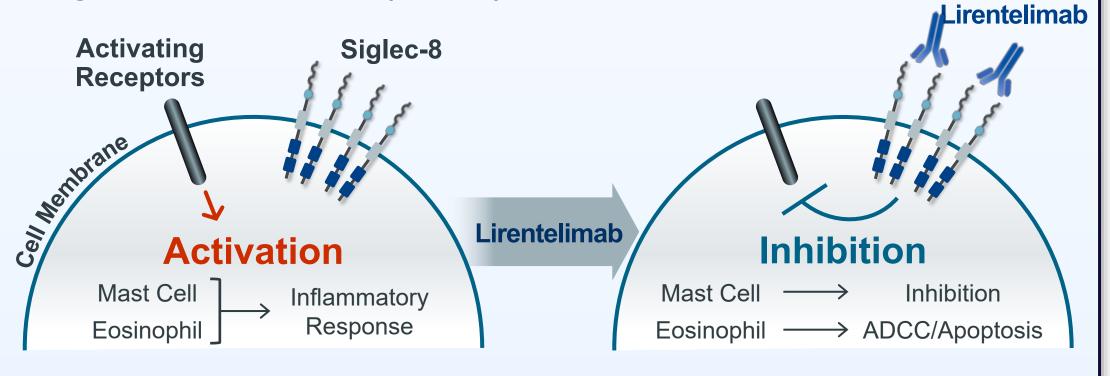
Phase 1b Study of Lirentelimab (AK002), an Anti-Siglec-8 Monoclonal Antibody, in Patients with Severe Allergic Conjunctivitis (KRONOS)

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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** Allergens 🏾 📍 Epithelium ACTIVATION AND RECRUITMENT OF OTHER TSLP IL-4 IL-13 Neuron Smooth Muscle Eosinophil Neutrophil Macrophage Mast Cell ECP, MBP, elastase, MMP TNF α , IL-1 β , TGF β Activated Histamine, LTC₄, B Cell PGD₂ and Tissue damage, fibrosis Bronchoconstriction, oroteases increased GI motility, pain, itch SENSITIZATION ACUTE AND CHRONIC INFLAMMATION

Figure 2. Lirentelimab (AK002) Mechanism of Action

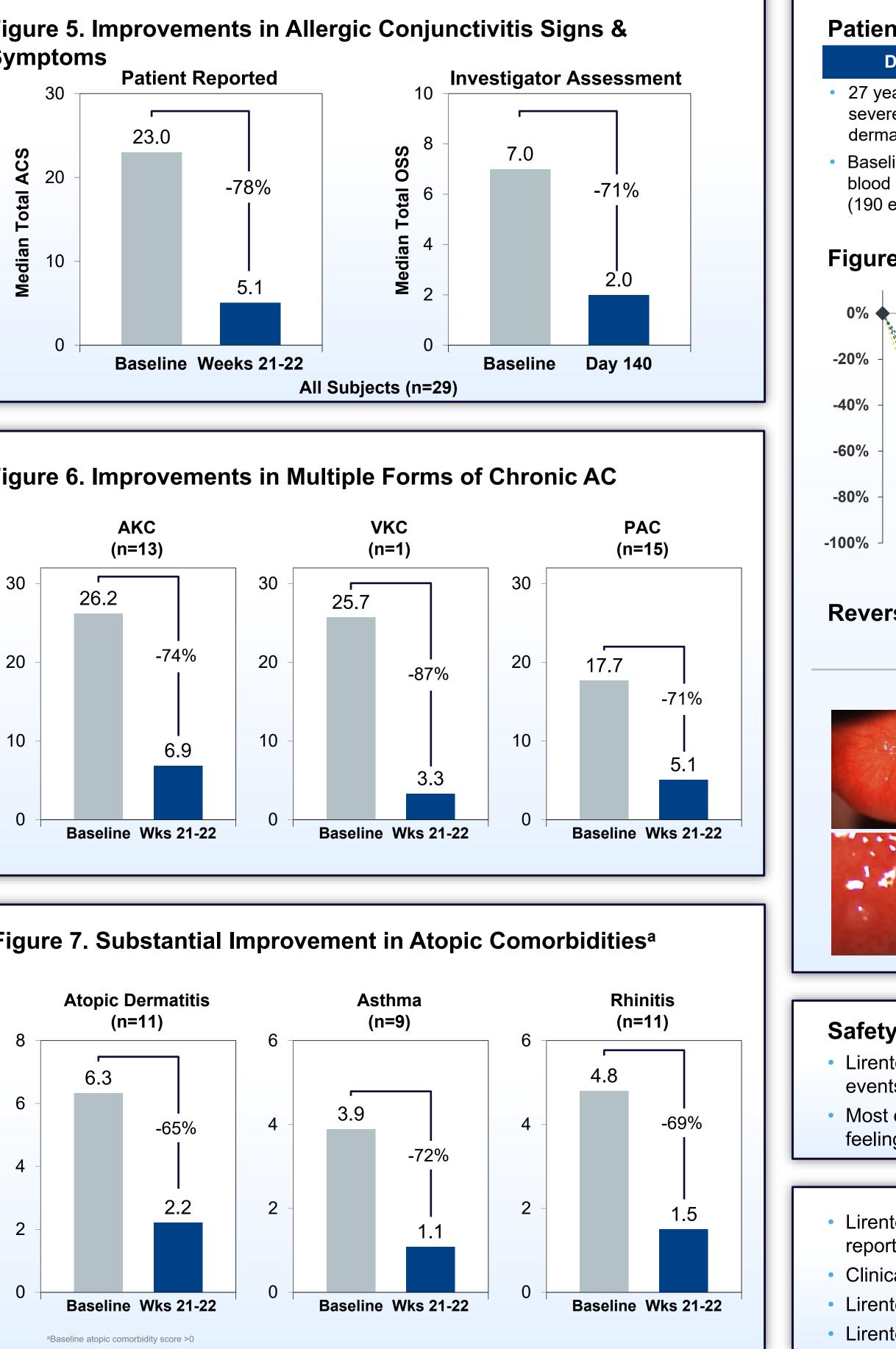


- Siglec-8 is an inhibitory receptor selectively expressed on human eosinophils and mast cells, and therefore represents a novel target for the treatment of AC
- Lirentelimab is a novel, humanized, non-fucosylated IgG1 monoclonal antibody to Siglec-8
- Engagement of Siglec-8 receptor by lirentelimab 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

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		-	ME	THC	DS			
Figure 3. Study Design								Fię
-Screening			Freatme	nt Pe	riod——		Follow-Up	Sy
2 – 4 weeks	6 mo	nthly do	oses of li	rentel	limab (mg	/kg)	5 months	
Pre-Treatment	0.3 mg/kg	1.0 mg/kg	1 or 3 mg/kg	1 or 3 mg/kg	1 or 3 mg/kg	1 or 3 mg/kg	Post-Treatment	
 Daily ACS questionnaire completion Baseline OSS assessment Screening and baseline assessments 	 Vital s adver Seconda Daily Daily Ital Month Ital Atopi 	signs, phys rse events ary Object ACS ques ching, photo crimation hly OSS (In ching, redne c comorbio	ives: tionnaire (P	atient re n body se assessm nd chemo sment:	bs, and collect ported-outcor ensation, ocular nent)	ne)	 Monthly visits Safety, tolerability, PD, and efficacy measures are assessed 	
Figure 4. Lire				Activ	vity Mea	sured	by PRO &	
	CONJU PTOM (A		TIS		0		SYMPTOM RE (OSS)	Fie
Daily patient					Monthly			
 Total ACS (0 - 	-).		-		gator assessment 3 point scale):	
 Itching (0-1) 	•)•			g (0-4)	5 point scale).	3
 Light sensition 	ivity (0-10))				ess (0-3)		
– Eye pain (0-	,	. (0.4)				ng (0-3)		S CS
 Foreign boo Watering ey 	•))		– Chen	nosis (0-3	3)	tal A
		,						an To
COMORBID ATOPIC DISEASE ASSESSMENTS Daily patient questionnaire for patients with comorbid atopic dermatitis, asthma								Median Total ACS
and/or rhinitis	questio	maire		IIIS W		olu alopi	ic dermatitis, astrina	
 0 – 10 point scale grading global disease severity 								
			R	ESUL	TS			
Table 1. Base	eline C	harac						Fi

		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/m²), Median (Range)		26 (20-43)	21	29 (19-40)	27 (19-43)
Total Symptom Score ^A	ACS, Median	26.2	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%



nt Case Study		
Demographics	Symptoms	Treatment History
ear-old male with re AKC, atopic atitis, and rhinitis line normal peripheral l eosinophils eos/µL)	 Itching, foreign body sensation, and watering Hyperemia (redness) and palpebral papillae Moderate comorbid atopic dermatitis & rhinitis 	 AKC: topical antihistamines, topical corticosteroids Atopic Dermatitis: oral antihistamines Rhinitis: oral antihistamines
Month 1 Month 2	t in Patient Reported S Month 3 Month 4 Month 5	Weeks 21-22
rsal of Neovascu	Iar and Inflammatory C	 Itching Light Sensitivity Eye Pain Foreign Body Watering 9% reduction in Total ACS Changes
Prior to AK00	-	3 Doses of AK002

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