Mast Cells in Addition to Eosinophils Are Markedly Elevated in Patients with Eosinophilic Gastritis and/or Gastroenteritis

Evans S. Dellon¹, Kathryn A. Peterson², Robert M. Genta³, Joseph A. Murray¹, Nirmala Gonsalves⁵, Mirna Chehade⁶, Marc E. Rothenberg⁷, Paneez Khoury⁸, Adam C. Bledsoe⁹, Camilla Shaw⁹, Henrik S. Rasmussen⁹, Bhupinder Singh⁹, Alan T. Chang⁹, Bradford A. Youngblood⁹, Ikku Hirano⁶

¹University of North Carolina, Chapel Hill, NC; ²University of Utah, Salt Lake City, UT; ³Baylor College of Medicine, Houston, TX; ⁴Mayo Clinic Rochester, Rochester, MN; ⁵Northwestern University, Chicago, IL; ⁶Icahn School of Medicine at Mount Sinai, New York City, NY; ⁷Cincinnati Children’s Hospital Medical Center, Cincinnati, OH; ⁸NIH/NIAID, Bethesda, MD; ⁹Allakos, Inc., Redwood City, CA

**BACKGROUND**
- Pathologic accumulation and over-activation of eosinophils are implicated in multiple chronic inflammatory diseases in the GI tract including eosinophilic esophagitis (EoE), gastritis (EG), gastroenteritis (EGE), and colitis - collectively termed eosinophilic gastrointestinal disorders (EGIDs)
- Patients with EGIDs have decreased quality of life due to debilitating symptoms such as dysphagia, abdominal pain, nausea, vomiting, and diarrhea
- While the pathogenesis of EGIDs has historically been thought to be driven by eosinophils, mast cells have also been shown to be elevated in EoE.¹ ²
- The role of mast cells in other EGIDs, has yet to be established

**OBJECTIVE**
- To quantify the extent of eosinophil and mast cell infiltration in gastric and duodenal biopsies from symptomatic patients diagnosed with EG/EGE

**METHODS**

**Symptom PRO**
- Subjects with prior diagnosis or suspected EG/EGE entered screening
- Subjects with an average weekly score of ≥3 for abdominal pain, diarrhea and/or nausea for 2 weeks on a PRO questionnaire (Fig. 4), qualified for an upper endoscopy (EoE) with biopsy

**EGD with Biopsy**
- Multiple biopsies were taken from each symptomatic subject according to a standardized protocol: 10 gastroscopic biopsies; 4 esophageal biopsies (only if subject had a history of EoE or EoE features were observed during EGD)
- Single pathologist evaluated stained biopsy samples and counted eosinophils (Fig. 5)
- Entry criteria:
  - ≥30 eos/hpf in 5 hpfs (stomach) and/or ≥30 eos/hpf in 3 hpfs (duodenum)
  - ≥15 eos/hpf in 1 hpf
- No other known cause for GI symptoms or tissue eosinophilia

**Histologic Criteria**

**RESULTS**

**Table 1. Baseline Characteristics**

<table>
<thead>
<tr>
<th>Age, Median Years (Range)</th>
<th>Female, n (%)</th>
<th>Race - White, n (%)</th>
<th>History of Atopic/Alergic Disease, n (%)</th>
<th>Peripheral Blood Eos (cells/µL)</th>
<th>Mean (Std. Dev.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>28 (14 - 74)</td>
<td>7 (77%)</td>
<td>10 (100%)</td>
<td>10 (100%)</td>
<td>318 (292)</td>
<td>978 (680)</td>
</tr>
</tbody>
</table>

**Figure 6. Study Diagnostic Criteria**

**Figure 7. Distribution of Patients by Diagnosis**

**Figure 8. Eosinophils and Mast Cells Are Consistently Elevated in Gastric and Duodenal Biopsies**

**CONCLUSIONS/DISCUSSION**

- 65 patients with active EG, EoE, or EG+EoE were enrolled in this Phase 2 randomized controlled trial
- In addition to elevated tissue eosinophils, 64 of 65 (98%) EG/EoE patients also had elevated mast cell counts in gastric and/or duodenal tissue biopsies
- In patients with EoE, mast cells were also elevated in eosinophilic gastritis
- These data suggest the potential for a pathogenic role for both mast cells and eosinophils in EGIDs and that treatments for EGIDs may need to target both cell types for optimal effect