High Discovery Rate of Eosinophilic Gastritis and/or Duodenitis Among Patients with Chronic Functional Gastrointestinal Symptoms

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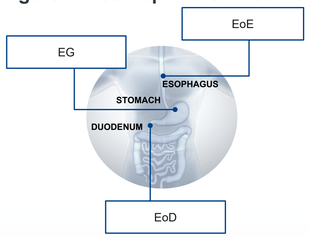
BACKGROUND

- Pathologic accumulation and over-activation of eosinophils and mast cells are implicated in chronic inflammatory diseases of the gastrointestinal (GI) tract, including eosinophilic esophagitis (EoE), gastritis (EG), duodenitis (EoD), and colitis—collectively termed eosinophilic gastrointestinal diseases (EGIDs)[1,2]
- Patients with EGIDs have decreased quality of life due to chronic and often debilitating symptoms such as dysphagia, abdominal pain, bloating, nausea, early satiety, vomiting, and diarrhea

Figure 1. Eosinophilic GI Disorders



EG, EoD, EoE

Eosinophil Infiltration of the Stomach, Duodenum, or Esophagus

- Eosinophils and mast cells cause GI symptoms, including abdominal pain, nausea, early satiety, loss of appetite, bloating, abdominal cramping, vomiting, diarrhea, and dysphagia
- There are no FDA-approved treatments for EG, EoD, or EoE
- These disorders are currently treated with restrictive diets and/or steroids

- EG and/or EoD are thought to affect 45,000–50,000 persons in the US; this could be an underestimate. There is evidence that these diseases are as common as inflammatory bowel diseases[3,4]
- EG and/or EoD have been described as rare conditions found in individuals with atopy and increased peripheral eosinophils and/or total IgE. However, this conclusion was based on retrospective studies that included patients already diagnosed with EG and/or EoD
- Current treatment options, such as diet restriction and corticosteroids, have limited efficacy and/or are inappropriate for chronic use
- New therapies are needed

Figure 2. High Rate of Detection of New Cases of EG and/or EoD in the ENIGMA Study Indicates Underdiagnosis of These Diseases[5]

51 patients without history of EG and/or EoD entered ENIGMA screening

↓

51% (26/51) met symptom criteria for endoscopy and biopsy

↓

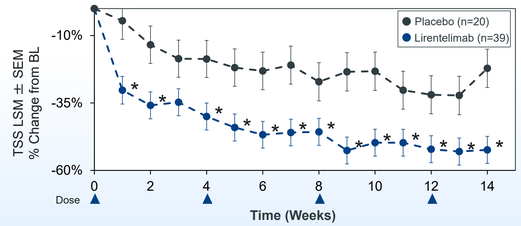
58% (15/26) EG and/or EoD[a]

- 29% (15/51) received a new diagnosis of EG and/or EoD
- Most patients without an established diagnosis of EG and/or EoD came from general GI practices
- These patients had a history of chronic nonspecific functional GI symptoms or diagnoses

a Patients who met symptom criteria and ≥30 eosinophils per high-power field (eos/hpf) in 5 gastric hpfs and/or ≥30 eos/hpf in 3 duodenal hpfs

- Lirentelimab is a humanized monoclonal antibody against Siglec-8, demonstrated histologic and symptom improvement in a Phase 2 randomized, placebo-controlled study in EG and/or EoD (ENIGMA)[5]
- A recent analysis of the ENIGMA screening data revealed that multiple biopsies are required to optimize diagnostic yield due to the patchiness of gastroduodenal eosinophils[6]
- We conducted a prospective study to evaluate the prevalence of EG and/or EoD among patients with moderate–severe chronic unexplained GI symptoms and clinical features, to inform diagnostic protocols

Figure 3. Lirentelimab Significantly Reduced Patient Symptoms in the ENIGMA Study[5]



* p <0.05

METHODS

- We performed a prospective, multi-center study to assess the prevalence of EG and/or EoD in patients with chronic moderate–severe GI symptoms (≥6-month history of GI symptoms without an identified cause and no response to pharmacologic or dietary interventions), or patients with previous diagnoses of irritable bowel syndrome and/or functional dyspepsia

EG/EoD GI Symptom Questionnaire©

- Developed in accordance with FDA guidance on development of patient-reported outcome measurements
- Captures patients' daily GI symptoms
- Measures each of the following symptoms on a scale of 0-10:
  - Abdominal pain
  - Vomiting
  - Loss of appetite
  - Bloating
  - Nausea
  - Early satiety
  - Abdominal cramping
  - Diarrhea
- Patients had daily scores of ≥3 (range 0–10) for any individual symptom and Total Symptom Scores (TSS) ≥10
- Controls had an average daily score ≤1 for all symptoms and no daily score ≥3, on any day, for any symptom

- Patients who reported active moderate–severe symptoms per the EG/EoD Questionnaire© qualified for systematic biopsy collection
- Biopsy samples were collected during esophagogastroduodenoscopy (EGD)
  - Minimum of 12 gastric and duodenum biopsies (4 gastric antrum, 4 gastric corpus, and 4 duodenum plus additional biopsies from areas of interest)
  - Up to 4 esophageal biopsies (2 distal and 2 mid/proximal) from patients with histories of EoE, esophageal abnormalities during EGD, or for other reasons
- Primary endpoints were the proportion of patients who underwent biopsy and met the histologic criteria for EG and/or EoD (≥30 eos/hpf in 5 gastric or 3 duodenal hpfs)
- We performed a study of healthy volunteers (controls) for comparison

RESULTS

Figure 4. High Prevalence of EG and/or EoD in Patients with Chronic GI Symptoms

Entered Screening n=556

73% Met Symptom Criteria and Biopsied n=405

45% Met Histologic Criteria for EG and/or EoD[a] n=181

EG w/o EoD n=16 (9%)	EG+EoD n=43 (24%)	EoD w/o EG n=122 (67%)
n=0/7 With EoE[b]	n=3/20 (15%) With EoE	n=9/51 (18%) With EoE

33% (181/556) of patients with chronic functional GI symptoms and 45% (181/405) of patients with moderate–severe symptoms who underwent biopsy met histologic criteria for EG and/or EoD

a Patients who met symptom criteria and ≥30 eos/hpf in 5 gastric hpfs and/or ≥30 eos/hpf in 3 duodenal hpfs
b 12 of 78 (15%) patients with esophageal biopsies met histologic criteria for EoE (≥15 eos in 1 hpf) and EG and/or EoD

Table 1. Features of Patients with EG and/or EoD and Controls

Patient Characteristics		Met Histologic[a] Criteria for EG and/or EoD n=181	Controls n=33
Mean age, years (range)		45 (19–78)	34 (18–51)
Female sex, %		73%	39%
White, %		85%	100%
Weight, median, kg		83	80
Blood eosinophils	Cells/μL, median (IQR)	170 (100–250)	70 (50–150)
	Blood eos ≥250 cells/μL, %	27%	9%
	Blood eos ≥500 cells/μL, %	4%	0
	Blood eos ≥1500 cells/μL, %	0	0
Immunoglobin E	kU/L, median (IQR)	34 (14–103)	18 (9–60)
	IgE ≥ 70 kU/L, %	36%	21%
TSS [0-80], mean ±SD		31.3±11.2	0.1±0.2
History of	GI symptoms[b], mean years	11	-
	GERD, IBS, FD, and/or EoE, %	93%	0
	GERD, %	65%	0
	IBS, %	55%	0
	FD, %	15%	0
	EoE, %	2%	0
	Atopy[c], %	48%	15%

a Patients who met symptom criteria and ≥30 eos/hpf in 5 gastric hpfs and/or ≥30 eos/hpf in 3 duodenal hpfs
b Diagnoses of other functional GI disorders, such as chronic abdominal pain or functional diarrhea
c Asthma, allergic rhinitis, atopic dermatitis and/or food allergy
GERD, gastroesophageal reflux disease; IBS, irritable bowel syndrome; FD, functional dyspepsia; IQR, interquartile range; NA, not applicable

Figure 5. Symptoms in Patients With EG, EoD, and EG+EoD

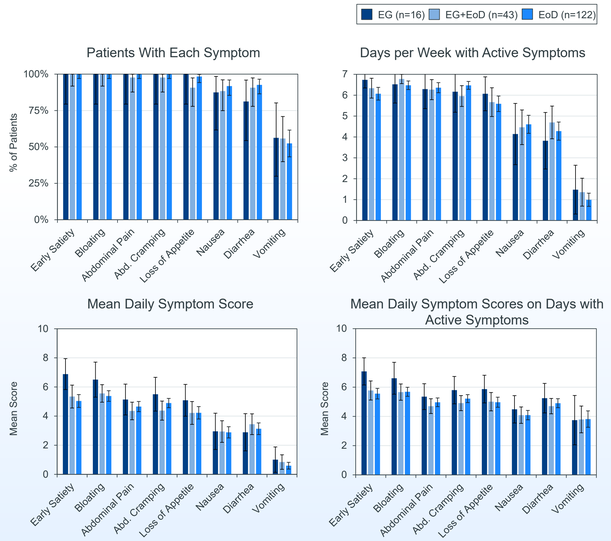
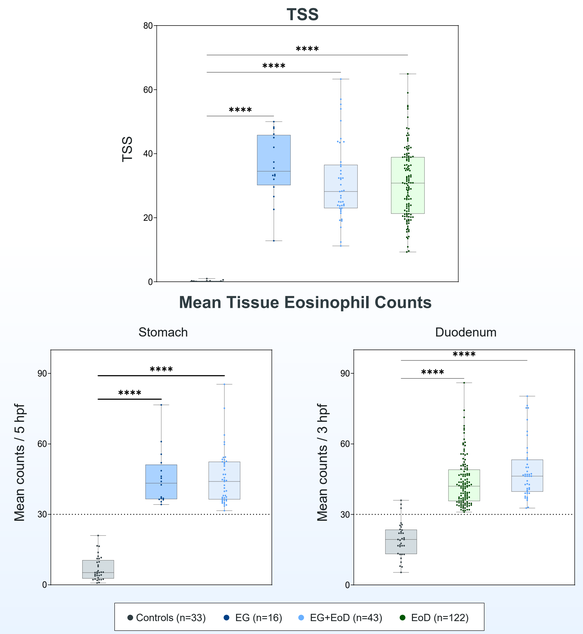


Figure 6. TSS & Mean Eosinophil Counts in Patients vs Controls



45% (181/405) of patients and 6% (2/33) of controls[a] met histologic criteria for EG and/or EoD (odds ratio, 12.52; 95% CI, 3.0–53.0; *P*<0.001)

a Patients and controls used the same patient-reported-outcome questionnaire and underwent identical biopsy protocols. Histologic evaluation for both groups were performed by the same central pathologists

* *P*<0.05; ** *P*<0.01; *** *P*<0.0001; **** *P*<0.0001

CONCLUSIONS/DISCUSSION

- Systematic endoscopy and biopsy of patients with moderate–severe GI symptoms found that 45% met histologic criteria EG and/or EoD
- Symptom burden, as measured by intensity and frequency, was similar among patients with EG, EoD, and EG and EoD
- Patients with EG, EoD, or EG and EoD had significantly higher symptom scores and gastric and duodenal eosinophil counts than controls.
- Patients with chronic moderate–severe GI symptoms should undergo EGD with collection of gastric and duodenal biopsies and counting of eosinophils to identify those with EG and/or EoD.
- Proper diagnosis of EG and/or EoD can lead to effective treatments, including targeted therapies

Reference: (1) Caldwell JM, et al. J Allergy Clin Immunol. 2014.; (2) Youngblood BA, et al. Gastroenterology. 2019.; (3) Jensen ET, et al. J Pediatr Gastroenterol Nutr. 2016.; (4) Licari AL, et al. JACI. 2020.; (5) Dellon ES, et al. NEJM. 2020.; (6) Dellon ES, et al. CGH. 2021.

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