320 (12.0)
2	0	610 (22.8)
3	1343 (50.2)	1288 (48.1)
4	1301 (48.6)	459 (17.1)
PP-NRS score (0-10), mean (SD)	7.1 (1.9)	5.0 (2.5)

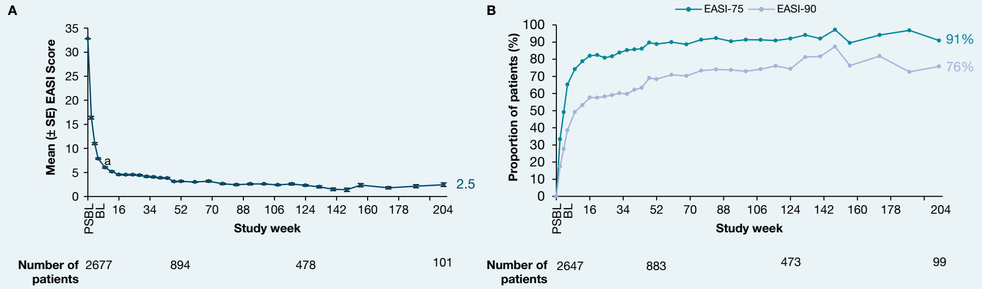
BMI, body mass index; EASI, Eczema Area and Severity Index; IGA, Investigator's Global Assessment; PP-NRS, Peak Pruritus Numerical Rating Scale; SD, standard deviation

Table 2. Patient disposition

n (%)	N = 2677
Patients who completed up to Week 52	2207 (82.4)
Patients who completed up to Week 100	1065 (39.8)
Patients who completed up to Week 148	557 (20.8)
Patients who completed up to Week 172	362 (13.5)
Patients who completed up to Week 204	352 (13.1)
Treatment duration > 204 weeks	240 (9.0)
Patients who completed the study	1114 (41.6)
Patients ongoing	201 (7.5)
Patients withdrawn from the study	1362 (50.9)
Study terminated by sponsor[a]	810 (30.3)
Withdrawal by subject[b]	238 (8.9)
Adverse event[c]	114 (4.3)
Lost to follow-up	69 (2.6)
Lack of efficacy	58 (2.2)
Protocol deviation	36 (1.3)
Pregnancy	20 (0.7)
Physician decision	12 (0.4)
Unknown	4 (0.1)
COVID-19 travel restriction	1 (0.04)

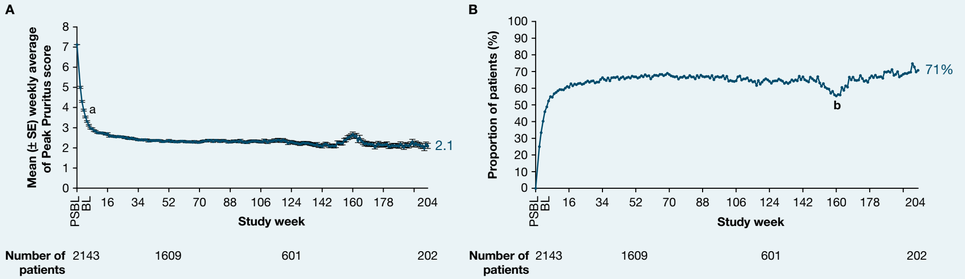
Patient attrition over time may enrich for patients who tolerate or respond well to dupilumab. The mean study drug injection compliance was high (98.1%), with most patients having ≥ 80% compliance during the study
[a]Regulatory approval/commercialization; [b]Includes reasons of relocation, desire for 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 safety follow-up period.

Figure 1. (A) Mean (± SE) EASI over time from the PSBL through Week 204; (B) Proportion of patients achieving EASI-75 and EASI-90 from the PSBL through Week 204



[a]Mean EASI (SE) at Week 8: 6.01 (0.16).
Following protocol amendments in June 2017 and January 2018, 113 and 272 patients re-entered the trial, with 102 and 207 patients having a treatment interruption of > 8 weeks between study weeks 148 and 164.
BL, current study baseline; EASI-75/90, ≥ 75%/90% improvement from PSBL in EASI; PSBL, parent study baseline; SE, standard error.

Figure 2. (A) Weekly mean (± SE) PP-NRS score by visit through Week 204; (B) Proportion of patients achieving ≥ 4-point reduction in PP-NRS score from PSBL through Week 204



[a]Mean PP-NRS (SE) at Week 2: 3.87 (0.05).
[b]Following protocol amendments in June 2017 and January 2018, 113 and 272 patients re-entered the trial, with 102 and 207 patients having a treatment interruption of > 8 weeks between study weeks 148 and 164.
BL, current study baseline; PP-NRS, Peak Pruritus NRS; PSBL, parent study baseline; SE, standard error.

Table 3. Overall safety in comparison with CHRONOS.

	OLE Dupilumab 300 mg qw (N = 2677)			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	14569	2273 (84.9)	167.5	1520	268 (85.1)	325.1	1500	263 (83.5)	322.4
Severe TEAE	383	263 (9.8)	4.96	46	28 (8.9)	10.3	24	17 (5.4)	5.9
SAE	383	278 (10.4)	5.20	24	16 (5.1)	5.75	11	10 (3.2)	3.40
SAE related to treatment	38	33 (1.2)	0.58	3	3 (1.0)	1.1	2	2 (0.6)	0.7
TEAE leading to discontinuation	120	99 (3.7)	1.76	30	26 (8.3)	8.31	10	9 (2.9)	2.58

nP/100PY, number of patients per 100 patient-years; SAE, serious adverse event; TEAE, treatment-emergent adverse event.

CONCLUSIONS

- **In this long-term (204 week) interim analysis of the 5 year OLE study, dupilumab demonstrated robust and sustained efficacy with progressive and incremental improvement in AD signs and symptoms (including skin lesions and pruritus) in adults with moderate-to-severe AD**
- **Mean EASI and weekly average PP-NRS score remained consistently 7 or below and 4 or below from Week 8 and Week 2, respectively, reflecting minimal disease activity with continuous long-term control evidenced by an increasing proportion of patients achieving and maintaining EASI-75 and EASI-90**
- **The safety profile was favorable and consistent with the known safety profile observed in previous dupilumab controlled studies**

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