Long-term Treatment of Patients with Eosinophilic Gastritis and/or Eosinophilic Duodenitis with Lirentelimab, a Monoclonal Antibody Against Siglec-8

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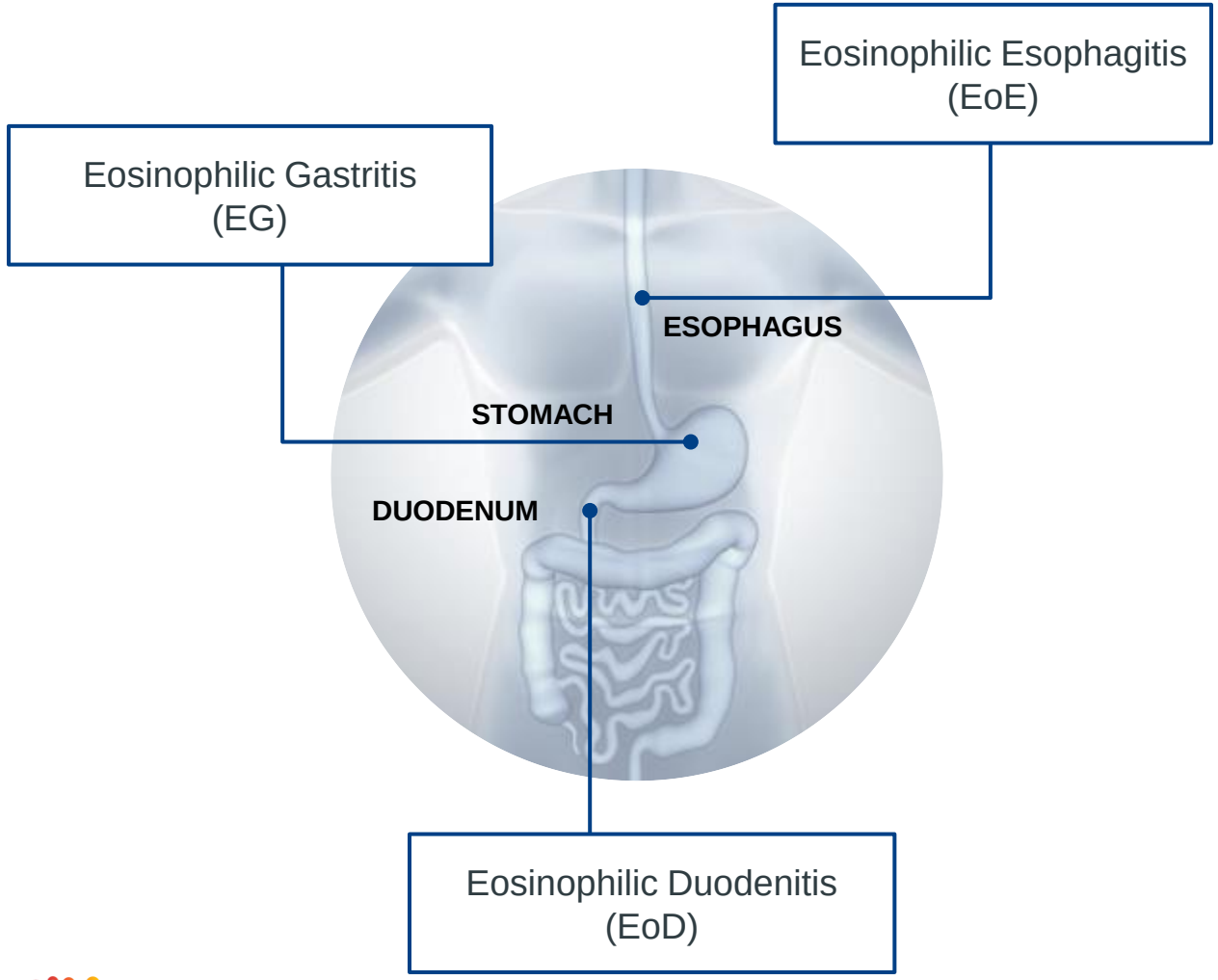
Disclosures

- Dr. Kathryn Peterson is an investigator in the ENIGMA study
- Lirentelimab is an investigational drug candidate and is not FDA/EMA approved
- This study is in progress. Data presented are current as of 3/3/2021

Eosinophilic Gastrointestinal Diseases (EGIDs)



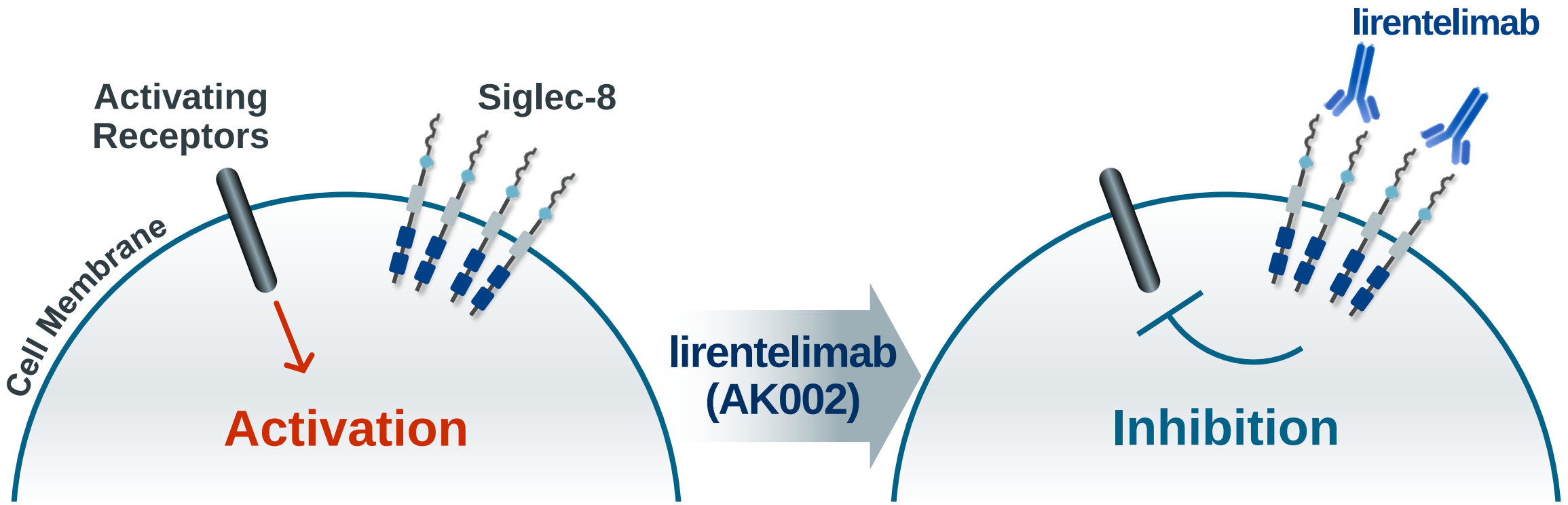
EG, EoD, EoE

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

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

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



Sources: BA Youngblood, et al. Int Arch Allergy Immunol. 2019;180(2):91-102. doi: 10.1159/000501637.
BA Youngblood, J Leung, R Falahati, et al. Discovery, Function, and Therapeutic Targeting of Siglec-8. 2021 Jan 10(1):19. doi: 10.3390/cells10010019.

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 lirentelimab
  - 22 patients 0.3, 1.0, 1.0, 1.0 mg/kg lirentelimab
  - 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		lirentelimab (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

SOURCE: Dellon ES, et al. New England Journal of Medicine. 2020;383:1624-34.

Open-Label Extension (OLE) Study Aim & Design

- **Study Aim**
  - Determine safety and efficacy of long-term use of lirentelimab for treatment of EG and/or EoD
- **Study Design**
  - Patients who completed ENIGMA had the option to receive lirentelimab in an OLE study
  - Patients enrolled in the OLE received up to 26 monthly lirentelimab infusions, administered intravenously every 28 days, titrated up to 3.0 mg/kg
  - Patients underwent an upper endoscopy with biopsy on Days 323 (week 46) and 659 (week 94) from entering ENIGMA

OLE Interim Analysis

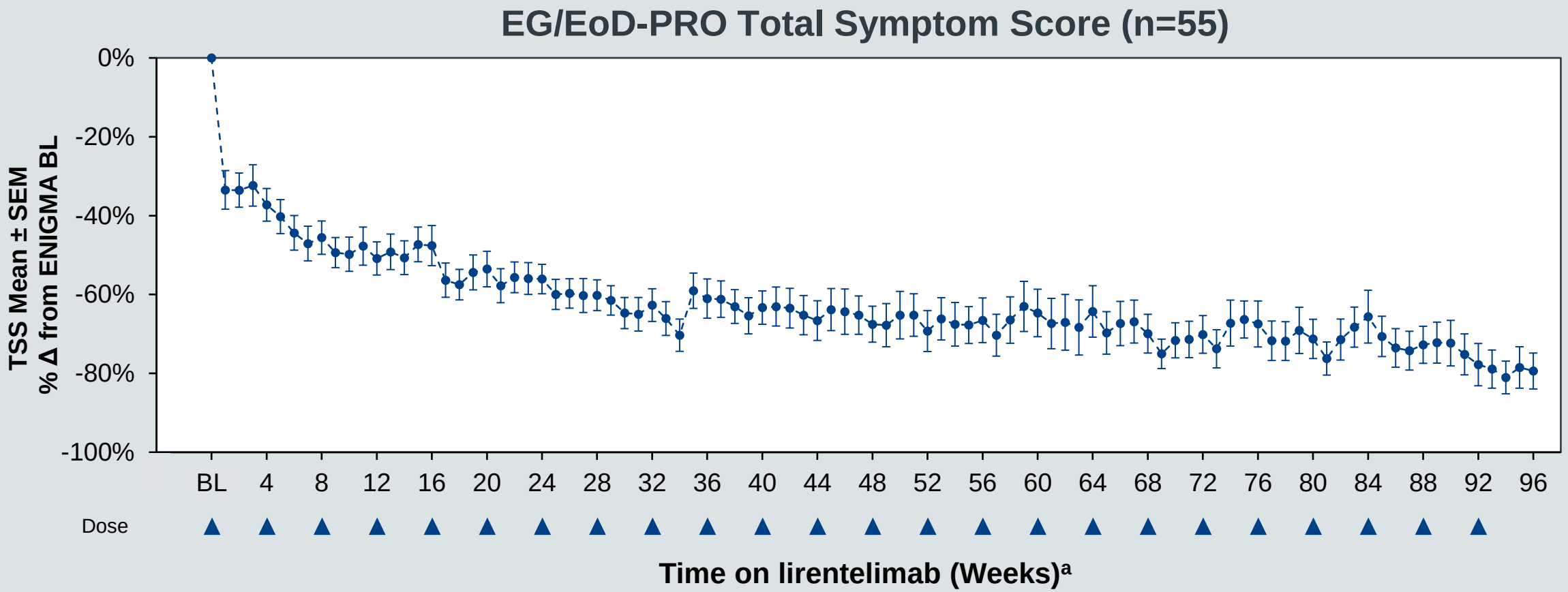
- **Patient Population**
  - 58 of 59 eligible patients entered the OLE study
  - As of 3/3/2021,
    - 34 patients ongoing
      - 26 patients have completed ≥94 weeks, average ~104 weeks
      - 8 patients with <94 weeks, average ~82 weeks
    - 24 patients no longer on treatment, average of ~49 weeks

Baseline Characteristics

Patient Characteristics		Enrolled in OLE (N=58)
Age, years 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)
% of Patients (n) with Histologic EoE[c]		36% (21)

a Gastrointestinal; Gastric (5 hpfs) or duodenum (3 hpfs) site with highest eosinophil or mast cell counts
b AEC: Absolute Eosinophil Count
c Patients with ≥15 eos in 1 esophageal hpf

Substantial Symptom Improvement Over Time



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

Change in Symptoms Over Time

Total lirentelimab Exposure (Weeks)[a]	TSS Mean Change from ENIGMA BL		
	Baseline	Absolute	Percent
13-14 (n=55)	32	-15	-51%
51-52 (n=38)	34	-22	-66%
93-94 (n=25)	35	-26	-75%

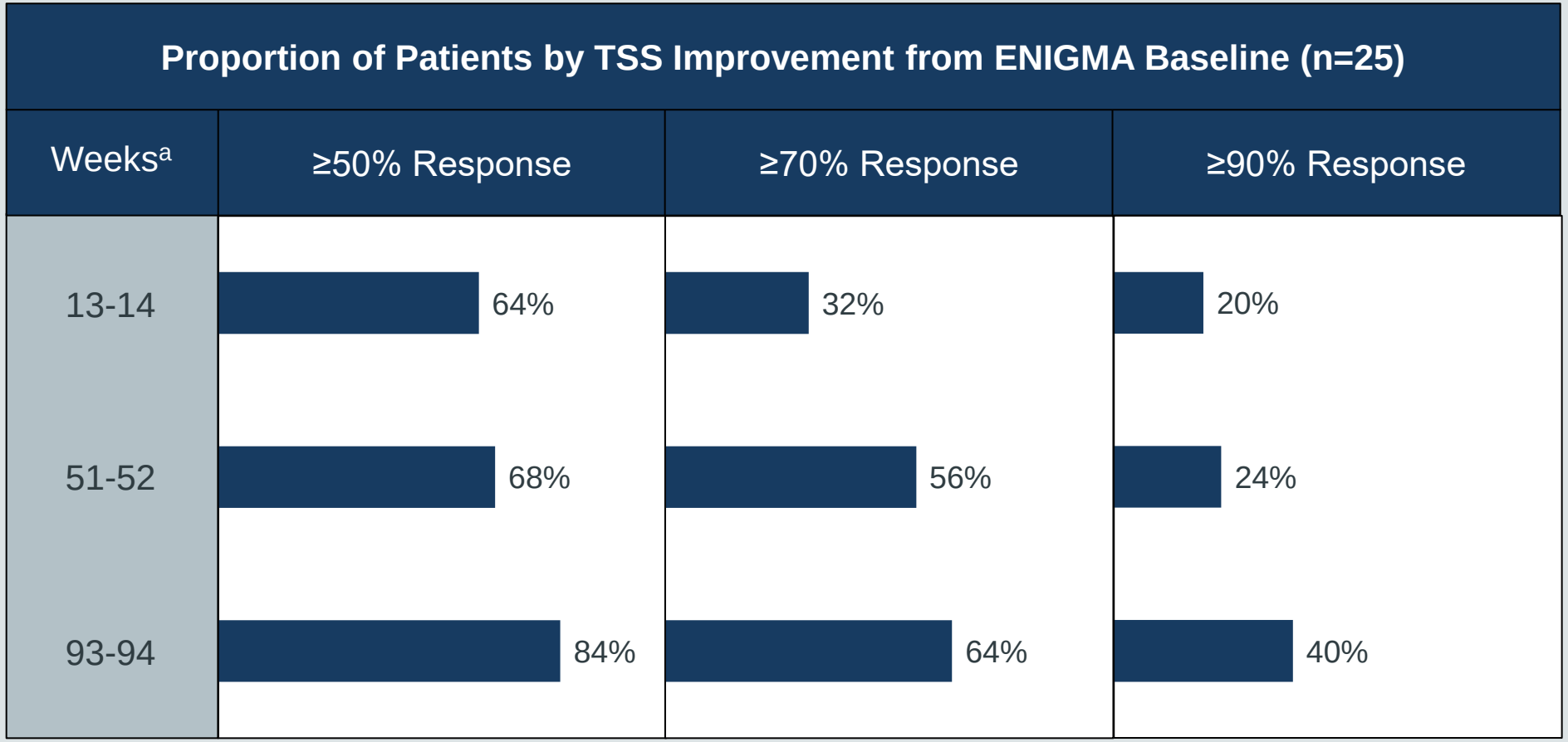
a Total lirentelimab exposure, inclusive of lirentelimab exposure during the Phase 2 ENIGMA study

Change in Symptom Response Rate Over Time

Total lirentelimab 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)
51-52 (n=38)	**74%** (28/38)	**55%** (21/38)	**18%** (7/38)
93-94 (n=25)	**84%** (21/25)	**64%** (16/25)	**40%** (10/25)

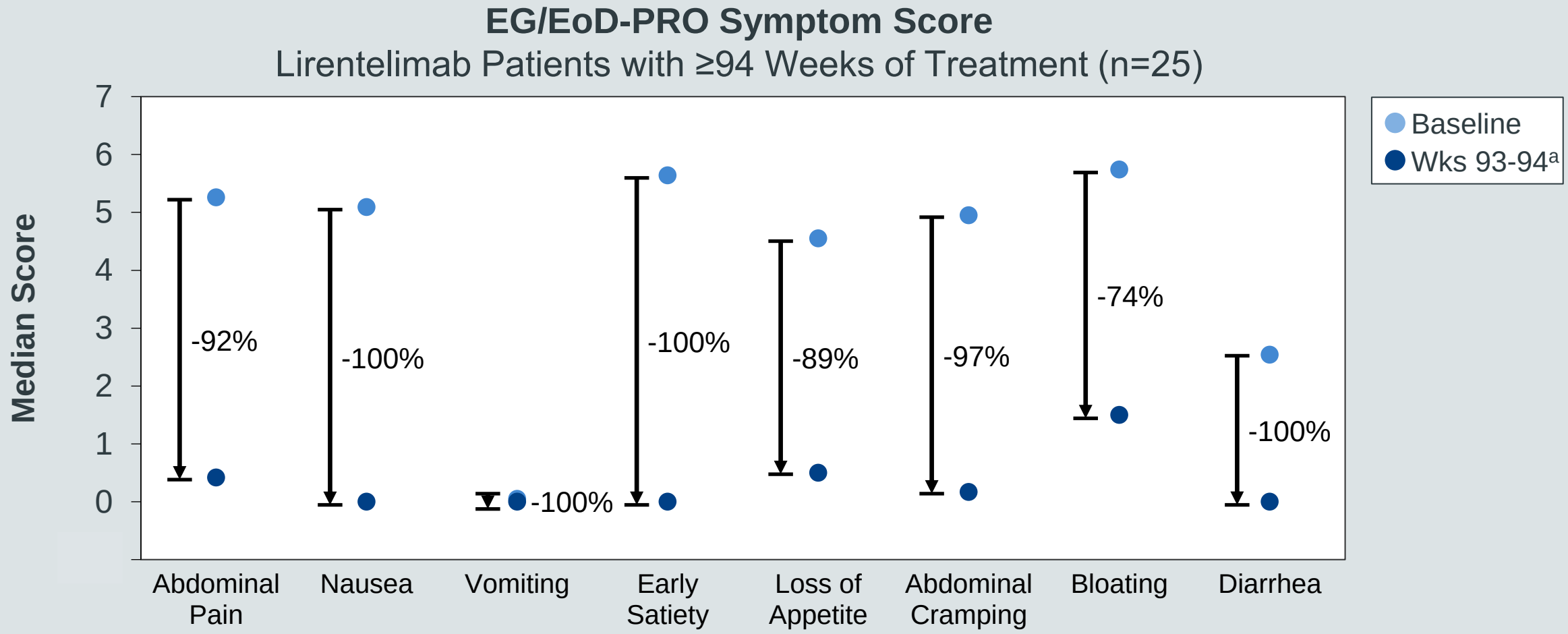
a Total lirentelimab exposure, inclusive of lirentelimab exposure during the Phase 2 ENIGMA study

Symptom Response Rate in Patients with ≥94 Weeks of Lirentelimab Treatment



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

Improvement Across All Symptoms

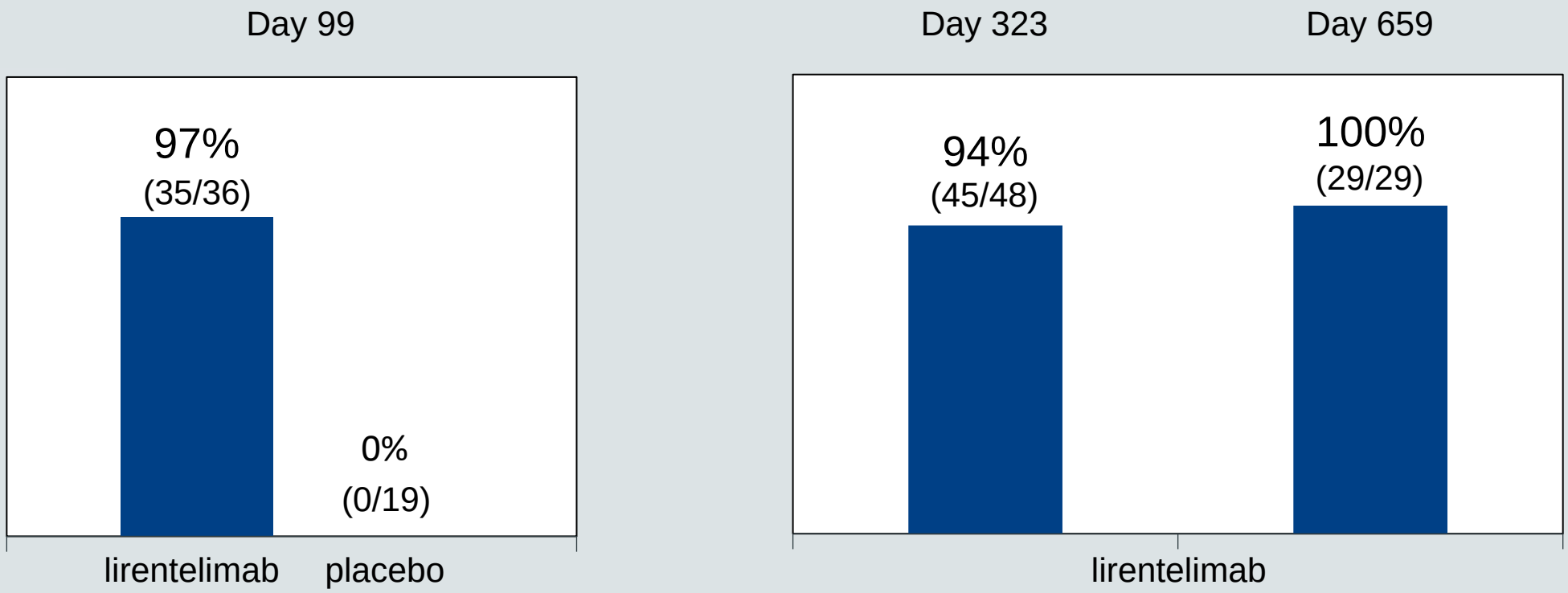


a Total lirentelimab exposure, inclusive of lirentelimab exposure during the Phase 2 ENIGMA study.

Sustained Histologic Remission on Lirentelimab

Proportion of Patients Meeting Histologic Remission Criteria

Eosinophils ≤4/hpf (Stomach) and/or ≤15/hpf (Duodenum)[a]



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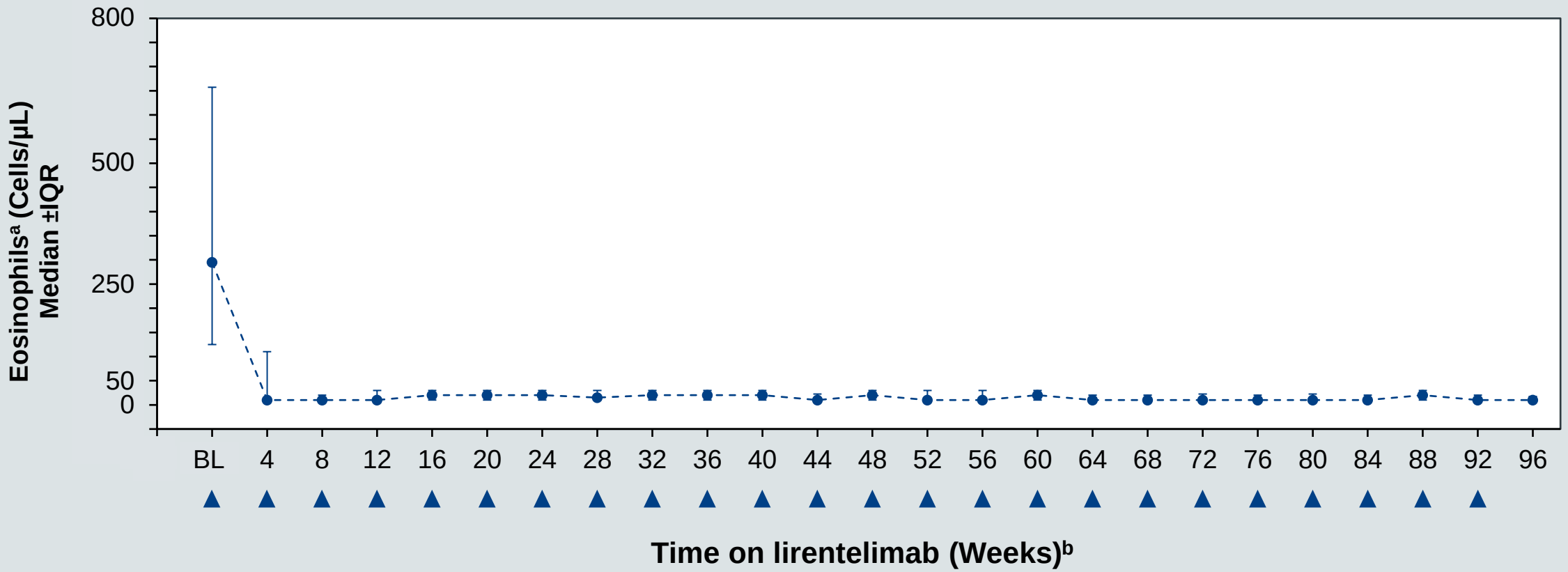
a Only patients enrolled in OLE displayed at day 99. 37/39 (95%) lirentelimab patients and 3/20 (15%) placebo patients met histologic remission criteria (predefined as <30 eos/hpf.) at the end of ENGIMA; SOURCE: Dellon ES, et al. New England Journal of Medicine. 2020;383:1624-34.

Sustained Depletion of Blood Eosinophils



a Blood eosinophils collected just prior to each infusion
b Total lirentelimab exposure, inclusive of lirentelimab 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	33% (19)
Headache	16% (9)
Nasopharyngitis	16% (9)
Nausea	12% (7)
Anxiety	10% (6)
Blood creatine phosphokinase increased	10% (6)
Diarrhea	10% (6)
Influenza	10% (6)
Rash	9% (5)
Sinusitis	9% (5)
Urinary tract infection	9% (5)
Anemia	7% (4)
Fatigue	7% (4)
Hypertension	7% (4)
Neutrophilia	7% (4)
Oropharyngeal pain	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 (prior to prednisone pre-treatment protocol)
- No drug-related serious AEs in OLE

Summary

- Long-term treatment with lirentelimab results in sustained histologic & symptomatic improvements in patients with EG and/or EoD with or without histologic EoE through week 94
  - Sustained response of blood and tissue eosinophil depletion
  - Symptomatic responses improved with increased duration of treatment
- Long-term treatment with lirentelimab was generally well-tolerated
- Additional lirentelimab studies:
  - Phase 3 randomized trial in EG and/or EoD (NCT04322604)
  - Phase 2/3 randomized trial in EoE (NCT04322708)

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