Eosinophilic Gastritis and Eosinophilic Duodenitis Exhibit a Similar Clinical Presentation, Underscoring the Need for Collection of Multiple Biopsies From Both the Stomach and Duodenum to Evaluate for Tissue Eosinophilia

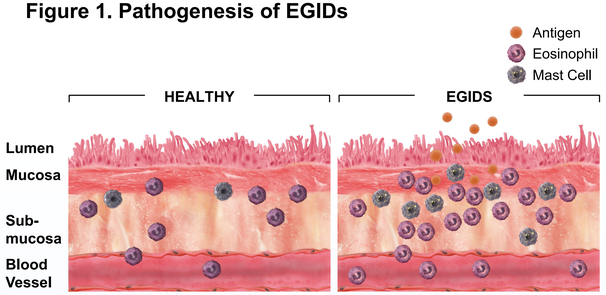
Nirmala Gonsalves MD[1], Mirna Chehade MD MPH[2], Marc E. Rothenberg, MD PhD[3], Ikuo Hirano MD[1], Kathryn A. Peterson MD[4], Gary W. Falk MD[5], Lauren T. Gehman PhD[6], Alan T. Chang[6], Bhupinder Singh MD[6], Henrik S. Rasmussen MD PhD[6], Robert M. Genta MD[7], Evan S. Dellon MD MPH[8]

[1]Northwestern University Feinberg School of Medicine, Chicago, IL; [2]Icahn School of Medicine at Mount Sinai, New York, NY; [3]Division of Allergy and Immunology, Cincinnati Children's Hospital, University of Cincinnati College of Medicine, Cincinnati, OH; [4]University of Utah, Salt Lake City, UT; [5]University of Pennsylvania Perelman School of Medicine, [6]Allakos, Inc., Redwood City, CA; [7]Baylor College of Medicine, Houston, TX; [8]University of North Carolina, Chapel Hill, NC

BACKGROUND

- Pathologic accumulation and over-activation of eosinophils and mast cells are implicated in multiple chronic inflammatory diseases in 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 debilitating and often nonspecific symptoms such as dysphagia, abdominal pain, abdominal cramping, bloating, early satiety, loss of appetite, nausea, vomiting, & diarrhea

Figure 1. Pathogenesis of EGIDs



- ENIGMA was a randomized controlled trial conducted in adult EG/EoD patients and it established the therapeutic potential of lirentelimab, a monoclonal Siglec-8 antibody that depletes eosinophils and inhibits mast cell activity[3]
- Patients enrolled in the ENIGMA phase 2 study were first screened for moderate-to-severe GI symptoms; if symptom criteria were met, the patient underwent upper endoscopy (EGD) with biopsy and histopathologic evaluation to confirm EG/EoD diagnosis (≥30 eosinophils per hpf in ≥5 hpfs in the gastric biopsies and/or in ≥3 hpfs in duodenal biopsies)
- Results from the ENIGMA study revealed that 45% of patients screened had no prior history of EG/EoD diagnosis and 29% of whom were found to have EG and/or EoD
- The high discovery rate of de novo EG/EoD coupled with studies reporting underdiagnosis of EG/EoD prompted further evaluation of screening data to examine symptom presentation of patients with confirmed EG/EoD
- Utilizing screening data from this prospective, multicenter, phase 2, randomized controlled trial, our primary aim was to better understand symptom presentation of EG/EoD patients and identify characteristics that can increase clinical suspicion of EG/EoD

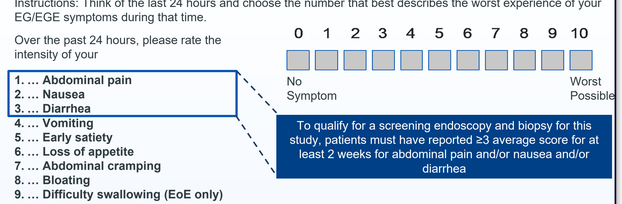
OBJECTIVE

- To characterize the symptoms and clinical presentation of subjects with EG and/or EoD (EG/EoD) using screening data from a randomized controlled trial of lirentelimab (AK002)

METHODS

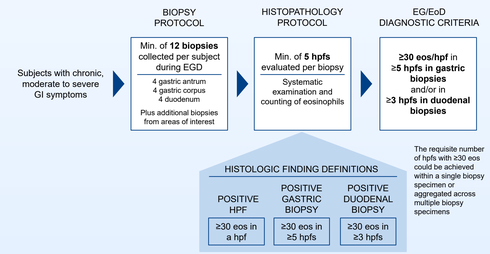
- Symptoms were assessed by an electronic patient-reported outcome (PRO) questionnaire developed to meet FDA Guidance and completed by patients on a daily basis
- The questionnaire assessed the daily severity of 8 GI symptoms: abdominal pain, nausea, vomiting, early satiety, loss of appetite, abdominal cramping, bloating, and diarrhea. Individual symptom scores ranged from 0 to 10 (0=no symptom, 10=worst possible), with a maximum daily Total Symptom Score (TSS) of 80 (higher score=greater severity)
- Moderate-to-severe GI symptoms was defined as an average daily individual symptom score of ≥3 (scale 0–10) over 7 days for at least 1 of 3 predefined symptoms (abdominal pain, diarrhea and/or nausea) for ≥2 of 4 weeks

Figure 2. Daily Symptom Questionnaire



- Histologic thresholds for diagnosis were ≥30 eos per high-powered field (hpf) in ≥5 hpfs for EG and ≥3 hpfs for EoD

Figure 3. Biopsy and Histopathology Protocol and EG/EoD Diagnostic Criteria



RESULTS

Figure 3. EG/EoD Diagnosis Rate

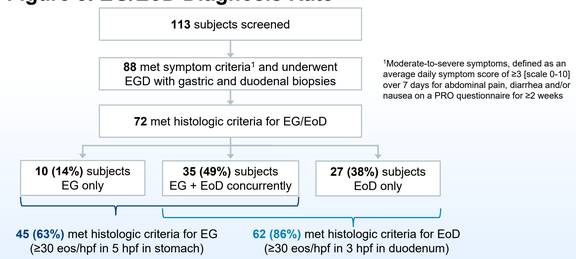


Table 1. Demographics and Characteristics

Patient Characteristics	Met EG/EoD Criteria N=72	Prior History of EG/EoD N=57	No Prior History N=15
Mean age, years (range)	42 (18-74)	40 (18-68)	48 (20-74)
Female sex, n (%)	43 (60%)	33 (58%)	10 (67%)
White, n (%)	66 (92%)	52 (91%)	14 (93%)
Weight, mean (range), kg	82 (47-171)	81 (47-171)	88 (59-136)
Total Symptom Score at baseline, mean ±SD	31 ±14	31 ±14	32 ±13
Atopy[a]	48 (67%)	37 (65%)	11 (73%)
Prior history, n (%)			
Eosinophilic gastritis and/or duodenitis (EG/EoD)	57 (79%)	57 (100%)	0 (0%)
Functional gastrointestinal disorder[b]	24 (33%)	17 (30%)	7 (47%)
GERD, acid reflux, or heartburn	24 (33%)	16 (28%)	8 (53%)
Peptic ulcer	9 (13%)	8 (14%)	1 (7%)
Chronic gastritis/duodenitis	4 (6%)	0 (0%)	4 (27%)
Physician-guided treatment, n (%)			
Proton pump inhibitor	35 (49%)	26 (46%)	9 (60%)
Diet modification	11 (15%)	9 (16%)	2 (13%)
Low-dose systemic corticosteroid[c]	7 (10%)	7 (12%)	0 (0%)
Topical steroid (budesonide) capsule	7 (10%)	7 (12%)	0 (0%)

[a] History of asthma, allergic rhinitis, atopic dermatitis, and/or food allergy
[b] Irritable bowel syndrome, functional abdominal pain, functional diarrhea, or functional constipation
[c] Prednisone ≤10mg daily or equivalent as a pre-existing regimen and taken throughout the study

Table 2. Symptom Presentation of All Subjects with Confirmed EG/EoD

Percent of Patients with Symptoms	EG/EoD (N=71)
Early Satiety	100%
Abdominal Pain	99%
Abdominal Cramping	99%
Bloating	97%
Loss of Appetite	97%
Nausea	94%
Diarrhea	89%
Vomiting	59%

Figure 4. Symptom Presentation of Subjects by EG and/or EoD Diagnosis

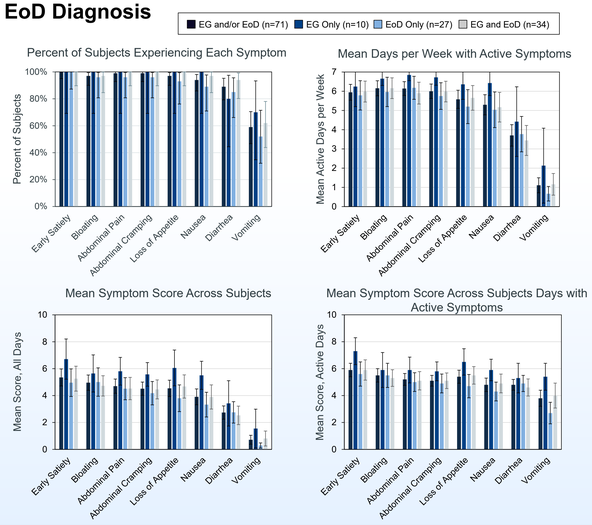


Figure 5. Symptom Presentation of Subjects by Prior Diagnosis of EG/EoD

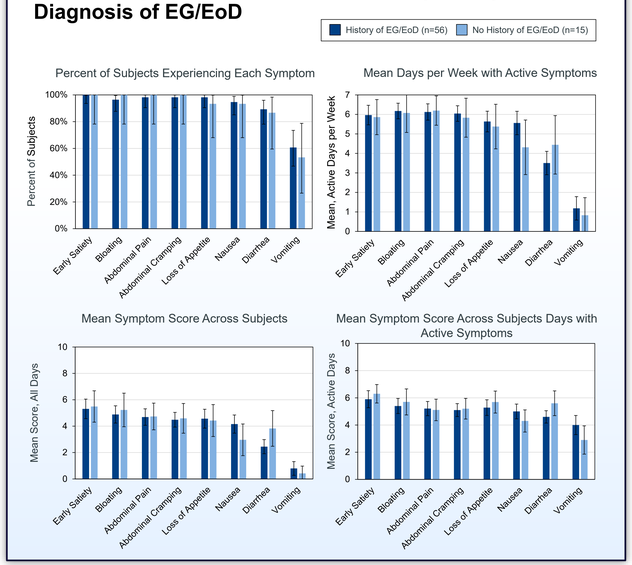
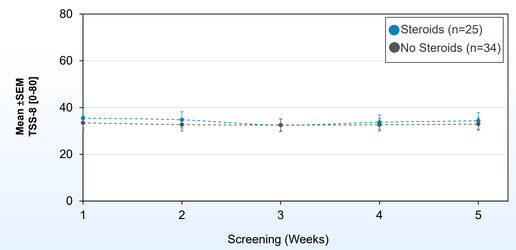


Figure 6. Total Symptom Score by Steroid Use



CONCLUSIONS/DISCUSSION

- This study is the first to prospectively evaluate the symptoms of EG/EoD subjects using data collected daily and with severity scoring using a validated PRO instrument
- Most subjects experienced a constellation of GI symptoms at moderate-to-severe intensity on most days
- Symptom presentation was clinically indistinguishable between subjects with only EG, only EoD, and concomitant EG+EoD, which shows that clinical presentation is the same regardless of the location of eosinophilia in the stomach, duodenum or both - underscoring the need to biopsy both organs
- These data demonstrate that patients with EG/EoD suffer from chronic symptoms despite treatment and that novel targeted therapies are needed

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Reference: (1) Caldwell JM, et al. J Allergy Clin Immunol. 2014.; (2) Youngblood BA, et al. Gastroenterology. 2019.; (3) Dellon ES, et al. NEJM. 2020.