Dupilumab improves inflammation in eosinophilic gastritis, but what about symptoms?

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Eosinophilic gastritis (EoG) remains a challenging diagnosis, often leaving patients with debilitating gastrointestinal symptoms and no approved treatment options. The condition, characterised by an infiltration of eosinophils into the stomach lining, is increasingly understood to be driven by type 2 inflammation. This mechanistic insight has spurred interest in targeted therapies.

A recent phase 2 trial, DEGAS, published in Lancet Gastroenterol Hepatol, investigated dupilumab, a monoclonal antibody that blocks IL-4 and IL-13, as a potential therapeutic agent for EoG. The drug has already demonstrated efficacy in other type 2 inflammatory diseases, including eosinophilic oesophagitis (EoE), raising expectations for its role in gastric inflammation.1

KEY TAKEAWAYS

- The Pivot: Dupilumab significantly reduced gastric eosinophil counts in patients with eosinophilic gastritis, marking the first targeted therapy to show this effect.
- The Data: 80% of dupilumab-treated patients achieved histological remission (peak eosinophil count <15 eos/hpf) compared to 20% on placebo (P=.001).
- The Action: Clinicians should consider dupilumab as a potential therapy for eosinophilic gastritis, particularly for its impact on histological inflammation, while awaiting further data on symptomatic improvement.

Eosinophilic gastritis is a chronic, immune-mediated inflammatory disorder of the stomach, defined by an abnormal accumulation of eosinophils within the gastric mucosa. Patients typically present with a range of non-specific gastrointestinal symptoms, including abdominal pain, nausea, vomiting, early satiety, and weight loss. The absence of approved treatments means management often relies on dietary restrictions, corticosteroids, or proton pump inhibitors, none of which offer a consistently effective or long-term solution. The underlying pathology involves a dysregulated type 2 immune response, with interleukin-4 (IL-4) and interleukin-13 (IL-13) identified as key cytokines driving eosinophil recruitment and activation.1,2

Dupilumab, a fully human monoclonal antibody, targets the alpha subunit of the IL-4 receptor, thereby inhibiting signalling from both IL-4 and IL-13. This dual blockade disrupts the central pathways of type 2 inflammation. Given its established efficacy in other eosinophil-driven conditions like EoE, atopic dermatitis, and asthma, investigators hypothesised that dupilumab could offer a targeted approach for EoG. The DEGAS trial aimed to assess this hypothesis, focusing on both histological and symptomatic endpoints.1,2

Designing the DEGAS trial

The DEGAS trial was a double-blind, placebo-controlled, phase 2, multicentre, randomised controlled trial. It enrolled 120 adults and adolescents (aged 12 years and older) with a confirmed diagnosis of eosinophilic gastritis. To qualify for inclusion, patients needed to have a peak gastric eosinophil count of at least 30 eosinophils per high-power field (eos/hpf) in at least five hpf, along with active gastrointestinal symptoms. Patients were randomised 1:1 to receive either dupilumab 300 mg subcutaneously every two weeks or placebo for 24 weeks. The primary endpoint was histological remission, defined as a peak gastric eosinophil count of less than 15 eos/hpf, combined with a 30% or greater reduction in the total symptom score from baseline.1

The trial design incorporated a comprehensive assessment of both objective and subjective measures. Endoscopic biopsies were taken at baseline and week 24 to quantify eosinophil counts, providing a direct measure of gastric inflammation. Symptom severity was tracked using a patient-reported outcome (PRO) instrument, specifically the Eosinophilic Gastritis Symptom Score (EGSS), which captured the frequency and severity of common EoG symptoms. This dual primary endpoint aimed to ensure that any observed histological improvement translated into meaningful clinical benefit for patients. Secondary endpoints included changes in individual symptom scores, endoscopic appearance, and safety profiles.1

The histological impact

Dupilumab demonstrated a clear and statistically significant effect on gastric eosinophil counts. At week 24, 80% of patients in the dupilumab group achieved histological remission (peak eosinophil count <15 eos/hpf), compared to only 20% in the placebo group (P=.001). This represents a substantial reduction in the inflammatory burden within the stomach lining. The mean reduction in peak eosinophil count from baseline was 92% in the dupilumab arm, versus 25% in the placebo arm. These numbers confirm that dupilumab effectively targets the underlying type 2 inflammatory process driving EoG.1

The histological response was consistent across various gastric regions, indicating a broad anti-inflammatory effect throughout the stomach. This is a critical finding, as eosinophil infiltration can be patchy, and a systemic reduction suggests a robust mechanism of action. The magnitude of the histological improvement mirrors what has been observed with dupilumab in eosinophilic oesophagitis, where similar reductions in tissue eosinophilia correlate with improved endoscopic appearance and reduced disease activity.1,2

But, the picture was less clear when it came to symptoms. While dupilumab significantly reduced gastric eosinophil counts, the combined primary endpoint, which required both histological remission and a 30% reduction in total symptom score, was met by 35% of dupilumab-treated patients compared to 15% of those on placebo (P=.02). This difference, while statistically significant, was driven primarily by the histological component. The symptomatic improvement, while present, was not as pronounced or as consistently achieved as the histological remission. This suggests a potential disconnect between the objective reduction in inflammation and the subjective experience of symptoms, a phenomenon not uncommon in chronic gastrointestinal conditions.1

Symptomatic relief and safety profile

Looking at symptomatic endpoints individually, dupilumab did show some benefit. The mean change from baseline in the EGSS total symptom score was -4.2 in the dupilumab group versus -2.1 in the placebo group (P=.04). This indicates

a modest but statistically significant improvement in overall symptom burden. Specific symptoms, such as abdominal pain and nausea, also showed trends towards improvement with dupilumab, though these were not always individually statistically significant. The variability in symptomatic response highlights the complex nature of EoG symptoms, which can be influenced by factors beyond eosinophil counts, including visceral hypersensitivity or concurrent functional gastrointestinal disorders.1

The safety profile of dupilumab in EoG was consistent with its known profile in other indications. The most common adverse events reported in the dupilumab group were injection site reactions (15% vs 5% with placebo), headache (10% vs 8%), and nasopharyngitis (8% vs 7%). No new safety signals emerged from this trial. Serious adverse events were infrequent and balanced between the two groups (3% in dupilumab vs 4% in placebo), with none considered related to the study drug. This reassuring safety profile is important for a chronic condition requiring long-term treatment.1

A systematic review and meta-analysis of monoclonal antibodies for eosinophilic oesophagitis and gastritis, published in the J Clin Gastroenterol, further supports the safety and efficacy trends observed with dupilumab. The review, which included data from multiple trials across both EoE and EoG, consistently highlighted the favourable safety profile of anti-IL-4/IL-13 agents. It also underscored the challenge of achieving complete symptomatic resolution, even when histological remission is robust. This reinforces the need for a careful interpretation of clinical trial endpoints in these complex conditions.2

Where it falls short

The DEGAS trial, while providing compelling evidence for dupilumab's histological efficacy in EoG, does have limitations. The phase 2 nature of the study means it was not powered to detect subtle differences in symptomatic improvement or rare adverse events. The relatively small sample size (N=120) also limits the generalisability of the findings to broader patient populations, particularly those with varying disease severities or comorbidities. A longer follow-up period would also be beneficial to assess the durability of both histological and symptomatic responses, as well as the potential for disease recurrence after treatment cessation.1

The disconnect between histological and symptomatic improvement remains a key area for further investigation. While a 30% reduction in symptom score was chosen as a clinically meaningful threshold, it is possible that different symptom assessment tools or a longer duration of treatment might yield more pronounced symptomatic benefits. The trial also did not explore the impact of dupilumab on quality of life, an important patient-centred outcome in chronic diseases. Future studies should incorporate more granular symptom assessment and quality of life measures to fully capture the patient experience. For clinicians managing these complex cases, having a comprehensive reference like the Oxford Handbook of Gastroenterology & Hepatology can be invaluable for navigating diagnostic and therapeutic challenges.1

The trial also did not specifically evaluate dupilumab in patients with concomitant eosinophilic oesophagitis or other type 2 inflammatory conditions. Many patients with EoG also have EoE, and understanding the combined impact of dupilumab in this multi-organ context would be clinically relevant. The current data focuses solely on gastric inflammation, leaving questions about its broader utility in patients with pan-eosinophilic gastrointestinal disease. The lack of a clear biomarker that correlates perfectly with symptomatic response also complicates treatment decisions and patient counselling.1

Still, the DEGAS trial represents a significant step forward. It provides the first robust evidence for a targeted biological therapy in eosinophilic gastritis, demonstrating a profound impact on the underlying inflammatory pathology. The

challenge now lies in translating this histological success into consistent and meaningful symptomatic relief for all patients, and in understanding which patient subgroups are most likely to benefit from this treatment. Future phase 3 trials will need to address these complexities, potentially refining patient selection criteria and exploring optimal dosing strategies.1

CLINICAL IMPLICATIONS

Dupilumab's ability to profoundly reduce gastric eosinophil counts in EoG is a welcome development for a condition with no approved treatments. This histological normalisation, seen in 80% of patients, directly addresses the core pathology. It offers a tangible, objective measure of treatment success that has been elusive with current off-label therapies.

But, the symptomatic response, while statistically significant, was less dramatic. A 35% response rate on the combined endpoint, driven largely by histology, means many patients may still experience bothersome symptoms despite clear anti-inflammatory effects. This disconnect underscores the complexity of patient-reported outcomes in chronic GI conditions and highlights the need for clinicians to manage patient expectations carefully.

The safety profile is reassuringly consistent with dupilumab's established record across other type 2 inflammatory diseases. This familiarity will ease adoption for specialists already prescribing the drug for conditions like EoE or atopic dermatitis. But, the cost implications of a long-term biologic for a chronic condition like EoG will undoubtedly be a significant consideration for healthcare systems and formulary committees.

This trial sets the stage for larger phase 3 studies, which must now focus on refining symptomatic endpoints and identifying predictors of robust clinical response. Until then, dupilumab offers a powerful tool for tackling the inflammation of EoG, even if the path to complete symptomatic relief remains somewhat less clear.

REFERENCES

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