Lirentelimab Reduces Levels of Inflammatory Cytokines in Tear Fluid From Patients With Allergic Conjunctivitis

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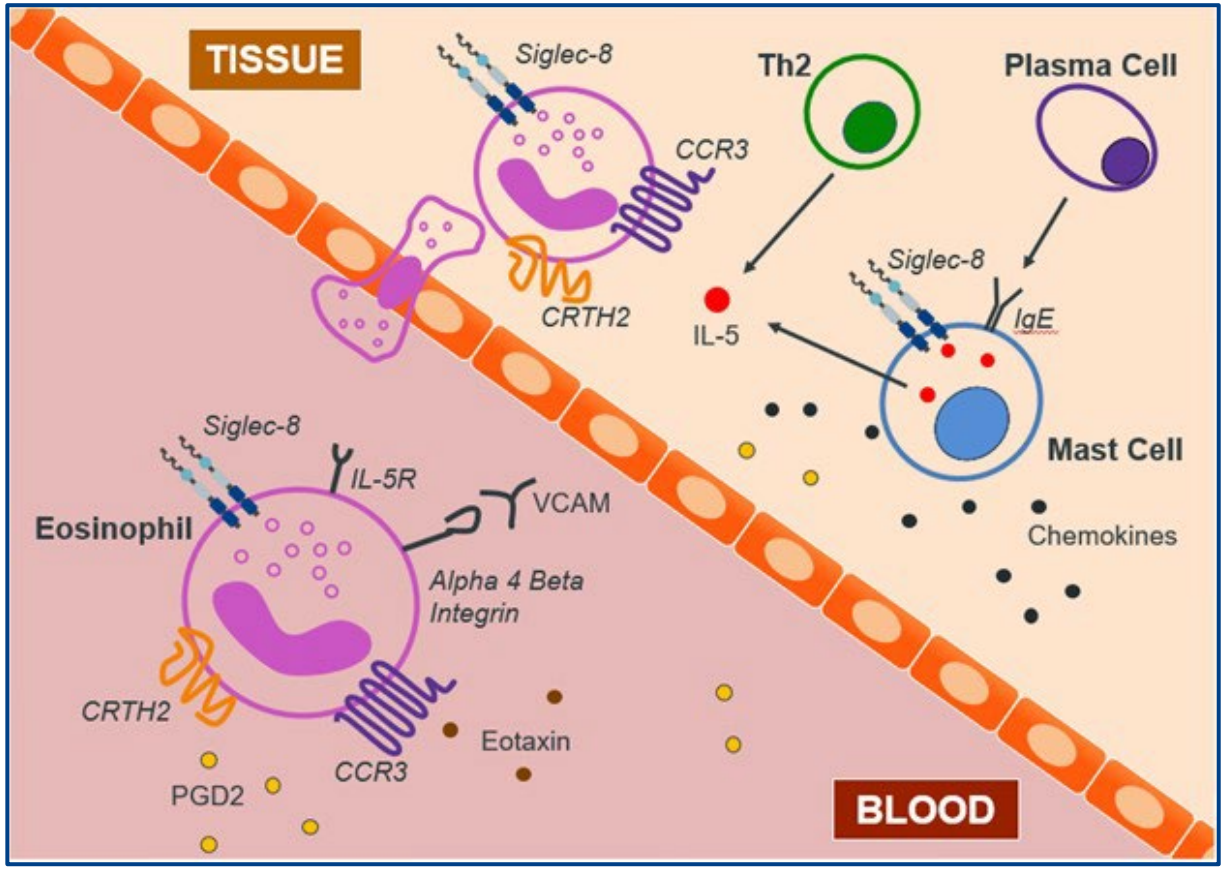
Disclosures

- Lirentelimab is an investigational drug candidate and is not FDA/EMA approved
- This study was funded by Allakos Inc.
  - University of Tennessee Health Science Center received funding from Allakos Inc. to perform the tear cytokine data analysis
- Final study publication is now available online at JACI (Anesi et al. 2022; in press)

Siglec-8 in Allergic Diseases

- Siglecs (Sialic acid-binding immunoglobulins) are glycan proteins on surface of immune cells
  - Involved in **inhibitory** cell signaling (negative regulation)
- Siglec-8 is expressed on mast cells and eosinophils



1. BA Youngblood, et al. Int Arch Allergy Immunol. 2019;180(2):91-102. doi: 10.1159/000501637.
2. Figure with permission from Fernandez, Roy, Asbell "Emerging Targets in Ocular Allergy" 2022 –in press

Eosinophils and Mast Cells Role in Chronic Eye Allergy

- Patients with VKC/AKC with greater infiltration of eosinophils into conjunctiva, sub-epithelium, and tears than patients with SAC/PAC
- Eosinophils release:
  - Eosinophil major basic protein
  - Eosinophil cationic protein
  - Eosinophil peroxidase
  - Eosinophil neurotoxin

→ Bind to basement membrane proteins and cause **cellular disaggregation** and **epithelial desquamation**

- Eosinophil cationic protein correlates with **Clinical Signs**
- Eosinophils Implicated in the **Cornea Sequelae** in VKC/AKC
  - Punctate keratitis, ulcers, plaques, epithelial toxicity
- Mast cell activation triggers an early type-1 hypersensitivity reaction and subsequent recruitment of inflammatory cells

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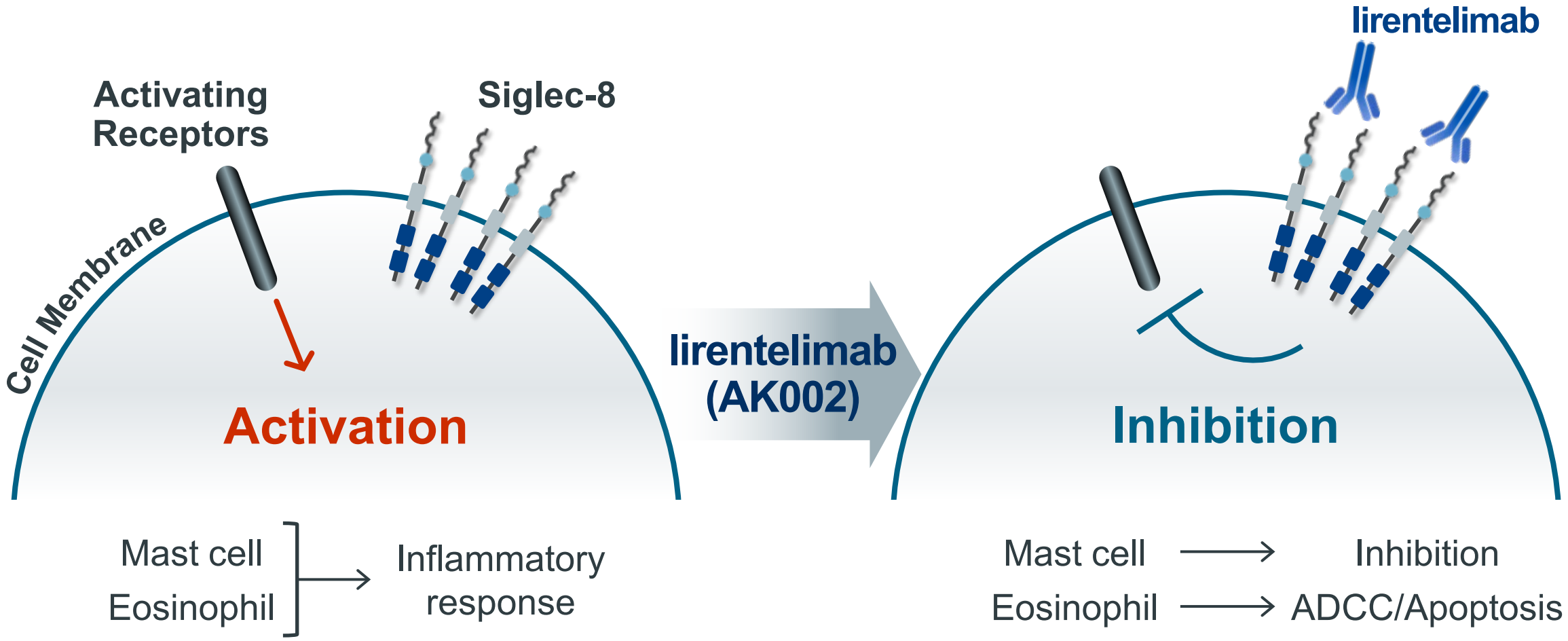
Lirentelimab (AK002) Targets Siglec-8 on Eosinophils and Mast Cells



1. BA Youngblood, et al. Int Arch Allergy Immunol. 2019;180(2):91-102. doi: 10.1159/000501637.
2. 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.

Lirentelimab in Allergic Conjunctivitis Phase 1 Study Overview

- **Study Aim**
  - To investigate the safety, tolerability, preliminary efficacy, and pharmacodynamics (PD) of lirentelimab in patients with severe and chronic allergic conjunctivitis.
  - **Exploratory analysis**
    - To assess changes in cytokine levels in tears upon lirentelimab treatment

- **Study Design**
  - Inclusion criteria: adults with chronic severe AKC, VKC, or PAC with history of topic or systemic corticosteroid use
  - Patients received 6 monthly lirentelimab infusions, administered intravenously every 28 days
    - Dose 1= 0.3 mg/kg, Dose 2= 1mg/kg, Subsequent doses= 1 or 3 mg/kg
  - Patients evaluated every 4 weeks during 20-week follow-up
    - Clinical activity measured by PRO & Investigator Assessments
      - Allergic Conjunctivitis Score (ACS) – daily patient questionnaire
      - Ocular Symptom Score (OSS) – monthly investigator assessment

AKC, Atopic Keratoconjunctivitis; VKC, Vernal Keratoconjunctivitis; PAC, Perennial Allergic Conjunctivitis

Anesi S, et al. JACI 2022; in press.

Baseline Characteristics

Patient Characteristics	Total (N=30)
Age, years Mean (Range)	52 (23-79)
Female	50%
White	93%
Duration with AC, years Median (Range)	6 (<1-38)
Blood absolute eosinophil count/mm^3	186±252
Atopic comorbidity diagnosis	
≥1 comorbidity	87%
≥2 comorbidities	60%
Atopic dermatitis	60%
Asthma	40%
Rhinitis	67%
Total ACS Score[a], ±SD	23±8
Total OSS Score, ±SD	6±3

[a]Total possible ACS score = 50. [b]Total possible OSS score = 13

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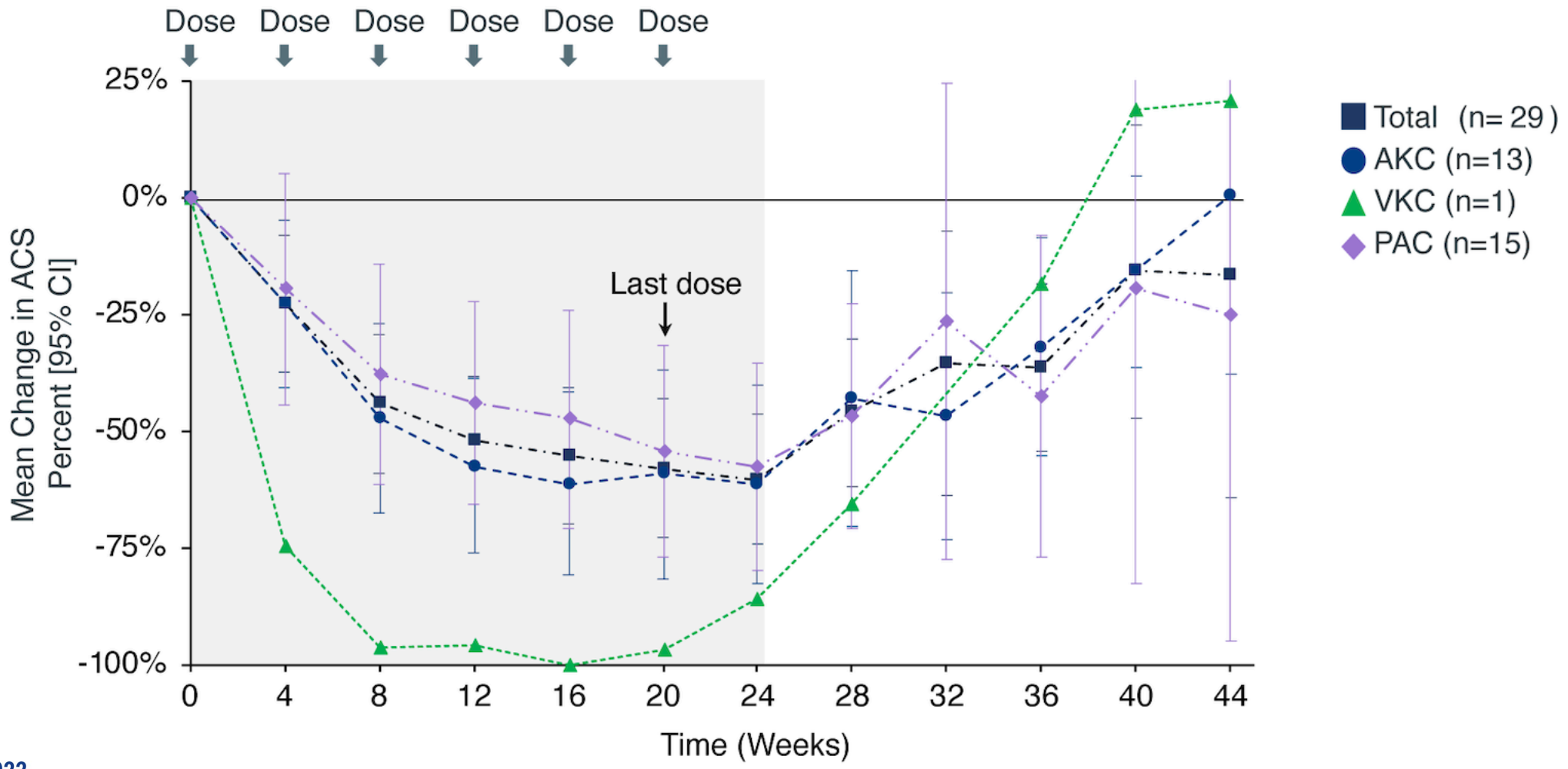
Patient Reported Symptoms Improved



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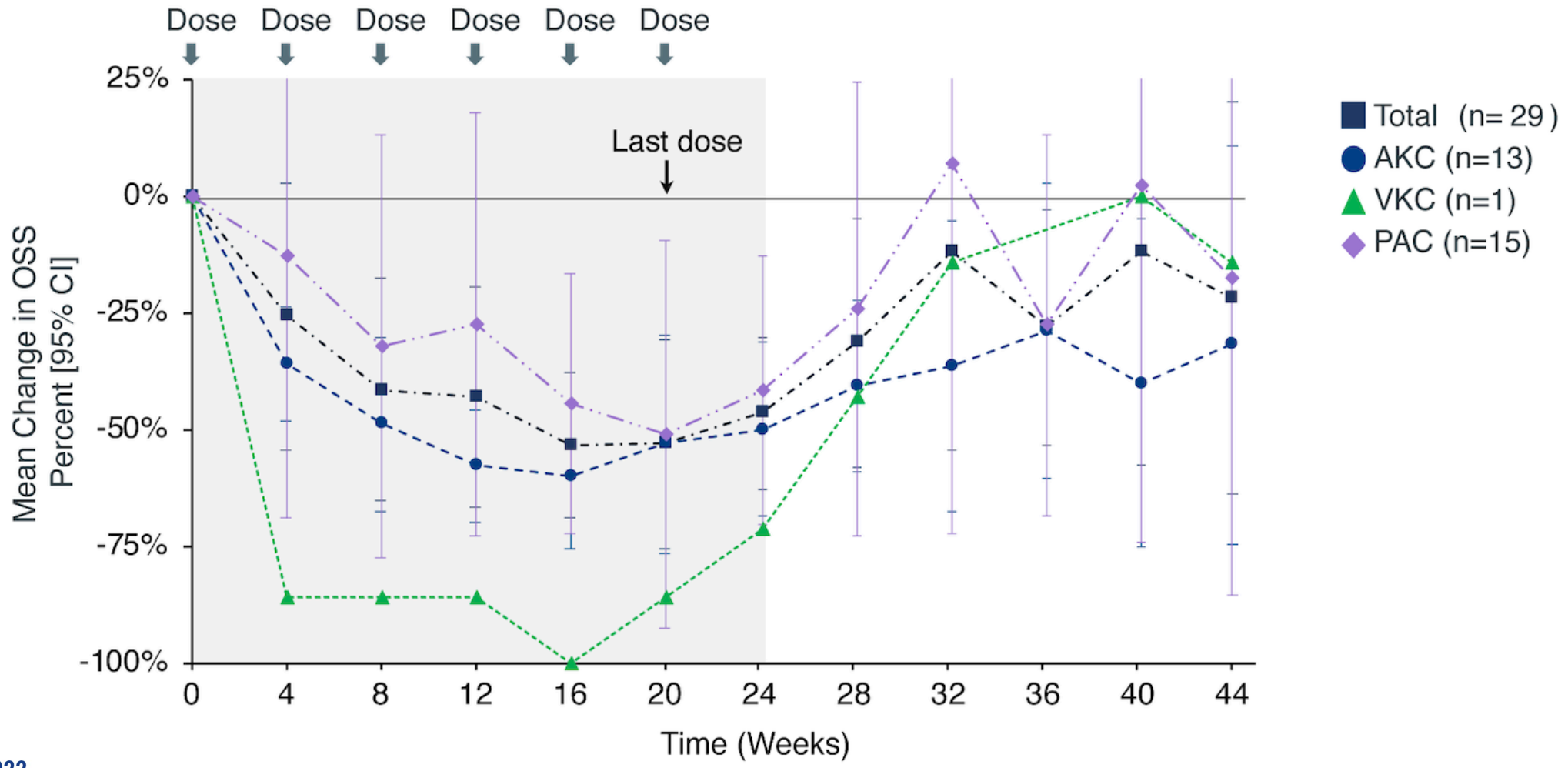
Investigator Assesses Signs & Symptoms Improved



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Safety Summary

Treatment-Emergent AEs in >5% of Patients

Adverse Event	Total (N=30)
Any Serious Event	3% (1)
Infusion related reaction	17% (5)
Blood creatine phosphokinase increased	10% (3)
Hypersensitivity	7% (2)
Sinusitis	7% (2)
Urinary tract infection	7% (2)

- Generally well-tolerated
- Most common AE infusion related reactions (IRR)
  - Included flushing, feeling of warmth, headache, nausea, or dizziness
  - Predominantly occurred on first infusion
- One Serious AE deemed not related to lirentelimab

Anesi S, et al. JACI 2022; in press.

Exploratory Analysis
Cytokine Response in Tears

- Tear fluid samples collected in 7 patients (2 AKC, 5 PAC)
  - Baseline, day 84, day 169 (last dose), day 309 (post-treatment follow-up)
  - Multiplex Bead Assay measured cytokine levels

- Cytokines analyzed:
  - **Type 1 (TH-1/Th17)**
    - IL-6, IL-8, CXCL-9, IL-10, IL-23, IL-17
  - **Type 2 (TH2)**
    - IL-4, IL-5, IL-13, IL-33
  - **Eosinophil function/migration**
    - VVL2 (MCP-1), CCL5 (RANTES), CCL11 (eotaxin-1), CCL24 (eotaxin-2), CCL26 (eotaxin-3), TARC (CCL17), CCL2, CCL3, CCL4, IP-10

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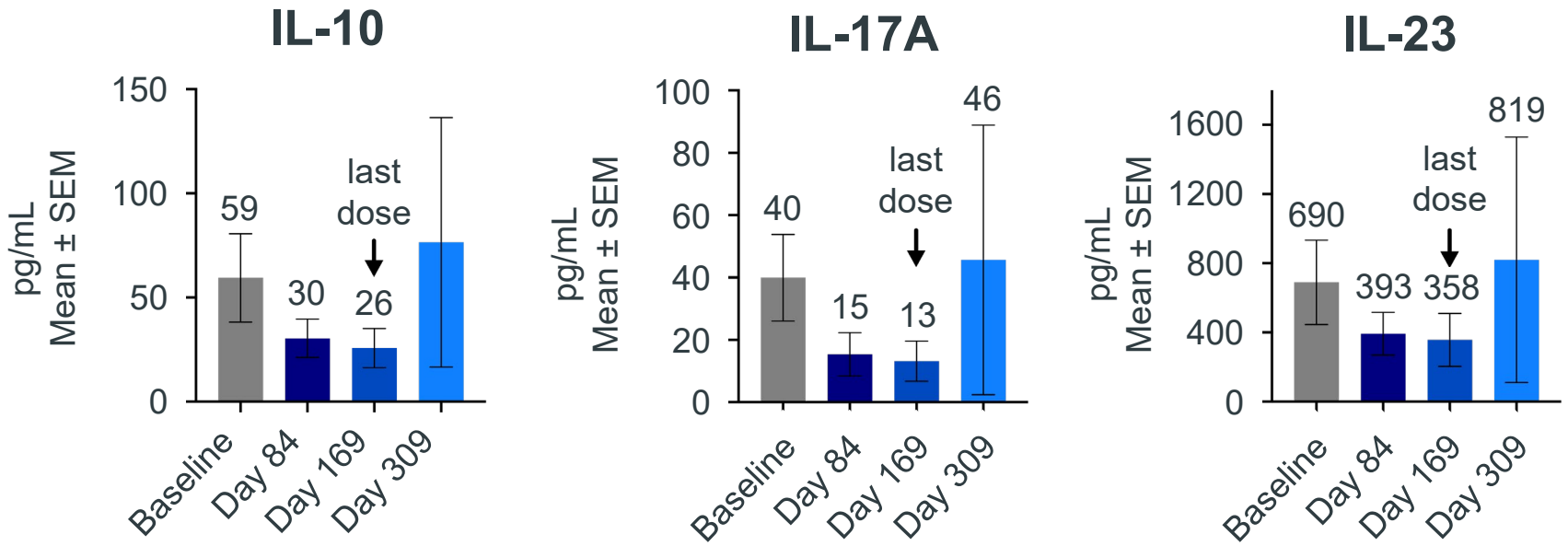
2. Anesi S, et al. JACI 2022; in press.

Reduction in Type 1 (TH-1/Th17) Cytokine Levels



- IL-10, IL17A, and IL-23 levels reduced during treatment
  - No change in levels observed for IL-6, IL-8, CXCL-9
- Treatment stopped at 6 months (Day 169)
- Cytokines rebounded to baseline levels after stopping drug (Day 309)

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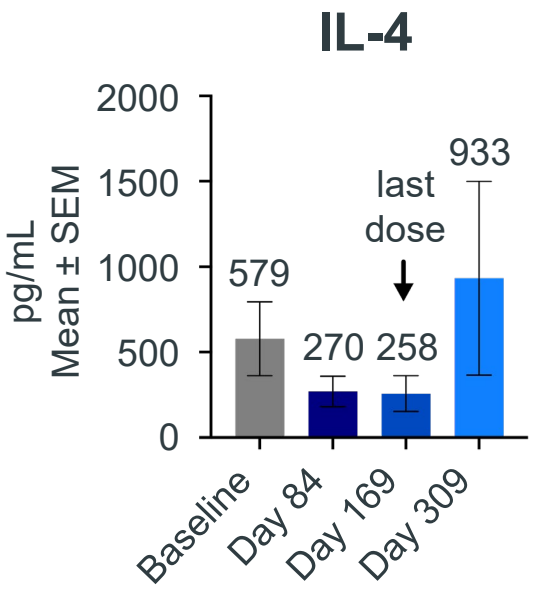
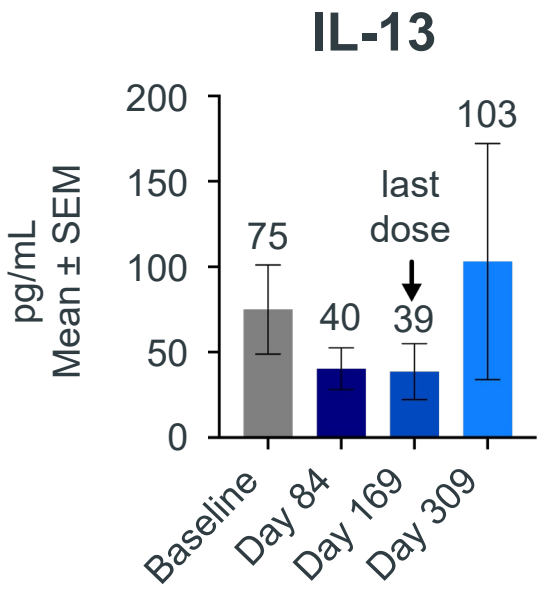
Reduction in Type 2 (TH2) Cytokine Levels

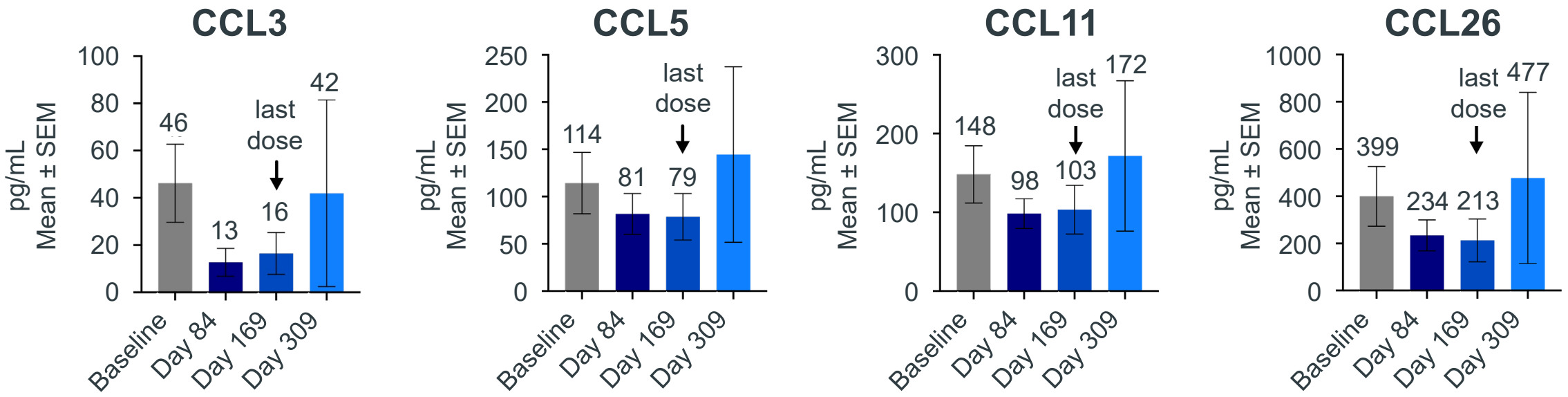




- IL-4 and IL-13 levels reduced during treatment
  - No change in levels observed for IL-5 and IL-33
- Treatment stopped at 6 months (Day 169)
- Cytokines rebounded to baseline levels after stopping drug (Day 309)

Anesi S, et al. JACI 2022; in press.

Reduction in Eosinophil Function/Migration Cytokines Levels



- CCL3, CCL5 (RANTES), CCL11 (eotaxin-1), and CCL26 (eotaxin-3) levels reduced during treatment
  - No change in levels observed for CCL2 (MCP-1), CCL24 (eotaxin-2), CCL17 (TARC), CCL2, CCL3, CCL4, IP-10
- Treatment stopped at 6 months (Day 169)
- Cytokines rebounded to baseline levels after stopping drug (Day 309)

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Summary

- In this phase 1 study, lirentelimab for chronic and severe allergic conjunctivitis was generally well tolerated
- Lirentelimab demonstrated improvements in both patient-reported and investigator-assessed signs and symptoms, including patients with comorbid atopic diseases
- Lirentelimab reduced local ocular inflammation as demonstrated in this pilot study by reduction in cytokine levels in tears
- These data support lirentelimab for further assessment in patients with comorbid atopic diseases commonly associated with ocular allergy (atopic dermatitis, asthma, rhinitis)

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

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