Dupilumab Treatment for up to 3 Years Demonstrates Sustained Efficacy in Adult Patients With Moderate-to-Severe Atopic Dermatitis: Results From LIBERTY AD Adult OLE

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BACKGROUND

- Long-term use of systemic immunosuppressants such as cyclosporin for treatment of atopic dermatitis (AD) is not recommended due to safety concerns
- Previous dupilumab studies have demonstrated favorable safety and sustained efficacy in adult patients for up to 76 weeks[1–3]

OBJECTIVES

- **To report long-term (up to 3 years) efficacy of dupilumab in adult patients with moderate-to-severe AD who participated in the R668-AD-1225 LIBERTY AD open-label extension (OLE) study (NCT01949311)**
- **To report long-term (up to 3 years) safety of dupilumab in adult patients with moderate-to-severe AD who participated in the OLE study**

METHODS

- LIBERTY AD OLE is an ongoing, phase 3, multicenter study assessing the long-term safety and efficacy of repeat doses of dupilumab 300 mg weekly (qw) in adults with moderate-to-severe AD who had previously participated in dupilumab studies (parent study) or had been screened for a phase 3 study, but could not be randomized because of randomization closure
- Eligible patients were ≥ 18 years of age who had previously participated in any dupilumab clinical trial, including early phase 1b trials
- This analysis examined patients given dupilumab 300 mg qw for up to 148 weeks at data cutoff (December 1, 2018)
- The study was conducted in accordance with the provisions of the Declaration of Helsinki, the International Conference on Harmonization Good Clinical Practice guideline, and applicable regulatory requirements; the protocol was reviewed and approved by institutional review boards/ethics committees at all study sites

Endpoints

- Primary endpoints were incidence and exposure-adjusted rates of adverse events (AEs)
- Secondary endpoints were incidence and exposure-adjusted rates of serious AEs (SAEs); proportion of patients with Investigator's Global Assessment (IGA) score 0–1 at Week 148; proportion of patients achieving ≥ 75% reduction in Eczema Area and Severity Index (EASI-75) from parent study baseline (PSBL) to Week 148; change in EASI score from PSBL to Week 148; change in Peak Pruritus Numerical Rating Scale (NRS) score from PSBL to Week 148
- Efficacy analyses were performed using all observed data at each timepoint without any imputation for missing values

RESULTS

- 2,678 patients were enrolled, of which 2,677 were treated (60.2% male, 72.3% white, mean age 39.2 years) (**Table 1**)
  - Baseline disease characteristics were consistent with considerable disease burden (**Table 1**)

Table 1. Baseline demographics and disease characteristics.

	Dupilumab 300 mg qw (N = 2,677)	
Age, mean (SD), years	39.2 (13.4)	
Male, n (%)	1,611 (60.2)	
Race, n (%)		
White	1,936 (72.3)	
Black/African American	147 (5.5)	
Asian	541 (20.2)	
Other/not reported	53 (1.9)	
BMI, mean (SD), kg/m^2	26.37 (5.6)	
	Current study	**Parent study**
AD duration, mean (SD), years	29.9 (14.8)	29.0 (14.8)
IGA score, mean (SD), range 0–4, n (%)	2.7 (1.0)	3.5 (0.5)
0 or 1	320 (12.0)	0
2	610 (22.8)	0
3	1,288 (48.1)	1,343 (50.2)
4	459 (17.1)	1,301 (48.6)
EASI (0–72), mean (SD)	16.4 (14.6)	32.8 (13.2)
Patients achieving EASI-75, n (%)	884 (33.0)	N/A
Peak Pruritus NRS score, mean (SD)	5.0 (2.5)	7.1 (1.9)

BMI, body mass index; N/A, not applicable; SD, standard deviation.

  - Overall, dupilumab was well tolerated with 3.5% of patients discontinuing dupilumab treatment due to treatment-emergent adverse events (TEAEs) (**Table 2**)
  - Long-term safety was consistent with previously observed dupilumab studies, and no new safety signals were detected with long-term dupilumab treatment (**Table 3**)
    - Exposure-adjusted incidence rates of the most common AEs were lower in the OLE study than in the LIBERTY AD CHRONOS treatment group
  - In total, 1,325 patients withdrew from the study; 807 patients withdrew due to study termination by the sponsor upon regulatory approval and commercialization of the study drug (**Table 4**)
- At Week 148 (n = 58), 74.1% of patients had an IGA score of ≤ 1 (clear or almost clear skin), and 94.8% had an IGA score ≤ 2 (mild) (**Figure 1A** and **B**)
- Mean percent change in EASI from PSBL to Week 148 (n = 58) was –95.4%, with 96.6% of patients achieving EASI-75 (**Figure 2A** and **B**)
- Additionally, mean EASI (standard error [SE]) was 1.4 (0.4) at Week 148 (**Figure 2C**)
- Mean percent change in weekly averaged daily Peak Pruritus NRS from PSBL to Week 148 (n = 218) was –65.4% (**Figure 3A**), while 75.0% (n = 224) of patients achieved ≥ 3-point improvement in Peak Pruritus NRS or a Peak Pruritus NRS score of 0 (**Figure 3B**)
- Mean weekly averaged daily Peak Pruritus NRS score was 2.2 (0.1) at Week 148, corresponding to no or very mild skin lesions and pruritus (**Figure 3C**)

Table 2. Safety overview: comparison between OLE and CHRONOS studies.

	OLE (AD-1225) Dupilumab 300 mg qw (N = 2,677)			CHRONOS (AD-1224) Week 52, final data set: Placebo + TCS (n = 315)			CHRONOS (AD-1224) Week 52, final data set: Dupilumab 300 mg qw + TCS (n = 315)		
	No. of events	n (%)	nP/ 100 PY	No. of events	n (%)	nP/ 100 PY	No. of events	n (%)	nP/ 100 PY
TEAE	13,826	2,264 (84.6)	173.74	1,520	268 (85.1)	325.08	1,500	263 (83.5)	322.43
Severe TEAE	355	246 (9.2)	5.08	46	28 (8.9)	10.31	24	17 (5.4)	5.88
SAE	354	256 (9.6)	5.28	24	16 (5.1)	5.75	11	10 (3.2)	3.40
SAE related to study drug	36	31 (1.2)	0.61	3	3 (1.0)	1.06	2	2 (0.6)	0.68
TEAE leading to study drug discontinuation	116	95 (3.5)	1.87	30	26 (8.3)	8.31	10	9 (2.9)	2.58

nP/100 PY, number of patients (nP) with events per 100 patient-years (100 PY); TCS, topical corticosteroids.

Table 3. The most common AEs: comparison between OLE and CHRONOS studies.

PT (≥ 5% of patients of OLE)	OLE (AD-1225) Dupilumab 300 mg qw (N = 2,677)		CHRONOS (AD-1224) Week 52, final data set: Placebo + TCS (n = 315)		CHRONOS (AD-1224) Week 52, final data set: Dupilumab 300 mg qw + TCS (n = 315)	
	n (%)	nP/100 PY	n (%)	nP/100 PY	n (%)	nP/100 PY
Nasopharyngitis	752 (28.1)	19.16	62 (19.7)	24.93	62 (19.7)	24.16
Conjunctivitis[a]	521 (19.5)	11.96	25 (7.9)	9.24	61 (19.4)	23.37
Atopic dermatitis	438 (16.4)	9.61	147 (46.7)	74.32	55 (17.5)	20.71
Upper respiratory tract infection	350 (13.1)	7.56	32 (10.2)	12.03	43 (13.7)	15.85
Headache	216 (8.1)	4.54	19 (6.0)	6.98	25 (7.9)	8.97
Oral herpes	188 (7.0)	3.91	9 (2.9)	3.20	15 (4.8)	5.21
Injection-site reaction	138 (5.2)	2.82	25 (7.9)	9.39	61 (19.4)	24.46

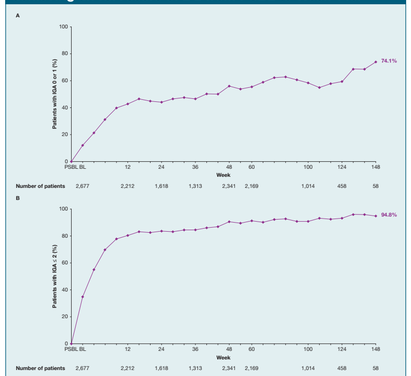
[a]Includes the following PTs: conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral, and atopic keratoconjunctivitis. MedDRA, Medical Dictionary for Regulatory Activities; PT, MedDRA Preferred Term.

Table 4. Patient disposition, [a]SAF.

Number of patients, n (%)	N = 2,677
Completed up to 1 year	2,207 (82.4)
Completed up to 2 years	1,028 (38.4)
Completed up to 3 years	347 (13.0)
Completed study	1,061 (39.6)
Patients ongoing	291 (10.9)
Withdrew from study	1,325 (49.5)
Study terminated by sponsor (regulatory approval/commercialization)	807 (30.1)
Withdrawal by subject[b]	221 (8.3)
Due to AE	109 (4.1)
Lost to follow-up	64 (2.4)
Lack of efficacy	57 (2.1)
Protocol deviation	32 (1.2)
Pregnancy	17 (0.6)
Physician decision	14 (0.5)
Unknown	4 (0.1)

[a]February 2019 database lock. [b]Includes reasons of relocation, desire for pregnancy, did not want to discontinue treatment for 12 weeks, work/school conflict, and personal reasons not specified. SAF, safety analysis set.

Figure 1. (A) Proportion of patients achieving an IGA Score of ≤ 1 from PSBL to Week 148, (B) proportion of patients achieving an IGA score of ≤ 2 from PSBL to Week 148.



BL, baseline of current study.

Figure 2. (A) Percent change in EASI from PSBL to Week 148, (B) proportion of patients achieving EASI-75 from PSBL to Week 148, (C) mean EASI over time from PSBL to Week 148.

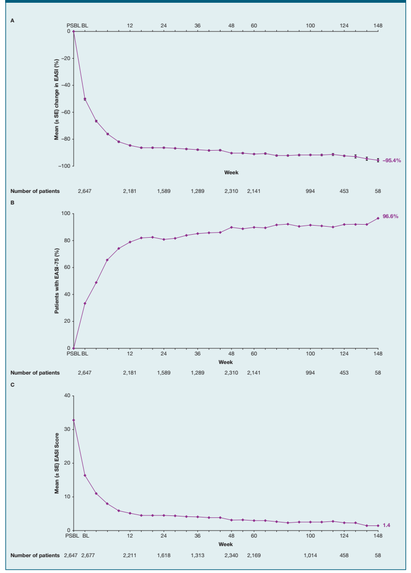
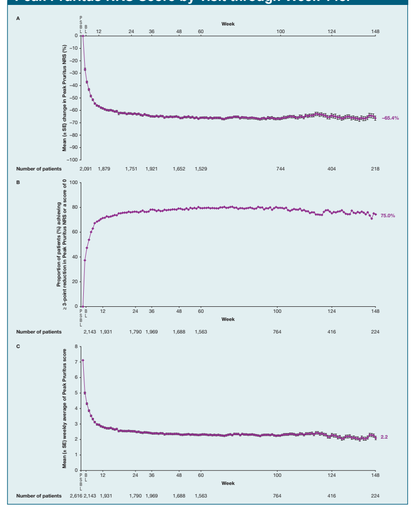


Figure 3. (A) Percent change in Peak Pruritus NRS from PSBL to Week 148, (B) proportion of patients achieving ≥ 3-point reduction in Peak Pruritus NRS or a score of 0 from PSBL to Week 148, (C) mean weekly average of Peak Pruritus NRS Score by visit through Week 148.



CONCLUSIONS

- **Treatment with dupilumab for up to 3 years showed a favorable risk–benefit profile and sustained efficacy with incremental improvement over time on multiple measures of disease assessment, reducing AD signs and symptoms in patients with moderate-to-severe AD**
- **The safety profile in this long-term study is consistent with the known safety profile of dupilumab previously observed in controlled studies; no new safety signals associated with the use of dupilumab in adult patients with moderate-to-severe AD were identified**

References

1. Simpson EL, et al. N Eng J Med. 2016;375:2335-48. 2. Blauvelt A, et al. Lancet. 2017;389:2287-303. 3. Deleuran M, et al. JAAD. 2020;82:377-88.

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