Primary Results of A Phase 1 Multicenter Open-Label Study of Antolimab, An Anti-Siglec-8 Antibody, for the Treatment of Patients With Chronic Gastrointestinal Symptoms and Elevated Gastric and/or Duodenal Mast Cells

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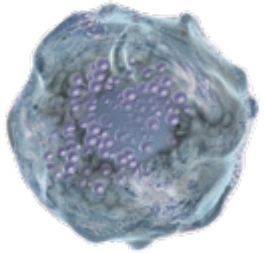
Disclosures

- Dr. Adam Bledsoe is an investigator in the ENIGMA study
- Antolimab (AK002) is an investigational drug candidate and is not FDA/EMA approved

Mast Cells and Eosinophils: Effector Cells Central to Initiating and Maintaining Inflammatory Responses

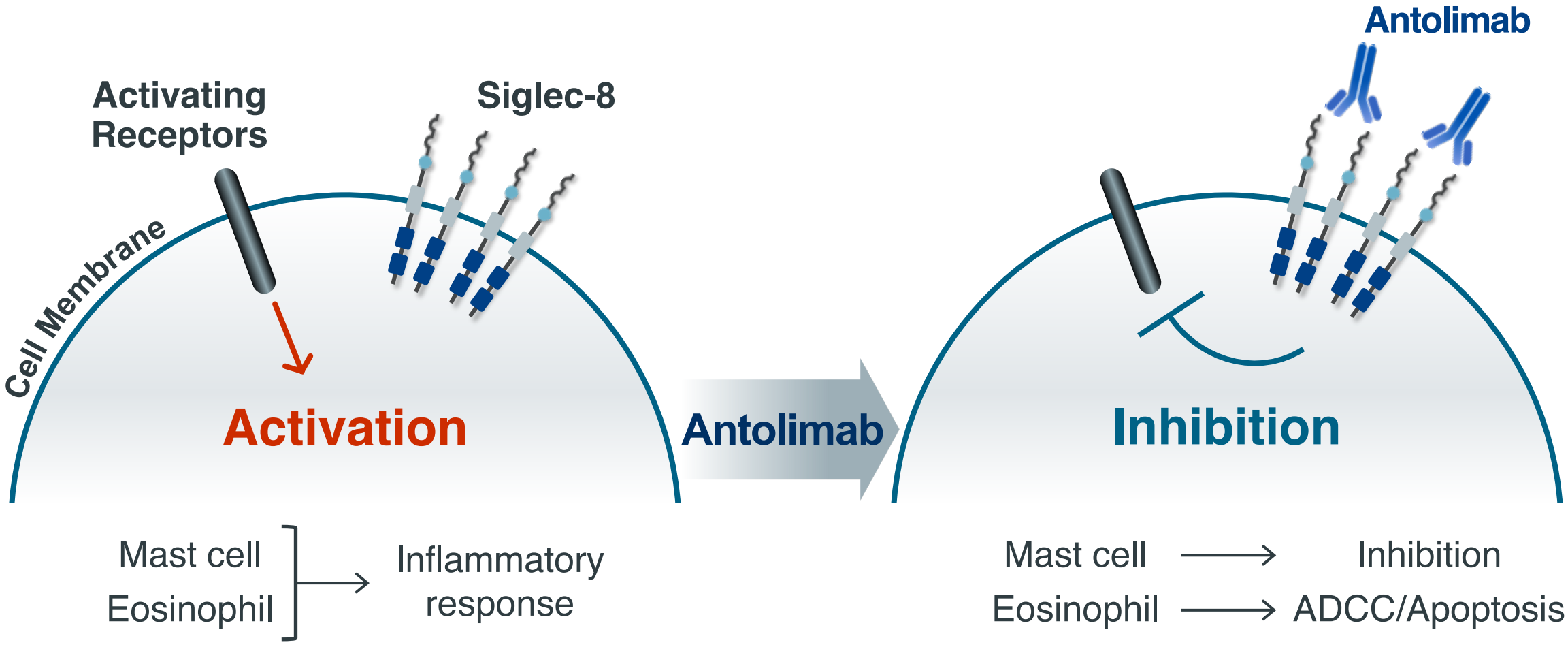


MAST CELLS

EOSINOPHILS

- Found at the Internal/External Interface of the Body
  - In particular, in tissues and surrounding blood vessels and peripheral nerves
- Produce a Broad Range of Inflammatory Mediators
  - Vasoactive amines, lipid mediators, proteases, cytokines and chemokines
- Participate in Acute and Chronic Inflammation
  - Including both innate and adaptive immune responses
- Key Drivers in Many Serious Diseases
  - Including gastrointestinal, ophthalmic, dermatologic, respiratory, and proliferative diseases

Antolimab (AK002) Targets Siglec-8 on Eosinophils and Mast Cells



ENIGMA Phase 2 Study in Eosinophilic Gastritis (EG) and/or Eosinophilic Duodenitis (EoD)

INCLUSION CRITERIA

- Patient-reported active moderate-to-severe symptoms per the **EG/EoD Questionnaire©**
  - Captures the symptoms of EG/EoD patients on a daily basis
  - Measures 8 symptoms each on a scale of 0-10; Total Symptom Score: (TSS) 80 points
    - Abdominal pain
    - Nausea
    - Vomiting
    - Early satiety
    - Loss of appetite
    - Abdominal cramping
    - Bloating
    - Diarrhea
  - Symptom criteria: weekly average ≥3 to 10 for abdominal pain, nausea, or diarrhea for at least 2 weeks
- Biopsy-confirmed EG and/or EoD
  - **EG:** ≥30 eos/hpf in 5 hpfs (stomach)
  - **EoD**: ≥30 eos/hpf in 3 hpfs (duodenum)

STUDY DESIGN

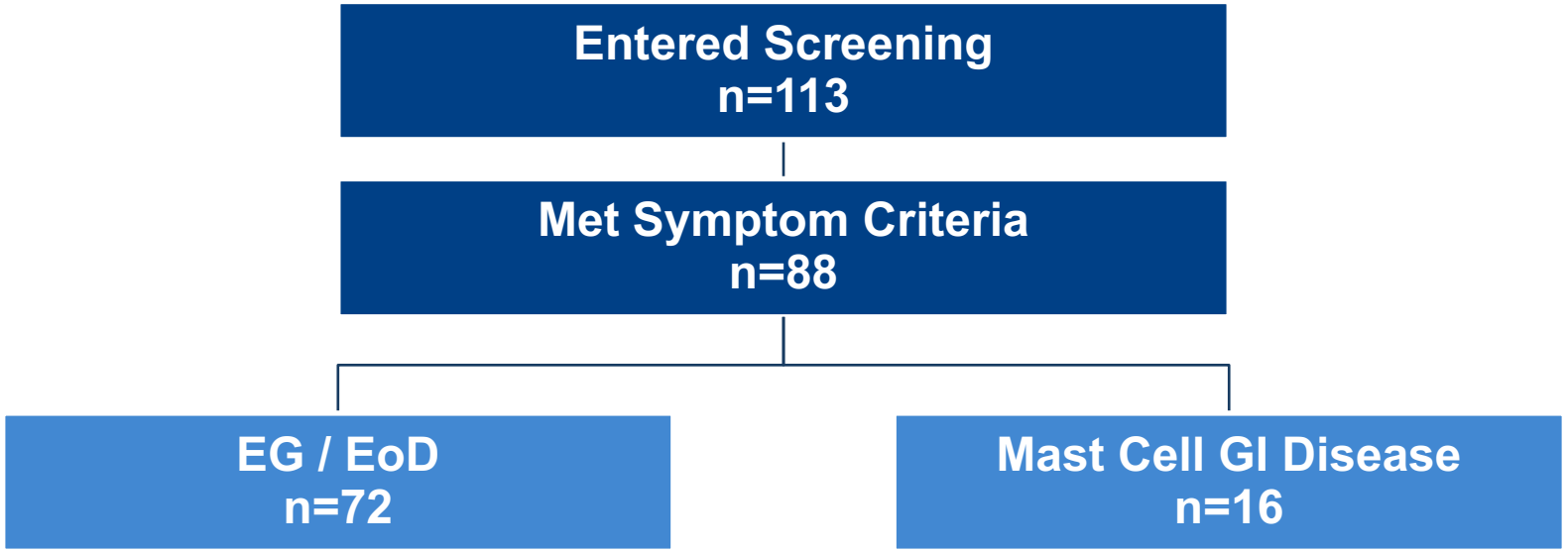
- Phase 2 multi-center, randomized, double-blind, placebo-controlled study
- 65 Patients – 3 arms, 4 monthly doses
  - 21 patients 0.3, 1.0, 3.0, 3.0 mg/kg antolimab
  - 22 patients 0.3, 1.0, 1.0, 1.0 mg/kg antolimab
  - 22 patients placebo
- Primary endpoint: Mean % reduction in tissue eosinophils from baseline to day 99
- Secondary endpoints
  - % Treatment responders (>75% reduction in tissue eosinophil counts AND >30% reduction in symptoms (TSS) from baseline to 2 weeks post-last dose)
  - Mean % reduction in TSS from baseline to 2 weeks post-last dose

RANDOMIZED STUDY RESULTS

Prespecified Endpoints		Antolimab (n=39)	Placebo (n=20)
1° - Tissue Eosinophils	% Δ	-95%	+10%
	p-value	**<0.0001**	-
2° - Treatment Responders	%	69%	5%
	p-value	**0.0008**	-
2° - TSS	% Δ	-53%	-24%
	p-value	**0.0012**	-

- All primary and secondary endpoints met in the first randomized trial in patients with EG and EoD
- Generally well tolerated

ENIGMA Screening Identified Symptomatic Patients With Elevated Mast Cells Without Eosinophilia



EG/EoD: ≥30 Eos & Mast Cells[1]

MGID: ≥30 Mast Cells[2]

16 of 88 symptomatic patients had elevated mast cells only
These patients were offered an open-label study of antolimab

1 65 met all enrollment criteria for ENIGMA; 1 patient had elevated eos only
2 ≥30 mast cells/hpf in 5 hpfs in the stomach and/or ≥30 mast cells/hpf in 3 hpfs in the duodenum

Phase 1 Mast Cell GI Disease (MGID) Study

Study Design

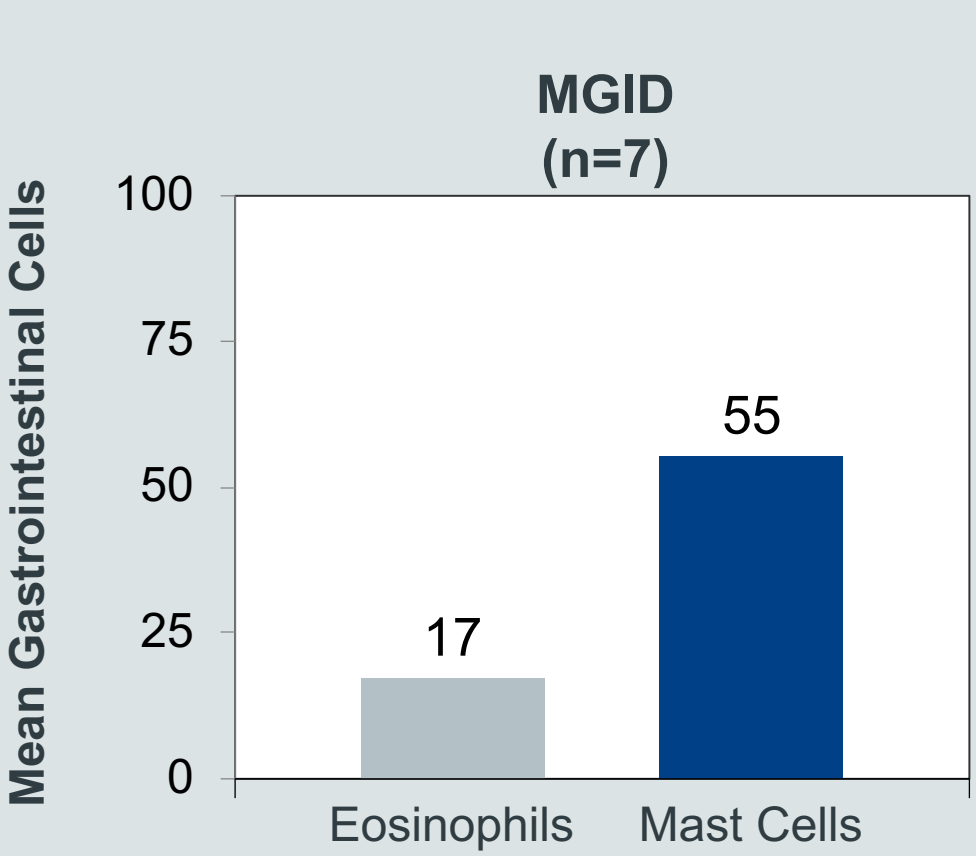
- Multi-center, open-label, multi-dose, Phase 1 study
- Active moderate to severe symptoms as measured by symptom questionnaire used in ENIGMA
- Biopsy confirmed elevated mast cells without tissue eosinophilia
  - Stomach: ≥30 mast cells/high powered field (hpf) in 5 hpfs, and/or
  - Duodenum: ≥30 mast cells/hpf in 3 hpfs
- 6 monthly doses
  - 0.3, 1.0, 3.0, 3.0, 3.0, 3.0 mg/kg antolimab

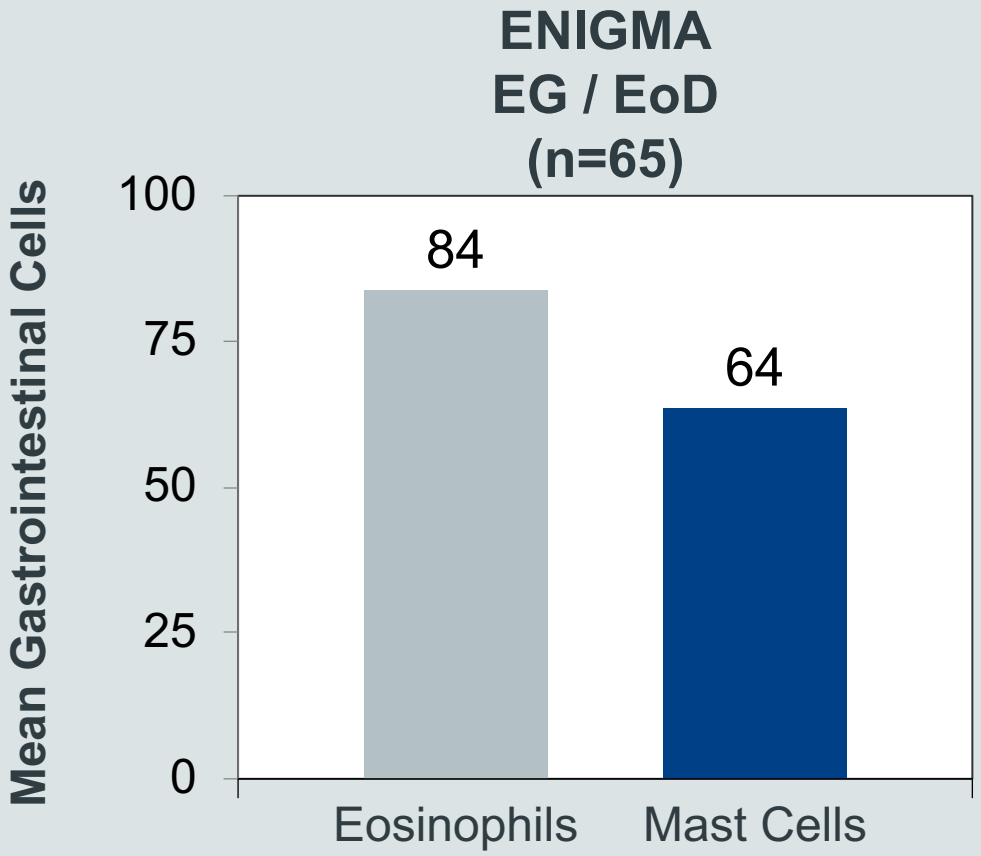
Baseline Characteristics

Mast Cell Gastritis Patients	n=7
Age, Mean (Range)	48 (19-79)
Female	100%
White	100%
Absolute Eosinophil Count /µL, Mean (Range)	127 (20-190)
Immunoglobulin-E (IU/mL)[1], Mean (Range)	28 (10-59)
Gastrointestinal[2] Eosinophils/hpf, Mean (Range)	17 (14-23)
Gastrointestinal[2] Mast Cells/hpf, Mean (Range)	55 (46-64)
Total Symptom Score (TSS) [0-80], Mean	27.1

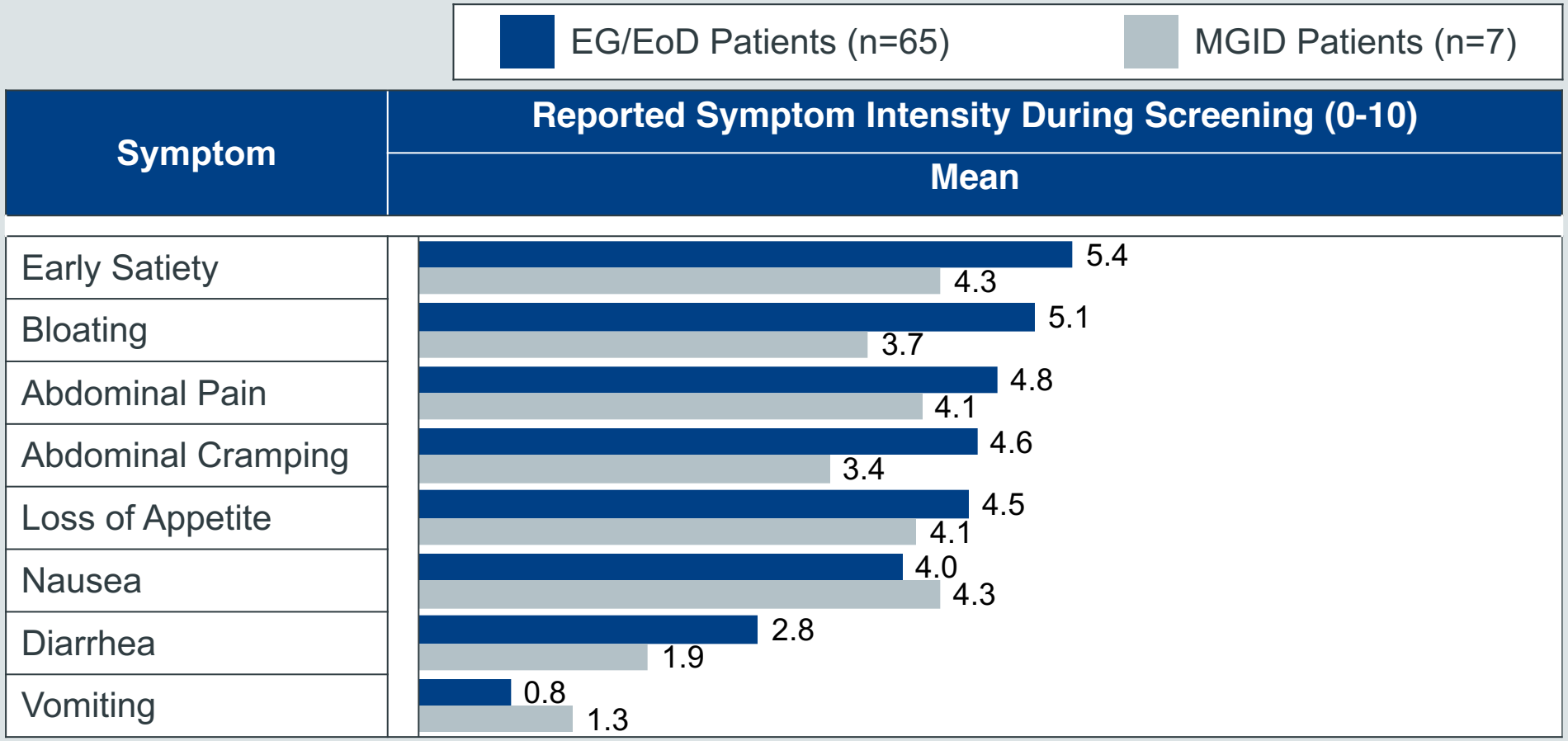
1 n=6
2 Gastric or duodenum site with highest eosinophil or mast cell counts

Baseline Gastrointestinal Eosinophils and Mast Cell Counts



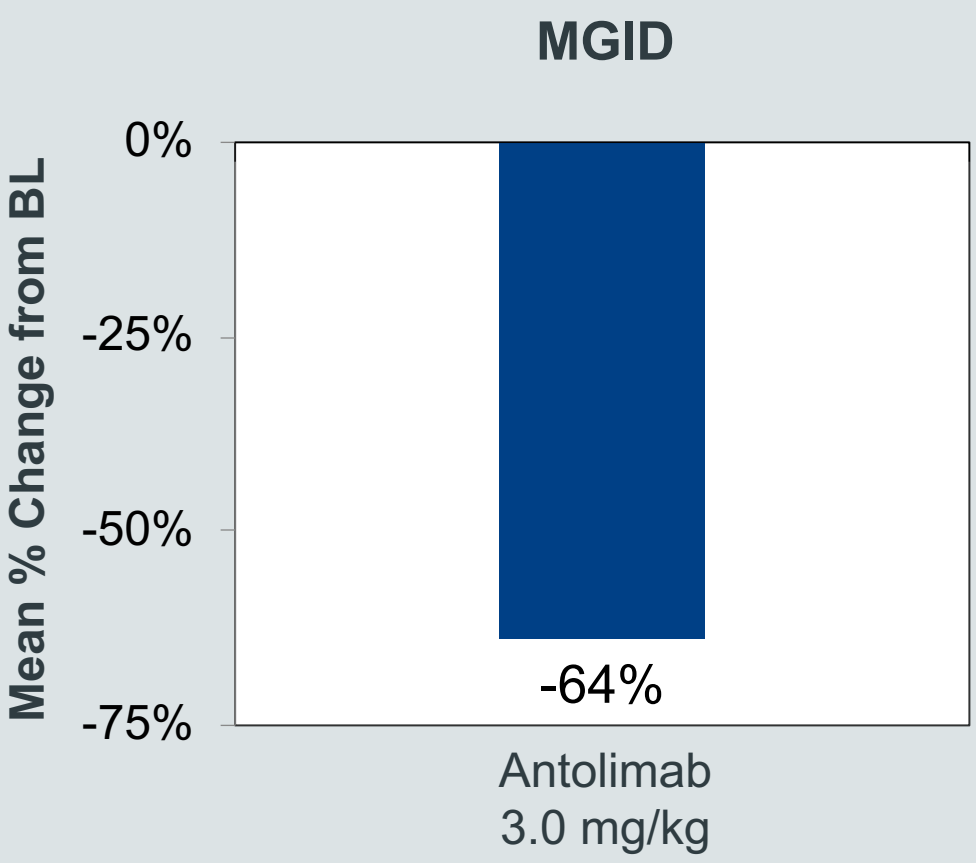


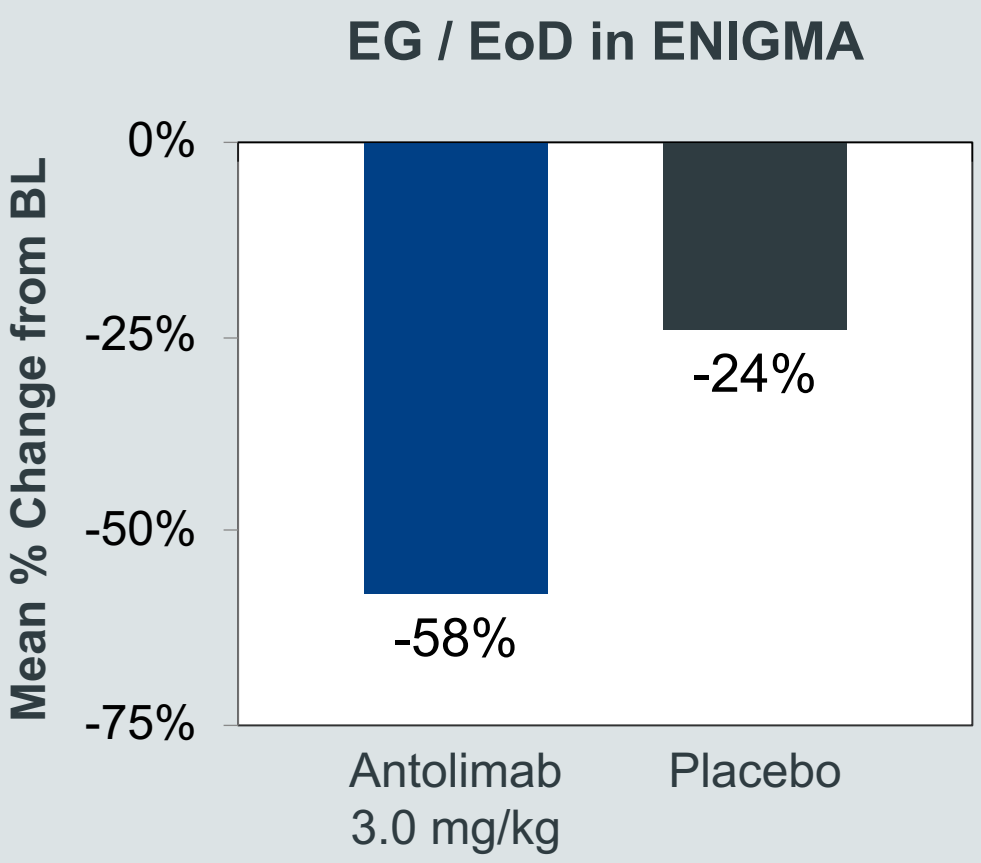
EG/EoD and MGID Patients Have Similar Symptomatic Burden



64% Improvement in Total Symptom Score

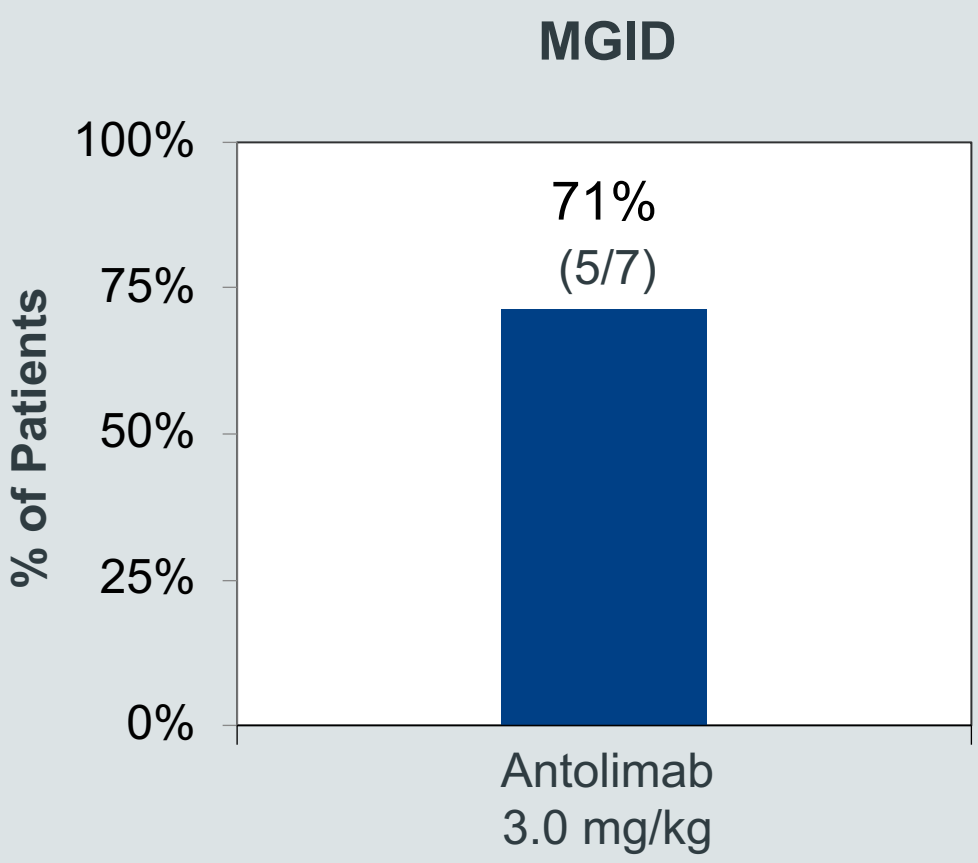
PRO TSS-8: Change from Baseline

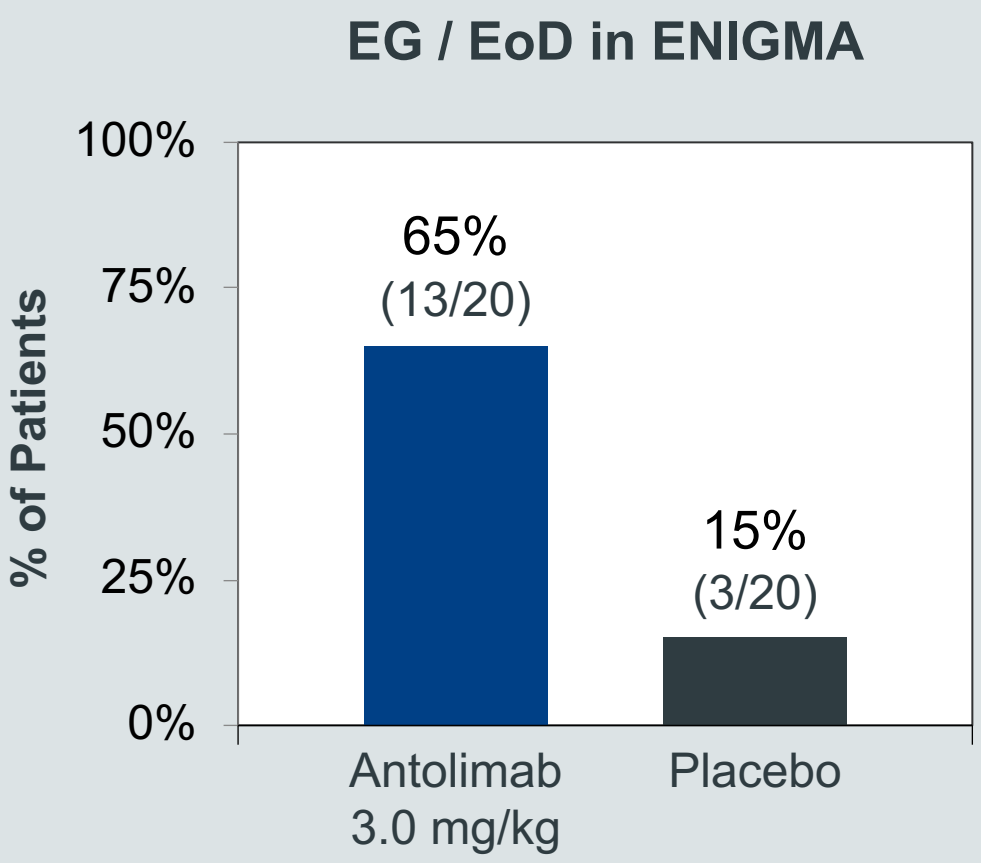




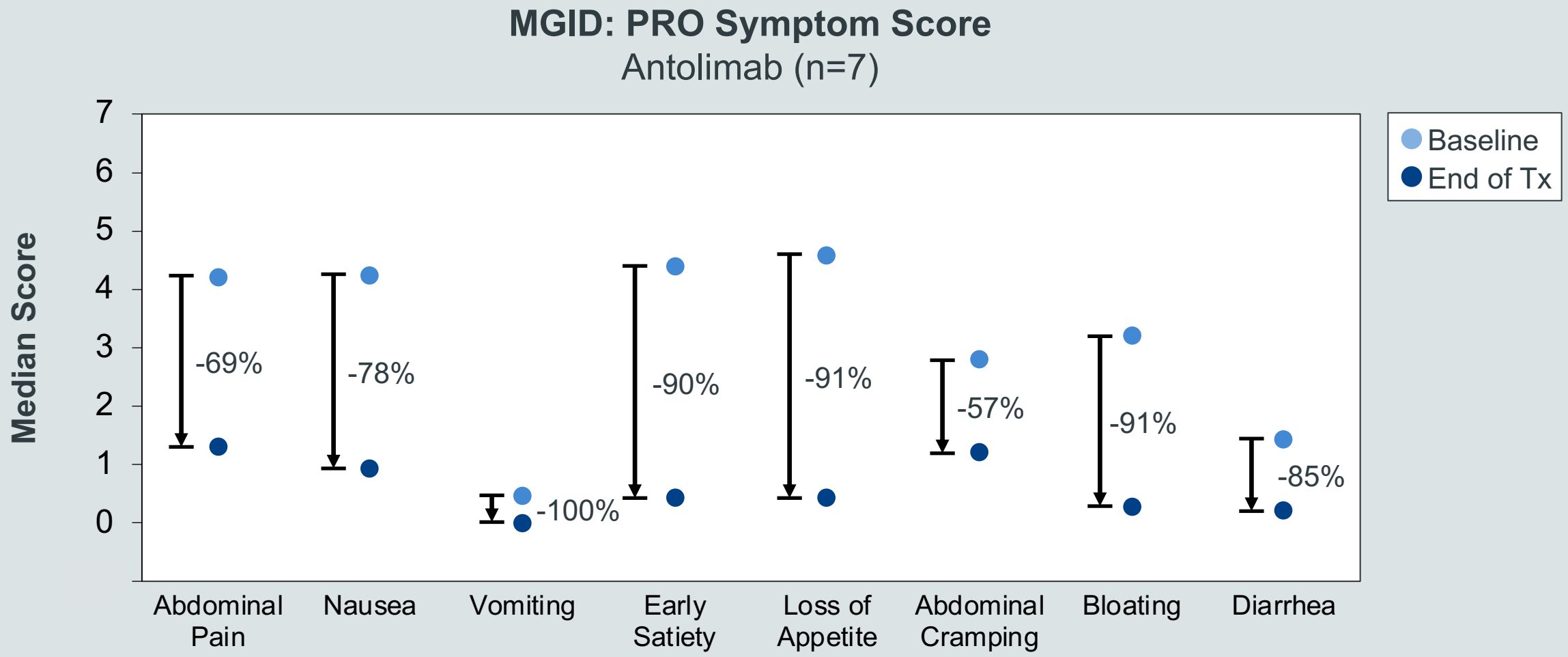
5 of 7 (71%) Patients with >50% Reduction in Symptoms

PRO Total Symptom Score: >50% Reduction

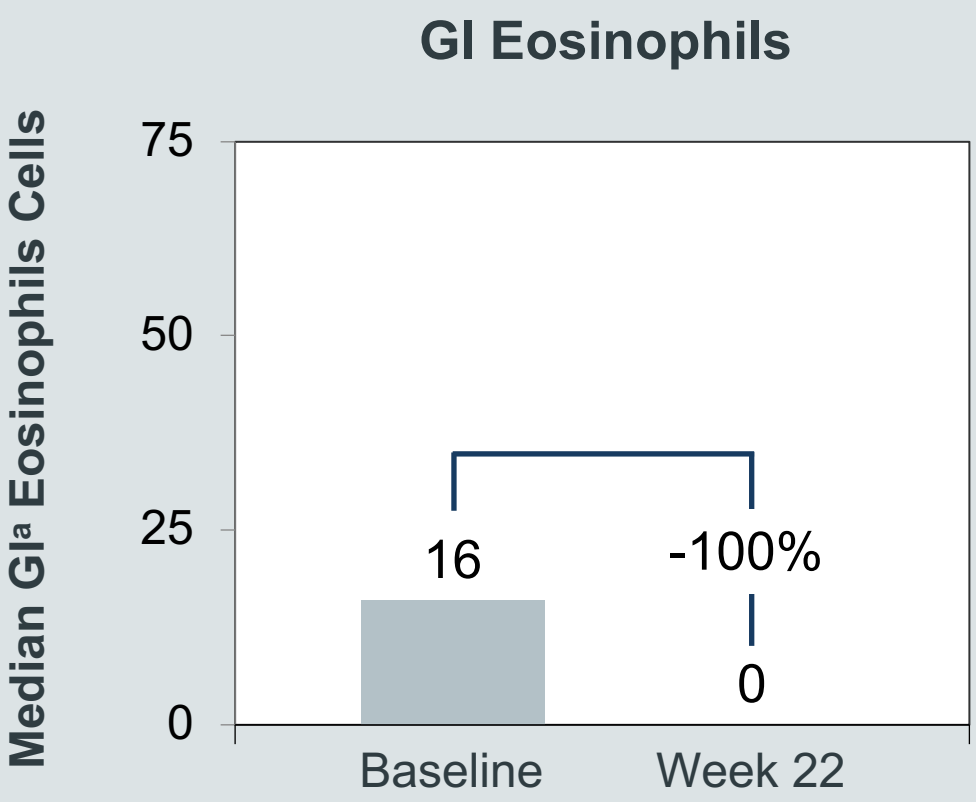


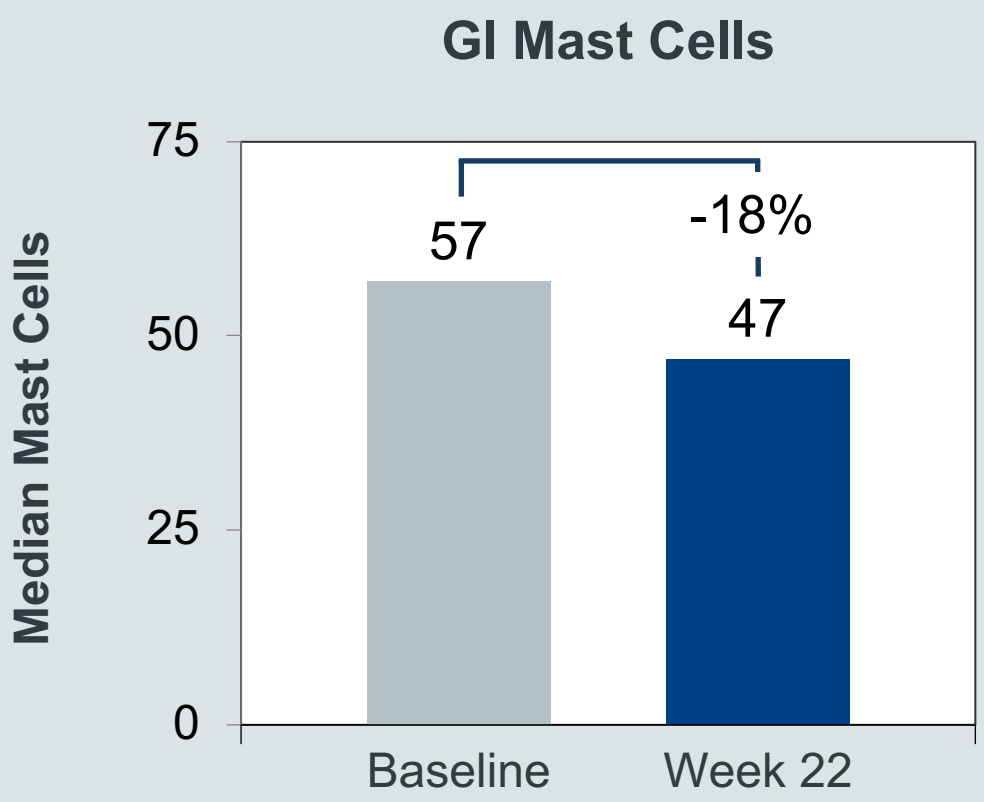


Improvement Across All Symptoms Measured



MGID: Histologic Results





a Gastrointestinal; Gastric (5 hpfs) or duodenum (3 hpfs) site with highest eosinophils or mast cell counts at baseline

MGID: Safety Summary

- Generally well tolerated
- Most common AE was infusion related reactions (flushing, feeling of warmth, headache, nausea, dizziness), all of which were mild
- No drug-related SAEs

Conclusions

- A group of symptomatic patients suspected of EG/EoD were found to have elevated mast cell counts without blood or tissue eosinophilia (MGID)
- Antolimab treatment resulted in substantial symptom improvement in a prospective, open-label study of patients with MGID
- Antolimab treatment was generally well tolerated
- These results suggest that mast cells may be the primary driver of symptoms in this disease and could contribute to symptoms in other GI diseases such as EGIDs
- Antolimab may be a promising targeted therapy for EG/EoD and MGID

We thank the patients who participated in this study, investigators, and study staff