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Long Term Efficacy and Safety of Dupilumab for Eosinophilic Esophagitis

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This summary reviews: Rothenberg ME, Dellon ES, Collins MH, et al. Efficacy and safety of dupilumab up to 52 weeks in adults and adolescents with eosinophilic oesophagitis (LIBERTY EoE TREET study): A multicentre, double-blind, randomised, placebo-controlled, phase 3 trial. Lancet Gastroenterol Hepatol 2023; 8: 990–1004.

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STRUCTURED ABSTRACT

Question: Does weekly or every 2-week dosing dupilumab maintain its efficacy and safety for eosinophilic esophagitis (EoE) over 52 weeks in adolescents and adults?

Design: Phase 3, multicenter, double-blind, randomized, placebo-controlled trial of participants enrolled in 24-week Part B of LIBERTY EoE TREET study who continued to 28-week part C (part B–C) extended active treatment.

Setting: Sixty-five centers across 10 countries (Australia, Canada, Europe, and the US), including tertiary and private care clinics.

Patients: The study included 227 patients (median age: 24 years, range 12–65; 33% adolescents, 64% male; 91% White) with EoE confirmed by ≥15 eosinophils per

high-power field (eos/hpf) despite 8 weeks of high-dose proton-pump inhibitor (PPI) therapy and moderate dysphagia (Dysphagia Symptom Questionnaire [DSQ] score ≥ 10). Patients were excluded if severe adverse events occurred during initial treatment or if they could not continue treatment with study drug for alternate reasons.

Exposure: Weekly or biweekly subcutaneous dupilumab 300 mg vs placebo during Part B. Patients on placebo during Part B transitioned to active treatment during Part C, either weekly or biweekly. Those on active treatment during Part B, continued on the same regimen for additional 28 weeks.

Outcome: There were no primary efficacy end points for part B-C. Instead, Part B's co-primary, key secondary, and efficacy endpoints were assessed at week 52 as secondary endpoints for Part C, the extended active treatment period. The previous primary endpoints were: (a) histological Remission: proportion of patients achieving a peak eosinophil count of ≤ 6 eos/hpf at Week 52; (b) symptom Improvement: absolute change from baseline in DSQ scores at Week 52. Previous secondary outcomes utilized here included**:** reduction in peak eosinophil counts to ≤ 1 eos/hpf and ≤ 15 eos/hpf. Change in Histology Scoring System, EREFS scores, health related quality of life (HRQol) measured by EoE Impact questionnaire (EoE-IQ), severity and frequency of symptoms measured by EoE symptom questionnaire (EoE-SQ), and EoE diagnostic panel (EDP) transcriptome signature from Part B baseline to week 52.

Data Analysis: Efficacy assessed via histological remission (≤ 6 eos/hpf), change in DSQ scores, and endoscopic and histological grading. Intention-to-treat analysis applied.

Funding: Sanofi and Regeneron Pharmaceuticals.

Results: Overall, 168 (74%) patients had previously used swallowed topical corticosteroids (tCs) for EoE and 112 (49%) patients had inadequate response, intolerance, or contraindication to tCs. Eighty (35%) had history of prior dilations. Those on weekly dupilumab with disease improvement after 24 weeks of treatment maintained or continued to improve with an additional 28 weeks of treatment with weekly dosing. All 65 (100%) patients on weekly dupilumab achieved peak ≤15 eos/hpf after 52 weeks of treatment. Weekly dupilumab significantly reduced dysphagia symptoms, with a mean DSQ score improvement of –30.3 points, and decreased peak eosinophil counts by over 95%. Biweekly dupilumab improved histological, endoscopic, and transcriptomic outcomes to a similar extent as weekly dupilumab did over a 52-week period, but was less effective in symptom relief. Overall safety was consistent with the known dupilumab safety profile. Dupilumab

was well-tolerated, with injection-site reactions being the most common adverse event with 14% in the weekly and 11% in the placebo/weekly group.

COMMENTARY

Why Is This Important?

EoE is a chronic, immune-mediated condition characterized by symptoms such as dysphagia, food impaction, and histological inflammation of the esophagus. Current treatment options, including proton pump inhibitors (PPIs), elimination diets, and topical corticosteroids, often fail to achieve sustained remission or are not well-tolerated. Dupilumab, a monoclonal antibody targeting IL-4 and IL-13 pathways, represents a promising option that directly addresses the underlying type 2 inflammation driving EoE.[1-3]

Despite dupilumab's approval based on short-term efficacy data from the first 2 phases of the LIBERTY EoE TREET study at 24 weeks compared to palcebo, the question regarding it's longer term efficacy and safety was unclear. Long-term management options for EoE have remained a significant unmet need in the field. This study bridges that gap by demonstrating that weekly 300 mg dupilumab is well tolerated and maintains its efficacy for up to 52 weeks, providing sustained histological, symptomatic, endoscopic, and molecular profile improvements that was achieved at 24 weeks with a favorable safety profile.

Key Study Findings

This study highlights the sustained efficacy of weekly dupilumab in managing EoE over 52 weeks. A significant proportion of patients (85%) receiving weekly dupilumab achieved histological remission (≤6 eos/hpf), compared to only 5% of placebo-treated patients at 24 weeks. Over 52 weeks, weekly dosing outperformed biweekly regimens, especially in symptom relief, emphasizing the importance of higher dosing frequency for optimal outcomes.

Improvements were also evident in symptoms, with a mean reduction of –30.3 points in the DSQ scores in the weekly dupilumab group, reflecting meaningful relief from swallowing difficulties. These benefits extended across endoscopic and molecular parameters, with significant reductions in eosinophil counts and improvements in EREFS. The safety profile was favorable, with injection-site reactions being the most common adverse event and no new safety concerns emerging over the 52-week treatment period. These findings position weekly dupilumab as a highly effective and well-tolerated long-term treatment for EoE.

Caution

The study population was predominantly White (91%), limiting the generalizability of findings to more diverse racial and ethnic groups. Additionally, the trial was conducted primarily in tertiary care settings, where patients may present with more severe disease and have greater access to specialized care than those in community settings. Furthermore, the safety data were reassuring, but the study was limited to 52 weeks.

My Practice

Dupilumab has become a cornerstone in my approach to managing EoE, especially in patients who fail standard treatments like PPIs, dietary treatment, and topical corticosteroids. For patients with moderate to severe disease—defined by persistent dysphagia, significant histological activity, or severe fibrostenotic disease characterized by recurrent food impactions and/or need for frequent dilation therapy—I would recommend weekly dupilumab based on this study's findings. The histological and symptomatic improvements achieved with weekly dosing in this study support this regimen. For patients who demonstrate partial response after 24 weeks, I emphasize the potential for continued improvement over time, as seen in the extended 52-week data.

However, for patients with less severe disease, I may consider biweekly dosing, as it still provides substantial benefits, albeit to a lesser degree. When initiating dupilumab, I counsel patients on expected outcomes, highlighting its ability to reduce inflammation, improve swallowing function, and potentially eliminate the need for frequent endoscopies. I also discuss the most common side effect, injection-site reactions, and reassure patients about the therapy's overall safety profile over 52-weeks. Ultimately, with the complexity of managing chronic therapies for a lifelong disease, individualized decision-making should be emphasized when considering dupilumab for EoE.

For Future Research

Future studies should focus on addressing several key gaps to optimize the use of dupilumab in EoE. Research is needed to explore its cost-effectiveness in real-world settings. Additionally, trials that include more racially and ethnically diverse populations are essential to confirm the generalizability of these findings. Long-term safety and efficacy data beyond one year would provide crucial insights into its suitability as a chronic therapy. Studies that investigate biomarkers or clinical predictors of response could help identify which patients derive the most benefit, enabling more personalized treatment approaches. Finally, comparisons between dupilumab and other emerging therapies for EoE could further refine treatment algorithms, ensuring the best outcomes for patients.

Conflict of Interest

Dr Eluri has no reported conflicts of interest related to this summary.

REFERENCES

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