Dupilumab Reduces Symptom Burden and Improves Health-Related Quality of Life in Patients With Eosinophilic Esophagitis: Results From Part A of a Randomized, Placebo-Controlled, Three-Part, Phase 3 Study

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BACKGROUND

- Eosinophilic esophagitis (EoE) is a chronic, allergic, type 2 inflammatory disease that is characterized by eosinophilic inflammation in the esophagus, leading to esophageal dysfunction and related symptoms that substantially impair patients' quality of life (QoL)[1–4]
- Dupilumab is a fully human VelocImmune®-derived[5,6] monoclonal antibody that blocks the shared receptor component for interleukin (IL)-4 and IL-13, thus inhibiting signaling of both IL-4 and IL-13, key and central drivers of type 2 inflammation in multiple diseases, including EoE[7,8]
- Part A of the 3-part, randomized, double-blind, placebo-controlled, phase 3 LIBERTY EoE TREET study (NCT03633617) evaluated the efficacy and safety of weekly dupilumab 300 mg vs placebo for 24 weeks in adolescent and adult EoE patients; co-primary endpoints – proportion of patients achieving peak esophageal intraepithelial eosinophil count ≤ 6 eosinophils/high-power field and change from baseline in Dysphagia Symptom Questionnaire score at Week 24 – were achieved, and dupilumab was well tolerated[9]

OBJECTIVE

- **To determine the effect of 24 weeks of dupilumab treatment compared with placebo on health-related QoL and symptoms experienced, other than dysphagia, in adult and adolescent patients with EoE**

METHODS

Study assessments

- Absolute change from baseline to Week 24 in:
  - The Eosinophilic Esophagitis Impact Questionnaire (EoE-IQ) score, which assesses the impact of EoE on a scale of 1 to 5; higher scores indicate greater health-related QoL impairment
  - The Eosinophilic Esophagitis Symptom Questionnaire for Frequency (EoE-SQ-Frequency) score, which assesses symptoms other than dysphagia on a scale of 5 to 25; higher scores indicate higher symptom burden
- Patient Global Impression of Change (PGIC) of Dysphagia since treatment initiation ranging from "Very much better" to "Very much worse"
- Development of the EoE-IQ and EoE-SQ-Frequency questionnaires was informed by a targeted literature review, expert advice meetings, and qualitative interviews of adolescent and adult EoE patients

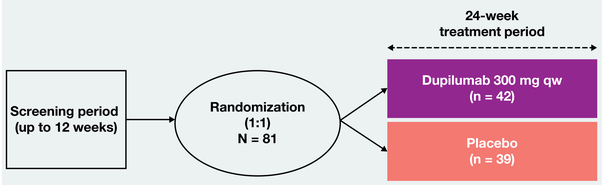
METHODS (CONT.)

Table. EoE-IQ and EoE-SQ-Frequency items and scoring.

Concepts measured in the EoE-IQ on a 5-point response option ranging from "Not at all" to "Extremely"	Concepts measured in the EoE-SQ-Frequency on a 5-point response option ranging from "Never" to "More than once a day
During the past 7 days, were you…	*During the past 7 days, how often did you experience…*
• Bothered by symptoms of EoE	• Chest pain
• Worried about trouble swallowing	• Stomach pain
• Worried about choking	• Burning feeling in your chest (heartburn)
• Embarrassed	• Food or liquid coming back up into your throat
• Worried about trouble swallowing while in a public place	• Throw up
• Difficulty taking part in social activities that involve eating food	
• Impact of EoE on relationships with family	
• Impact of EoE on relationships with friends	
• Difficulty keeping up with things at work or school	
• Missing work or school	
• Sleep disruption	

RESULTS

Figure 1. Study design showing Part A of the dupilumab EoE phase 3 TREET study (NCT03633617).[9]



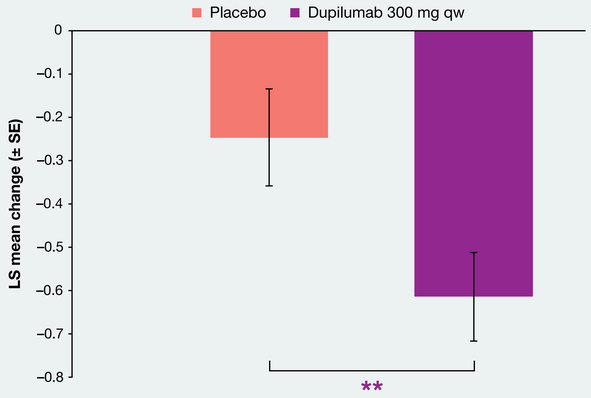
qw, weekly.

Study design

Part A of the TREET study enrolled 81 patients aged ≥ 12 years with a documented diagnosis of EoE by endoscopic biopsy and unresponsive to 8-week treatment with high-dose proton-pump inhibitors; a peak eosinophil count of ≥ 15 eosinophils/high-power field in at least 2 of the 3 regions sampled; no other causes of eosinophilic gastrointestinal disease; stable diet; a history of ≥ 2 episodes of dysphagia per week over 4 weeks; ≥ 4 episodes of dysphagia in the 2 weeks prior to baseline, ≥ 2 of which required medical attention; Dysphagia Symptom Questionnaire score ≥ 10.

RESULTS (CONT.)

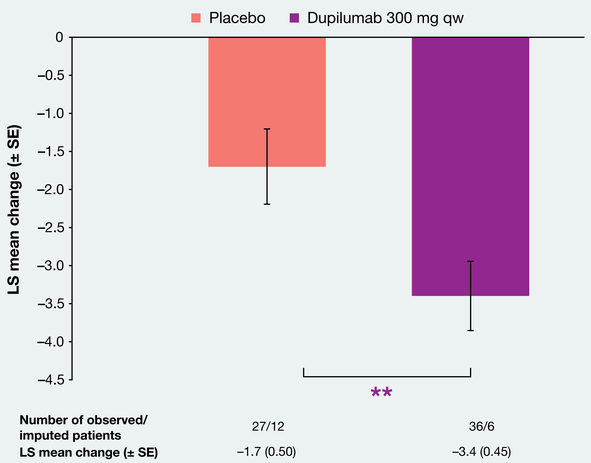
Figure 2. Absolute change from baseline to Week 24 in EoE-IQ score.



Number of observed/imputed patients	27/12	36/6
LS mean change (± SE)	−0.25 (0.11)	−0.61 (0.10)

**$P < 0.01$, derived using the ANCOVA model with baseline measurement as covariate, and the treatment and randomization stratification factors as fixed factors. Data were imputed using multiple imputations with values after first rescue treatment used were set to missing. Imputed patients – 5 patients in the placebo group received rescue treatment, 2 early terminations, 1 pending Week 24 assessments due to COVID-19 pandemic restrictions, and 4 missing Week 24 assessments; data after rescue treatment were set to missing and their Week 24 data were imputed.
LS, least squares; SE, standard error.

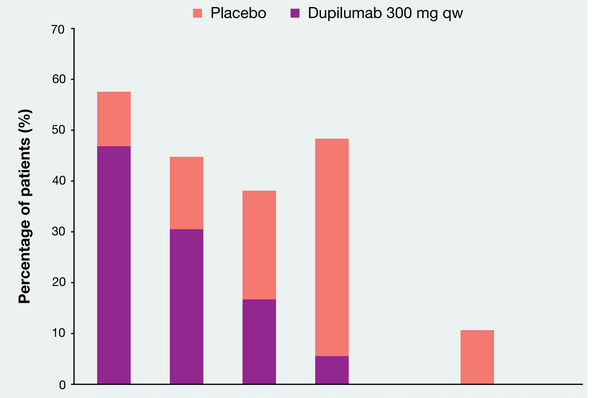
Figure 3. Absolute change from baseline to Week 24 in EoE-SQ-Frequency score.



Number of observed/imputed patients	27/12	36/6
LS mean change (± SE)	−1.7 (0.50)	−3.4 (0.45)

**$P < 0.01$, derived using the ANCOVA model with baseline measurement as covariate, and the treatment and randomization stratification factors as fixed factors. Data were imputed using multiple imputations with values after first rescue treatment used were set to missing. Imputed patients – 5 patients in the placebo group received rescue treatment, 2 early terminations, 1 pending Week 24 assessments due to COVID-19 pandemic restrictions, and 4 missing Week 24 assessments; data after rescue treatment were set to missing and their Week 24 data were imputed.

Figure 4. Descriptive summary of PGIC of Dysphagia from baseline to Week 24 based on observed data.



Number reporting outcome/number of patients (%)							
Dupilumab	17/36 (47.2)	11/36 (30.6)	6/36 (16.7)	2/36 (5.6)	0/36	0/36	0/36
Placebo	3/28 (10.7)	4/28 (14.3)	6/28 (21.4)	12/28 (42.9)	0/28	3/28 (10.7)	0/28

Data after rescue treatment were set to missing. No imputation performed for patients with missing data.

OVERALL SAFETY

- The incidence of treatment-emergent adverse events was similar across the intervention groups (dupilumab 85.7% vs placebo 82.1%), with the most frequent being injection-site reactions (dupilumab 16.7% vs placebo 10.3%) and nasopharyngitis (11.9% vs 10.3%)

CONCLUSIONS

- **In adolescent and adult patients with EoE over the 24-week treatment period:**
  - **Dupilumab improved health-related QoL as assessed by the EoE-IQ vs placebo**
  - **Dupilumab reduced the frequency of symptoms as assessed by the EoE-SQ-Frequency vs placebo**
  - **Dupilumab increased the proportion of patients reporting their dysphagia as "very much better" vs placebo**

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