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Clinical Activity of Lirentelimab (AK002), an Anti-Siglec-8 Monoclonal Antibody, in Treatment-Refractory Chronic Urticaria

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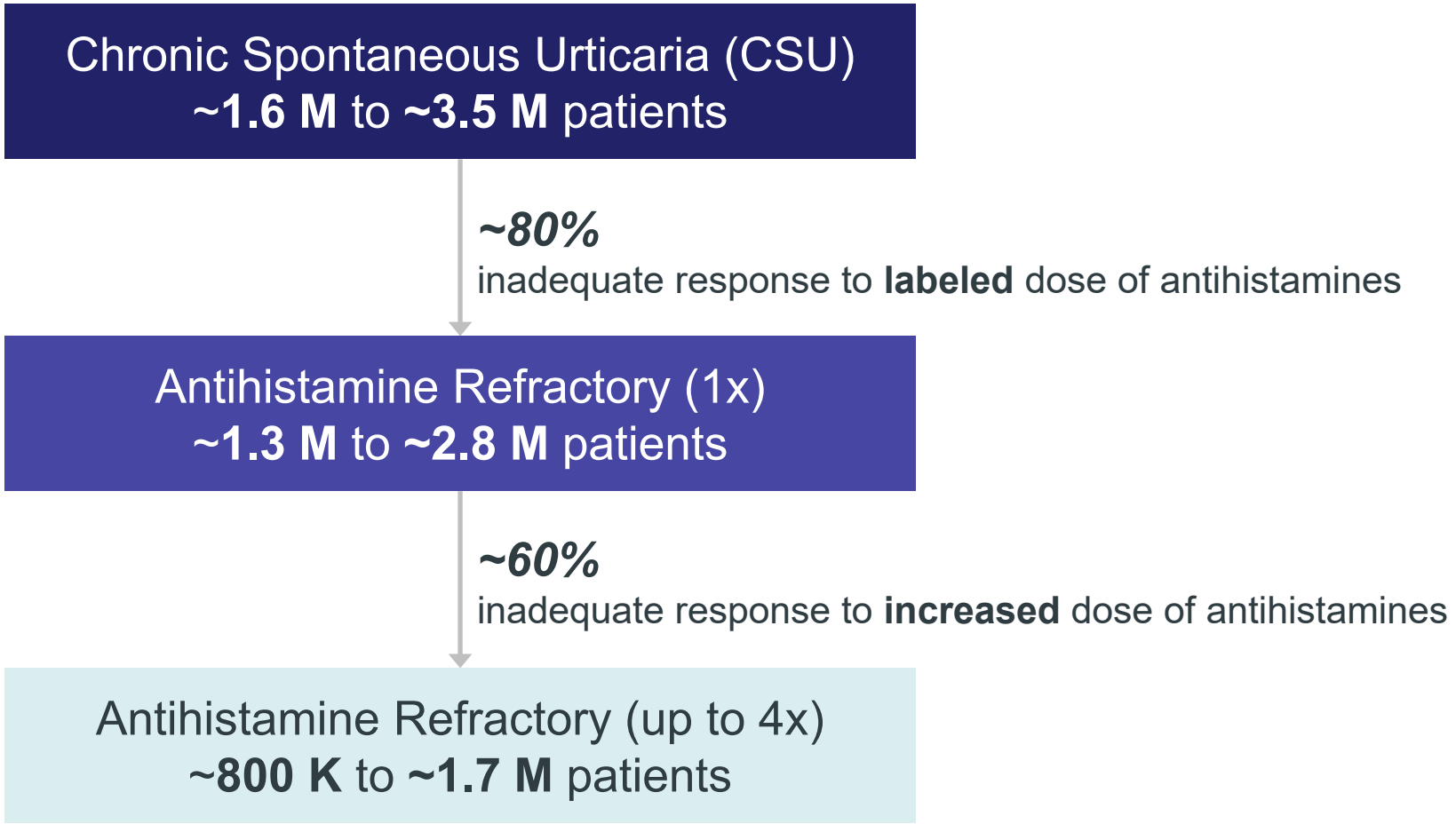
Disclosures

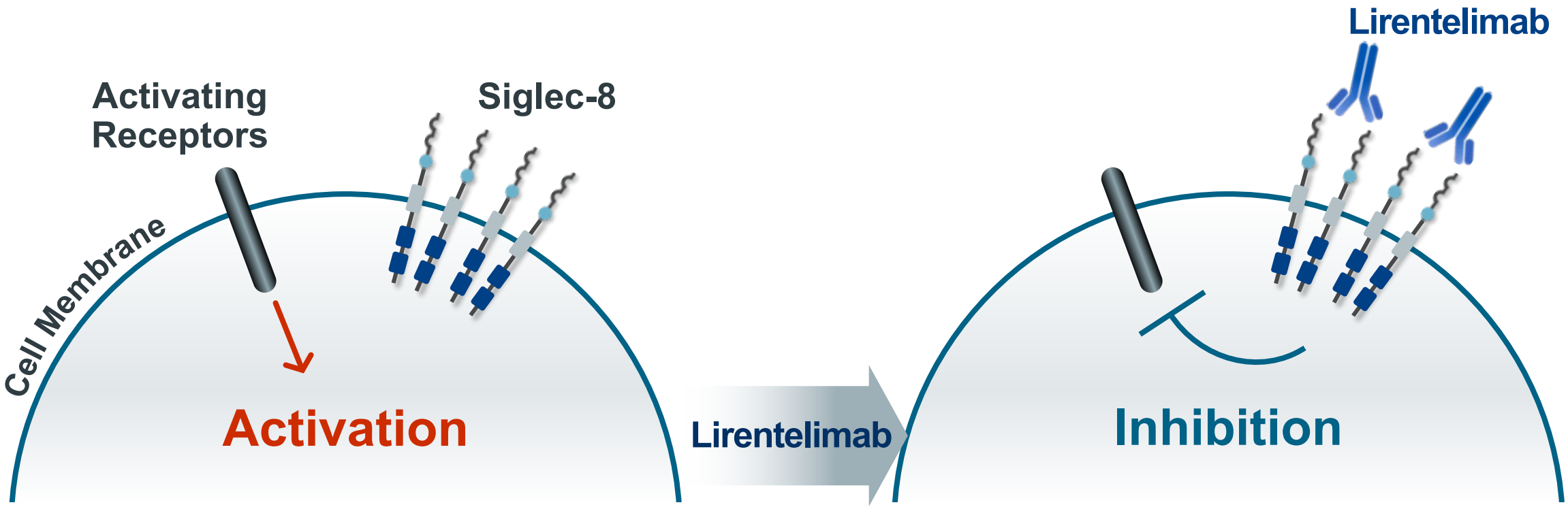
- Sabine Altrichter is an investigator for this study
- Lirentelimab (AK002) is an investigational drug candidate and is not FDA/EMA approved

Prevalence of Antihistamine-Refractory CSU in US



Source: Maurer et al. *Allergy*. 2011 Mar;66(3):317-30; Staevska et al. *J Allergy Clin Immunol*. 2010 Mar;125(3):676-82; Van den Elzen et al. *Clin Transl Allergy* (2017) 7:4

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



Study Design

Design	Key Endpoints	

• Open-label
• 45 patients – 4 cohorts
  - Omalizumab-naïve CSU
  - Omalizumab-refractory[1] CSU
  - Cholinergic urticaria
  - Symptomatic Dermographism
• One month screening period
• Dosed once monthly for 6 months
• 8 weeks safety follow up
• 0.3 mg/kg starting AK002 dose; increased to 1.0 mg/kg (dose 2 and 3); if UCT <12, increased to 3.0 mg/kg (dose 4, 5, and 6)
	Primary	• Change in Urticaria Control Test (UCT) Week 22 from BL
		  - Complete Response: UCT score ≥12 and ΔUCT ≥ 3
		  - Partial Response: ΔUCT ≥ 3
		  - No Response: ΔUCT < 3

	Secondary	• Change in disease activity by UAS7 (CSU only) • Safety and tolerability

1 Patients refractory to omalizumab (n=11): AH treatment up to 4x labeled dose, OMA doses up to 600 mg, average OMA treatment duration ~10 months; UCT on OMA: 4.1

Urticaria Disease Assessment Tools

URTICARIA CONTROL TEST (UCT)

- Measures disease control (symptoms and quality of life)
- Used in clinical practice
- Can be used in both chronic spontaneous urticaria and chronic inducible urticarias (e.g. cholinergic and symptomatic dermographism

URTICARIA ACTIVITY SCORE (UAS)

- Comprised of measures of itch & hives:
  - Itch Severity Score (ISS)
  - Hives Severity Score (HSS)
- UAS7 used as primary endpoint for regulatory approval in CSU (can only be used in CSU)

UCT and UAS7 recommended by EAACI CU Guidelines to assess CSU disease

Baseline Patient Characteristics

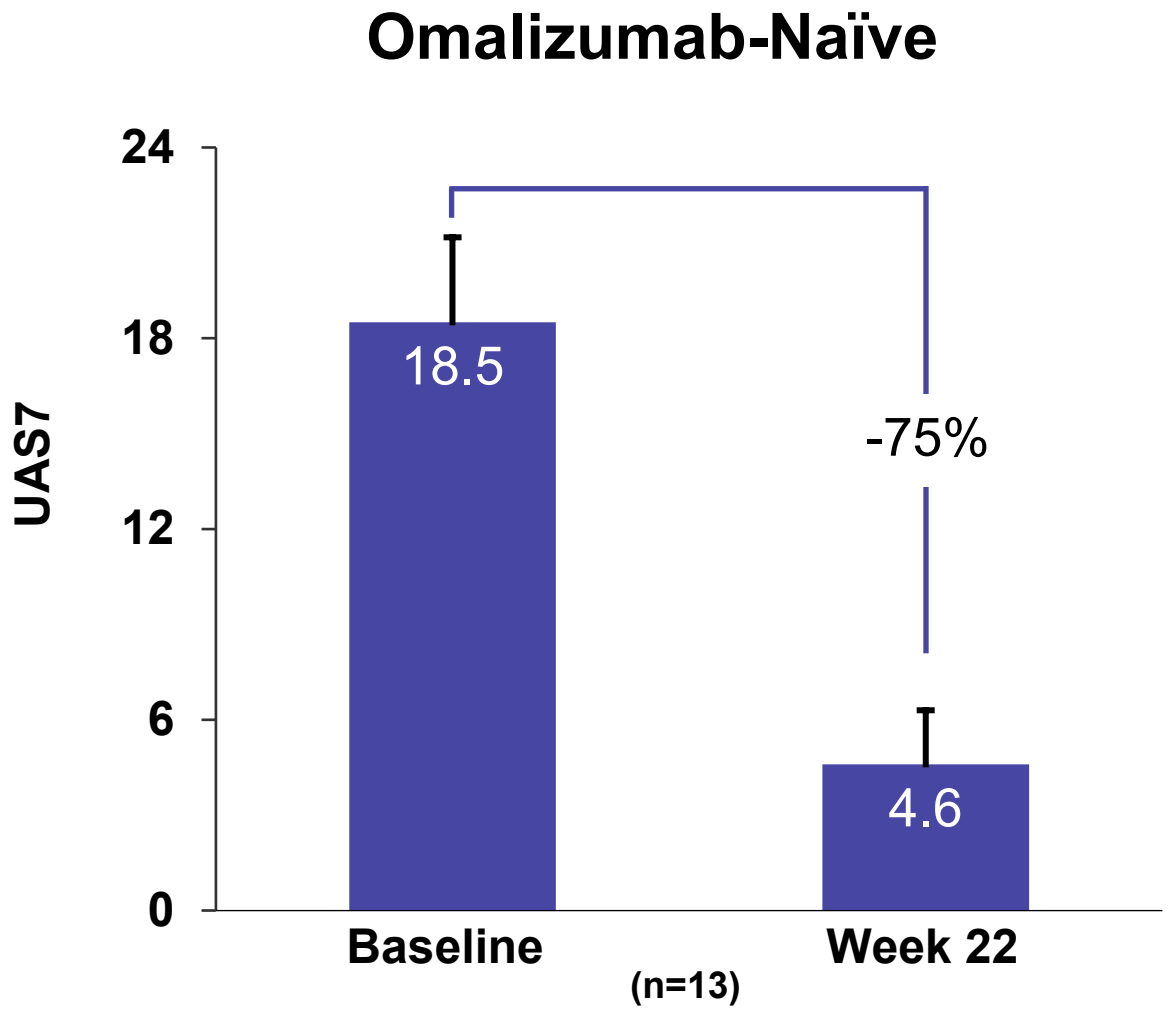
	Chronic Spontaneous Urticaria		Chronic Inducible Urticaria	
	Omalizumab Naïve (n=13)	Omalizumab Refractory (n=11)	Cholinergic Urticaria (n=11)	Symptomatic Dermographism (n=10)
Age	65 (30-75)	29 (22-60)	33 (18-62)	27 (19-56)
Female	100%	82%	55%	60%
BMI	32 (20-44)	26 (20-42)	27 (23-39)	30 (22-36)
UCT	3.2	3.7	5.4	5.7
UAS7	18.5 (8.6-41.0)	28.7 (18.1-35.8)	-	-

High Response Rate by UCT with Lirentelimab in CSU

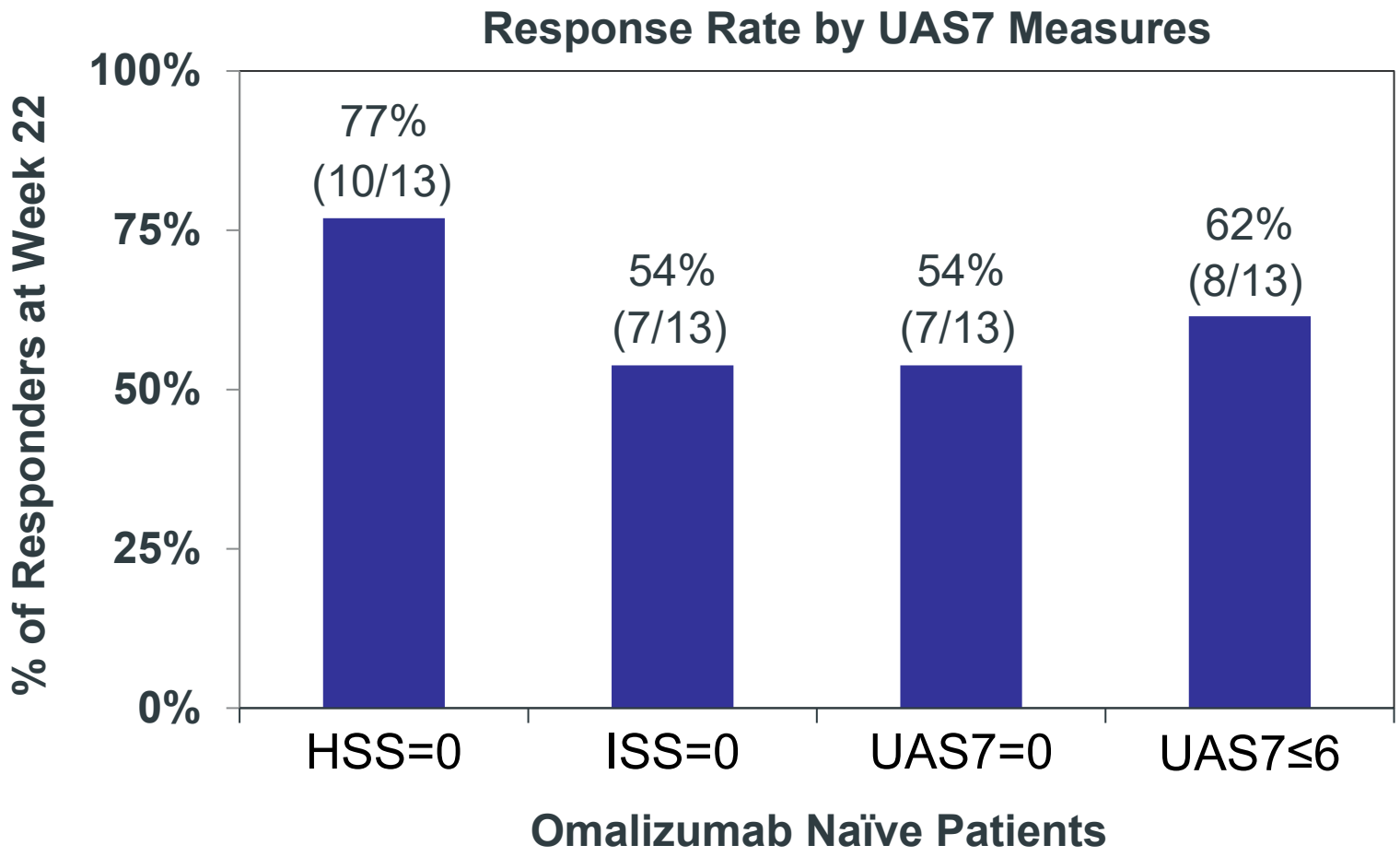
	Chronic Spontaneous Urticaria[1]	
Urticaria Control Test Response[1]	Omalizumab Naïve (n=13)	Omalizumab Refractory (n=7)
Complete Response	92%	57%
Partial Response	0%	29%
No Response	8%	14%

1 Patients who received all 6 doses
2 UCT complete response: ≥3-point improvement from baseline and score ≥12; partial response ≥3-point improvement from baseline; no response <3-point improvement from baseline

Omalizumab Naïve CSU: Substantial Improvement in UAS7



Omalizumab Naïve CSU: Response by UAS7 Measures



Omalizumab Refractory CSU Cohort – Medical History

Inadequate disease control despite extensive use of omalizumab (OMA)

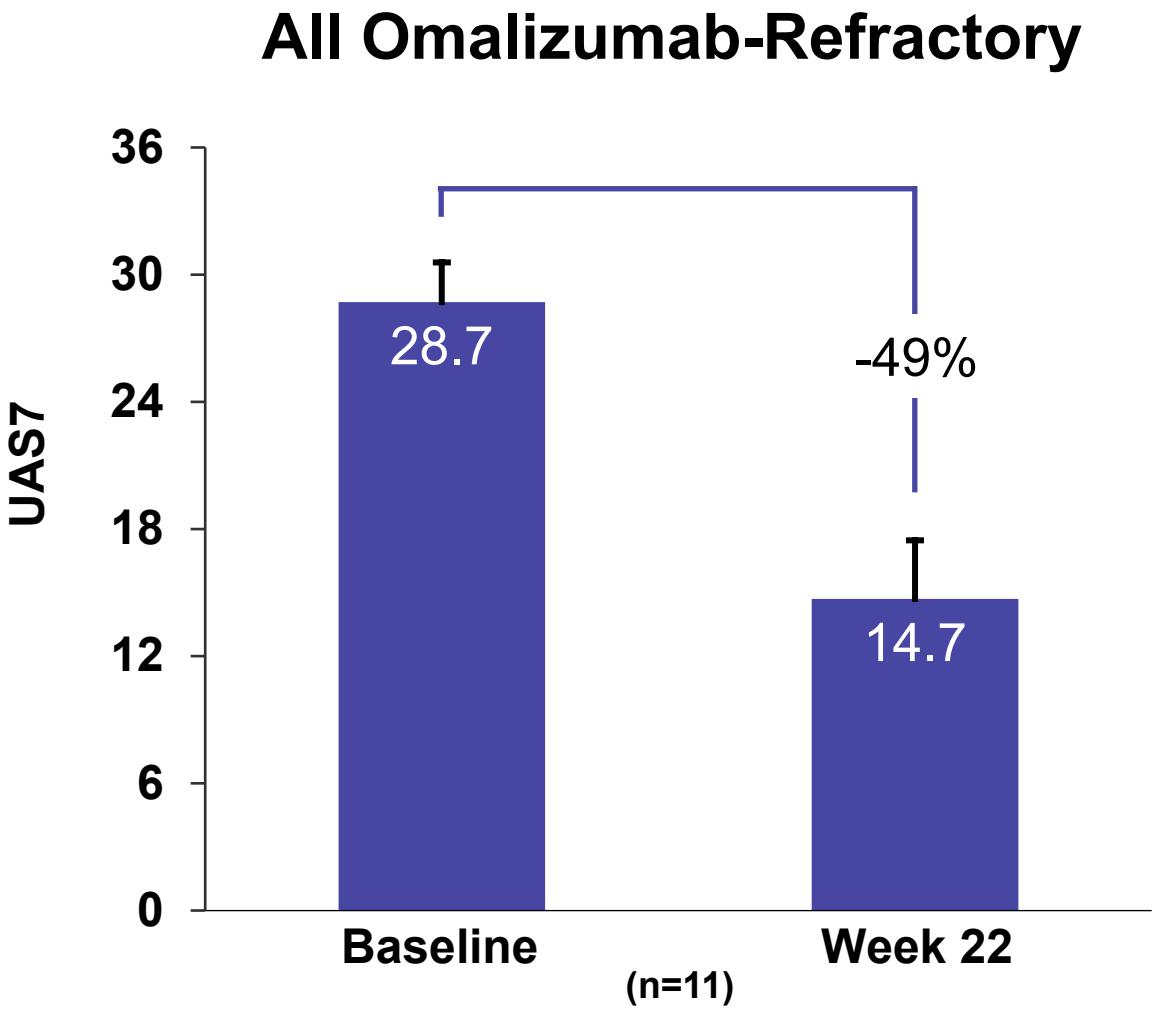
Prior OMA Treatment Experience

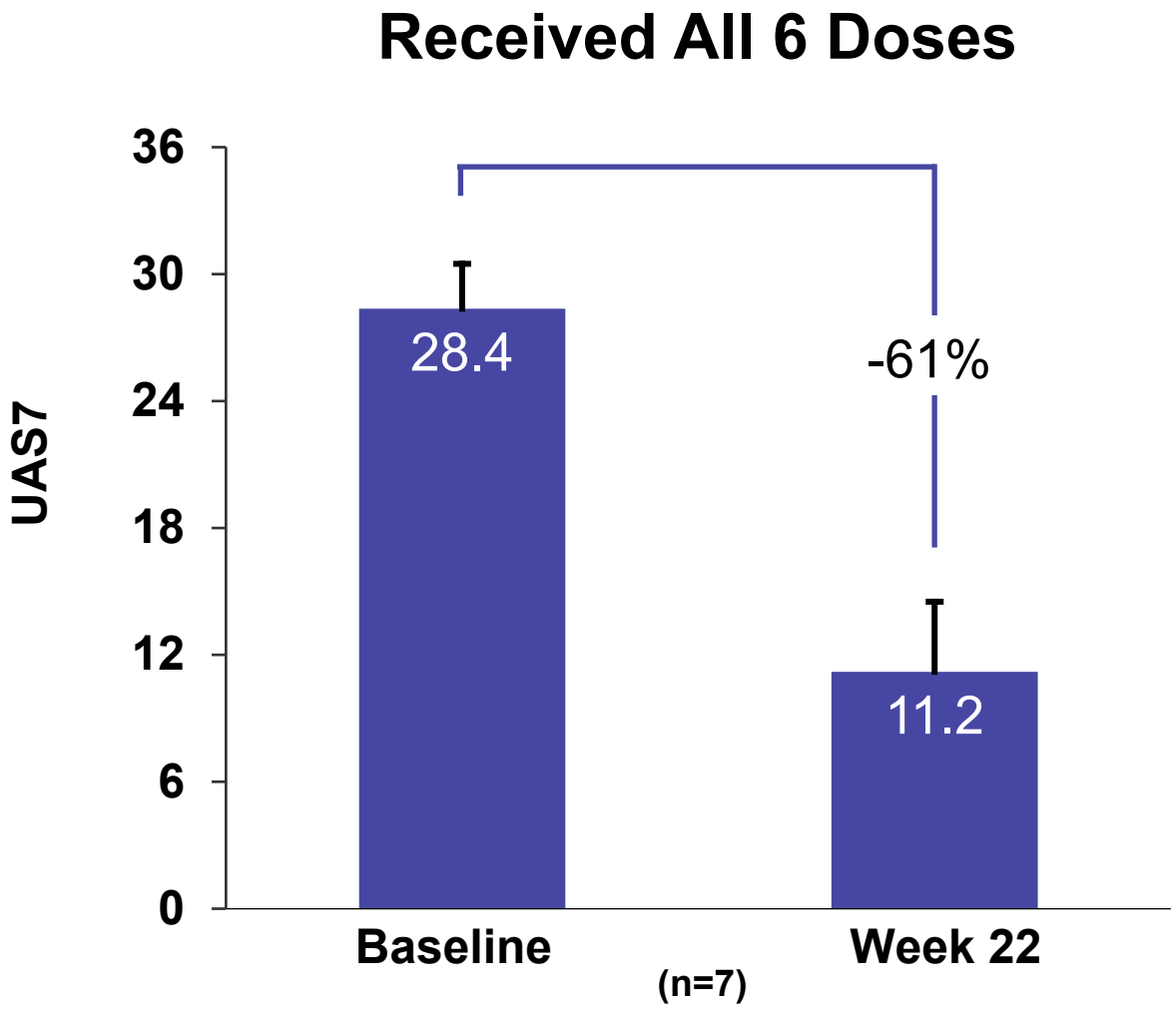
- **Average treatment duration:** ~10 months
- **Treatment regimen:**
  - Omalizumab: up to 600 mg
  - Antihistamine: up to 4x labeled dose
- **Average UCT score on Omalizumab:** 4.1

Lirentelimab (AK002) Experience

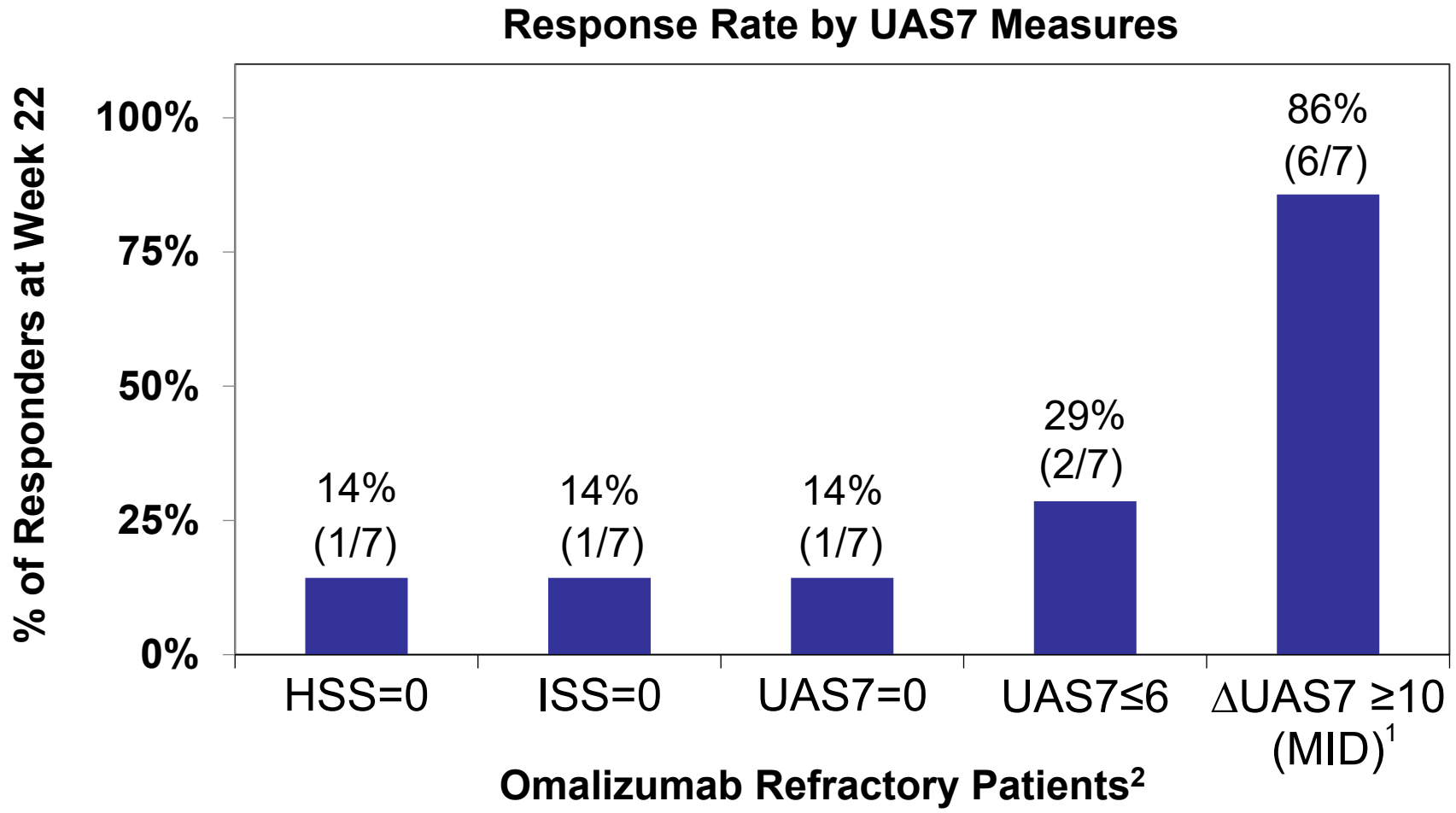
- **Time since last OMA dose:** >2 months
- **Treatment regimen:**
  - Antihistamine: up to 4x labeled dose
- **Average UCT score at baseline:** 3.7
- **Average UCT score after 6 doses**: 11.4

Omalizumab Refractory CSU: Substantial Improvement in UAS7





Omalizumab Refractory CSU: Response by UAS7 Measures



1 Minimally Important Difference: Mathias, Maurer et al. Ann Allergy Asthma Immunol 108 (2012) 20-24
2 Patients who received all 6 doses; In entire OMA-refractory CSU cohort, 8 of 11 patients met MID change in UAS7 ≥10

High Response Rate by UCT with Lirentelimab in CIndU

	Chronic Inducible Urticaria	
Urticaria Control Test Response[1]	**Cholinergic (n=11)**	**Symptomatic Dermographism (n=10)**
Complete Response	82%	40%
Partial Response	0%	30%
No Response	18%	30%

1 UCT complete response: ≥3-point improvement from baseline and score ≥12; partial response ≥3-point improvement from baseline; no response <3-point improvement from baseline

Cholinergic Urticaria: 100% Response Rate by PCE[1] Test

	Baseline		End of Study	
	Provocation[2] Response < 10 mins	Number of Wheals after 30 mins	Provocation Response < 10 mins	Number of Wheals after 30 mins
CholU-1	+	21 - 50	-	0
CholU-2	+	1 - 20	-	0
CholU-3	+	1 - 20	-	0
CholU-4	+	>50	-	0
CholU-5	+	Positive	-	0
CholU-6	+	>50	-	0
CholU-7	+	>50	-	21-50

1 Pulse Control Ergometry
2 Provocation - exercise on stationary bike elevates body temperature to trigger symptoms, positive response if hives occur ≤10 minutes from start of sweating. Test terminated at 30 mins

Safety Summary

- Generally well-tolerated
- No drug-related Serious Adverse Events
- Most common adverse event was mild to moderate infusion-related reactions (IRRs; flushing, feeling of warmth, headache, nausea, or dizziness)

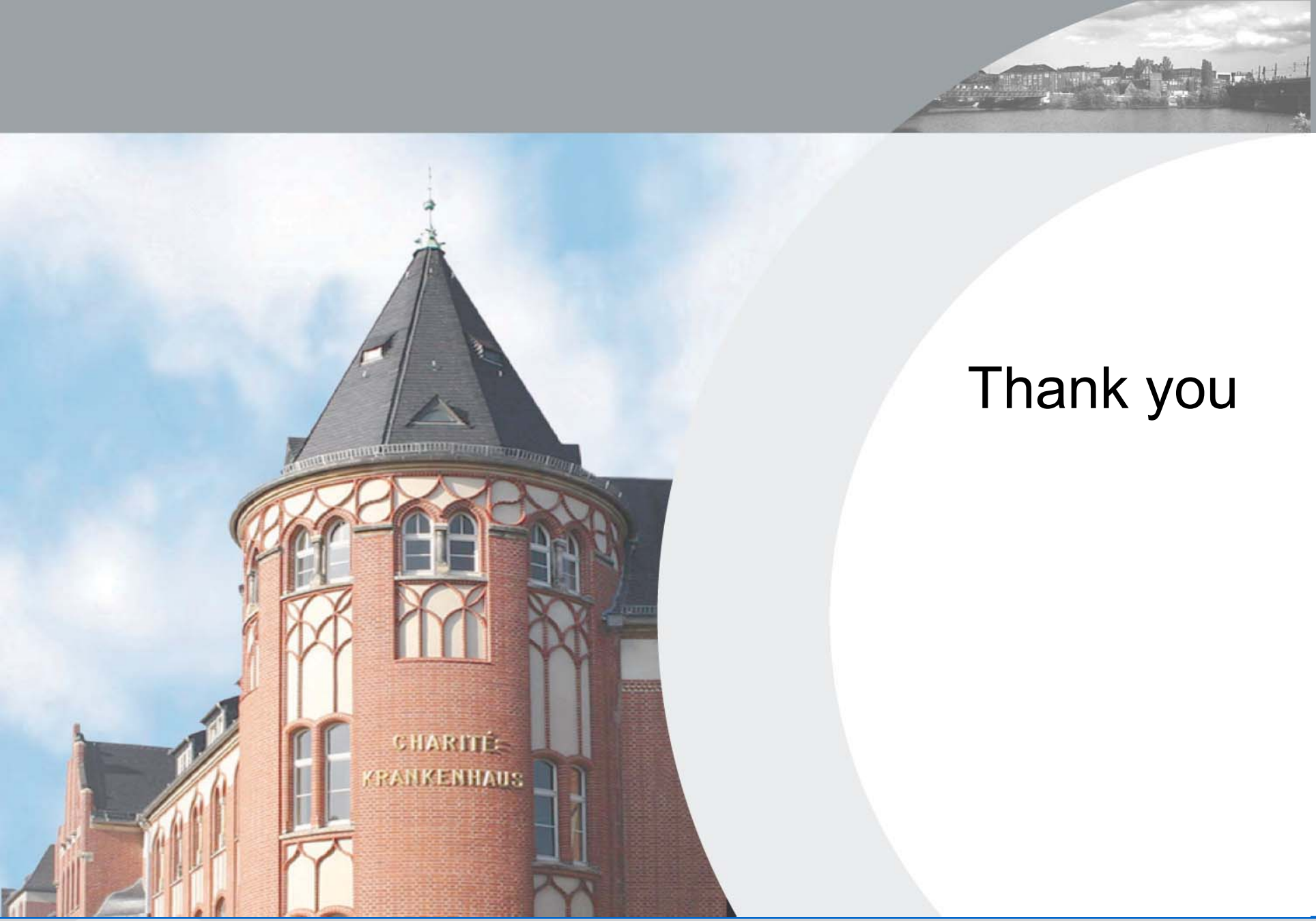
Lirentelimab in Chronic Urticaria

Demonstrated activity in all forms of antihistamine-refractory Chronic Urticaria tested

Substantial activity in patients refractory to omalizumab

Continued activity observed in 12-month open-label extension

Lirentelimab is potentially a front-line biologic treatment for Chronic Urticaria



Thank you