Dupilumab Reduces the Emotional and Dysphagia-Related Impacts of Eosinophilic Esophagitis to Improve Health-Related Quality of Life

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BACKGROUND

- Eosinophilic esophagitis (EoE) is a chronic, progressive, allergic, type 2 inflammatory disease of the esophagus that substantially impairs quality of life (QoL)[1]
- Dupilumab is a fully human monoclonal antibody[2,3] that blocks the shared receptor component for interleukin (IL)-4 and IL-13, key and central drivers of type 2 inflammation in multiple diseases[4,5]
- In Parts A and B of the three-part, phase 3 LIBERTY EoE TREET (NCT03633617) study, dupilumab 300 mg qw vs placebo demonstrated significant, clinically meaningful improvements in symptomatic and histologic aspects of the disease in adolescents and adults with EoE up to 24 weeks, and was generally well tolerated

OBJECTIVE

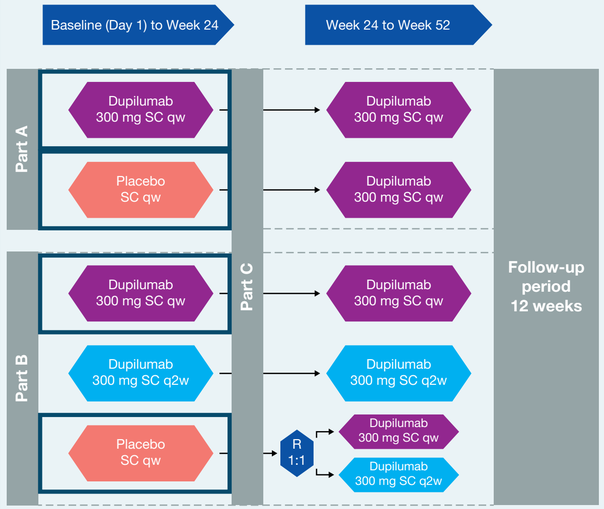
- **To assess the effect of dupilumab vs placebo on improving aspects of QoL using the EoE Impact Questionnaire (EoE-IQ), a novel disease-specific measure of health-related QoL in EoE patients, during the 24-week double-blind treatment period in Parts A and B of LIBERTY EoE TREET**

METHODS

- In Part A 42 patients received dupilumab 300 mg qw and 39 received placebo, and in Part B 80 patients received dupilumab 300 mg qw and 79 received placebo, for 24 weeks (**Figure 1**)
- The EoE-IQ is a patient-reported 11-item questionnaire that measures the impact of EoE on the following domains over a 7-day recall period: emotional (individual items 1–5), social (items 6–8), work and school (items 9–10), and sleep (item 11) (**Table**)

METHODS (CONT.)

Figure 1. Study design of the phase 3 LIBERTY-EoE-TREET trial (NCT03633617).



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) before entering a 12-week follow-up period. Non-eligible patients who did not enter Part C also entered a 12-week follow-up period. q2w, every 2 weeks; qw, weekly; SC, subcutaneously; R, randomized.

- The EoE-IQ was developed in line with best practices in the field of clinical outcomes assessment and includes the most relevant QoL impacts of EoE, as identified through literature review and discussion with therapeutic area experts and confirmed via patient interviews
- Response to each item is on a 5-point scale ranging from 1 to 5 with a higher score indicating a more negative impact on QoL, with the overall score as an average of item scores

Table. EoE-IQ items at baseline and after 24 weeks of treatment with weekly dupilumab 300 mg.

	Dupilumab 300 mg qw			
EoE-IQ Item	Mean absolute value at baseline	Mean absolute value at Week 24	LS mean difference vs placebo	*P* value vs placebo
Part A				
1. Bothered	**3.08**	**1.80**	**–0.64**	**0.0043**
2. Worried swallowing	**2.88**	**1.69**	**–0.73**	**0.0011**
3. Worried choking	**2.42**	**1.60**	**–0.61**	**0.0040**
4. Embarrassed	1.91	1.34	–0.21	0.2336
5. Worried swallowing public	**2.80**	**1.46**	**–0.90**	**0.0001**
6. Social activities	**2.06**	**1.40**	**–0.43**	**0.0311**
7. Family	1.44	1.29	–0.20	0.2560
8. Friends	1.39	1.28	–0.31	0.0813
9. Keep up work/school	1.48	1.30	–0.28	0.1379
10. Miss work/school	1.37	1.34	–0.09	0.5504
11. Sleep disruption	**1.82**	**1.21**	**–0.42**	**0.0027**
Part B				
1. Bothered	**3.50**	**1.97**	**–0.53**	**0.0004**
2. Worried swallowing	**3.10**	**1.60**	**–0.65**	**<0.0001**
3. Worried choking	**2.72**	**1.45**	**–0.57**	**<0.0001**
4. Embarrassed	**2.21**	**1.28**	**–0.28**	**0.0141**
5. Worried swallowing public	**2.96**	**1.53**	**–0.45**	**0.0020**
6. Social activities	**2.34**	**1.35**	**–0.30**	**0.0117**
7. Family	1.72	1.22	0.01	0.8765
8. Friends	1.68	1.19	–0.06	0.4409
9. Keep up work/school	1.81	1.32	–0.08	0.4170
10. Miss work/school	1.32	1.18	–0.09	0.3390
11. Sleep disruption	**1.94**	**1.36**	**–0.22**	**0.0409**

EoE-IQ at baseline and after 24 weeks of treatment with weekly dupilumab 300 mg. Values after first rescue treatment use were set to missing (censoring), then multiple imputation was used to impute missing values. All *P* values are nominal. EoE-IQ, EoE Impact Questionnaire; LS, least squares.

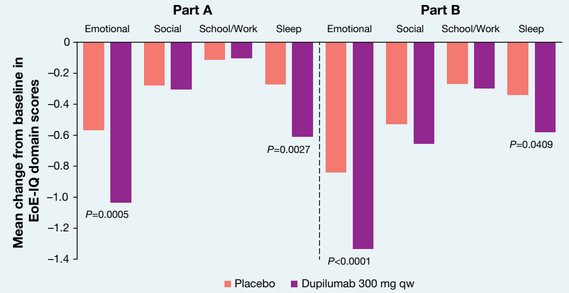
RESULTS

- At baseline, the most burdensome impacts of EoE were related to overall emotional impact and anxiety around dysphagia (items 1-5) (**Table**)

RESULTS (CONT.)

- Dupilumab 300 mg qw showed a nominally significant reduction in total average score vs placebo (Part A LS mean change –0.614, *P*=0.0077; Part B –0.887, *P*=0.0002)
- Dupilumab showed a nominally significant reduction vs placebo in 6 individual EoE-IQ items in Parts A and B: "bothered", "worried about swallowing", "worried about choking", "worried about swallowing in public", "social activities", and "sleep disruption"; and in 1 additional item in Part B: "embarrassed" (**Table**)
- Dupilumab showed a nominally significant reduction vs placebo in emotional and sleep domains of the EoE-IQ (**Figure 2**)
- Treatment effect was generally larger for dupilumab vs placebo on most questionnaire items

Figure 2. Change from baseline in EoE-IQ domains after 24 weeks of treatment with weekly dupilumab 300 mg or placebo.



Values after first rescue treatment use were set to missing (censoring), then multiple imputation was used to impute missing values. EOE-IQ, eosinophilic esophagitis impact questionnaire; qw, weekly.

CONCLUSION

- **This analysis of the EoE-IQ from Parts A and B of the phase 3 TREET trial demonstrated that EoE QoL was improved among patients on dupilumab 300 mg qw, with improvement driven by emotional and social impacts and sleep**

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