Dupilumab Improves **Inflammatory and Remodeling Aspects** of Endoscopic Disease Activity in **Eosinophilic Esophagitis:** 52-Week Results From the Phase 3 LIBERTY EoE TREET Study

Eosinophilic Esophagitis

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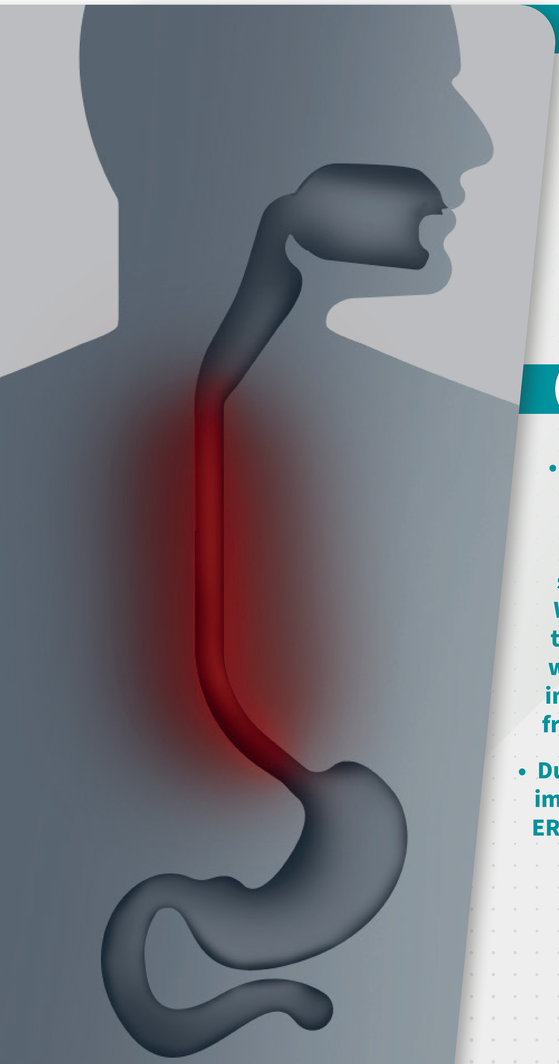
Background

- EoE is a chronic, progressive, type 2 inflammatory disease that can lead to progressive remodeling and fibrostenosis of the esophagus[1–3]
- EREFS is a validated classification system for the major endoscopic features of EoE, which includes subscores that assess inflammation and remodeling[4]
  - By convention, EREFS has been scored as a summation of proximal and distal esophageal sites[4]
  - EREFS scored by worst observed region may be more responsive to change in disease state than traditional EREFS scoring[5]
- Dupilumab, a fully human monoclonal antibody,[6] is approved in the USA for the treatment of EoE in adult and pediatric patients aged ≥1 year, weighing ≥15 kg, and in the EU for adults and adolescents aged ≥12 years, weighing ≥40 kg[7,8]
- In Parts A and B of the phase 3 LIBERTY EoE TREET study, dupilumab 300 mg qw improved histologic, symptomatic, and endoscopic aspects of EoE vs placebo at Week 24 in adults and adolescents with EoE; patients who completed Parts A and B and continued to the active treatment extension Part A–C/B–C received a further 28 weeks' dupilumab treatment[9]
- For more information on methods, please scan the QR code below.



Objective

- **This analysis assessed the effect of dupilumab on EREFS inflammatory and remodeling severity up to Week 52, using EREFS by worst observed region, in participants of the LIBERTY EoE TREET study**

Conclusions

- **Dupilumab demonstrated improvements in worst observed EREFS total score, and inflammation and remodeling subscores, vs placebo at Week 24, which were maintained through Week 52 for patients who continued dupilumab, and improved in those who switched from placebo to dupilumab**
- **Dupilumab also led to improvements in individual EREFS features at Week 52**

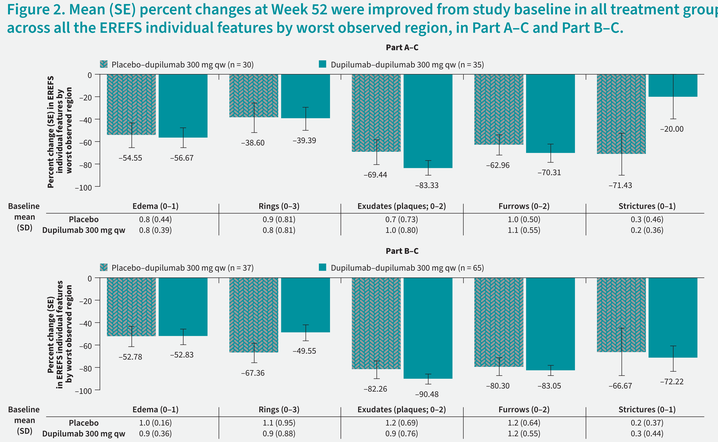
Results

Table. Baseline demographics and disease characteristics were generally well balanced between groups.

	Part A–C		Part B–C	
	Placebo–dupilumab 300 mg qw (N = 37)	Dupilumab–dupilumab 300 mg qw (N = 40)	Placebo–dupilumab 300 mg qw (N = 37)	Dupilumab–dupilumab 300 mg qw (N = 74)
Age, years, mean (SD)	29.0 (12.8)	34.3 (15.7)	28.6 (12.7)	28.6 (14.0)
Adolescents ≥12 to <18 years, n (%)	9 (24.3)	10 (25.0)	10 (27.0)	24 (32.4)
Female sex, n (%)	16 (43.2)	14 (35.0)	13 (35.1)	26 (35.1)
Race, n (%)				
White	35 (94.6)	39 (97.5)	34 (91.9)	65 (87.8)
Black/African American	1 (2.7)	1 (2.5)	1 (2.7)	2 (2.7)
Other/missing	1 (2.7)	0	2 (5.4)	7 (9.5)
History of prior swallowed topical steroid use for EoE, n (%)	30 (81.1)	28 (70.0)	27 (73.0)	51 (68.9)
History of prior esophageal dilations, n (%)	16 (43.2)	18 (45.0)	18 (48.6)	23 (31.1)
Eos count of three regions (/hpf), mean (SD)	71.57 (41.59)	59.78 (34.04)	60.00 (28.81)	62.70 (31.47)
DSQ score, mean (SD)[a]	34.9 (12.4)	31.6 (12.6)	36.7 (9.7)	38.0 (10.7)
EREFS total score, mean (SD)[b]	6.0 (2.4)	6.5 (3.3)	8.0 (3.4)	6.9 (3.1)
EREFS total score by worst observed region, mean (SD)[b]	3.7 (1.4)	3.9 (1.6)	4.6 (1.7)	4.1 (1.6)
EREFS inflammation subscore, mean (SD)[c]	4.2 (2.3)	5.0 (2.8)	6.0 (2.2)	5.0 (2.2)
EREFS inflammation subscore by worst observed region, mean (SD)[c]	2.5 (1.2)	2.9 (1.3)	3.4 (1.0)	2.9 (1.2)
EREFS remodeling subscore, mean (SD)[d]	1.8 (1.6)	1.5 (1.6)	2.0 (2.0)	1.9 (1.8)
EREFS remodeling subscore by worst observed region, mean (SD)[d]	1.2 (1.1)	1.0 (1.0)	1.2 (1.1)	1.2 (1.1)
EoE-HSS grade score, mean (SD)[e]	1.34 (0.47)	1.28 (0.41)	1.31 (0.35)	1.31 (0.40)
EoE-HSS stage score, mean (SD)[e]	1.39 (0.40)	1.31 (0.33)	1.30 (0.30)	1.29 (0.34)

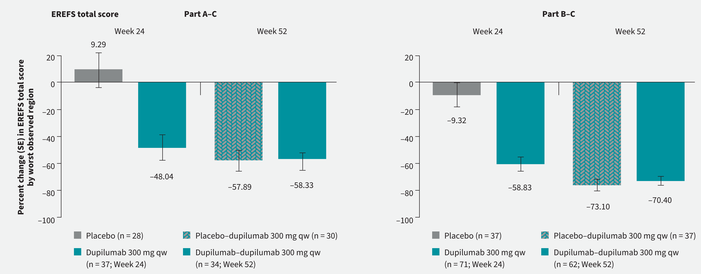
[a]The DSQ assesses the frequency and severity of dysphagia. The biweekly total DSQ score ranges from 0 to 84; lower scores indicate less dysphagia-related symptom burden. [b]EREFS assesses the severity of endoscopic features. Scores range from 0 to 18 (traditional) or from 0 to 9 (worst observed region); higher scores indicate greater severity. [c]EREFS inflammation subscore is comprised of the inflammatory features: edema, exudates, and furrows. Scores range from 0 to 10 (traditional) or from 0 to 5 (worst observed region); higher scores indicate greater severity. [d]EREFS remodeling subscore is comprised of the remodeling features: rings and strictures. Scores range from 0 to 8 (traditional) or from 0 to 4 (worst observed region); higher scores indicate greater severity. [e]EoE-HSS assesses the severity (grade) and extent (stage) of histologic features summed over 3 regions. Scores range from 0 to 3; 0 represents normal and 3 maximum change. Both scores exclude lamina propria fibrosis.

Figure 2. Mean (SE) percent changes at Week 52 were improved from study baseline in all treatment groups, across all the EREFS individual features by worst observed region, in Part A–C and Part B–C.



- In patients who had a worst observed EREFS total score of ≥1 at baseline, 75% and 62% in Part A–C, and 80% and 95% in Part B–C, had improved scores from baseline at Week 52, in the dupilumab-dupilumab 300 mg qw and placebo-dupilumab 300 mg qw groups, respectively

Figure 1. Dupilumab improved worst observed EREFS total score, and inflammation and remodeling subscores, vs placebo; improvements were maintained through Week 52.



DSQ, Dysphagia Symptom Questionnaire; EoE, eosinophilic esophagitis; eos, eosinophils; EREFS, EoE-Endoscopic Reference Score; hpf, high-power field; HSS, Histologic Scoring System; qw, weekly; SD, standard deviation; SE, standard error.

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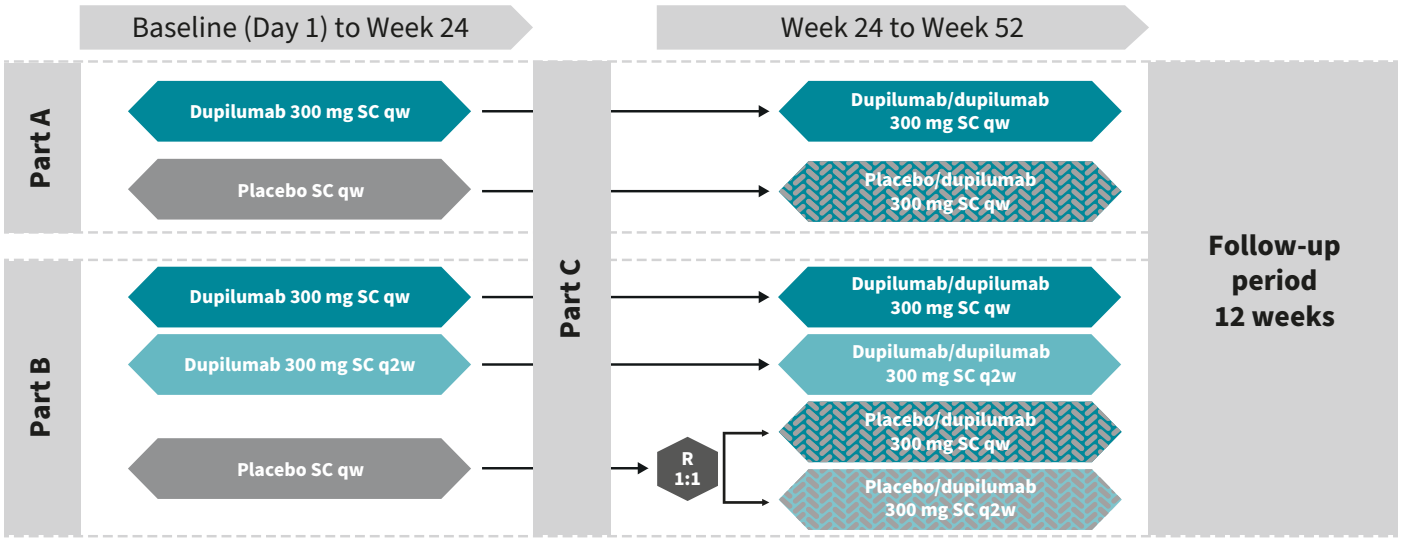
Supplementary Methods

- This analysis included patients who continued to Part A–C or Part B–C of the TREET study, and who received placebo or dupilumab 300 mg qw up to Week 24, and dupilumab 300 mg qw through Week 52 **(Figure S1)**

Figure S1. Study design of Parts A, B, and C of the LIBERTY-EoE-TREET trial.



- Edema (score range 0–1), rings (0–3), exudates (0–2), furrows (0–2), and strictures (0–1) were assessed by endoscopy in the proximal and distal regions at screening, and at Weeks 24 and 52, and were scored locally
- Worst observed scores (highest score for each individual endoscopic feature from either region) were used for EREFS total score (range 0–9), and inflammation (0–5) and remodeling (0–4) subscores