

Phase 1b Study of Lirentelimab (AK002), an Anti-Siglec-8 Monoclonal Antibody, in Patients with Severe Allergic Conjunctivitis (KRONOS)

Terry Levine¹; Joseph Tauber²; Quan Dong Nguyen³; Stephen D. Anesi⁴; Peter Chang⁴; Gregg J. Berdy⁵; Charles Lin³; David S. Chu⁶; Andrea M. Kantor⁷; Henrik S. Rasmussen⁷; Bhupinder Singh⁷; Alan T. Chang⁷; Amol P. Kamboj⁷; Bennie H. Jeng⁸; Vishal Jhanji⁹; C. Stephen Foster⁴

¹Allergy & Asthma Care, PA, Overland Park, Kansas; ²Tauber Eye Center, Kansas City, MO; ³Byers Eye Institute, Stanford University, Palo Alto, CA; ⁴Massachusetts Eye Research & Surgery Institution, Waltham, MA; ⁵Ophthalmology Associates, St. Louis, MO; ⁶Metropolitan Eye Research & Surgery Institute, Palisades Park, NJ; ⁷Allakos, Inc., Redwood City, CA; ⁸University of Maryland; ⁹University of Pittsburgh

BACKGROUND

- Atopic Keratoconjunctivitis (AKC), Vernal Keratoconjunctivitis (VKC) and Perennial Allergic Conjunctivitis (PAC) are forms of chronic allergic conjunctivitis (AC), an inflammatory disease characterized by extreme itching, pain, watering, redness and swelling of the conjunctiva
- In severe cases, corneal damage and permanent vision loss can occur
- Patients with severe AC often have allergic comorbidities which contribute to a reduced quality of life
- Eosinophil recruitment and mast cell activation are key drivers of signs and symptoms in severe AC (Figure 1)
- Current treatments are often ineffective in chronic AC and are associated with significant side effects
- There is a substantial unmet need for novel treatments for chronic AC

Figure 1. Mast Cells and Eosinophils Are Key Drivers of Inflammatory Disease

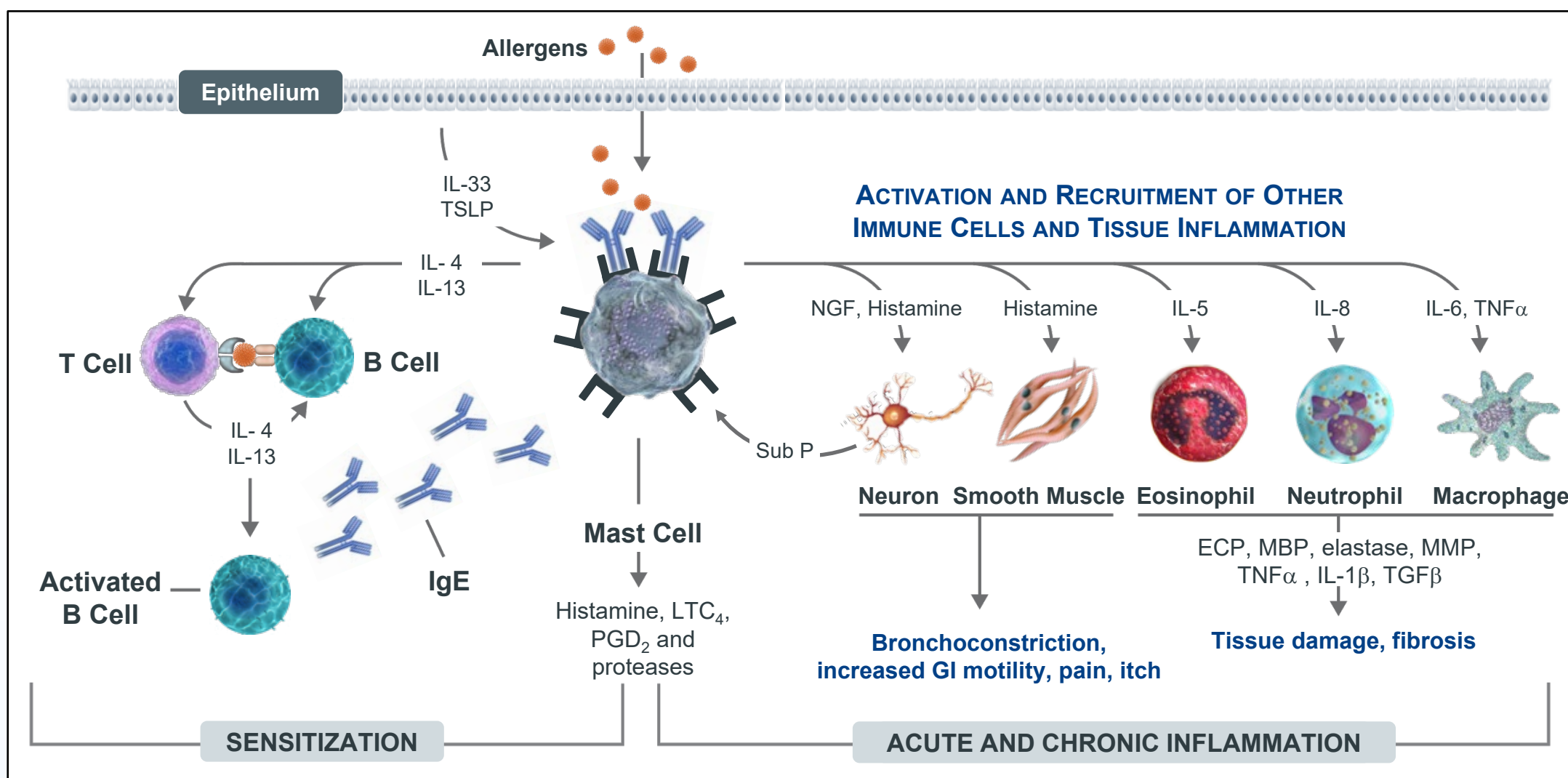
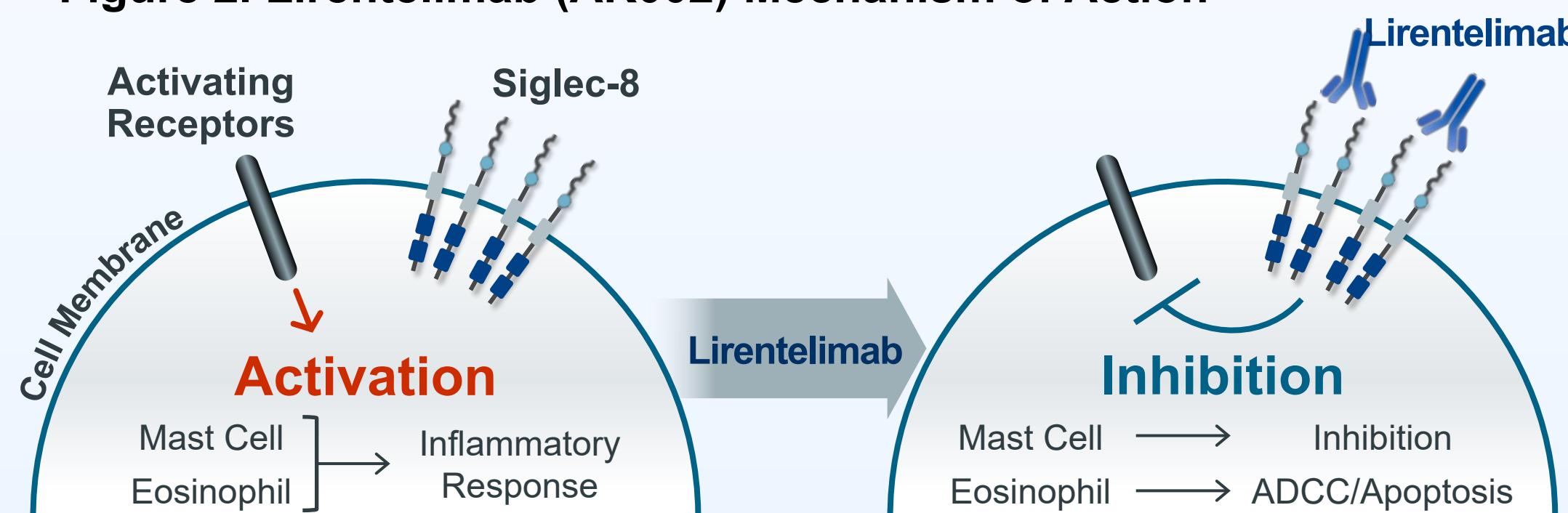


Figure 2. Lirentelimab (AK002) Mechanism of Action



- Siglec-8 is an inhibitory receptor selectively expressed on human eosinophils and mast cells, and therefore represents a novel target for the treatment of AC
- Lirentelimab is a novel, humanized, non-fucosylated IgG1 monoclonal antibody to Siglec-8
- Engagement of Siglec-8 receptor by lirentelimab triggers:
 - Antibody dependent cell mediated cytotoxicity (ADCC) against eosinophils (blood)
 - Inhibition of mast cells and apoptosis of tissue eosinophils (tissue)
- Here we present results from KRONOS, a Phase 1 multi-center, open-label study of lirentelimab in patients with chronic AC

METHODS

Figure 3. Study Design

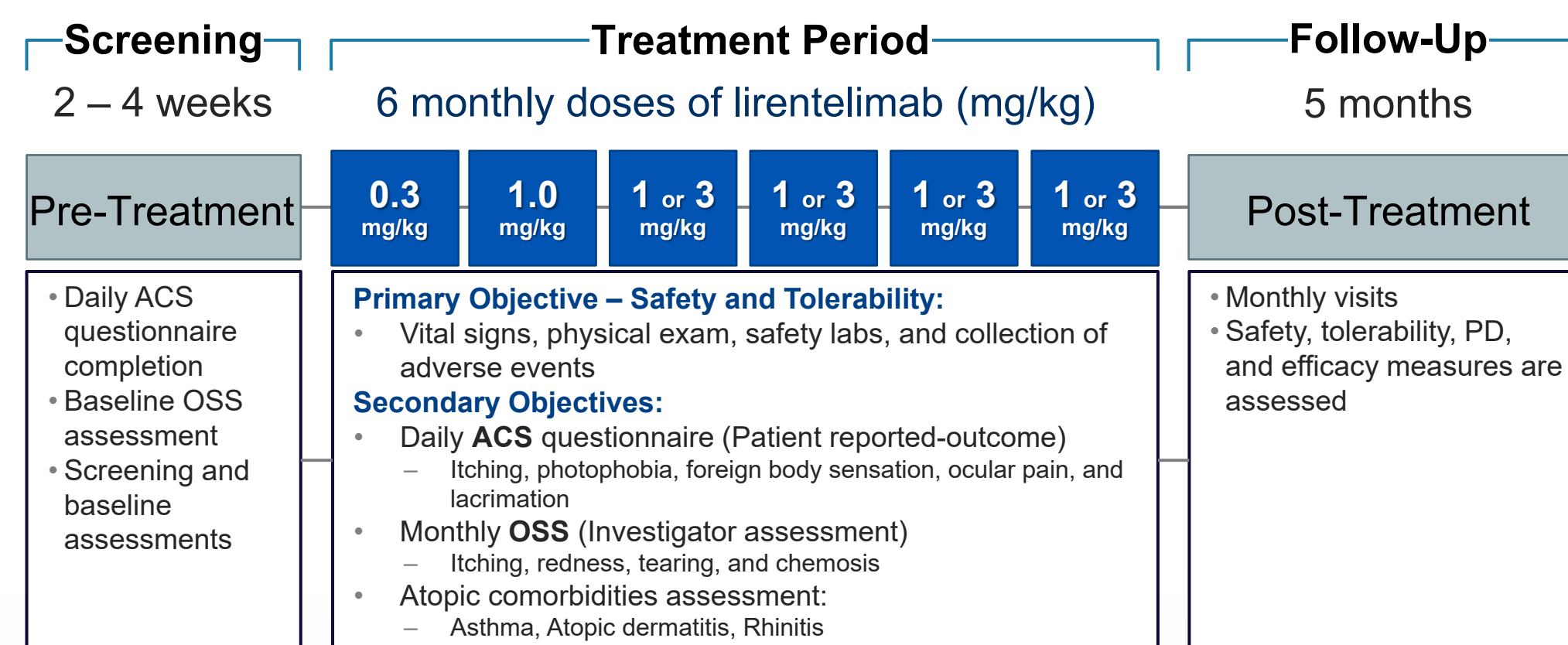


Figure 4. Lirentelimab Clinical Activity Measured by PRO & Investigator Assessments

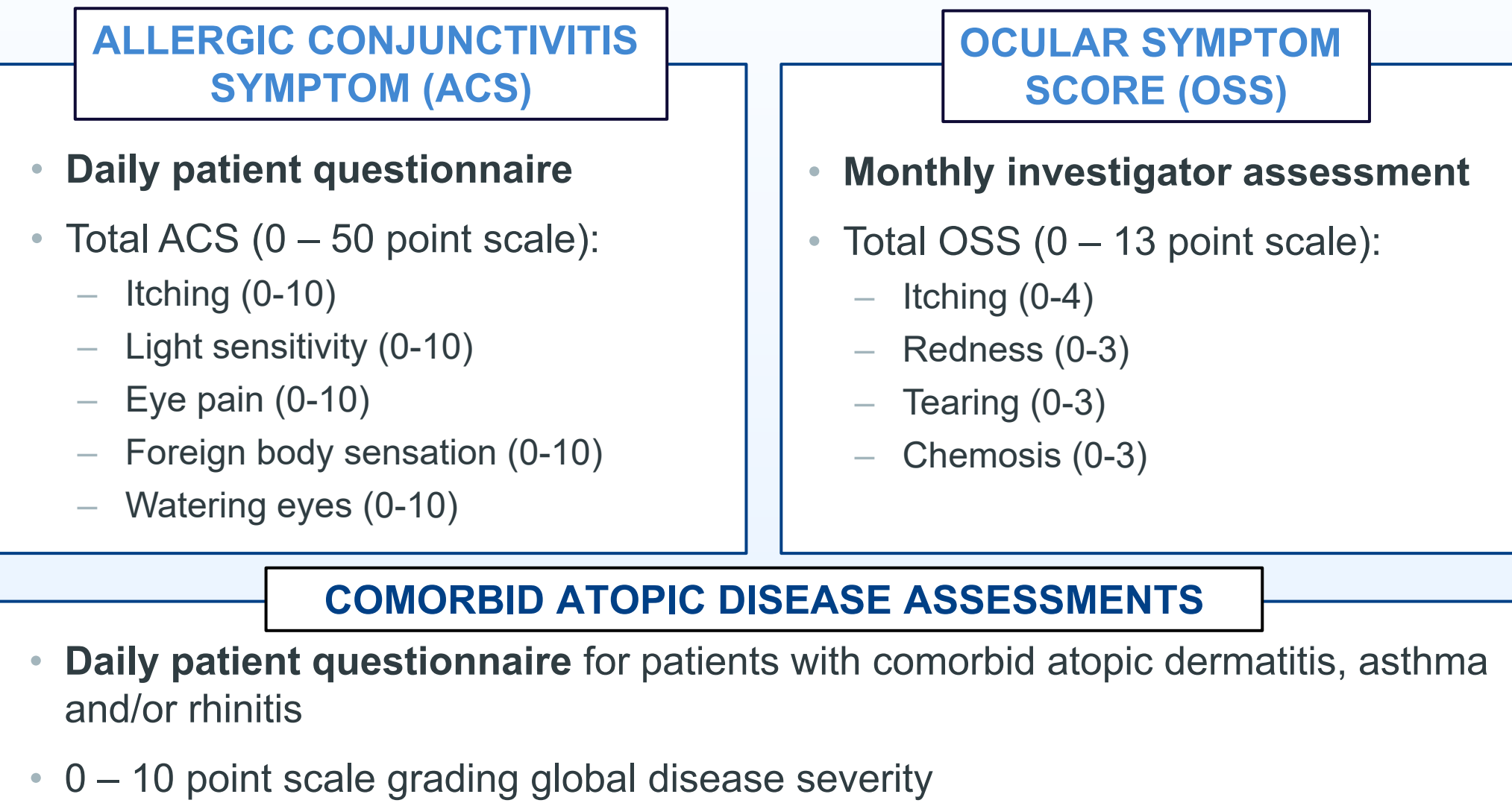


Figure 5. Improvements in Allergic Conjunctivitis Signs & Symptoms

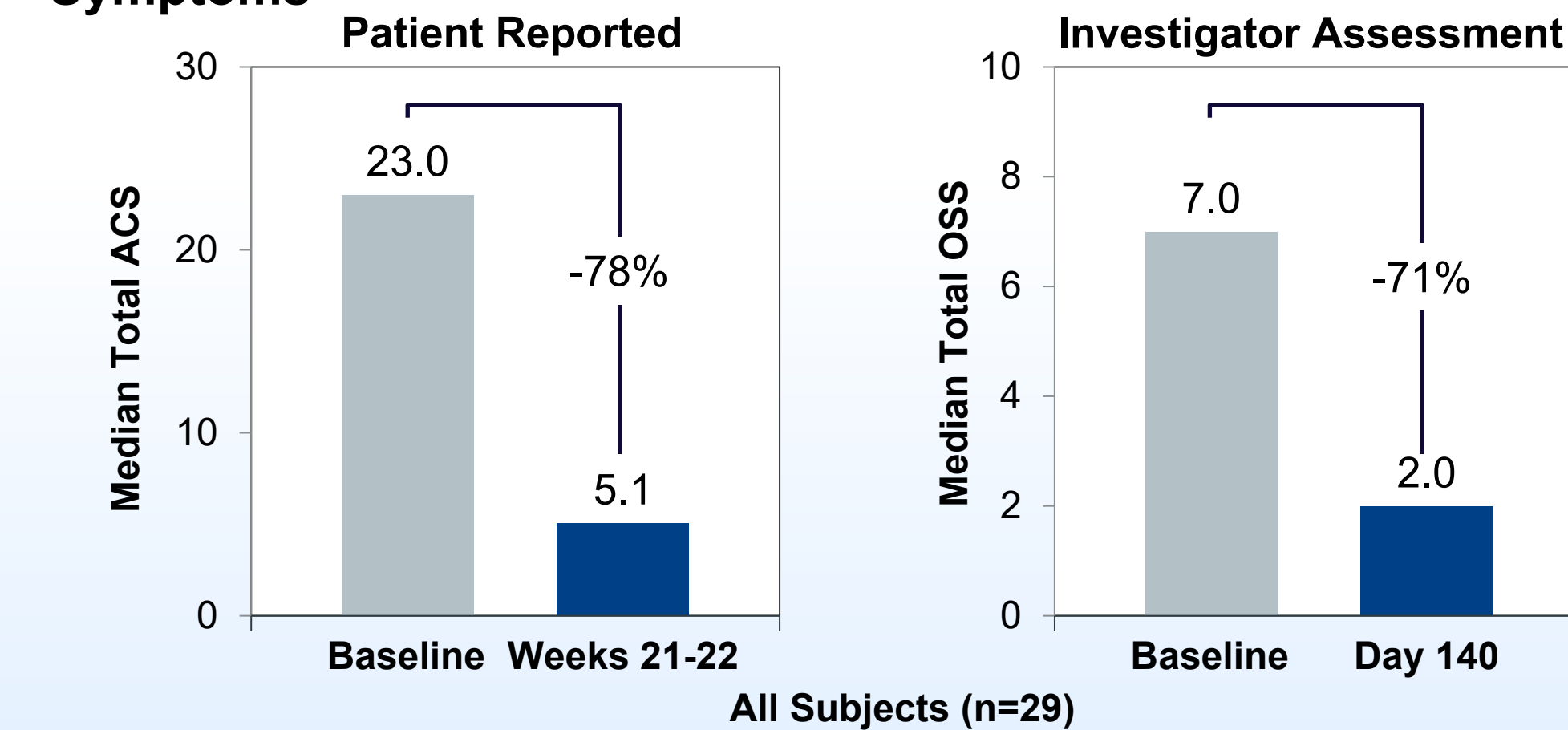


Figure 6. Improvements in Multiple Forms of Chronic AC

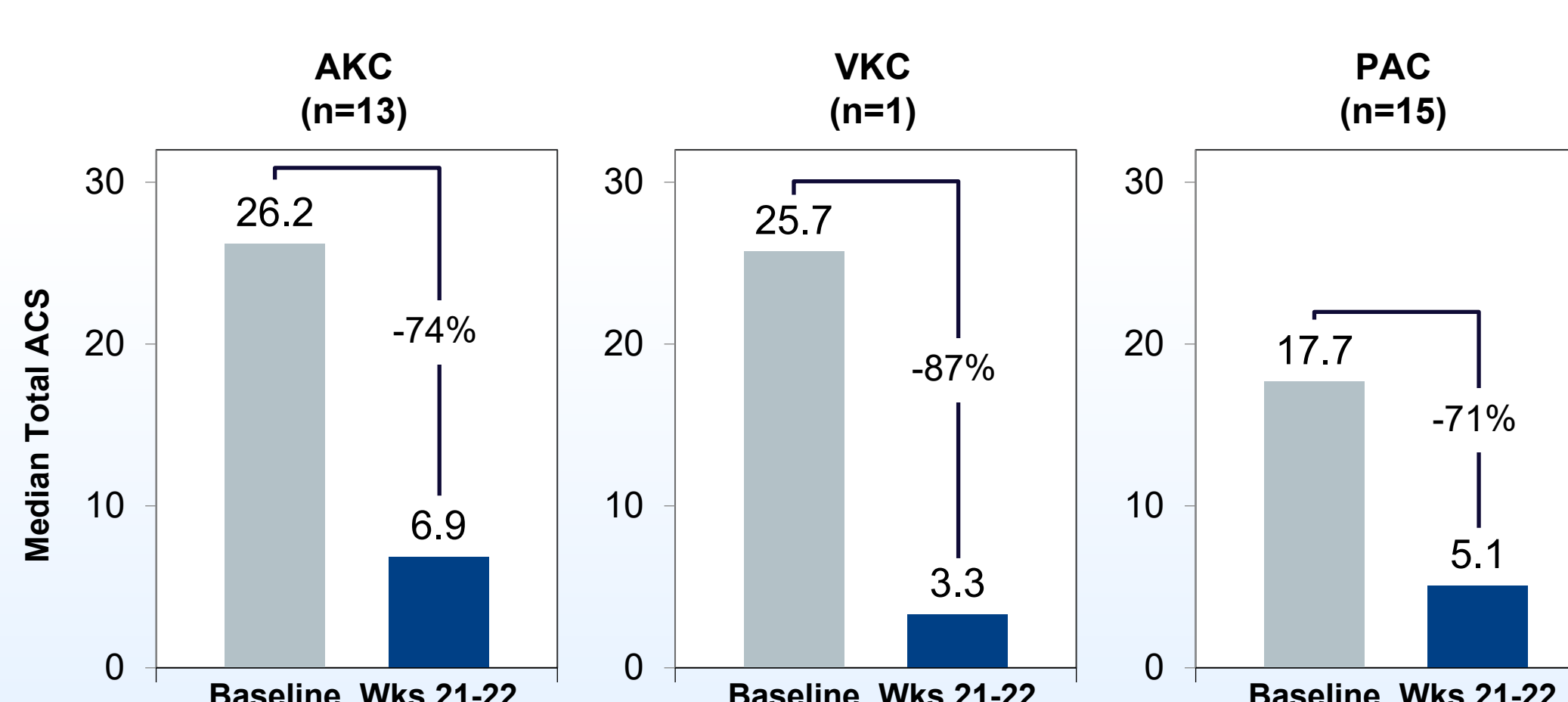
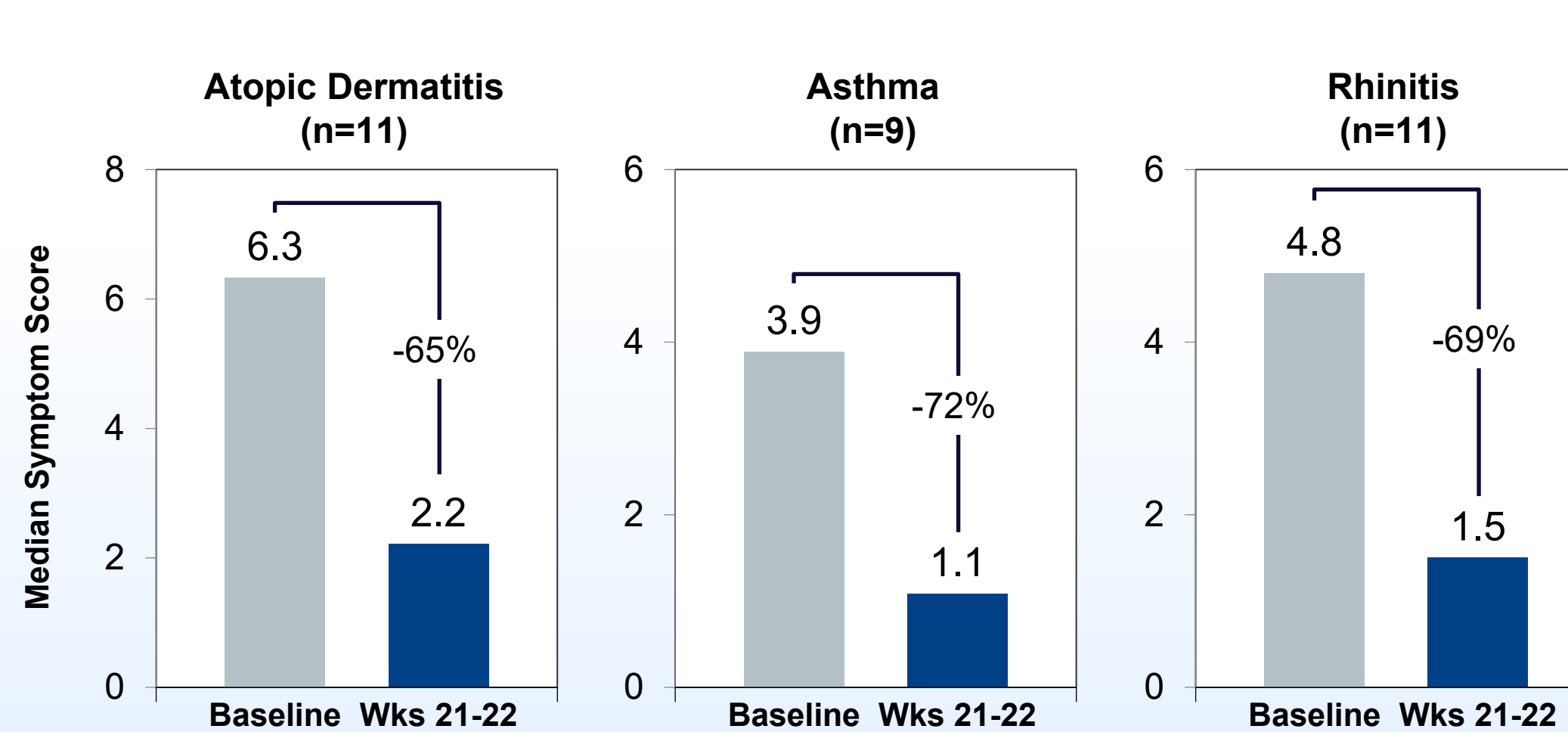


Figure 7. Substantial Improvement in Atopic Comorbidities^a



RESULTS

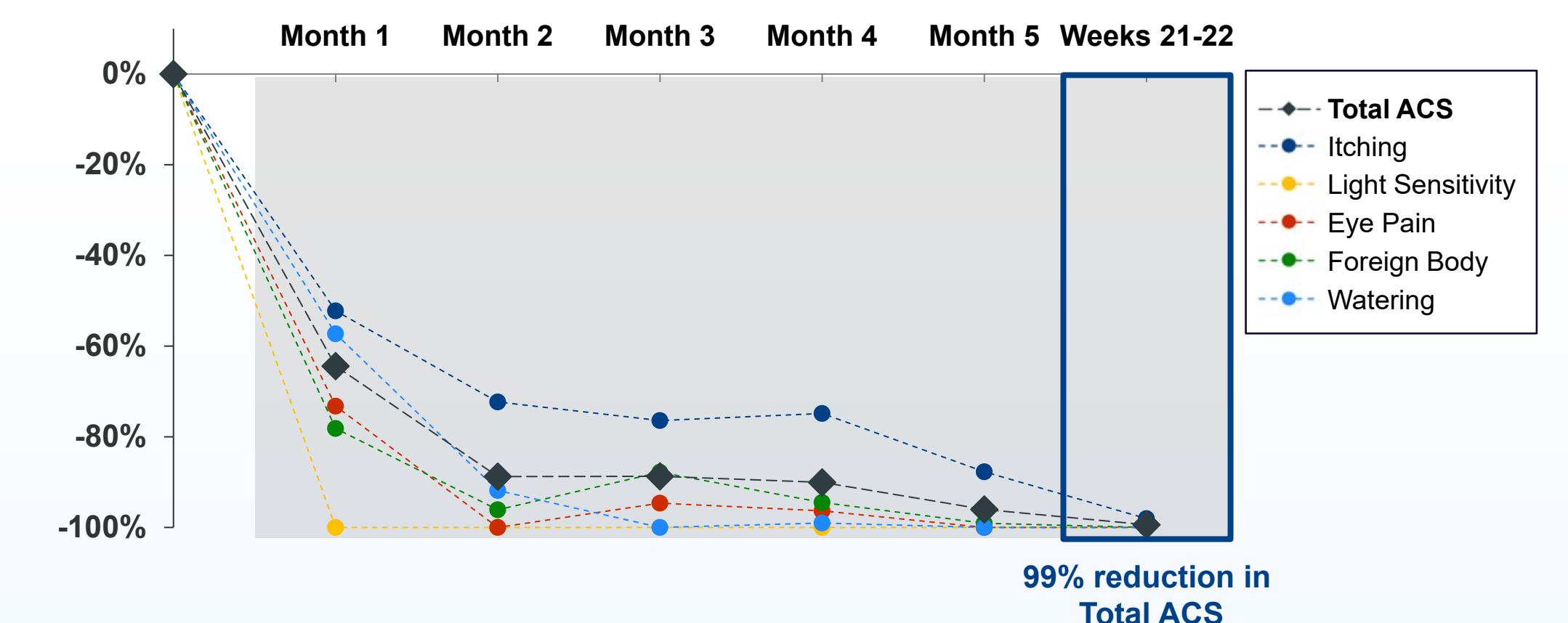
Table 1. Baseline Characteristics

	AKC (N=13)	VKC (N=1)	PAC (N=15)	Total (n=29)	
Age, Median (Range)	50 (23-72)	25	53 (29-66)	51 (23-72)	
Female	38%	0	67%	52%	
Weight (kg), Median (Range)	81 (50-107)	68	84 (52-108)	81 (50-108)	
BMI (kg/m ²), Median (Range)	26 (20-43)	21	29 (19-40)	27 (19-43)	
Total Symptom Score ^A	ACS, Median	25.7	17.7	23.0	
	OSS, Median	7.0	7.0	6.0	7.0
Atopic Comorbidities by Medical History	≥1 Comorbidity	85%	100%	87%	86%
	Atopic Dermatitis	85%	0	40%	59%
	Asthma	54%	100%	27%	41%
Rhinitis	54%	100%	73%	66%	

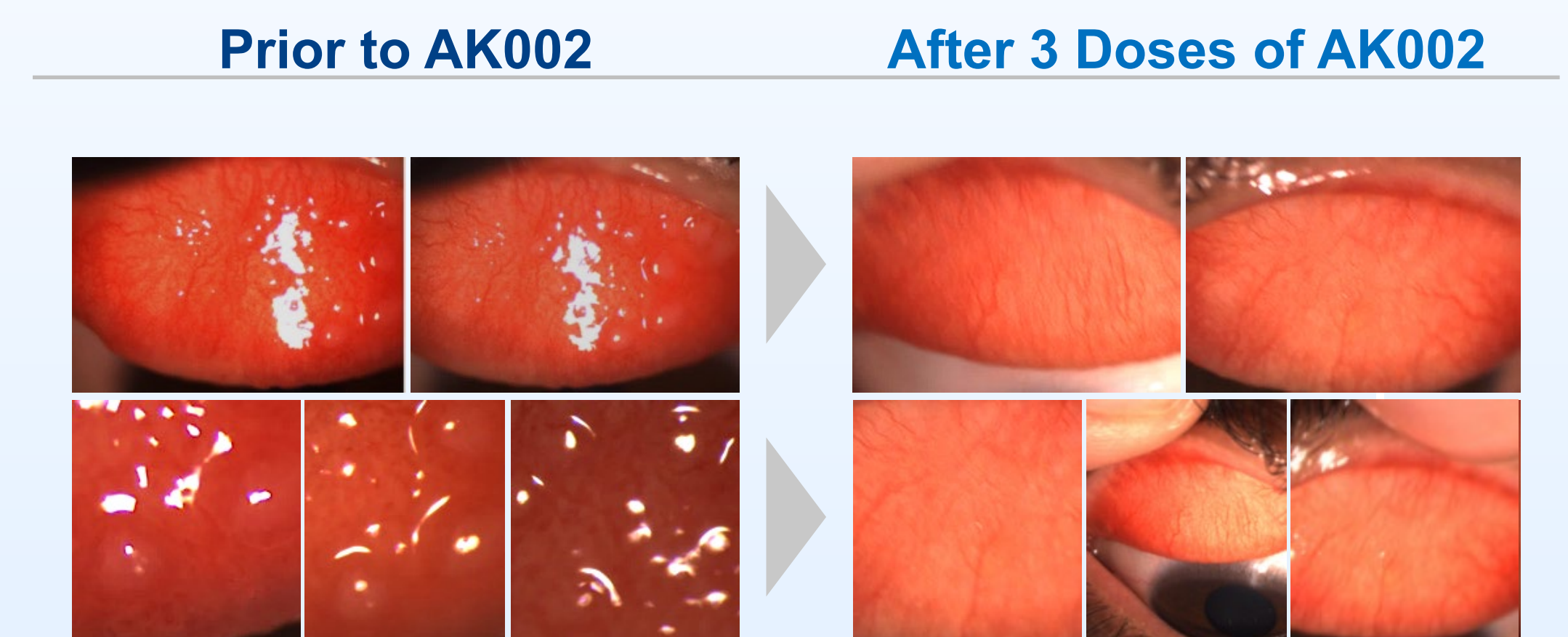
Patient Case Study

Demographics	Symptoms	Treatment History
<ul style="list-style-type: none"> 27 year-old male with severe AKC, atopic dermatitis, and rhinitis Baseline normal peripheral blood eosinophils (190 eos/μL) 	<ul style="list-style-type: none"> Itching, foreign body sensation, and watering Hyperemia (redness) and palpebral papillae Moderate comorbid atopic dermatitis & rhinitis 	<ul style="list-style-type: none"> AKC: topical antihistamines, topical corticosteroids Atopic Dermatitis: oral antihistamines Rhinitis: oral antihistamines

Figure 8. Improvement in Patient Reported Symptoms (ACS)



Reversal of Neovascular and Inflammatory Changes



Safety Summary:

- Lirentelimab was generally well-tolerated, with no drug-related serious adverse events (AEs)
- Most common AE was mild to moderate infusion-related reactions (IRRs; flushing, feeling of warmth, headache, nausea, or dizziness)

CONCLUSIONS/DISCUSSION

- Lirentelimab demonstrated substantial improvements in signs and symptoms as reported by patients and investigators in multiple forms of chronic AC
- Clinical activity observed in comorbid atopic dermatitis, asthma, and rhinitis
- Lirentelimab was generally well-tolerated
- Lirentelimab may be a promising treatment for severe AC as well as atopic conditions