Interim Results of an Open-label Extension Study of Antolimab, an Anti-Siglec-8 Antibody, for the Treatment of Patients with Eosinophilic Gastritis and/or Eosinophilic Duodenitis (ENIGMA OLE; NCT03664960)

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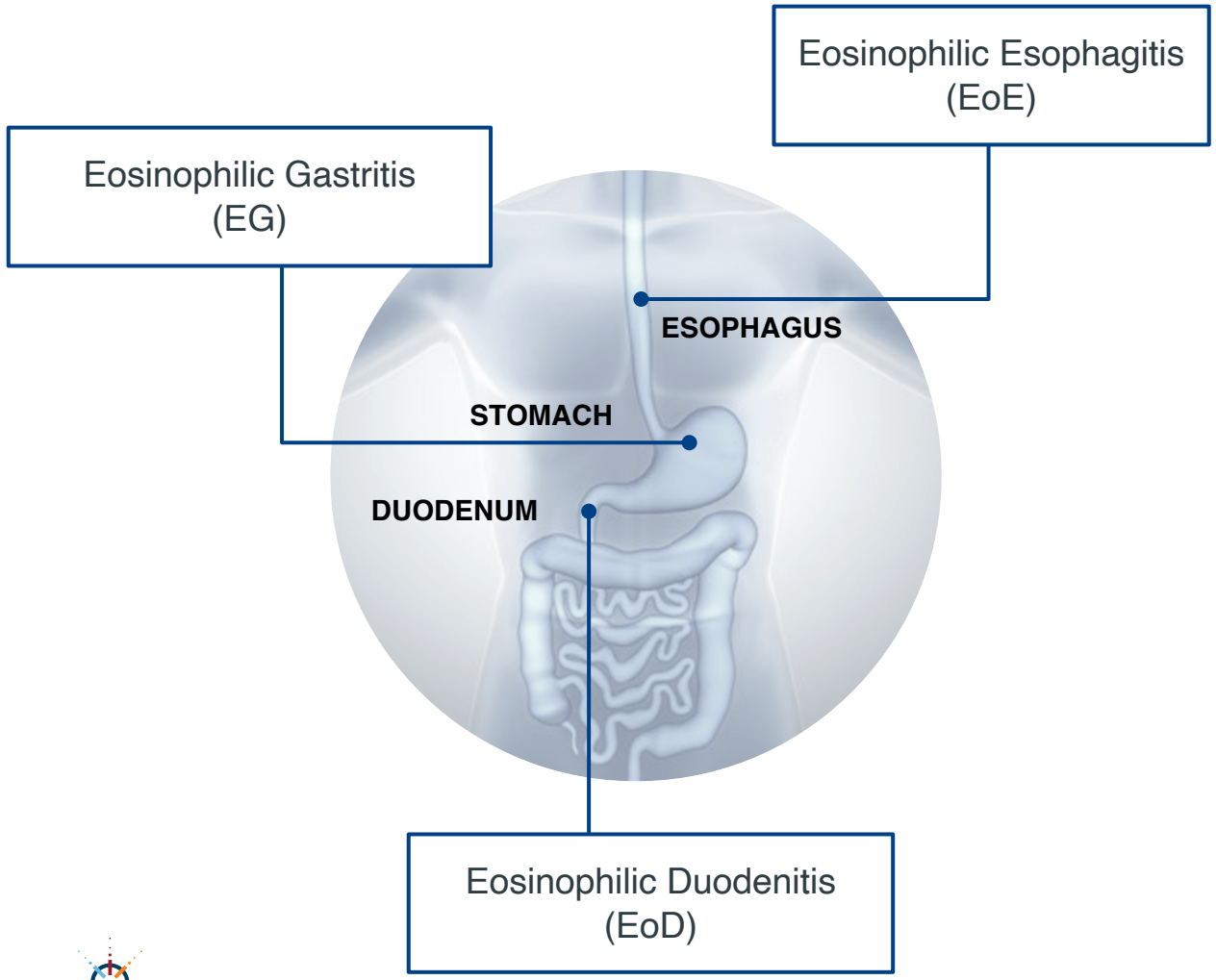
Digestive Disease Week
May 2–5, 2020 | Exhibit Dates: May 3–5

Disclosures

- Dr. Nirmala Gonsalves is an investigator in the ENIGMA study
- Antolimab (AK002) is an investigational drug candidate and is not FDA/EMA approved
- This study is in progress. Data presented are current as of 4/28/2020

Eosinophilic Gastrointestinal Diseases (EGIDs)



EG, EoD, EoE

Chronic Eosinophilic Inflammation of the Stomach, Duodenum, or Esophagus

- Eosinophils and mast cells are important drivers of disease
- Symptoms: abdominal pain, nausea, early satiety, loss of appetite, bloating, abdominal cramping, vomiting, diarrhea, and dysphagia
- No FDA approved treatment for EG, EoD, or EoE
- Current standard of care: diet and/or steroids

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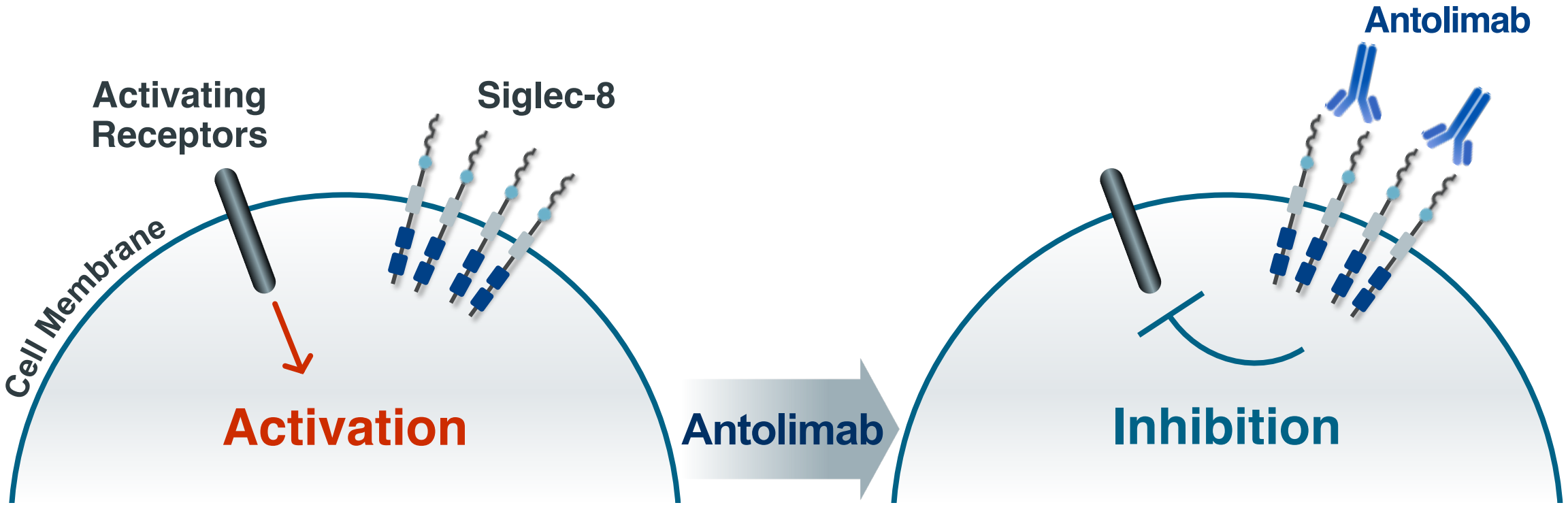
Source: Egan M, Furuta GT. Ann Allergy Asthma Immunol 121(2018) 162-167; Gonsalves M. Clin Rev. Allergy Immunol. 2019.

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



ENIGMA Phase 2 Study Summary

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

Open-Label Extension (OLE) Study Aim & Design

- **Study Aim**
  - Determine safety and efficacy of long-term use of antolimab for treatment of EG and/or EoD
- **Study Design**
  - Patients who completed ENIGMA had the option to receive antolimab in an OLE study
  - Patients enrolled in the OLE received up to 20 monthly antolimab infusions, administered intravenously every 28 days, titrated up to 3.0 mg/kg
  - Patients underwent an upper endoscopy with biopsy on Days 323 and 659 from entering ENIGMA

OLE Interim Analysis

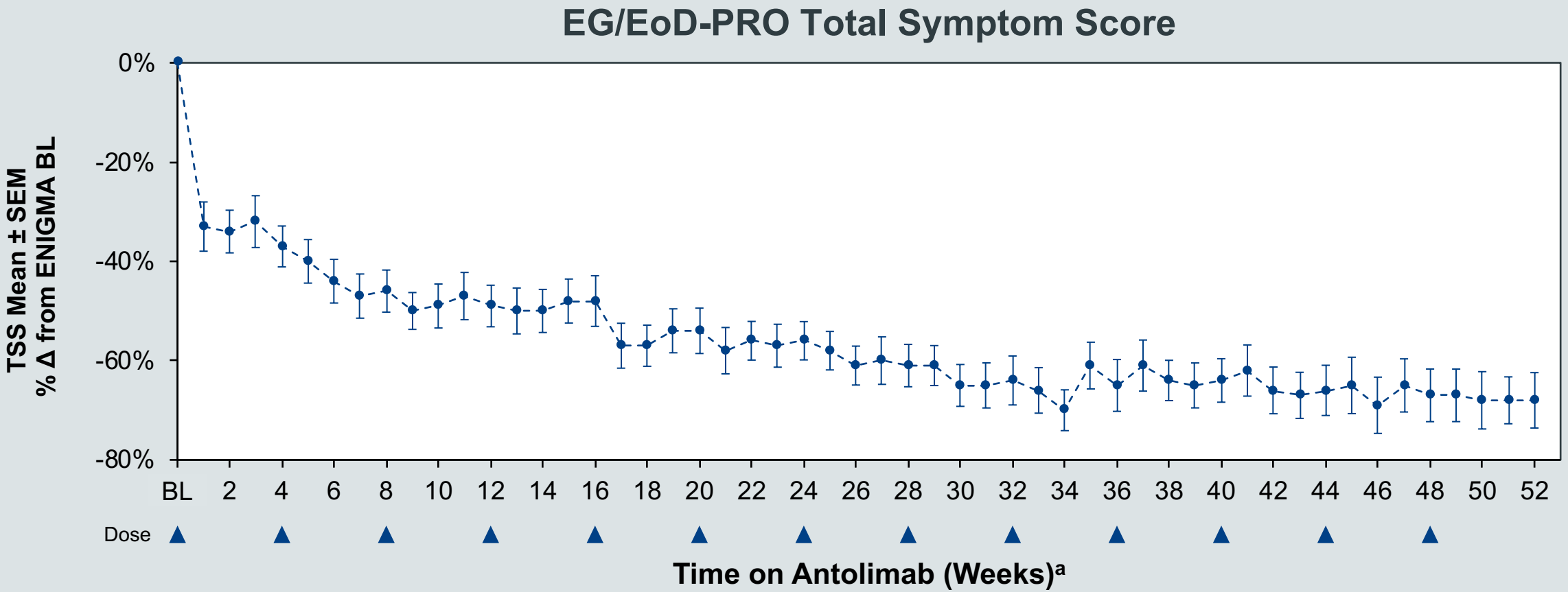
- **Patient Population**
  - 58 of 59 eligible patients entered the OLE study
  - As of 4/28/2020,
    - 35 patients have completed ≥52 weeks of antolimab treatment (includes ENIGMA exposure)
      - Average 64 weeks of antolimab treatment
    - 12 patients have discontinued <52 weeks of antolimab treatment
      - Average 33 weeks of antolimab treatment
    - 11 patients have <52 weeks of treatment and are still on study
      - Average 47 weeks of antolimab treatment

ENIGMA Baseline Characteristics

Patient Characteristics		Enrolled in OLE (N=58)
Age, Mean (Range)		41 (18-74)
Female		60%
White		93%
GI[a] Eosinophils/hpf, Mean (Range)		74 (33-201)
GI[a] Mast Cells/hpf, Mean (Range)		60 (20-114)
Total Symptom Score [0-80], Mean (Range)		32 (6-61)
% of Patients (n) by AEC[b]/µL	<500	69% (40)
	≥500	31% (18)

a Gastrointestinal; Gastric (5 hpfs) or duodenum (3 hpfs) site with highest eosinophil or mast cell counts
b AEC: Absolute Eosinophil Count

Substantial Symptom Improvement Over Time



a Total antolimab exposure, inclusive of antolimab exposure during the Phase 2 ENIGMA study

Change in Symptoms Over Time

Total Antolimab Exposure (Weeks)[a]	TSS Mean Change from ENIGMA BL		
	Baseline	Absolute	Percent
13-14 (n=55)	32	-16	-51%
29-30 (n=45)	31	-19	-63%
51-52 (n=30)[b]	33	-22	-68%

a Total antolimab exposure, inclusive of antolimab exposure during the Phase 2 ENIGMA study
b 5 of 35 patients with ≥52 weeks did not complete PRO on weeks 51-52, and therefore were excluded

Change in Symptom Response Rate Over Time

Total Antolimab Exposure (Weeks)[a]	% of Patients (n) by TSS Improvement		
	≥50%	≥70%	≥90%
13-14 (n=55)	**58%** (32/55)	**25%** (14/55)	**15%** (8/55)
29-30 (n=45)	**69%** (31/45)	**44%** (20/45)	**18%** (8/45)
51-52 (n=30)[b]	**70%** (21/30)	**57%** (17/30)	**30%** (9/30)

a Total antolimab exposure, inclusive of antolimab exposure during the Phase 2 ENIGMA study
b 5 of 35 patients with ≥52 weeks did not complete PRO on weeks 51-52, and therefore were excluded

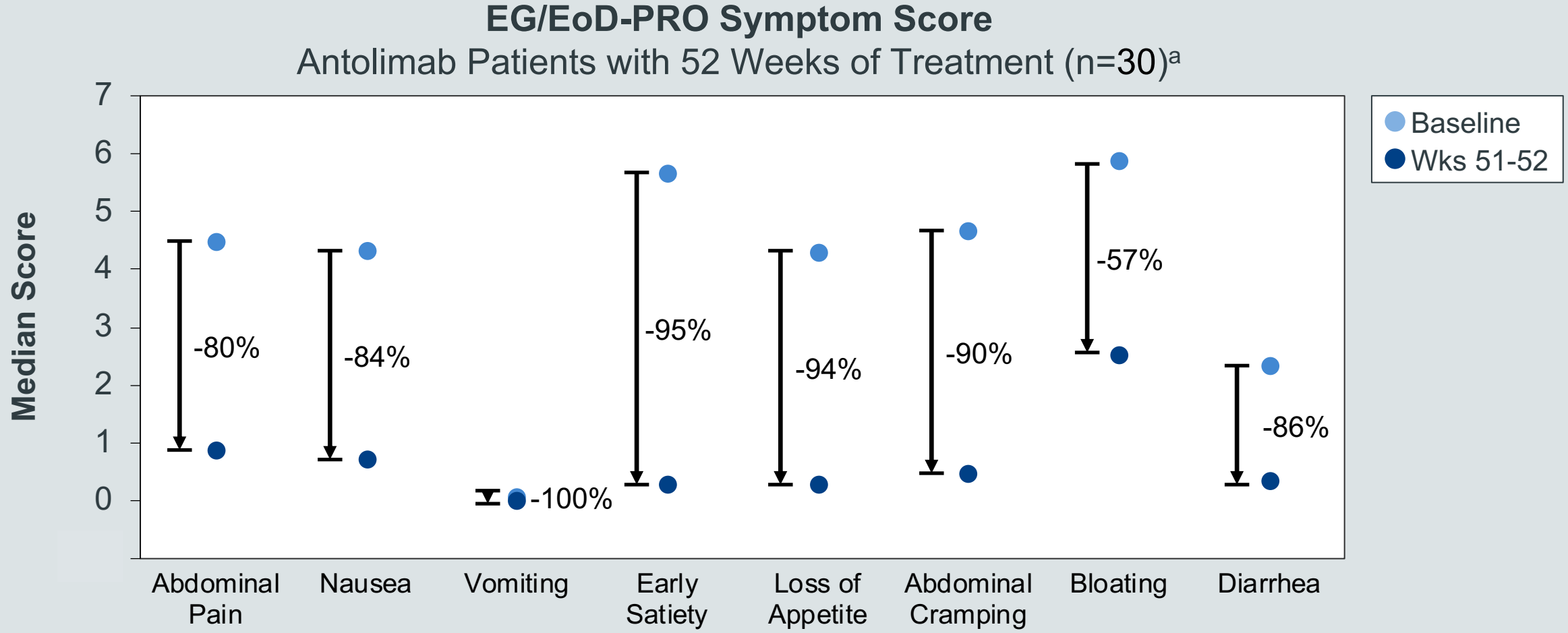
Symptom Response Rate in Patients with 52 Weeks of Antolimab Treatment

Proportion of Patients by TSS Improvement from ENIGMA Baseline[a]

Weeks[b]	≥50% Response	≥70% Response	≥90% Response
13-14 (n=30)	73%	30%	20%
29-30 (n=30)	77%	50%	23%
51-52 (n=30)	70%	57%	30%

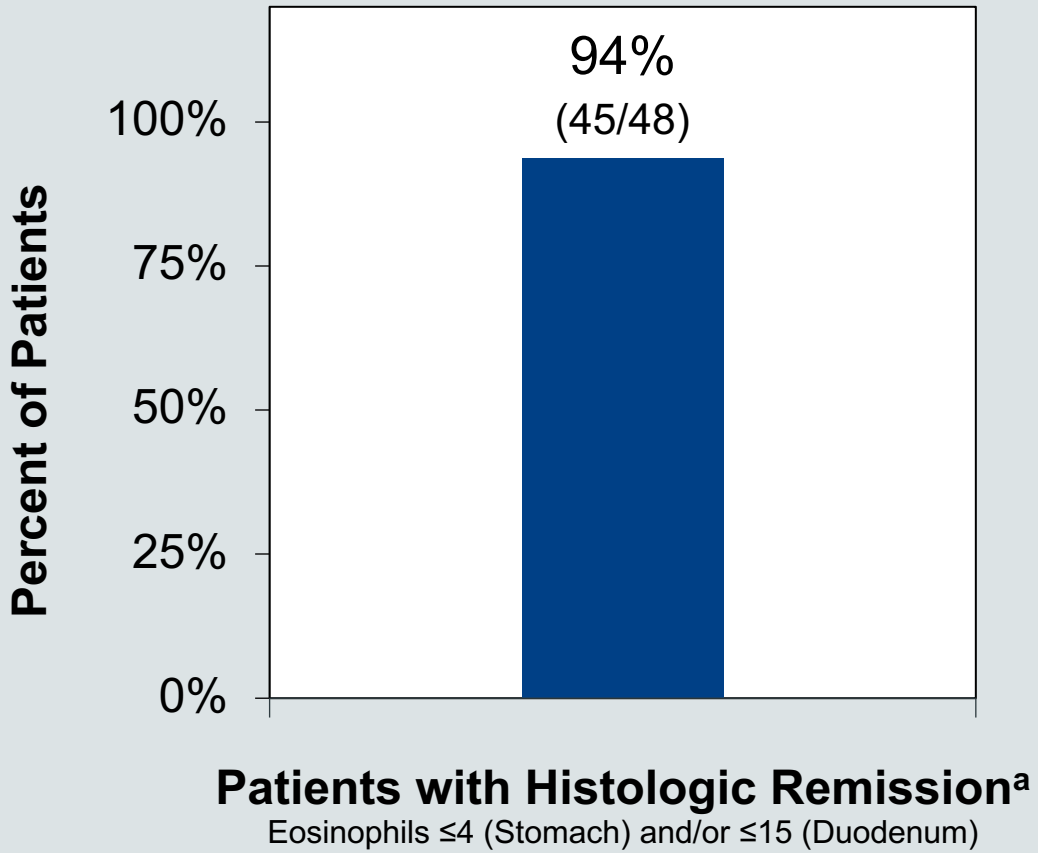
a 5 of 35 patients with ≥52 weeks did not complete PRO on weeks 51-52, and therefore were excluded
b Total antolimab exposure, inclusive of antolimab exposure during the Phase 2 ENIGMA study

Improvement Across All Symptoms



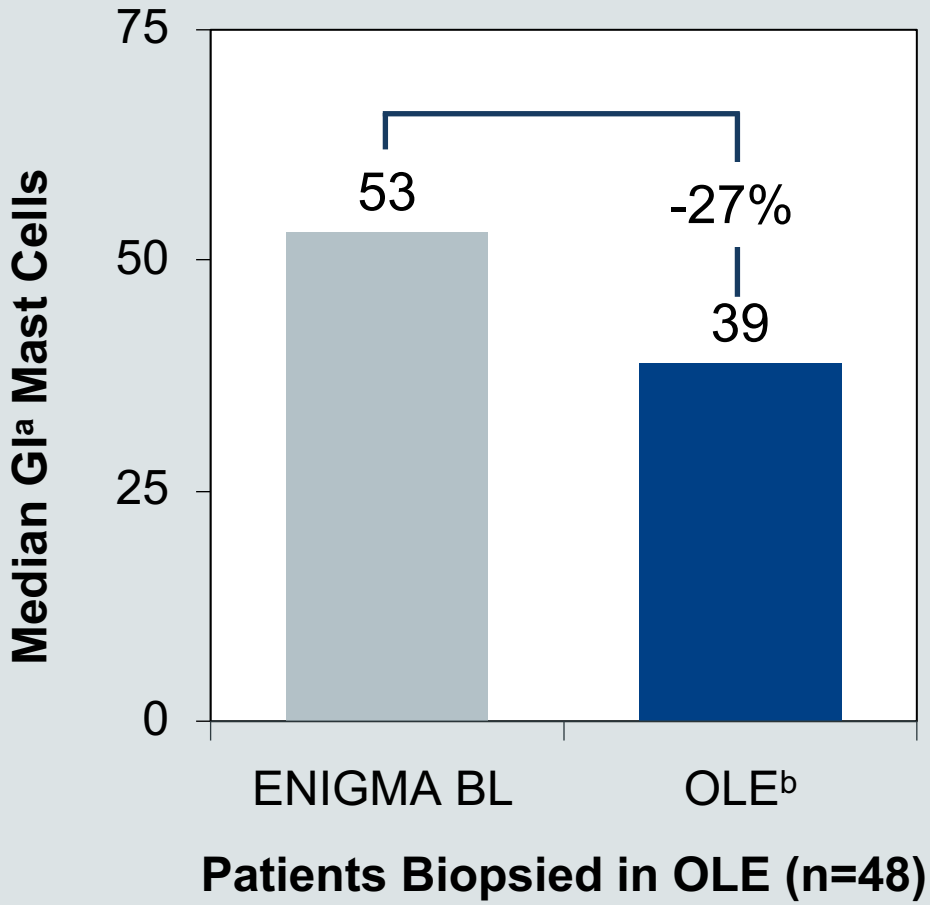
a Total antolimab exposure, inclusive of antolimab exposure during the Phase 2 ENIGMA study
5 of 35 patients with ≥52 weeks did not complete PRO on weeks 51-52, and therefore were excluded

Sustained Histologic Remission on Antolimab



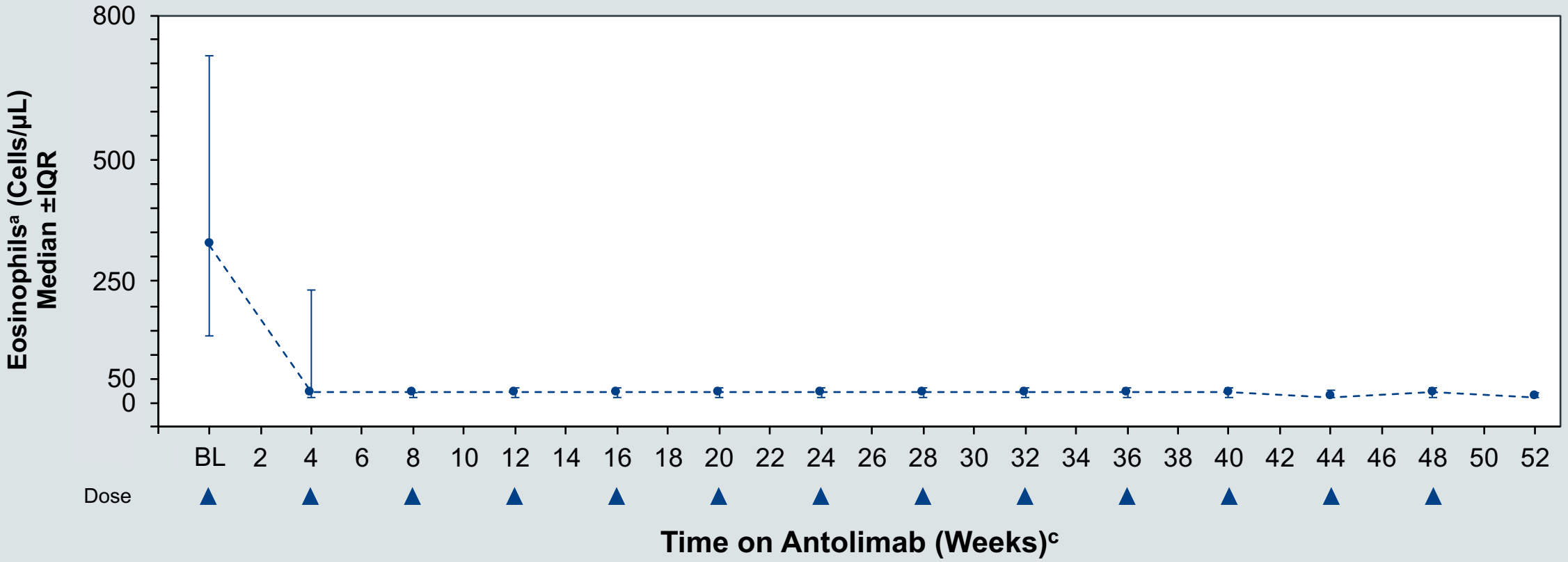
a Biopsies taken on Day 323

Change in Tissue Mast Cell Counts



a Gastrointestinal; Gastric (5 hpfs) or duodenum (3 hpfs) site with highest mast cell counts at baseline
b Biopsies taken on Day 323

Sustained Depletion of Blood Eosinophil Counts



a Blood eosinophils collected just prior to each infusion
b BL: ENIGMA baseline
c Total antolimab exposure, inclusive of antolimab exposure during the Phase 2 ENIGMA study

Safety Summary

Treatment-Emergent AEs in >5% of Patients

% of Patients, (n)	Total (n=58)
Infusion related reaction	29% (17)
Headache	12% (7)
Nasopharyngitis	12% (7)
Nausea	12% (7)
Influenza	10% (6)
Anxiety	9% (5)
Diarrhea	9% (5)
Anemia	7% (4)
Blood creatine phosphokinase increased	7% (4)
Fatigue	7% (4)
Neutrophilia	7% (4)
Oropharyngeal pain	7% (4)
Sinusitis	7% (4)
Urinary tract infection	7% (4)
Vomiting	7% (4)

- Generally well-tolerated
- Most common AE was mild to moderate infusion related reactions (IRR)
  - All were mild to moderate (flushing, feeling of warmth, headache, nausea, dizziness)
  - Mostly on first two infusions, greatly reduced or does not occur on subsequent infusions
  - No IRRs in 20 patients who received single-dose oral prednisone night before first infusion
- No drug related SAEs

Summary

- Long-term treatment of antolimab was generally well-tolerated
- Antolimab treatment resulted in durable symptomatic improvements and sustained blood and tissue eosinophil depletion
- Symptomatic responses improved with increased duration of antolimab treatment
- Additional antolimab studies:
  - Phase 3 randomized trial in EG/EoD (NCT04322604)
  - Phase 2/3 randomized trial in EoE (NCT04322708)

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