# Safety and Efficacy of Long-Term Treatment With Lirentelimab, a Monoclonal Antibody Against Siglec-8, in Patients With Eosinophilic Gastritis/Duodenitis

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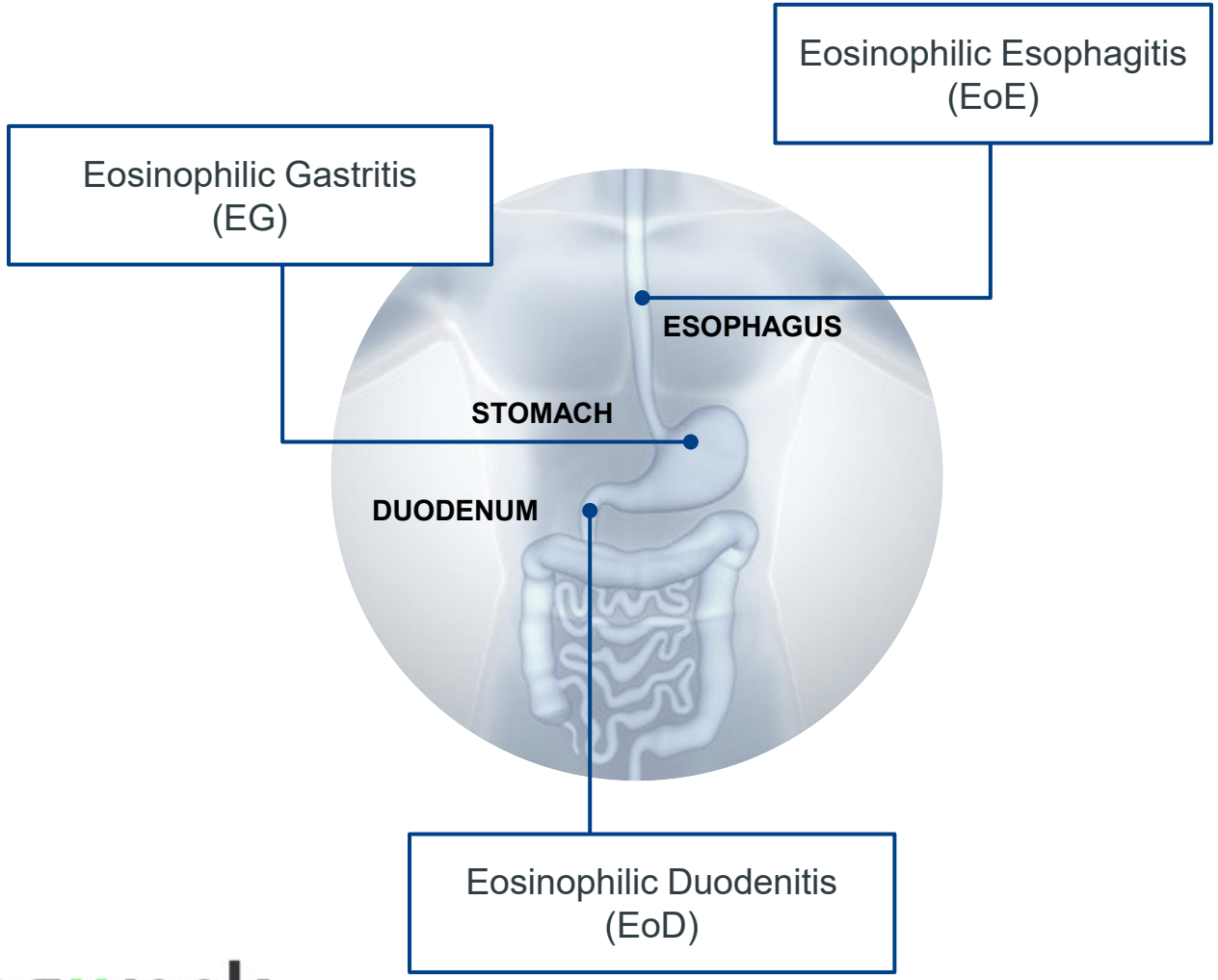
# Disclosures

- Dr. Evan S. Dellon 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 7/7/2021

# Eosinophilic Gastrointestinal Diseases (EGIDs)




## EG, EoD, EoE

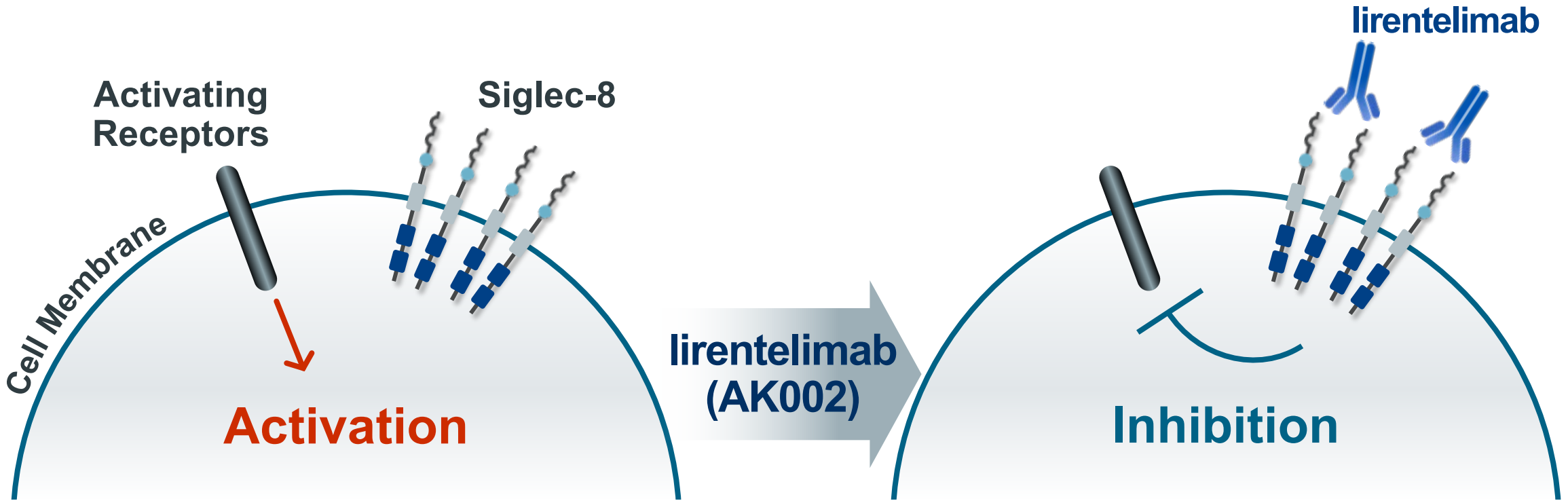
**Chronic Eosinophilic Inflammation of the Stomach, Duodenum, or Esophagus**

- 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

- ENIGMA was a phase 2 multi-center, randomized, double-blind, placebo-controlled study of lirentelimab in 65 patients with EG and/or EoD
  - Active moderate to severe symptoms (average weekly score over ≥2 weeks of ≥3 for either abdominal pain, diarrhea and/or nausea) using the daily 8 symptom EG/EoD-SQ© Questionnaire
  - Biopsy confirmed EG and/or EoD: ≥30 eos/hpf in 5 stomach hpfs and/or 3 duodenum hpfs
- Lirentelimab met the primary & secondary endpoints, and was well tolerated
- Results from ENIGMA are available in the New England Journal of Medicine



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 lirentelimab treatment for 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

# Baseline Characteristics

| Patient Characteristics[a] | | Enrolled in OLE (N=58) |
|---|---|---|
| Age, years Mean (Range) | | 41 (18-74) |
| Female | | 60% |
| White | | 93% |
| GI[b] Eosinophils/hpf, Mean (Range) | | 74 (33-201) |
| GI[b] Mast Cells/hpf, Mean (Range) | | 60 (20-114) |
| Total Symptom Score [0-80], Mean (Range) | | 32 (6-61) |
| % of Patients (n) by AEC[c]/μL | <500 | 69% (40) |
| | ≥500 | 31% (18) |
| % of Patients (n) with Histologic EoE[d] | | 36% (21) |

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

# OLE Interim Analysis Population

58 of 59 eligible patients entered the OLE study; as of 7/7/21

- 29 patients ongoing
  - 27 patients have completed ≥94 weeks, average ~117 weeks
  - 2 patients with <94 weeks, average ~87 weeks
- 29 patients no longer on treatment, average of ~58 weeks
  - 8 patients completed the study
  - 21 patients discontinued

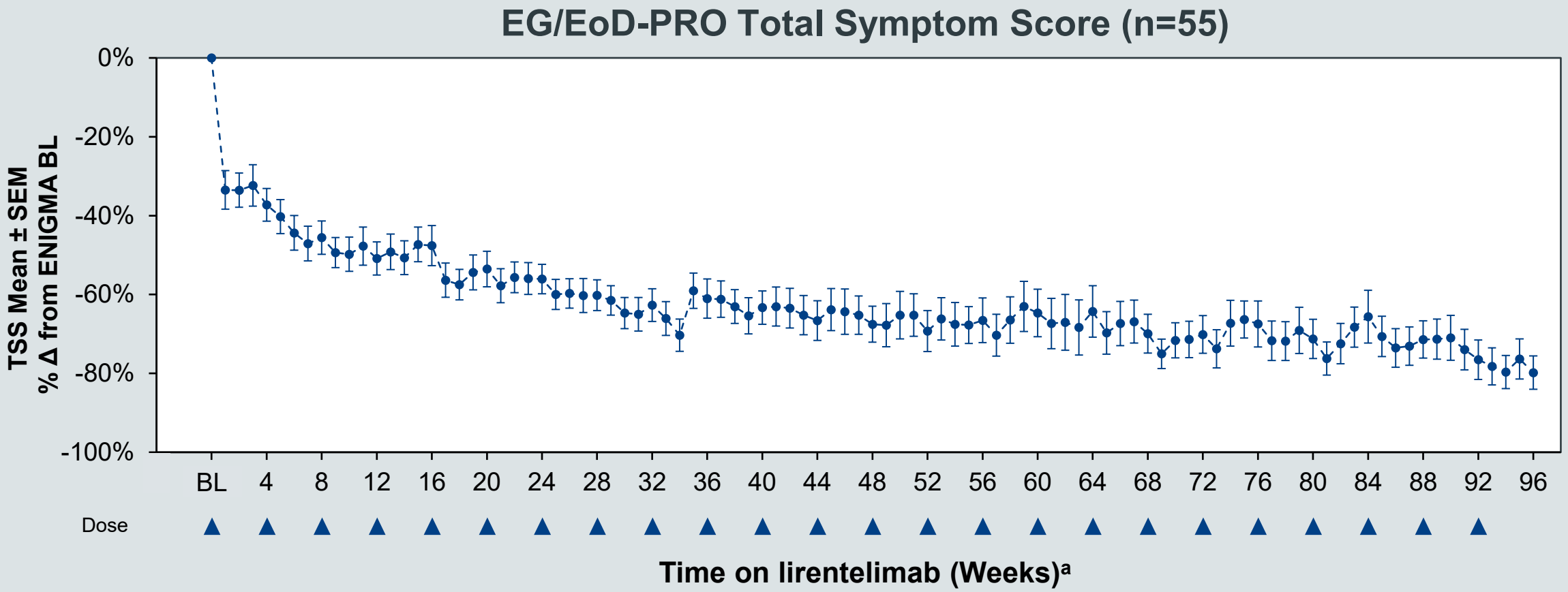
# Reasons for Withdrawal

| Reasons for Withdrawal | Discontinued Patients (n=21) |
|---|---|
| Personal Reasons | 15 |
| Adverse Event* | 3 |
| Study non-compliance | 2 |
| Lost to follow-up | 1 |



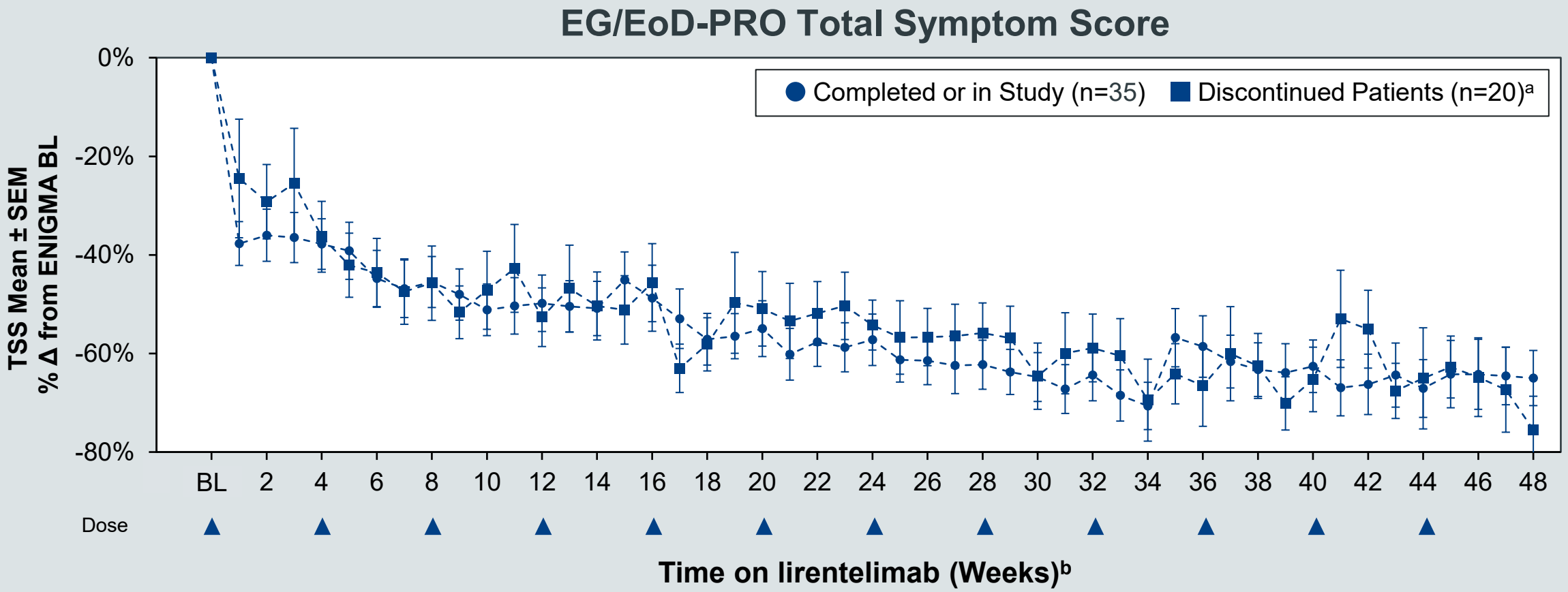
* None considered related to study drug

# Substantial Symptom Improvement Over Time




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

# Similar Responses in Discontinued Patients




a Data shown from timepoints with responses from ≥5 patients
b Total lirentelimab exposure, inclusive of 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=31) | 35 | -26 | -75% |



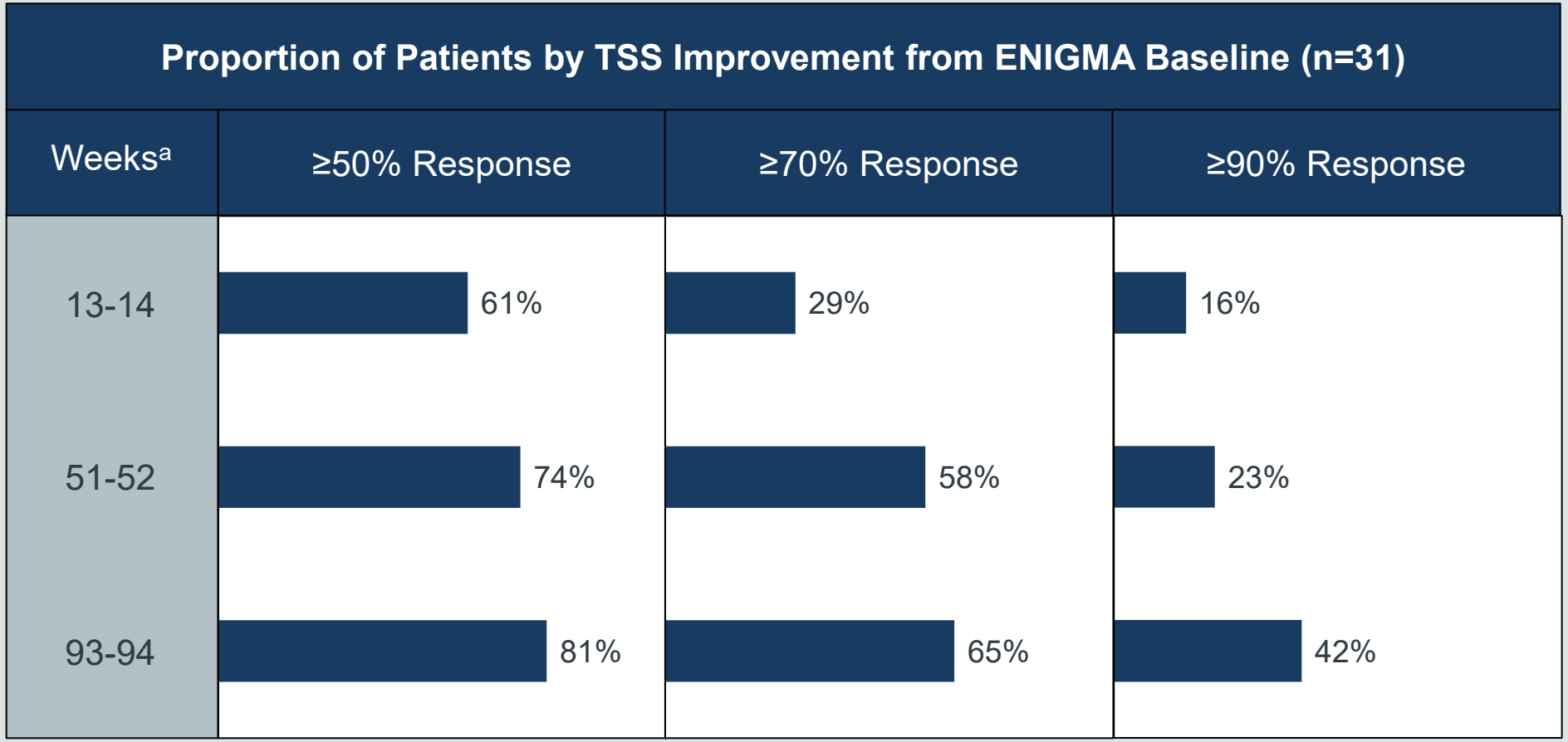
a Total lirentelimab exposure, inclusive of the Phase 2 ENIGMA study

# 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=31) | **81%** (25/31) | **65%** (20/31) | **42%** (13/31) |

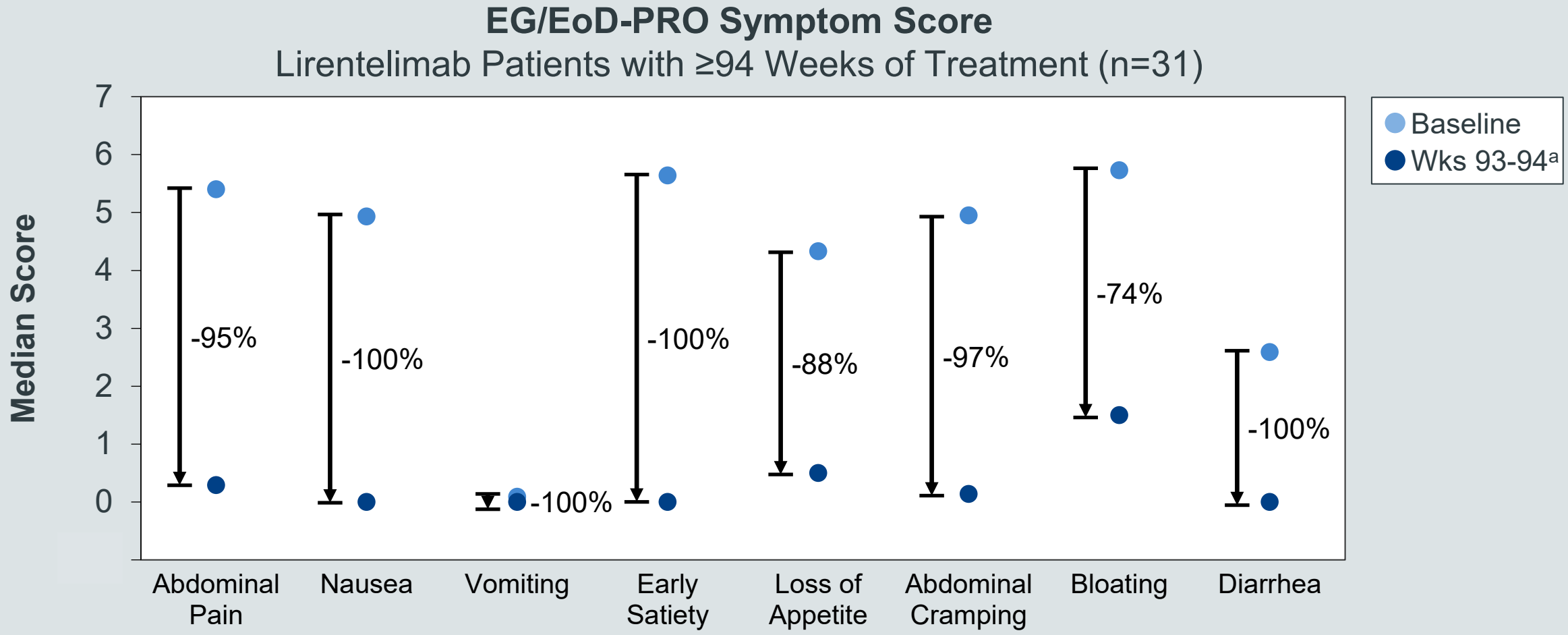
a Total lirentelimab exposure, inclusive of the Phase 2 ENIGMA study

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




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

# Improvement Across All Symptoms

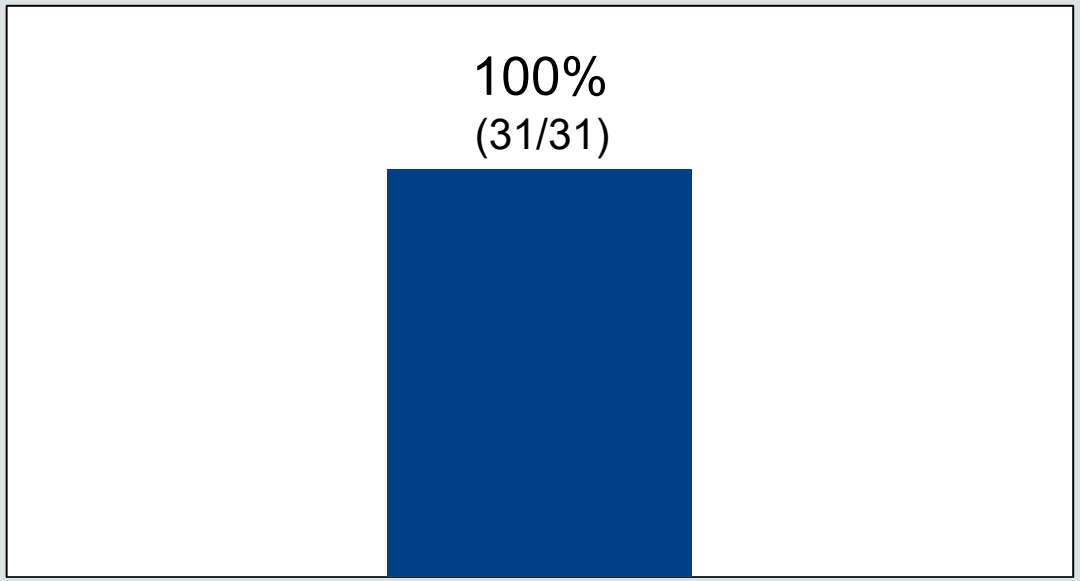



a Total lirentelimab exposure, inclusive of the Phase 2 ENIGMA study

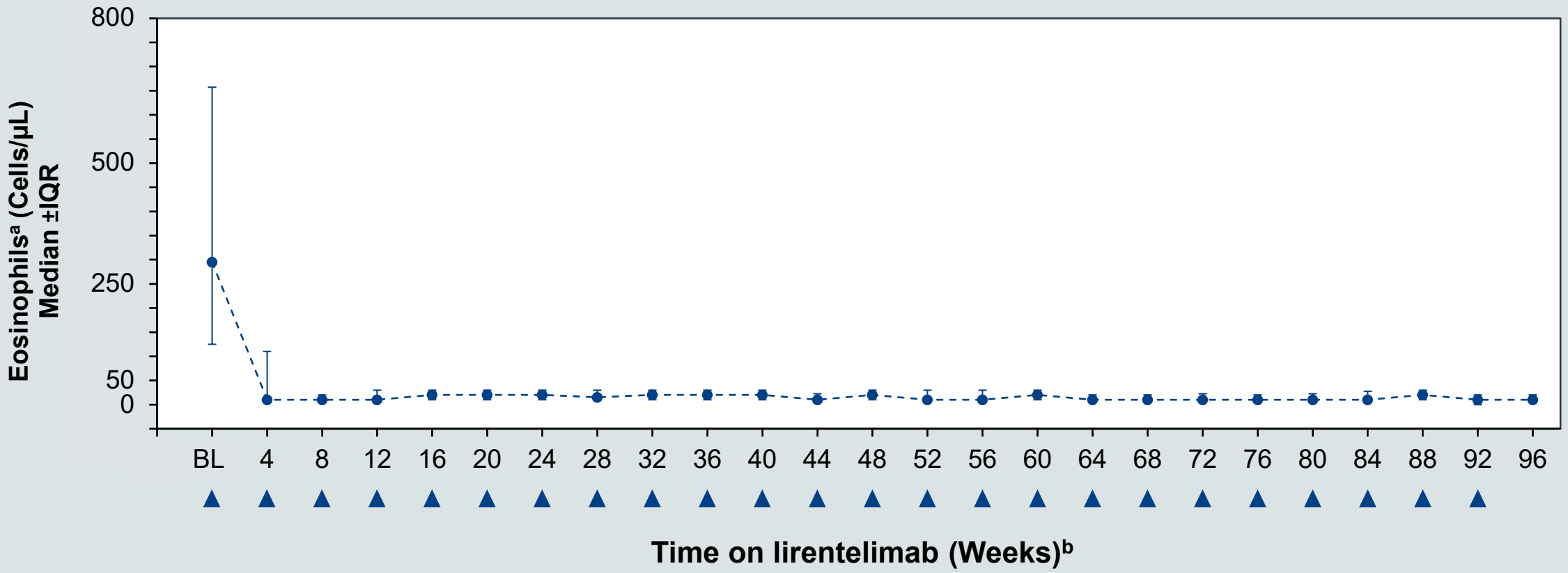
# Histologic Remission Maintained

**Proportion of Patients Meeting Histologic Remission Criteria**

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



# Sustained Depletion of Blood Eosinophils




a Blood eosinophils collected just prior to each infusion
b Total lirentelimab exposure, inclusive the Phase 2 ENIGMA study

# OLE Safety Summary

**Treatment-Emergent AEs in >5% of Patients**

| % of Patients, (n) | Total (n=58) |
|---|---|
| Infusion related reaction | 34% (20) |
| Nasopharyngitis | 17% (10) |
| Headache | 16% (9) |
| Nausea | 12% (7) |
| Rash | 10% (6) |
| Influenza | 10% (6) |
| Diarrhea | 10% (6) |
| Anxiety | 10% (6) |
| Blood creatine phosphokinase increased | 10% (6) |
| Sinusitis | 9% (5) |
| Fatigue | 9% (5) |
| Vomiting | 9% (5) |
| Anemia | 9% (5) |
| Urinary tract infection | 9% (5) |
| Abdominal pain | 7% (4) |
| Neutrophilia | 7% (4) |
| Hypertension | 7% (4) |
| Oropharyngeal pain | 7% (4) |
| Chest pain | 7% (4) |

- Generally well-tolerated
- Most common adverse event was mild to moderate infusion-related reactions (IRRs)[a]; mostly occurred on first infusion, greatly reduced or did not occur on subsequent infusions
- No drug-related serious AEs in OLE
- No other significant adverse events



a Symptoms included flushing, feeling of warmth, headache, nausea, and/or dizziness

# Summary

- Long-term treatment with lirentelimab results in sustained histologic & symptomatic improvements in patients with EG and/or EoD 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