Continued Treatment with Dupilumab for Atopic Dermatitis Improves Efficacy in Week 16 Non-Responders

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INTRODUCTION

- Patients with moderate-to-severe atopic dermatitis (AD) often require long-term disease management
  - However, many systemic and topical treatments for AD are not recommended for continuous long-term use due to safety concerns and lack of long-term efficacy data[1]
- Standard efficacy endpoints in randomized, phase 3, placebo-controlled trials of dupilumab[2,3] include proportions of patients achieving ≥ 75% improvement from baseline in Eczema Area and Severity (EASI) scores (EASI-75), and proportions of patients achieving Investigator's Global Assessment (IGA) of 0 or 1
- The 16-week treatment period in short-term clinical trials of dupilumab may not be sufficient for some patients with moderate-to-severe AD to achieve optimal efficacy

OBJECTIVE

- **To report dupilumab efficacy up to Week 100 of an ongoing open-label extension (OLE) study (NCT01949311) in patients with moderate-to-severe AD who did not achieve the following outcomes at Week 16 in 2 parent studies:[4] EASI-75 or IGA 0 or 1**

METHODS

Study design

- The study design, efficacy, and safety of the identically designed parent studies LIBERTY AD SOLO 1 (NCT02277743) and LIBERTY AD SOLO 2 (NCT02277769), have been previously reported[4]
  - Treatment in these trials consisted of placebo, dupilumab 300 mg every 2 weeks (q2w), or dupilumab 300 mg every week (qw)
- LIBERTY AD OLE (NCT01949311) is an ongoing OLE trial assessing the long-term safety and efficacy of dupilumab
  - A loading dose of 600 mg was administered to:
    - Patients with a treatment gap of > 4 weeks between the end of the parent study and OLE baseline
    - Patients who had previously completed treatment per amendment 7 and who resumed treatment under amendment 7 or 8 with a treatment gap of > 4 weeks
  - Treatment in this trial is 300 mg qw[5]
  - Use of TCS and TCI was permitted
  - Patients were eligible for participation in LIBERTY AD OLE if they had participated in 1 of 14 previous dupilumab trials (including SOLO 1 or 2) and if they had adequately completed all protocol pre-specified assessments of the parent study
    - Data presented here are from patients who originally participated in SOLO 1 or 2 and continued into the OLE

Endpoints

- Outcomes assessed in this analysis include proportions of patients achieving EASI-75 or IGA 0 or 1 through Week 100 of the OLE among patients who did not achieve these endpoints at Week 16 of the parent study

Analysis

- Data are presented based on assigned treatment regimen in the original parent study
- Patients were included in this analysis if they received at least 1 dose of study drug in the OLE (safety analysis set)
- All analyses presented here were performed using all observed values at the indicated time point (only patients with measurements performed were included), with no imputation for missing values
- All endpoints were calculated based on the baseline values from the parent SOLO study
- Data are reported based on a cut-off date of December 15, 2018 (database lock February 2019)

RESULTS

- In total, 2,677 patients were enrolled and treated in the OLE
- Here, we present data from patients in the OLE who previously were enrolled from the SOLO 1 and 2 parent studies.
  - A total of 460, 457, and 462 patients were enrolled in SOLO 1 or 2 in the placebo, dupilumab 300 mg q2w, and dupilumab 300 mg qw groups, respectively.[4]
- Most patients who achieved the primary endpoints of SOLO 1 or 2 continued into SOLO-CONTINUE (NCT02395133); most patients who did not achieve the primary endpoints of SOLO 1 or 2 entered into OLE
  - 334, 213, and 178 patients enrolled in the OLE from SOLO 1 or 2 (patients received placebo, dupilumab 300 mg q2w, and dupilumab 300 mg qw in SOLO 1 or 2, respectively)

Table 1. Baseline demographics and disease characteristics of patients who did not achieve EASI-75 or IGA 0 or 1 at Week 16 of SOLO who were subsequently enrolled in the OLE, and are included in this analysis

	Non-achievers at Week 16 of SOLO	
	EASI-75 (n = 694)	IGA 0 or 1 (n = 715)
Age, mean (SD), years	39.1 (13.6)	39.2 (13.7)
Gender, male, n (%)	436 (62.8)	449 (62.8)
Race, n (%)		
White	455 (65.6)	469 (65.6)
Black/African American	36 (5.2)	38 (5.3)
Asian	186 (26.8)	191 (26.7)
Other/not reported	17 (2.4)	17 (2.4)
BMI, mean (SD), kg/m^2	26.5 (5.6)	26.5 (5.6)
Duration of AD, mean (SD), years	30.0 (14.5)	30.0 (14.6)
EASI (range 0–72), mean (SD)	23.8 (15.2)	23.4 (15.2)
EASI-75, n (%)	62 (8.9)	71 (9.9)
IGA (range 0–4), mean (SD)	3.2 (0.6)	3.1 (0.6)
IGA, n (%)		
0 or 1	3 (0.4)	6 (0.8)
2	53 (7.6)	60 (8.4)
3	471 (67.9)	482 (67.4)
4	167 (24.1)	167 (23.4)

BMI, body mass index; SD, standard deviation. Data shown as total patients included in this analysis per efficacy endpoint not-achieved, regardless of treatment received in SOLO 1 or 2.

- Included in this analysis are the following number of patients who enrolled in the OLE from SOLO 1 or 2, who did not achieve the below outcomes at Week 16 of SOLO 1 or 2:
  - EASI-75: 195/213 (91.5%) 300 mg q2w, and 169/178 (94.9%) 300 mg qw
  - IGA 0 or 1: 207/213 (97.2%) 300 mg q2w, and 176/178 (98.9%) 300 mg qw
- The baseline demographics and disease characteristics of patients originally enrolled in SOLO 1 or 2 who subsequently enrolled in the OLE are shown in **Table 1**

Efficacy

- A large proportion of patients who did not achieve EASI-75 or IGA 0 or 1 at Week 16 in SOLO 1 and 2 achieved these respective endpoints after treatment with dupilumab 300 mg qw by Week 12 in the OLE (**Figure, A and B**)
  - A proportion of patients had achieved EASI-75 or IGA 0 or 1 at OLE baseline, due to rescue treatment during the parent study or during the drug holiday between parent study and OLE
- The proportions of patients achieving EASI-75 increased over time in the OLE (**Figure, A**)
  - The proportions of patients with EASI-75 at Week 100 of the OLE were 91.0%, and 91.1% for the SOLO dupilumab 300 mg q2w, and dupilumab 300 mg qw treatment groups, respectively
- A tendency for improvement in AD signs as assessed by proportion of patients with IGA scores of 0 or 1 was also seen in the OLE (**Figure, B**)
  - At Week 100 of the OLE, the proportions of patients with IGA scores of 0 or 1 were 44.8%, and 49.0% for the patients who received dupilumab 300 mg q2w, and dupilumab 300 mg qw, respectively, in SOLO
- Patients included in this analysis who also had an uninterrupted treatment period (i.e. a treatment gap < 6 weeks between the end of SOLO 1 and 2, and the start of OLE) are depicted in **Figure** by the dashed lines
  - Efficacy results were similar when comparing the uninterrupted treatment subset of patients to all patients included in this analyses

Safety

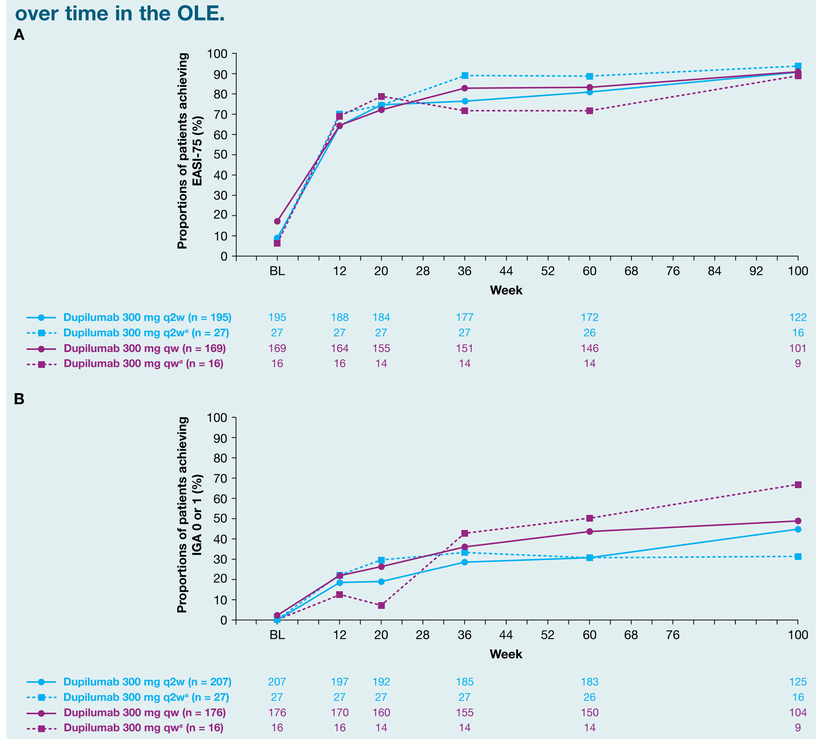
- The safety results from the overall OLE population are shown in **Table 2**
- Treatment discontinuations due to adverse events were uncommon, and safety for long-term dupilumab treatment was consistent with the known dupilumab safety profile
- The most common adverse events were nasopharyngitis, AD exacerbations, upper respiratory tract infection, headache, conjunctivitis, injection-site reactions, and herpes viral infections (**Table 2**)

Table 2. Safety assessed in the overall dataset of the OLE population.

	Dupilumab 300 mg qw (N = 2,677)			
	Events, n	Patients with ≥ 1 event, n (%)	nE/100 PY	nP/100 PY
TEAEs	13,826	2,264 (84.6)	270.1	173.7
Serious TEAEs	354	256 (9.6)	6.92	5.28
Severe TEAEs	355	246 (9.2)	6.94	5.08
TEAEs leading to study drug discontinuation	116	95 (3.5)	2.27	1.87
Serious TEAEs related to treatment	36	31 (1.2)	0.70	0.61
Death[a]	2	2 (< 0.1)	N/A	N/A
Most common TEAEs by PT (≥ 5% of patients)				
Nasopharyngitis	1,543	752 (28.1)	30.14	19.16
Atopic dermatitis	736	438 (16.4)	14.38	9.61
Upper respiratory tract infection	532	350 (13.1)	10.39	7.56
Headache	408	216 (8.1)	7.97	4.54
Conjunctivitis[b]	826	521 (19.5)	16.14	11.96
Injection-site reactions (HLT)	855	260 (9.7)	16.70	5.58
Herpes viral infections (HLT)	715	333 (12.4)	13.97	7.21

[a]1 death due to natural causes in an 88-year-old female and 1 due to unknown causes in a 58-year-old female approximately 5 months after the final dose of study drug.
[b]Includes PT: conjunctivitis, conjunctivitis allergic, conjunctivitis bacterial, conjunctivitis viral and atopic keratoconjunctivitis.
HLT, MedDRA High-Level Term; MedDRA, Medical Dictionary for Regulatory Activities; N/A, not applicable; nE, number of events; nP, number of patients; PT, MedDRA Preferred Term; PY, patient-years; TEAE, treatment-emergent adverse event.

Figure. Proportions of patients who, at Week 16 of SOLO, did not achieve (A) EASI-75, (B) IGA scores of 0 or 1; but who did achieve these outcomes over time in the OLE.



[a]The dashed lines depict the sub-set of patients included in this analysis who had uninterrupted treatment (a treatment gap of < 6 weeks between the end of SOLO 1 and 2, and the start of OLE).
BL, baseline of the OLE study.

CONCLUSIONS

- **Among patients with moderate-to-severe AD not achieving EASI-75 or IGA 0 or 1 at Week 16 in SOLO 1 and 2, a large proportion achieved these respective endpoints after continued treatment with dupilumab 300 mg qw, regardless of treatment received in the parent study**
- **The OLE data suggest that long-term treatment with dupilumab improves AD signs and symptoms in patients who do not respond optimally in the short term**
- **Due to the study design, and that this study is ongoing, a limitation of these analyses is a diminishing patient population over time. Data from patient withdrawals (due to study termination by sponsor, personal reasons, adverse events, lack of efficacy and other reasons) that occurred after week 16 but before week 100 would not be captured**

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