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Summary

Eosinophilic GI disorders: Pathophysiology and beyond – are drugs for eosinophilia enough?

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This presentation reviewed the pathophysiology of eosinophilic GI disorders and demonstrated that therapies targeting eosinophil depletion (anti-IL-5 agents, Siglec-8) achieve near-complete tissue eosinophil elimination but fail to improve symptoms or endoscopy, indicating eosinophils are not the primary disease driver.

KEY POINTS

- Eosinophilic GI disorders share a type 2 inflammatory pathway involving alarmins (TSLP, IL-33), Th2 cytokines (IL-4, IL-13, IL-5), and JAK-STAT signaling, with transcriptomic studies revealing complex roles for eosinophils and mast cells beyond simple degranulation.
- The speaker reported that Mepolizumab and Benralizumab achieved pronounced eosinophil depletion (up to 90% of patients near-complete) but did not reduce symptoms above placebo, and eosinophilic esophagitis persisted in the complete absence of eosinophils.
- Siglec-8 antibody reduced tissue eosinophils to fewer than 6 per high-power field in over 90% of patients at high dose but showed no symptom benefit over placebo.
- Mast cell depletion and anti-IgE therapy similarly failed to improve symptoms or endoscopy despite target engagement, suggesting classical atopic effector cells are not therapeutic targets.
- The speaker stated that Dupilumab (anti-IL-4 receptor) and TSLP receptor blockade are effective EOE treatments, and recommended targeting upstream mechanisms such as alarmins and epithelial barrier dysfunction rather than eosinophils alone.
- Eosinophilic colitis has minimal transcriptomic overlap with upper GI eosinophilic disorders and lacks the strong type 2 immune signature, though preliminary data in four patients suggested Dupilumab may improve symptoms and histology.

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