Dupilumab improves clinical, symptomatic, endoscopic and histologic aspects of EoE, regardless of prior swallowed topical steroid use

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BACKGROUND

- Eosinophilic esophagitis (EoE) is a chronic, progressive, allergic, type 2 inflammatory disease of the esophagus[1]
- Swallowed topical corticosteroids (STC) are a first-line treatment for EoE, but are not uniformly effective
- Dupilumab is a fully human VelocImmune®-derived[2,3] monoclonal antibody that blocks the shared receptor component for IL-4 and IL-13, key and central drivers of type 2 inflammation in multiple diseases[4,5]
- In a pooled analysis of Parts A and B of the three-part, phase 3 LIBERTY EoE TREET study dupilumab 300 mg qw vs placebo demonstrated significant, (all p<0.0001) improvements in clinical, symptomatic, histologic, and endoscopic aspects of the disease in adolescents/adults with EoE up to 24 weeks and was generally well tolerated
- Dupilumab is approved by the FDA for the treatment of adults and adolescents aged ≥12 years and weight ≥ 40 kg with EoE[6]

OBJECTIVE

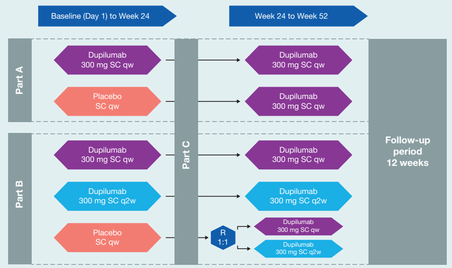
- **The objective of this pre-specified analysis of LIBERTY EoE TREET was to assess the efficacy of dupilumab 300mg qw vs placebo at Week 24 in pooled patients from Parts A and B with and without prior history of STC use, and with or without a history of inadequate response, intolerance, or contraindication to STC**

METHODS

- In Part A, 81 participants with EoE were randomized 1:1 to 24 weeks of subcutaneous dupilumab 300 mg qw (n=42) or placebo (n=39); In Part B, 240 participants with EoE were randomized 1:1:1 to 24 weeks of subcutaneous dupilumab 300 mg qw (n=80), dupilumab 300 mg every 2 weeks (q2w) (n=81), or placebo (n=79) (**Figure 1**)
- Patients with and without a history of STC use from Parts A and B, and with and without a history of inadequate response, intolerance, or contraindication to STCs from Part B, were evaluated
  - Prior STC use was defined as use of any swallowed topical corticosteroid prior to study participation
  - All patients were required to washout of STC for 8 weeks prior to study baseline
  - The study was not powered for analysis of these subgroups

METHODS (CONT.)

Figure 1. Study design of the phase 3 LIBERTY-EoE-TREET trial.



Study drug was administered to patients without a loading dose. At the end of the treatment period, patients from Part A or Part B had the option to continue to an ongoing extended treatment period of 28 weeks (Part C). Non-eligible patients who did not enter Part C entered a 12-week follow-up period.
QW, weekly; Q2W, every 2 weeks; SQ, subcutaneously.

- Endpoints at Week 24 included the proportion of patients achieving peak esophageal intraepithelial eosinophil count ≤6/high-power field (hpf); absolute and % change in Dysphagia Symptom Questionnaire (DSQ) score; % change in peak esophageal intraepithelial eosinophil count; absolute change in Histologic Scoring System (HSS) grade and stage scores; and absolute change in Endoscopic Reference Score (EREFS)

RESULTS

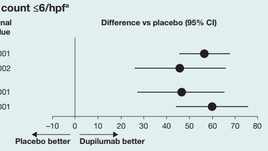
- At baseline, in Parts A and B combined, 84/122 patients (69%) in the dupilumab qw group, and 87/118 patients (74%) in the placebo group had a history of STC use for EoE
- At baseline, in Part B, 38/80 patients (48%) in the dupilumab qw group, and 39/79 patients (49%) in the placebo group had a history of inadequate response, intolerance, or contraindication to STC
- Dupilumab qw improved outcomes vs placebo for primary and key secondary efficacy endpoints, with generally comparable results observed in subgroups of patients with and without prior STC use, and with and without a history of inadequate response, intolerance, or contraindication to STC (**Figure 2**)

RESULTS (CONT.)

Figure 2. Dupilumab efficacy at Week 24 on primary endpoints (A) proportion of patients achieving peak esophageal intraepithelial eos count ≤6/hpf and (B) absolute change from baseline in DSQ score, and secondary endpoints including (C) % change in peak eos count, (D) % change in DSQ score, EoE-HSS (E) grade and (F) stage scores, and (G) absolute change in EREFS, in adults and adolescents with EoE, by subgroups based on history of prior STC use and history of inadequate response, intolerance, or contraindication to STC.

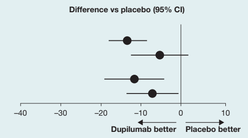
A. Proportion of patients achieving peak esophageal intraepithelial eosinophil count ≤6/hpf[a]

	Placebo n	Dupilumab n	Difference vs placebo (95% CI)	Nominal P-value
Prior STC use				
Yes	87	84	56.7 (45.52, 67.88)	<0.0001
No	31	38	46.0 (25.82, 66.20)	0.0002
Inadequate response/Intolerrant/Contraindication to STC				
Yes	39	38	46.3 (27.13, 65.54)	<0.0001
No	40	42	59.9 (43.91, 75.80)	<0.0001



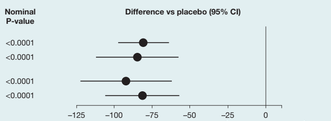
B. Absolute change from baseline in DSQ score[a]

	Placebo n	Dupilumab n	Difference vs placebo (95% CI)	Nominal P-value
Prior STC use				
Yes	87	84	−13.27 (−18.033, −8.504)	<0.0001
No	31	38	−5.21 (−12.406, 1.996)	0.1565
Inadequate response/Intolerrant/Contraindication to STC				
Yes	39	38	−11.55 (−19.055, −4.036)	0.0026
No	40	42	−7.08 (−13.747, −0.415)	0.0374



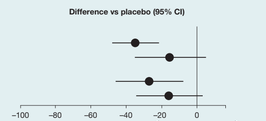
C. Percent change from baseline in peak eosinophil count[a]

	Placebo n	Dupilumab n	Difference vs placebo (95% CI)	Nominal P-value
Prior STC use				
Yes	87	84	−80.76 (−97.769, −63.750)	<0.0001
No	31	38	−84.87 (−112.157, −57.581)	<0.0001
Inadequate response/Intolerrant/Contraindication to STC				
Yes	39	38	−92.29 (−122.477, −62.103)	<0.0001
No	40	42	−81.49 (−106.023, −56.963)	<0.0001



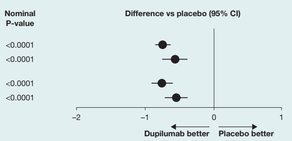
D. Percent change from baseline in DSQ score[b]

	Placebo n	Dupilumab n	Difference vs placebo (95% CI)	Nominal P-value
Prior STC use				
Yes	87	84	−34.5 (−47.75, −21.22)	<0.0001
No	31	38	−14.9 (−35.21, 5.36)	0.1492
Inadequate response/Intolerrant/Contraindication to STC				
Yes	39	38	−26.8 (−45.98, −7.65)	0.0061
No	40	42	−15.9 (−35.22, 3.52)	0.1087



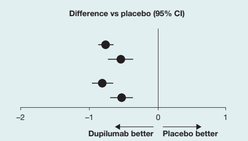
E. Absolute change from baseline in EoE-HSS grade score[a,d]

	Placebo n	Dupilumab n	Difference vs placebo (95% CI)	Nominal P-value
Prior STC use				
Yes	87	84	−0.766 (−0.8733, −0.6589)	<0.0001
No	31	38	−0.574 (−0.7665, −0.3814)	<0.0001
Inadequate response/Intolerrant/Contraindication to STC				
Yes	39	38	−0.778 (−0.9416, −0.6148)	<0.0001
No	40	42	−0.554 (−0.7240, −0.3841)	<0.0001



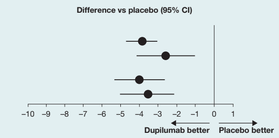
F. Absolute change from baseline in EoE-HSS stage score[a,d]

	Placebo n	Dupilumab n	Difference vs placebo (95% CI)	Nominal P-value
Prior STC use				
Yes	87	84	−0.765 (−0.8680, −0 .6617)	<0.0001
No	31	38	−0.548 (−0.7343, −0 .3623)	<0.0001
Inadequate response/Intolerrant/Contraindication to STC				
Yes	39	38	−0.807 (−0.9651, −0.6496)	<0.0001
No	40	42	−0.535 (−0.6993, −0.3702)	<0.0001



G. Absolute change from baseline in EoE EREFS total score[c]

	Placebo n	Dupilumab n	Difference vs placebo (95% CI)	Nominal P-value
Prior STC use				
Yes	87	84	−3.86 (−4.699, −3.021)	<0.0001
No	31	38	−2.59 (−4.156, −1.018)	0.0012
Inadequate response/Intolerrant/Contraindication to STC				
Yes	39	38	−4.00 (−5.358, −2.641)	<0.0001
No	40	42	−3.54 (−4.996, −2.087)	<0.0001



[a]Pinch biopsies were collected from 3 esophageal regions (proximal, mid, distal) at screening and Wk24 for histology and RNA sequencing.
[b]The Dysphagia Symptom Questionnaire is a patient-reported outcome measure that is administered daily and assesses the frequency and severity of dysphagia. The biweekly total DSQ score ranges from 0 to 84; higher scores indicate greater dysphagia-related symptom burden.
[c]Endoscopies were performed at screening and Wk24, and the proximal and distal esophageal regions scored for edema, rings, exudates, furrows, and strictures. The overall score ranges from 0 to 18; higher scores indicate greater severity.
[d]Biopsies were scored for eosinophil density, basal zone hyperplasia, eosinophil abscesses, eosinophil surface layering, dilated intercellular spaces, surface epithelial alteration, dyskeratotic epithelial cells, and lamina propria fibrosis. Each region was scored separately from 0 to 1, and the 3 regions were summed for the final score which ranges from 0 to 3; 0 represents normal and 3 maximum change.

CONCLUSION

- **Regardless of history of prior STC use, in this pooled analysis from Part A and Part B of the EoE TREET Phase 3 Study, dupilumab 300mg qw demonstrated substantial improvements in clinical, histologic, and endoscopic study endpoints at Week 24 in adults and adolescents with EoE**

References: 1. Lucendo AJ, et al. United European Gastroenterol J. 2017;53:335-358. 2. Macdonald LE, et al. Proc Natl Acad Sci U S A. 2014;111(14):5147-52. 3. Murphy AJ, et al. Proc Natl Acad Sci U S A. 2014;111(14):5153-8. 4. Gandhi NA, et al. Expert Rev Clin Immunol. 2017;13(5):425-37. 5. Le Floc'h A, et al. Allergy. 2020;75(5):1188-204. 6. Dupilumab. Highlights of Prescribing Information. US Food and Drug Administration 2022. Available from: https://www.regeneron.com/downloads/dupixent_fpi.pdf

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