Long-Term Safety Data for Dupilumab 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 cumulative safety concerns
- Data from an open-label extension (OLE) study (NCT01949311) have previously demonstrated favorable safety and sustained of dupilumab efficacy in adult patients for up to 172 weeks

OBJECTIVE

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

METHODS

Study design

- LIBERTY AD OLE (NCT01949311) is an ongoing, phase 3, multicenter study assessing long-term safety and efficacy of dupilumab 300 mg weekly (qw) in adults with moderate-to-severe AD who previously participated in dupilumab clinical trials (parent studies), including in the placebo group[1]
- Protocol amendments in June 2017 and January 2018 allowed for patient re-entry and treatment extension for up to 5 years in certain countries
- This interim data includes the full safety analysis set at time of database cutoff in April 2021 for the overall study population
- In 2019, 226 ongoing patients transitioned from 300 mg 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
- 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; NRS, 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. [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.

Table 3. Safety summary

	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.

Table 4. Analysis of most common TEAEs

TEAEs reported in ≥ 5% of patients by PT	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)	
	Patients ≥ 1 event, n (%)	**nP/100PY**	**Patients ≥ 1 event, n (%)**	**nP/100PY**	**Patients ≥ 1 event, n (%)**	**nP/100PY**
Nasopharyngitis	773 (28.9)	17.95	62 (19.7)	24.9	62 (19.7)	24.2
Conjunctivitis[a]	536 (20.0)	11.4	25 (7.9)	9.24	61 (19.4)	23.37
Atopic dermatitis	444 (16.6)	8.95	147 (46.7)	74.32	55 (17.5)	20.7
Upper respiratory tract infection	362 (13.5)	7.15	32 (10.2)	12.0	43 (13.7)	15.8
Headache	218 (8.1)	4.14	19 (6.0)	7.0	25 (7.9)	9.0
Oral herpes	199 (7.4)	3.77	9 (2.9)	3.2	15 (4.8)	5.2
Injection site reaction	138 (5.2)	2.54	25 (7.9)	9.4	61 (19.4)	24.5

[a]Includes the following PTs: conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, and atopic keratoconjunctivitis.
MedDRA, Medical Dictionary for Regulatory Activities; PT, MedDRA Preferred Term.

Table 5. Assessment of conjunctivitis

Assessment of conjunctivitis[a]	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)	
Number of events	888		29		91	
Not recovered/not resolved	83 (9.3)		1 (3.4)		7 (7.7)	
Recovered/resolved	775 (87.3)		27 (93)		81 (89)	
Recovered/resolved with sequelae	10 (1.1)		0		1 (1.1)	
Recovering/resolving	18 (2.0)		1 (3.4)		2 (2.2)	
	n (%)	**nP/100PY**	**n (%)**	**nP/100PY**	**n (%)**	**nP/100PY**
Number of patients with ≥ 1 event of conjunctivitis	536 (20)	11.4	25 (7.9)	9.2	61 (19.4)	22.6
Related to study drug	258 (9.6)	4.9	5 (1.6)	1.8	15 (4.8)	5.2
Mild	248 (9.3)	4.7	15 (4.8)	5.4	31 (9.8)	11.0
Moderate	262 (9.8)	5.0	9 (2.9)	3.2	28 (8.9)	10.0
Severe	26 (1.0)	0.5	1 (0.3)	0.4	2 (0.6)	0.7
Resulting in permanent discontinuation of study drug	14 (0.5)	0.2	0	0	0	0

[a]Includes the following PTs: conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, and atopic keratoconjunctivitis.

CONCLUSIONS

- **Safety data from this 4-year interim analysis of an open label study of adults with moderate-to-severe AD are generally consistent with the known favorable dupilumab safety profile**
- **Exposure-adjusted incidence rates of TEAEs were generally lower than previously reported rates of AEs in a 52-week controlled trial and declined over time**
- **Exposure-adjusted incidence rates of conjunctivitis remained stable despite the extended treatment period**
- **More than 95% of patients with conjunctivitis reported their severity as mild/moderate, over 85% of conjunctivitis events were reported as recovered/resolved, and only 0.5% of patients discontinued treatment due to conjunctivitis**

References: 1. Beck LA, et al. Am J Clin Dermatol. 2020;21:567-77.

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