Lirentelimab, A Monoclonal Antibody Against Siglec-8, Depletes Blood and Tissue Eosinophils in Patients With Allergic or Inflammatory Diseases

Marc E. Rothenberg MD PhD[1], Marcus Maurer MD[2], Frank Siebenhaar MD[2], Stephen D. Anesi MD[3], Sabine Altrichter MD[2], Evan S. Dellon MD MPH[4], Bhupinder Singh MD[5], Cory Mekelburg[5], Bradford A. Youngblood PhD[5], Henrik S. Rasmussen MD PhD[5]

[1]University of Cincinnati College of Medicine, Cincinnati, OH; [2]Dermatologial Allergology, Allergie-Centrum-Charité, Charité - Universitätsmedizin Berlin, Germany; [3]Massachusetts Eye Research & Surgery Institution, Waltham, MA; [4]University of North Carolina, Chapel Hill, NC; [5]Allakos, Inc, Redwood City, CA

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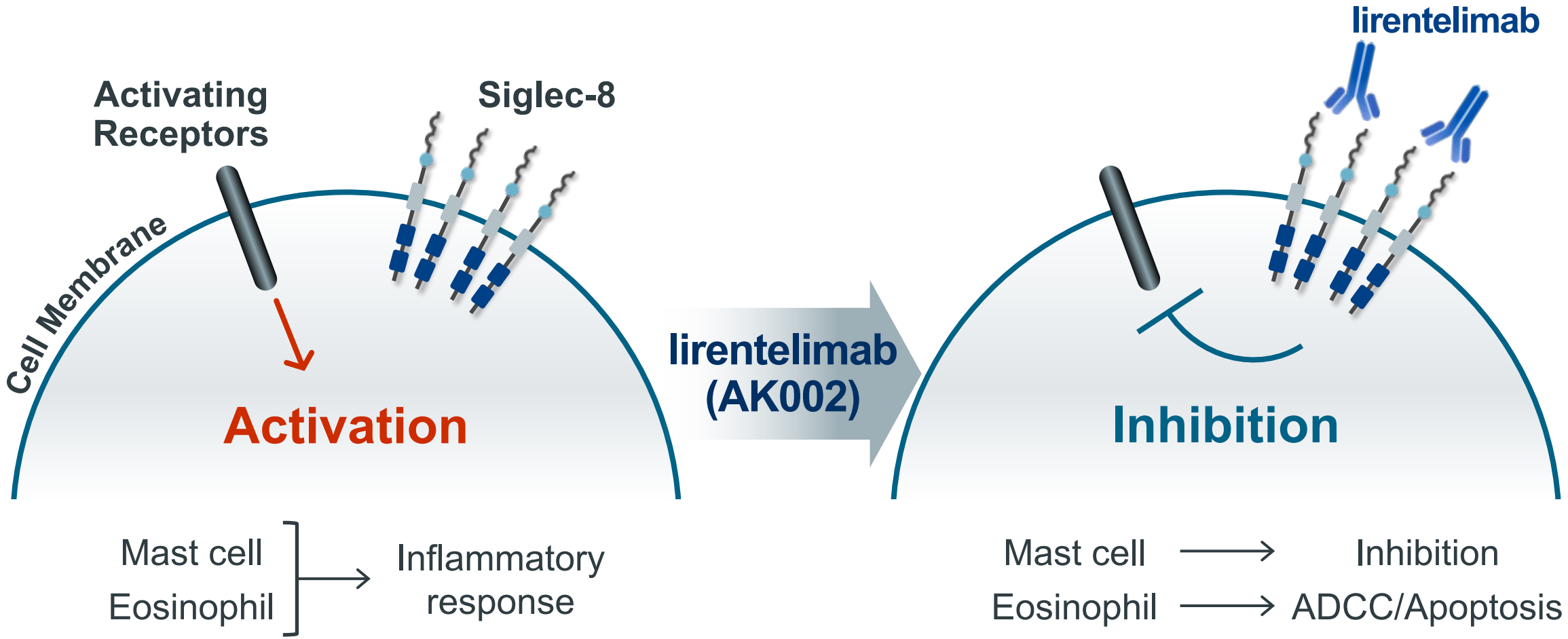
Disclosures

- Dr. Marc E. Rothenberg is an investigator in the ENIGMA study
- Lirentelimab is an investigational medicine and is not FDA/EMA approved
- ENIGMA open-label extension is in progress. Data presented are current as of 7/7/2021

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



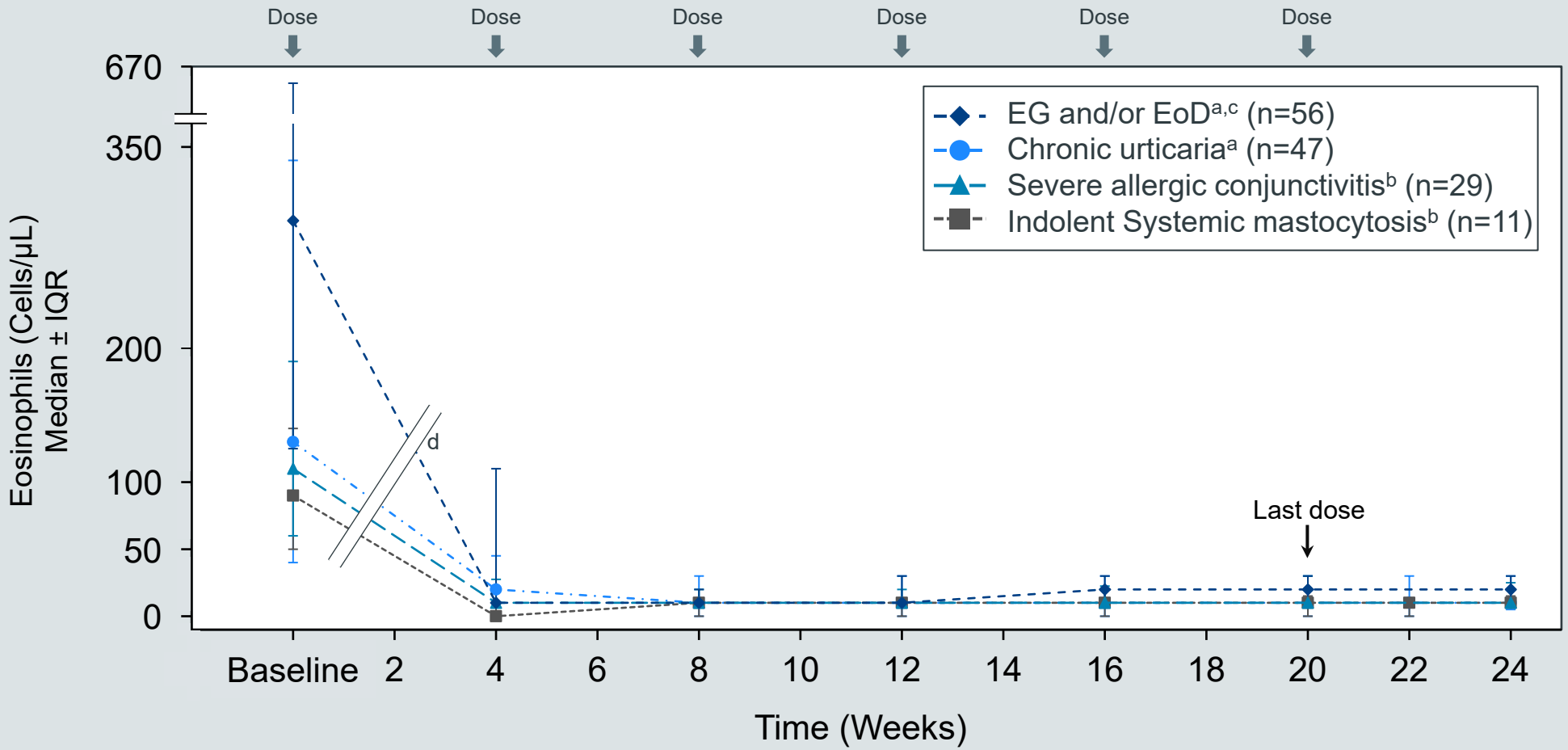
Sources: BA Youngblood, et al. Int Arch Allergy Immunol. 2019;180(2):91-102. doi: 10.1159/000501637.
BA Youngblood, J Leung, R Falahati, et al. Discovery, Function, and Therapeutic Targeting of Siglec-8. 2021 Jan 10(1):19. doi: 10.3390/cells10010019.

Summary of Lirentelimab Clinical Studies Design

	EG and/or EoD[a,b]	Chronic Urticaria[c]	Allergic Conjunctivitis[d]	Indolent Systemic Mastocytosis[e]
Patients	58	47	30	12
Monthly Dosing	• Randomized: 4 (0.3 – 3 mg/kg) • OLE: Up to 20 (0.3 – 3 mg/kg)	6 (0.3 – 3 mg/kg)	6 (0.3 – 3 mg/kg)	6 (1 – 6 mg/kg)
Endpoints	Primary • Change in GI tissue eos from baseline to day 99 (week 16); randomized vs. placebo Secondary • Treatment response (reduction in tissue eos and TSS)[f] • Symptom improvement (Mean% reduction in TSS)[g]	Primary[h] • Change in UCT @ week 22 vs baseline Secondary[i] • Change in UAS7 • Safety	Primary • Safety and tolerability Secondary • Symptom improvement: a) Patient reported (ACS)[j] b) Investigator reported (OSS)[k]	Primary • Safety and tolerability Secondary • Change in: a) Symptoms (MSQ)[l] b) Activity (MAS)[m] c) QoL (MC-QoL)[n]
Blood Sampling	Baseline and just prior to infusion	Baseline and just prior to infusion	Baseline and 1 day prior to infusion	Baseline and 1 day prior to infusion
Tissue (Biopsy)	OLE: Baseline, day 99, 323, and 659	Not collected	Not collected	Not collected

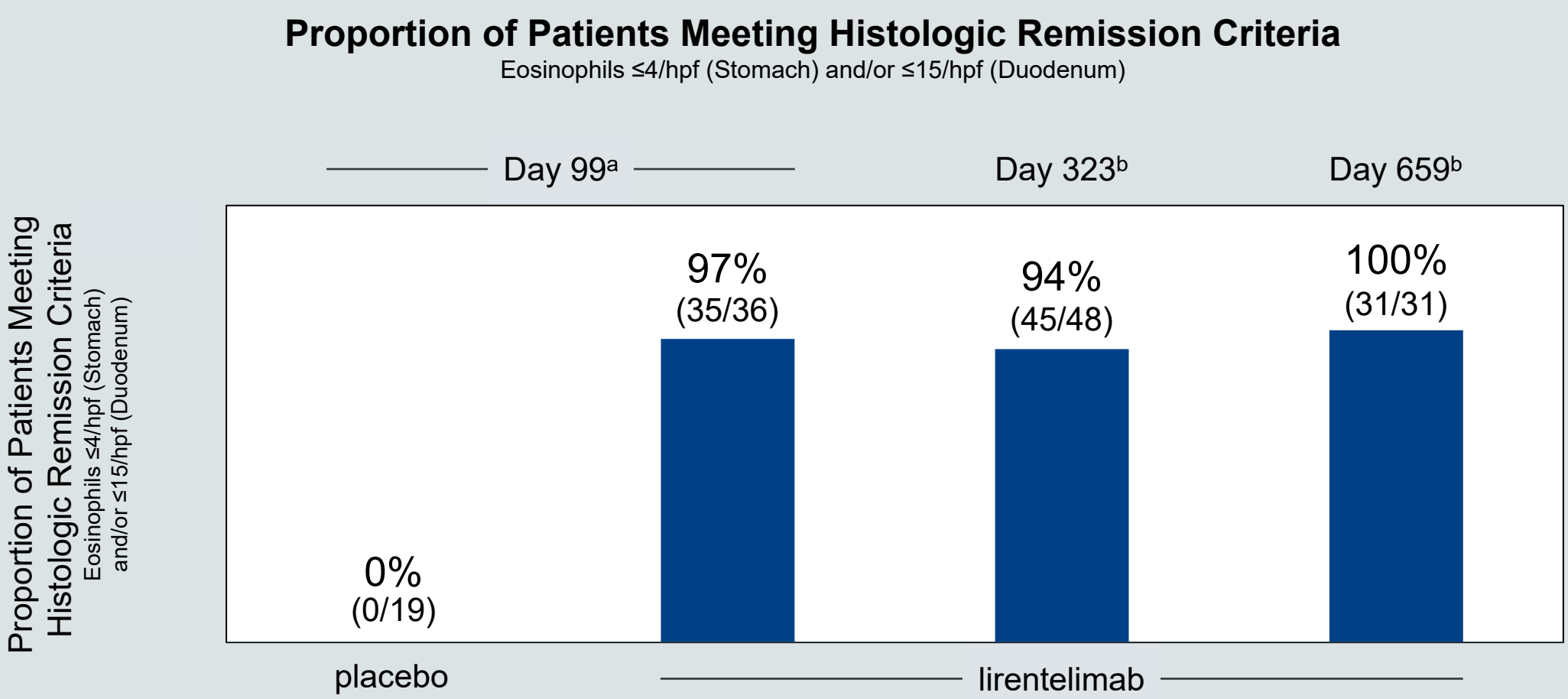
[a] EG and/or EoD, ENIGMA Phase 2 ClinicalTrials.gov #NCT03496571; b Dellon ES., et al. Siglec-8 Antibody for Eosinophilic Gastritis and Duodenitis. NEJM. 2020 Oct 22;383(17):1624-1634
[c] Chronic urticaria, CURSIG Phase 2a ClinicalTrials.gov # NCT03436797
[d] Severe allergic conjunctivitis, KRONOS Phase 1b ClinicalTirals.gov # NCT03379311
[e] Indolent systemic mastocytosis, ASIGMA Phase 1 Clinical Trials.gov # NCT02808793
[f] Treatment response defined as >75% reduction in tissue eosinophil counts AND >30% reduction in symptoms from baseline to 2 weeks post-last dose; [g] TSS, total symptom score;
[h] UTC, urticaria control test; [i] UAS7, Patient-reported urticaria activity scores (for patients with chronic CU); [j] ACS, Patient-reported allergic conjunctivitis symptom questionnaire;
[k] OSS, monthly investigator-assessed ocular symptom scores; [l] MSQ, mastocytosis symptom questionnaire; [m] MAS, mastocytosis activity score; [n] MC-QoL, mastocytosis quality of life

Sustained Depletion of Blood Eosinophils



a. Blood eosinophils collected just prior to each infusion.
b. Blood eosinophils collected 1-day prior to infusion
c. Total lirentelimab exposure, inclusive the Phase 2 ENIGMA study
d. Depletion of eosinophils is not linear and occurs more rapidly than depicted; slope reflects baseline and next monthly infusion visit

Sustained Depletion of Eosinophils in Gastric and Duodenal Tissues From Patients With EG and/or EoD



a Only patients enrolled in ENIGMA 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.

b Day 323 and 659 biopsy collected from patients in the OLE; by day 659 29 patients were no longer in treatment in the OLE (8 completed the study and 21 patients discontinued [n=15 due to personal reasons, n=3 due to AEs not related to study drug, n=2 due to study non-compliance, and n=1 lost to follow-up])

Summary

- Lirentelimab depleted blood eosinophils in 4 separate studies of patients with allergic or inflammatory diseases through 24 weeks
- In patients with EG/EoD, monthly dosing of lirentelimab maintained complete or almost complete depletion of blood and tissue eosinophils through 94 weeks
- Additional ongoing 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 these studies, the investigators, and all study staff