Optimization of Eosinophilic Gastritis/Duodenitis Detection Requires Evaluation of Multiple High-Powered Fields in Each of 8 Gastric and 4 Duodenal Biopsies: Analysis from a Randomized Trial

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BACKGROUND

- Pathologic accumulation and over-activation of eosinophils and mast cells are implicated in chronic inflammatory diseases in the gastrointestinal (GI) tract, including eosinophilic esophagitis (EoE), gastritis (EG), duodenitis (EoD), and collaterally termed eosinophilic gastrointestinal diseases (EGIDs).
- Patients with EGIDs have decreased quality of life due to chronic debilitation and often non-specific symptoms such as dysphagia, abdominal pain, abdominal cramping, bloating, early satiety, loss of appetite, nausea, vomiting, and diarrhea

METHODS

ENIGMA was a randomized, controlled, phase 2 trial of adult patients with EG and/or EoD that established the therapeutic potential of interleukin-5 (IL-5) monoclonal antibody against siglec-8 that depletes eosinophils and inhibits mast cell activity.
- Patients enrolled in the ENIGMA study were first screened for moderate-severe GI symptoms.
- Patients who met the symptom criteria underwent esophagogastroduodenoscopy (EGD) with biopsy and histopathologic evaluation to confirm diagnoses of EG and/or EoD (≥30 eosinophils per hpf in ≥35 hpfs in gastric biopsies and/or in ≥35 hpfs in duodenal biopsies).
- Among patients enrolled in the ENIGMA study, 45% had no previous diagnoses of EG and/or EoD, 29% of these patients were found to have EG and/or EoD in the study.

Figure 1. Pathogenesis of EGIDs

Lumen

Healthy

SUBMUCOSA

Mucosa

Vessel

EGDS

Antigen

Eosinophil

Mast Cell

Figure 2. De Novo EG and/or EoD Diagnosis in ENIGMA

This high discovery rate of EG and/or EoD, along with other studies reporting underdiagnosis of EG and/or EoD, prompted further evaluation of the screening protocol.

- Using screening data from this prospective, multicenter, phase 2, randomized controlled trial, we assessed rates of diagnosis and defined the number of biopsies required to optimize detection of EG and/or EoD

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

Biopsy Protocol

GASTRIC PROTOCOL

1. Biopsies taken in an organized and systematic manner (from the proximal greater curvature to the distal greater curvature).

Stomach

Duodenum

• ENIGMA was a randomized, controlled, phase 2 trial of adult patients with EG and/or EoD that established the therapeutic potential of interleukin-5 (IL-5) monoclonal antibody against siglec-8 that depletes eosinophils and inhibits mast cell activity.

RESULTS

The high detection rate in previously undiagnosed patients and pathiness of gastric and duodenal eosinophilia suggest that a biopsy protocol of a minimum of 8 gastric and 4 duodenal biopsies and quantification of tissue eosinophils will increase EG and/or EoD diagnostic yield.

- In contrast to previous reports, EoD was found as frequently as EG, and was also found in some subjects without concomitant eosinophilia of other regions of the GI tract

Figure 4. Histopathologic Evaluation Process

Histopathologic Evaluation Process: Steps for EG and/or EoD

- Patients with eosinophilic gastritis and/or duodenitis: Histopathology diagnosis of EG and/or EoD is made when ≥30 eos/hpf in ≥5 hpf in gastric mucosal specimens and/or ≥30 eos/hpf in ≥5 hpf in duodenal mucosal specimens.

- Eosinophilic gastritis and/or duodenitis: Histopathology diagnosis of EG and/or EoD is made when ≥30 eos/hpf in ≥5 hpf in gastric mucosal specimens and/or ≥30 eos/hpf in ≥5 hpf in duodenal mucosal specimens.

Figure 5. Ideal Biopsy Specimen

Gastric Antrum

Gastric Corpus

Duodenum

Ideal specimen: A biopsy oriented on edge that includes surface epithelium, mucosa, and muscularis mucosae of intestinal and duodenal tissue.

Figure 6. EG and/or EoD Diagnosis Rate in Patients

<table>
<thead>
<tr>
<th>Stomach</th>
<th>Duodenum</th>
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<td>EG only</td>
<td>EoD only</td>
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Table 1. Patient Demographics

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<th>Patient Characteristics</th>
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<tr>
<td>History of asthma, allergic rhinitis, atopic dermatitis, and/or food allergy</td>
<td>48 (67%)</td>
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<td>History of GERD, inflammatory bowel disease, celiac disease, autoimmune disorders, inflammatory bowel disease, or a history of eosinophilia of the GI tract</td>
<td>31 (44%)</td>
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<td>History of chronic gastritis/duodenitis</td>
<td>35 (51%)</td>
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Figure 7. Distribution of Patients With and Without a Prior Diagnosis of EG and/or EoD

- Due to the pathiness of gastric and duodenal eosinophilia, insufficient biopsy sampling in clinical practice might produce false-negative results and missed diagnoses.

Figure 8. Number of Biopsies Required for EG and/or EoD Diagnosis

- A minimum of 8 gastric and 4 duodenal biopsies are required.

CONCLUSIONS/DISCUSSION

- The high detection rate in previously undiagnosed patients and pathiness of gastric and duodenal eosinophilia suggest that a biopsy protocol of a minimum of 8 gastric and 4 duodenal biopsies and quantification of tissue eosinophils will increase EG and/or EoD diagnostic yield.

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