Histologic and Symptomatic Improvement Across Multiple Forms of Eosinophilic Gastrointestinal Diseases in ENIGMA, a Randomized, Double-Blind, Placebo-Controlled Trial of Antolimab (AK002) (ENIGMA; NCT03496571)

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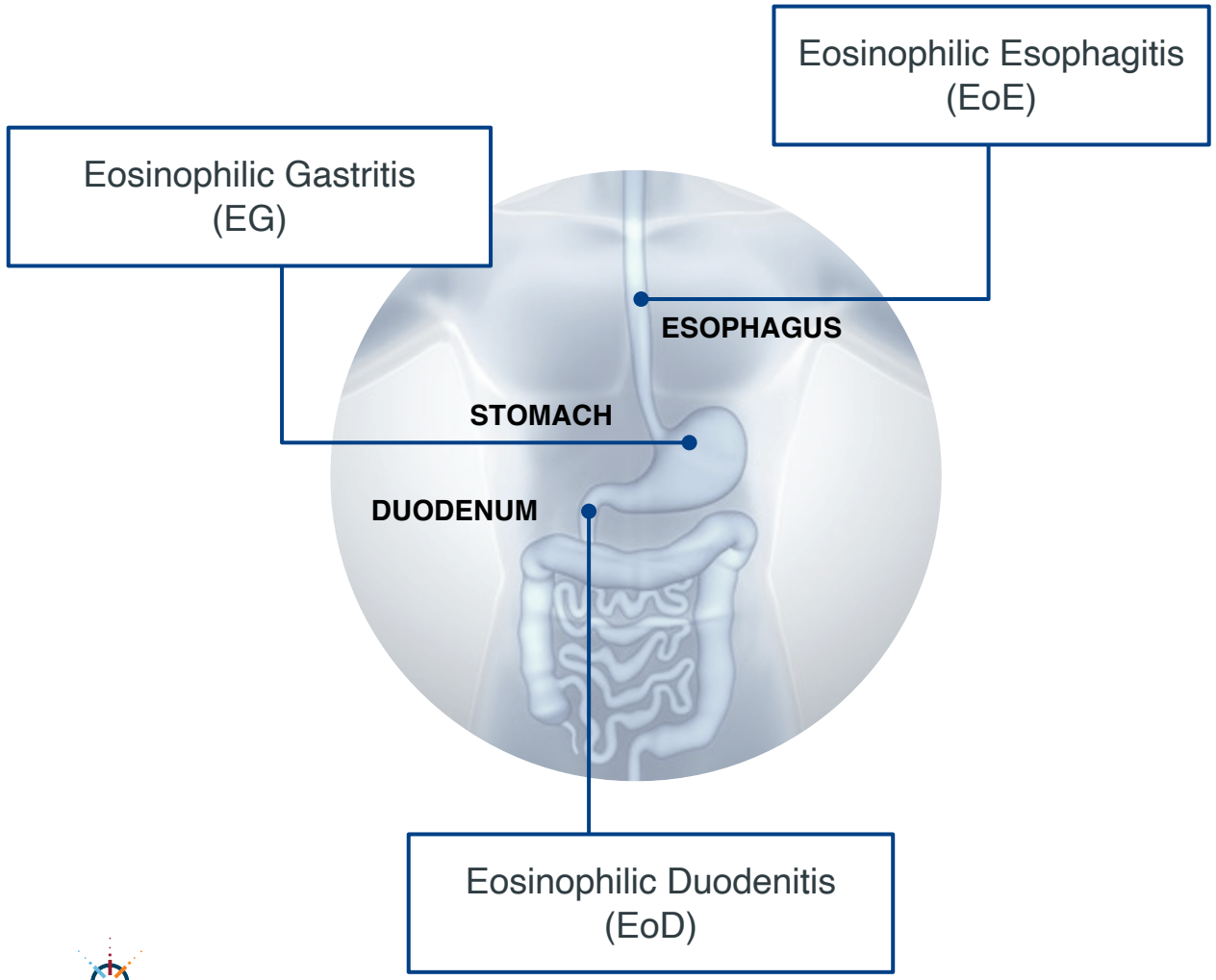
Disclosures

- Dr. Evan Dellon is a principal investigator in the ENIGMA study
- Antolimab (AK002) is an investigational drug candidate and is not FDA/EMA approved

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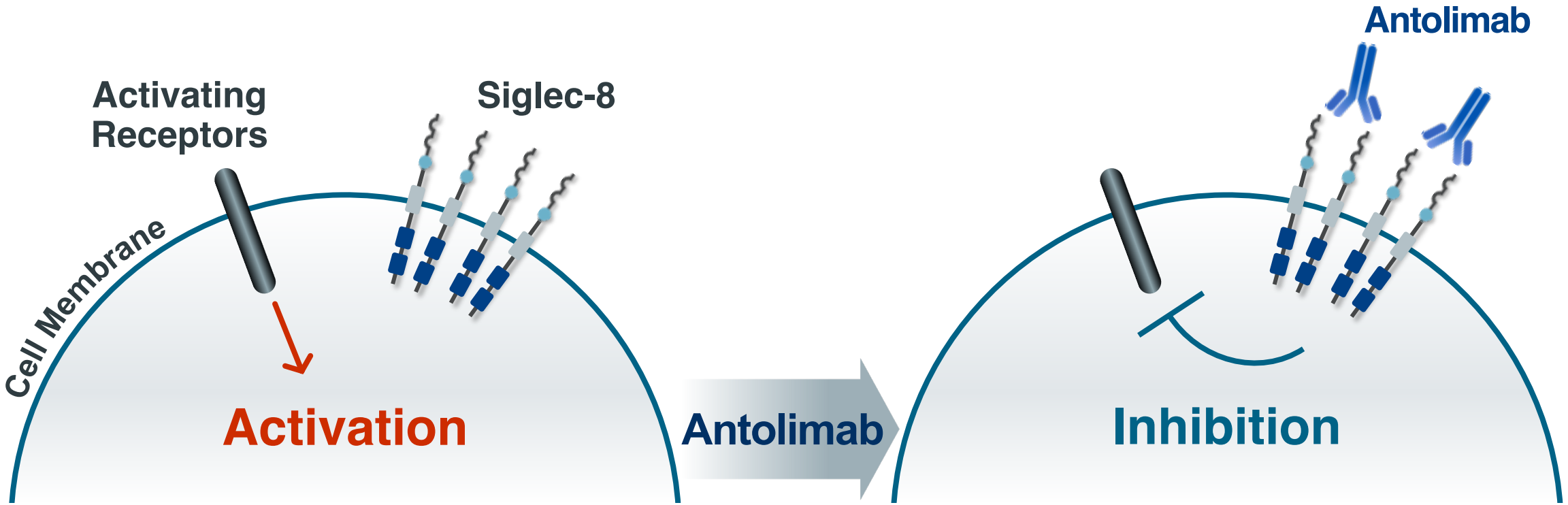
Source: Egan M, Furuta GT. Ann Allergy Asthma Immunol 121(2018) 162-167; Gonsalves M. Clin Rev. Allergy Immunol. 2019.

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



ENIGMA Phase 2 Study Aim and Inclusion

Study Aim

- Determine safety and efficacy of antolimab (AK002) for treatment of EG and/or EoD

Key Inclusion Criteria

- Active moderate to severe symptoms[1] using the daily 8 symptom EG/EoD Questionnaire©
- Biopsy confirmed
  - Stomach: ≥30 eos/hpf in 5 hpfs, and/or
  - Duodenum: ≥30 eos/hpf in 3 hpfs

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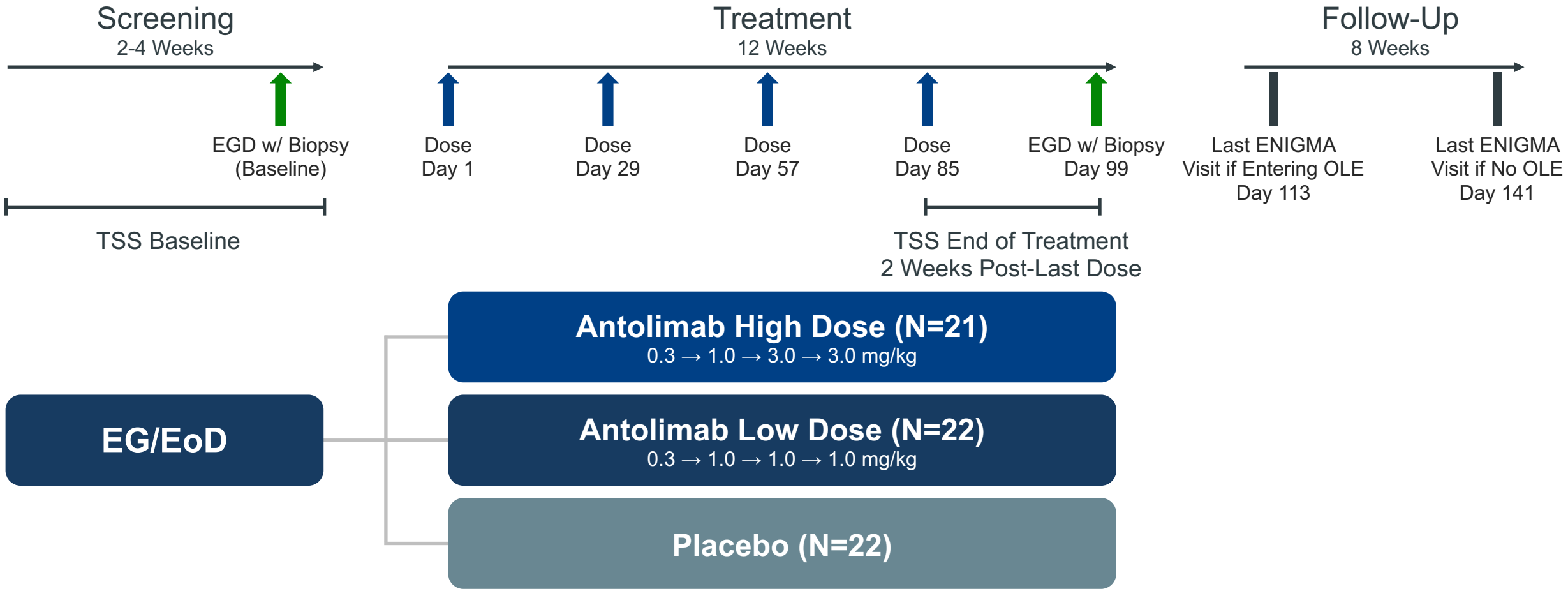
1 PRO entry criteria: average weekly score of ≥3 for either abdominal pain, diarrhea and/or nausea over ≥2 weeks

ENIGMA Phase 2 Study Design



Symptoms Assessed Using a PRO Questionnaire

EG/EoD Questionnaire©

- Developed in accordance with FDA guidance on PRO development
- 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

- Patients with concomitant eosinophilic esophagitis received a daily question to report severity of dysphagia on a scale of 0-10

Endpoints

Primary Endpoint

- Mean percent change in gastrointestinal eosinophil counts from baseline

Responder Secondary Endpoint

- Proportion of patients who have >75% decrease in tissue eosinophils
  AND >30% benefit in Total Symptom Score (TSS)

Symptoms Secondary Endpoint

- Mean percent change in TSS from baseline

Post-hoc analysis: histologic and symptomatic (TSS) changes in EG/EoD subgroups

- Proportion of patients with tissue eosinophils below threshold;
  ≤4 (stomach) and/or ≤15 (duodenum)
- Mean percent change in TSS from baseline

Baseline Characteristics of EG/EoD Patients

		antolimab (AK002) Dose Groups			Placebo (n=20)	Total (N=59)
		High 0.3-3.0 mg/kg (n=20)	Low 0.3-1.0 mg/kg (n=19)	Combined High/Low (n=39)		
Age, Mean (Range)		42 (20-67)	43 (18-74)	42 (18-74)	40 (18-67)	41 (18-74)
Female		60%	84%	72%	50%	64%
White		85%	95%	90%	100%	93%
Mean Gastrointestinal[1] Eosinophils/hpf		76	80	78	75	77
Mean Gastrointestinal[1] Mast Cells/hpf		59	70	64	56	62
Mean Total Symptom Score (TSS) [0-80]		34.1	34.7	34.4	30.1	32.9
% of Patients (n) by AEC[2]/μL	<250	45% (9)	26% (5)	36% (14)	45% (9)	39% (23)
	250 to <500	35% (7)	42% (8)	38% (15)	15% (3)	31% (18)
	500 to <1500	20% (4)	21% (4)	21% (8)	35% (7)	25% (15)
	≥1500	0%	11% (2)	5% (2)	5% (1)	5% (3)

1 Efficacy population; one patient withdrew after the 1st OLE dose with no qualifying weeks with symptom scores
2 Gastrointestinal; Gastric or duodenum site with highest eosinophil or mast cell counts
3 AEC: Absolute Eosinophil Count

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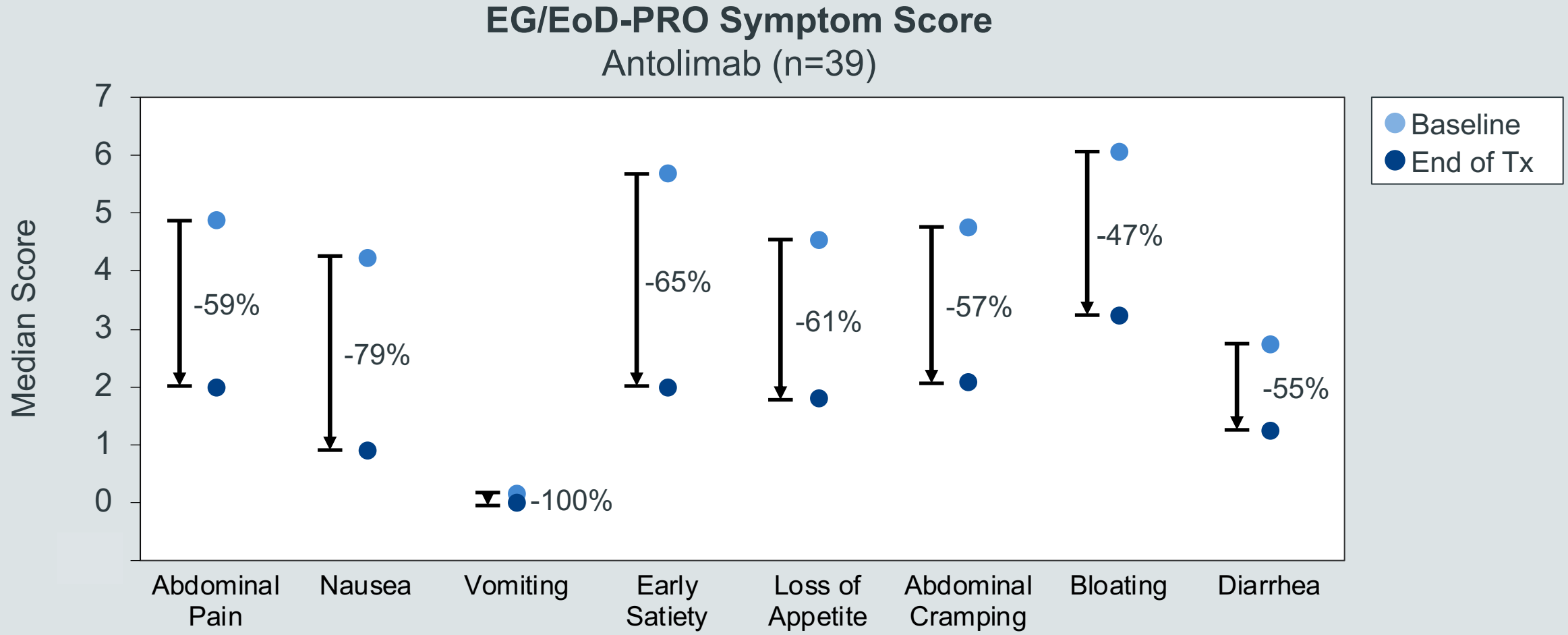
Antolimab Met ENIGMA Primary and Secondary Endpoints

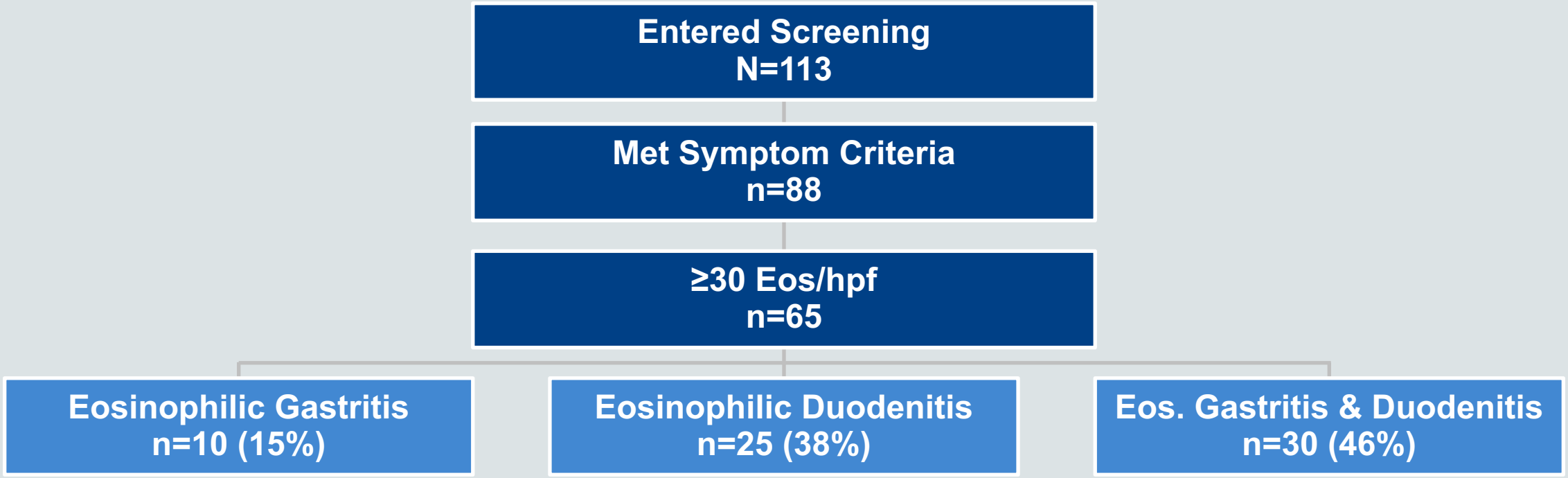
Prespecified Endpoints		Antolimab Dose Groups			
		High (n=20)	Low (n=19)	Combined (n=39)	Placebo (n=20)
1° - Tissue Eosinophils[1] % Δ from BL to Day 99	Baseline	76	80	78	75
	% Δ	-97%	-92%	-95%	+10%
	p-value	**<0.0001**	**<0.0001**	**<0.0001**	-
2° - Treatment Responders (Eos Δ >-75% & TSS Δ >-30%)	%	70%	68%	69%	5%
	p-value	**0.0009**	**0.0019**	**0.0008**	-
2° - Total Symptom Score % Δ from BL to End of Study	Baseline	34	35	34	30
	% Δ	-58%	-49%	-53%	-24%
	p-value	**0.0012**	**0.0150**	**0.0012**	-

1 Average count of the highest readings from the Day 99/End of study biopsy that correspond in location to the location with the highest average count at baseline

Improvement Across All Symptoms on Antolimab



ENIGMA Patient Distribution

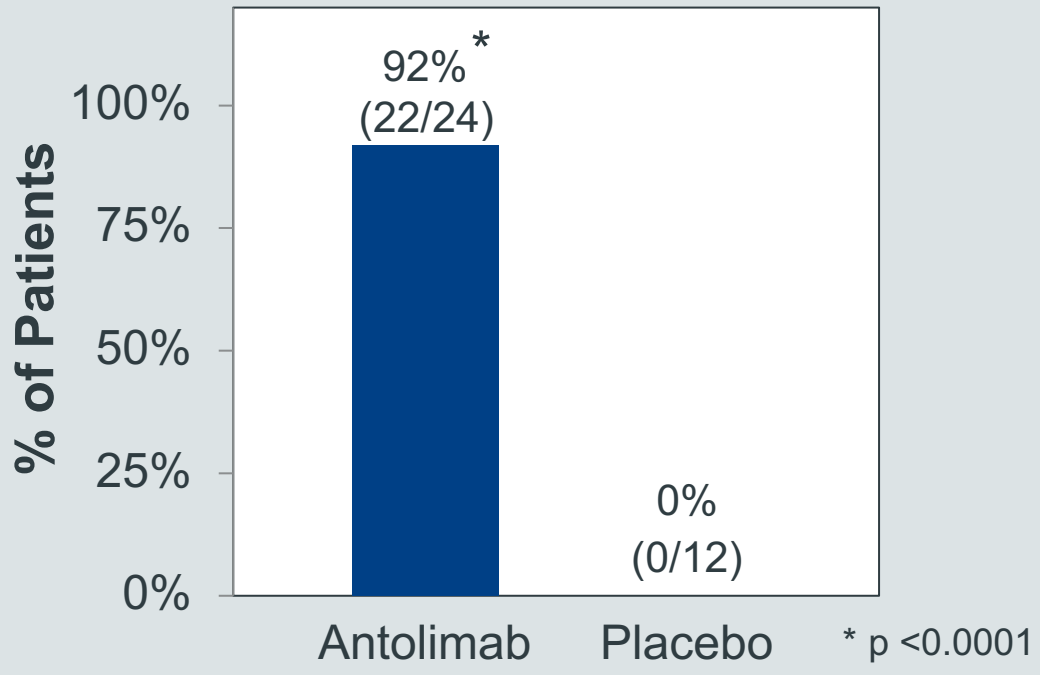


61% (40/65) of patients had gastric eosinophilia (+/- duodenal eosinophilia)

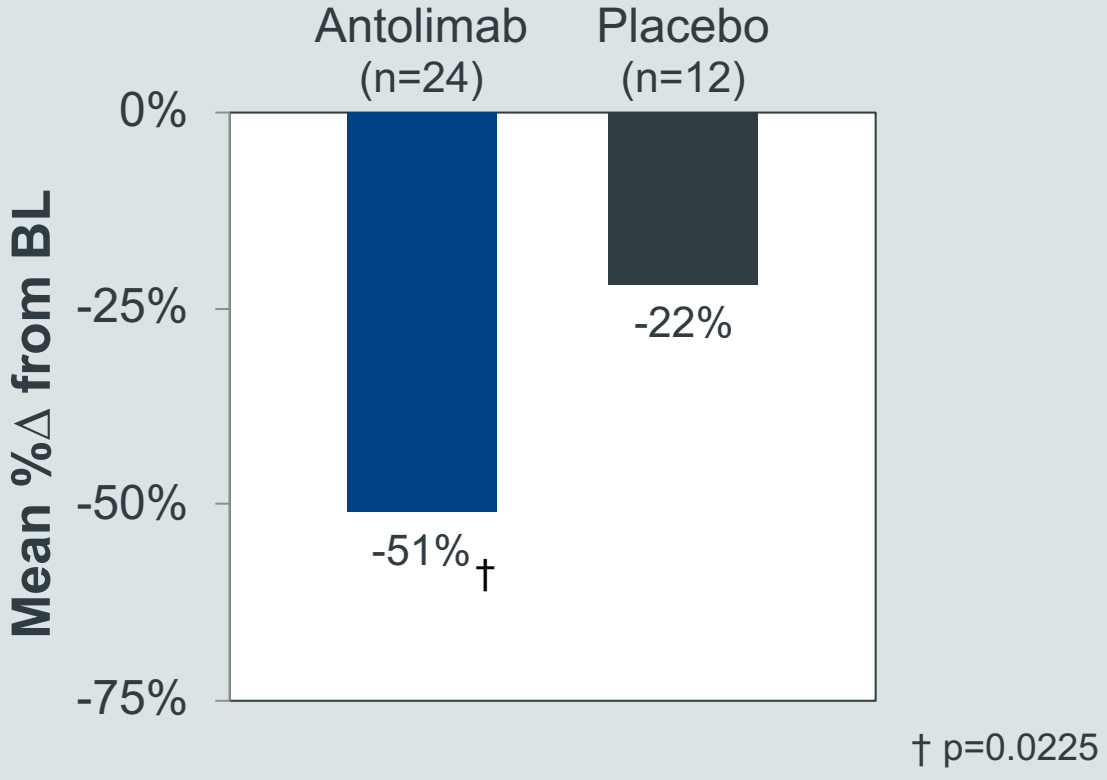
85% (55/65) of patients had duodenal eosinophilia (+/- gastric eosinophilia)

Response in Eosinophilic Gastritis (EG)[1]

Gastric Eos ≤ 4/hpf

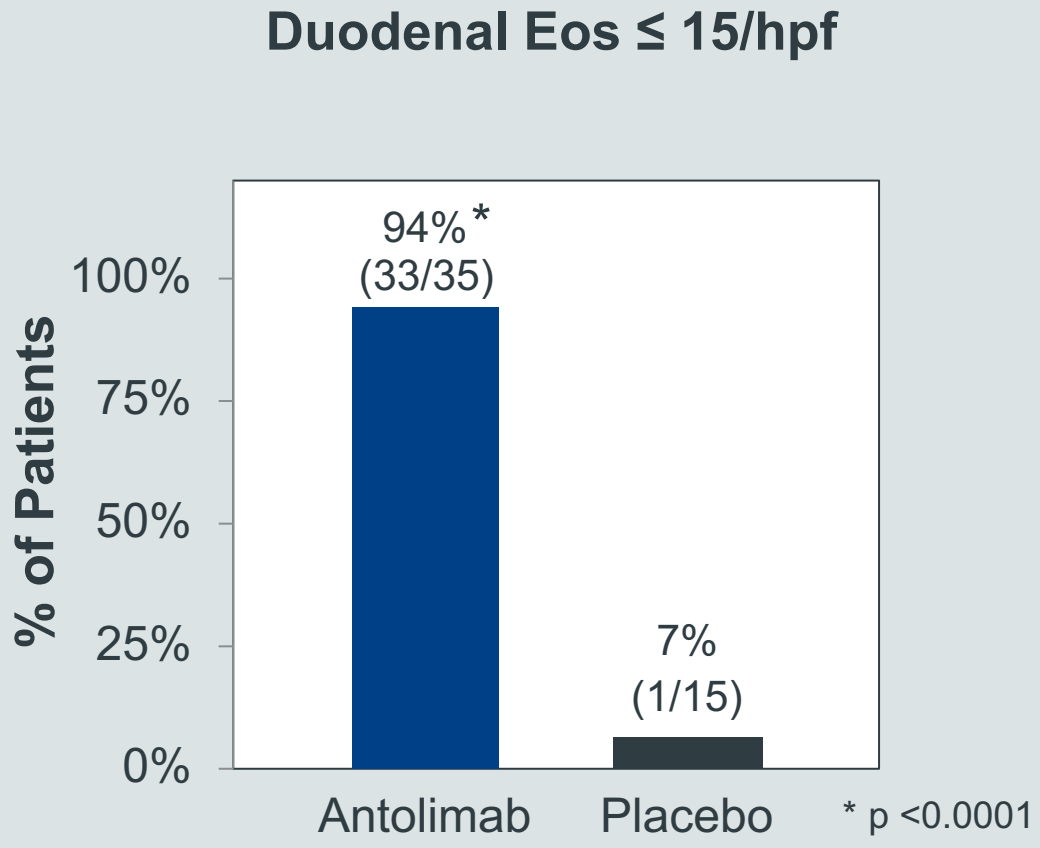


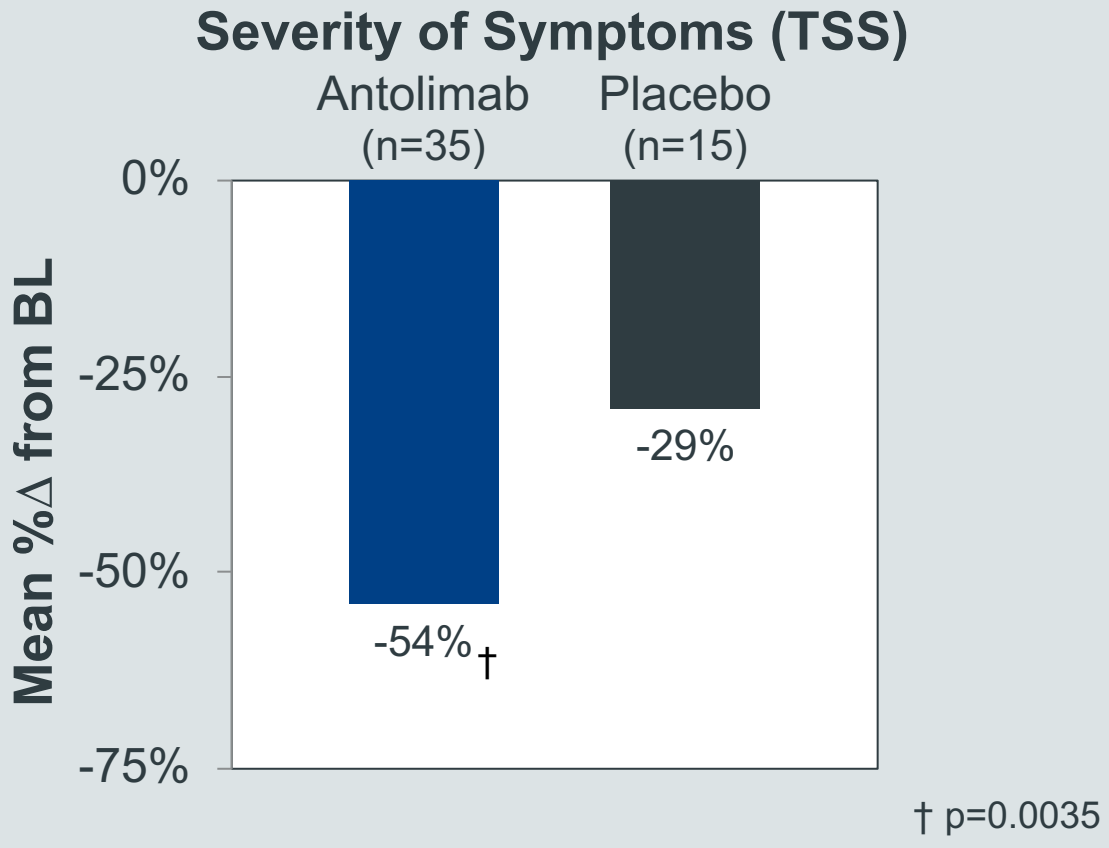
Severity of Symptoms (TSS)



1 Patients with gastric eosinophilia at baseline: ≥30 eos/hpf in 5 hpfs in the stomach

Response in Eosinophilic Duodenitis (EoD)[1]

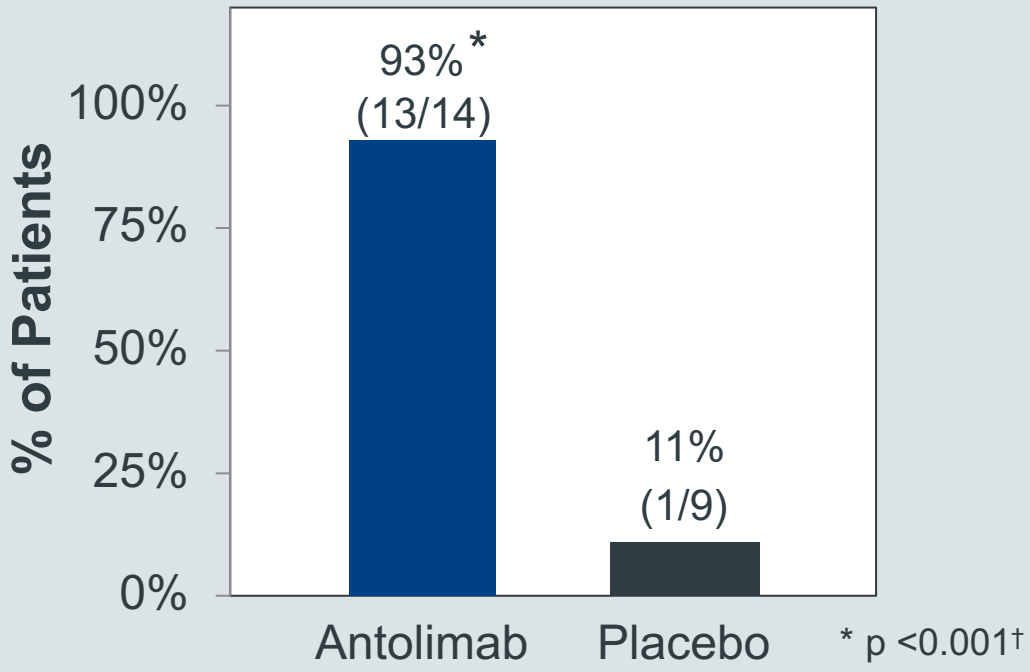




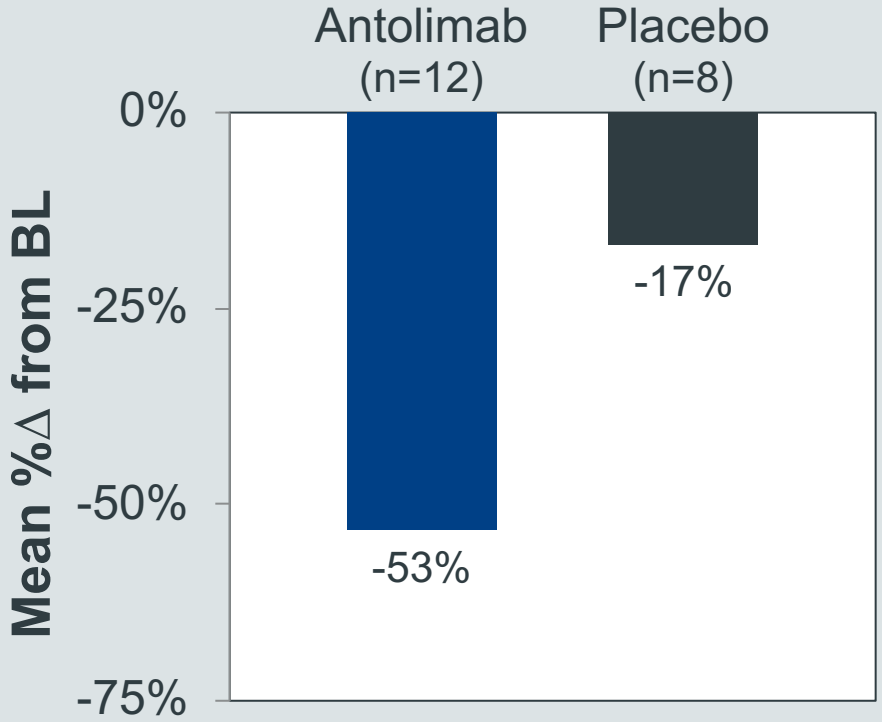
1 Patients with duodenal eosinophilia at baseline: ≥30 eos/hpf in 3 hpfs in the stomach

Exploratory: Response in Concomitant EoE[1]

Esophageal Eos ≤ 6/hpf[2]



Severity of Dysphagia[3]



1 25 patients with concomitant EoE (≥15 eos/hpf or history of EoE) and baseline dysphagia
2 Excludes patients with eos < 6/hpf at baseline. At end of treatment, 10/14 AK002 patients had 0 eos/hpf; 2/14 AK002 patients had 1 eos/hpf; 1/14 AK002 patients had 3 eos/hpf; 1/14 AK002 patients had 105 eos/hpf (biopsy occurred 6 weeks post last dose instead of 2 weeks per protocol); 1/9 placebo patients had 2 eos/hpf; 8/9 placebo patients had 19 – 200 eos/hpf
3 All EoE patients with end of treatment dysphagia scores
† p = 0.00015

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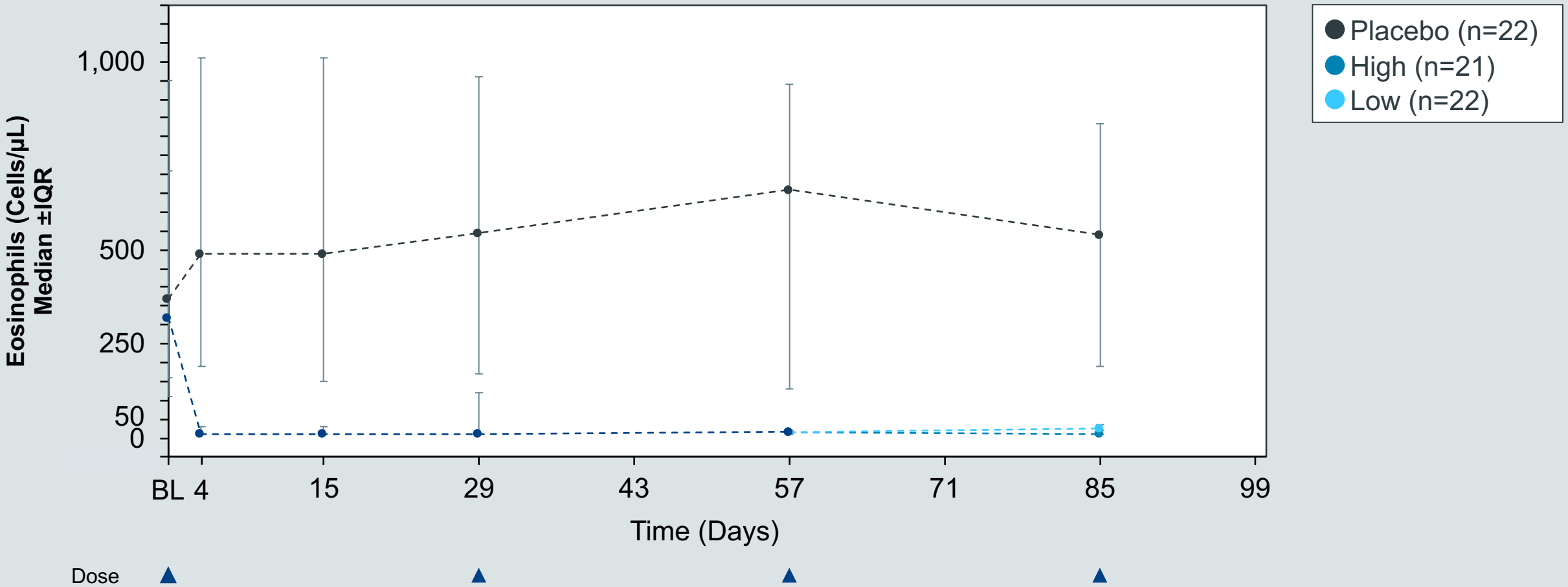
Absolute Blood Eosinophil Counts



a Blood eosinophils collected just prior to each infusion and days 4 and 15.

Safety Summary

Treatment-Emergent AEs in ≥5% of Patients

% of Patients, (n)	Antolimab (n=43)	Placebo (n=22)
Infusion related reaction	60% (26)	23% (5)
Headache	9% (4)	9% (2)
Upper respiratory tract infection	9% (4)	9% (2)
Urinary tract infection	9% (4)	5% (1)
Nausea	7% (3)	14% (3)
Fatigue	7% (3)	9% (2)
Diarrhea	5% (2)	9% (2)
Nasopharyngitis	5% (2)	9% (2)
Abdominal pain	2% (1)	9% (2)
Dehydration	2% (1)	9% (2)
Gastroenteritis viral	2% (1)	9% (2)
Pyrexia	2% (1)	9% (2)
Sinusitis	2% (1)	9% (2)
Cough	0% (0)	9% (2)
Influenza	0% (0)	9% (2)
White blood cell count increased	0% (0)	9% (2)

- Generally well tolerated
- Most common AE was mild to moderate infusion related reactions (IRR)
  - 93% mild to moderate (flushing, feeling of warmth, headache, nausea, dizziness)
  - Mostly on first infusion, greatly reduced or does not occur on subsequent infusions
  - 1 drug-related serious adverse event, an IRR which recovered within 24 hours with no further sequelae
- Treatment-emergent SAEs: 9% on AK002, 14% on Placebo
- No other significant AEs

Summary

- The ENIGMA study met all prespecified endpoints, demonstrating significant histologic and symptomatic improvement in EG and/or EoD
- Eosinophils were reduced in blood and throughout the upper gastrointestinal tract (esophagus, stomach, and duodenum)
- Generally well-tolerated
- These results build on clinical activity of antolimab (AK002) observed in chronic urticaria, severe allergic conjunctivitis, asthma, atopic dermatitis, and indolent systemic mastocytosis
- Additional antolimab studies in EGIDs:
  - 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