

# AK002 (Antolimab) in Adult Patients with Active Eosinophilic Gastritis and/or Eosinophilic Gastroenteritis: Primary Results from a Randomized, Double-Blind, Placebo-Controlled Phase 2 Trial (ENIGMA Study; NCT03496571)

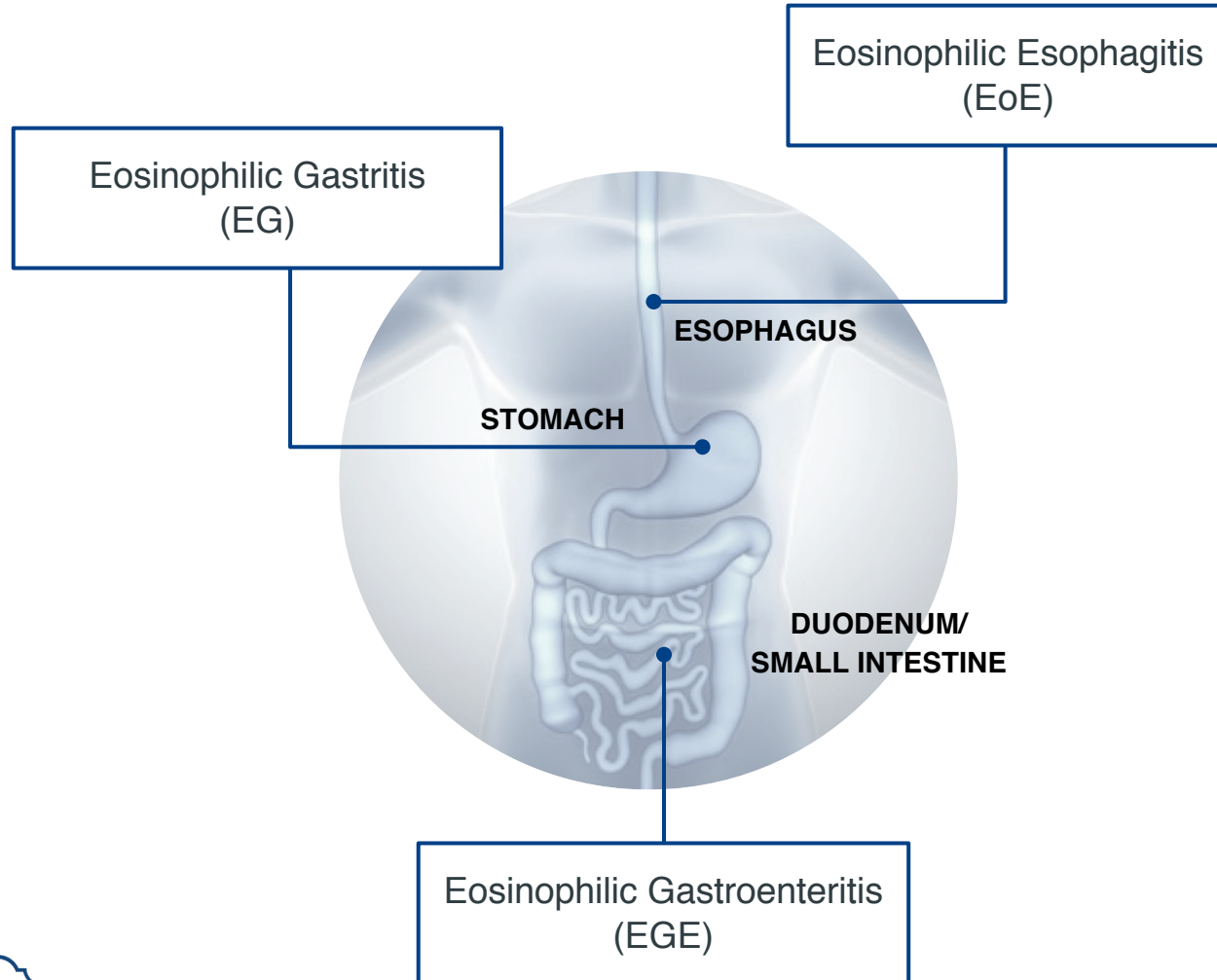
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# Eosinophilic Gastrointestinal Diseases (EGIDs)

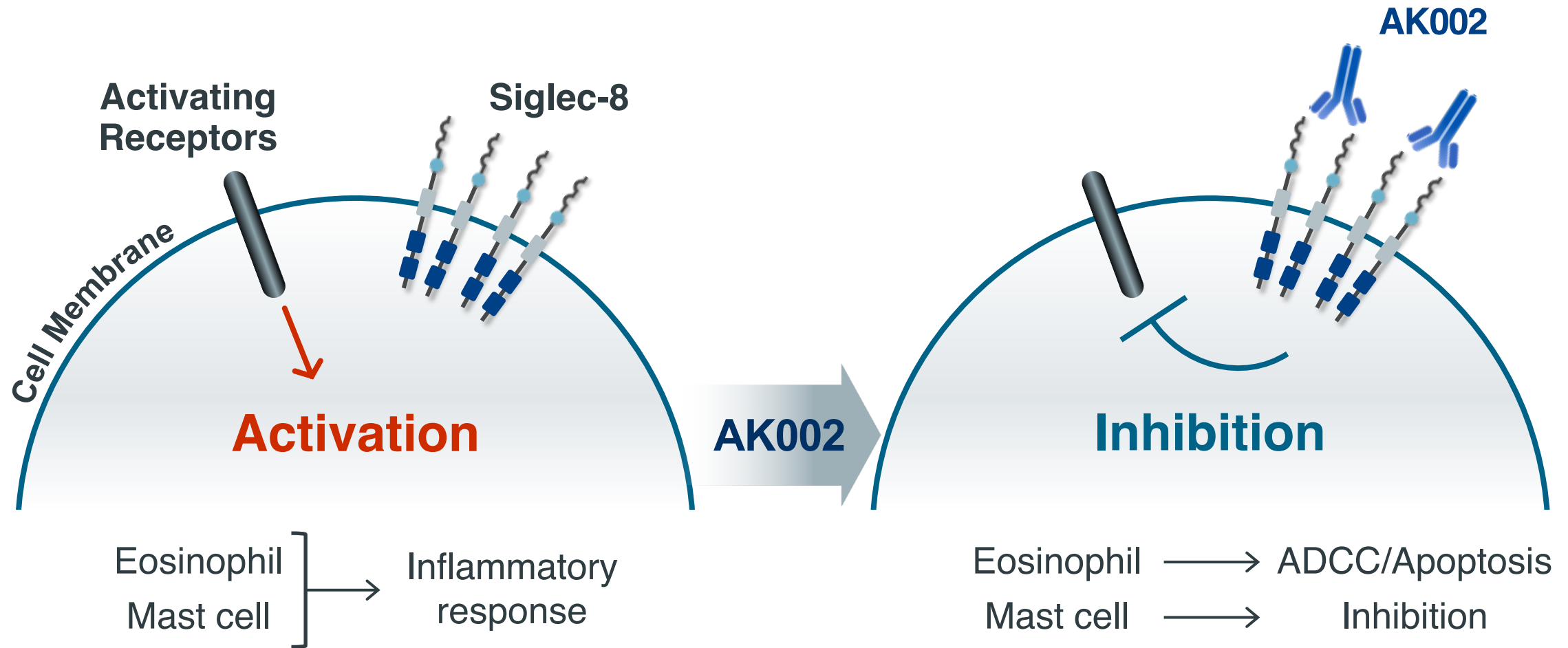


## EG, EGE, EoE

### Chronic Eosinophilic Inflammation of the Stomach, Small Intestine, or Esophagus

- Symptoms: abdominal pain, nausea, early satiety, loss of appetite, bloating, abdominal cramping, vomiting, diarrhea, and dysphagia
- Eosinophils and mast cells are important drivers of disease
- Current standard of care: steroids; diet
- No FDA-approved treatment for EG, EGE, or EoE

# AK002 Targets Siglec-8 on Eosinophils and Mast Cells



# ENIGMA Phase 2 Study Aim and Inclusion

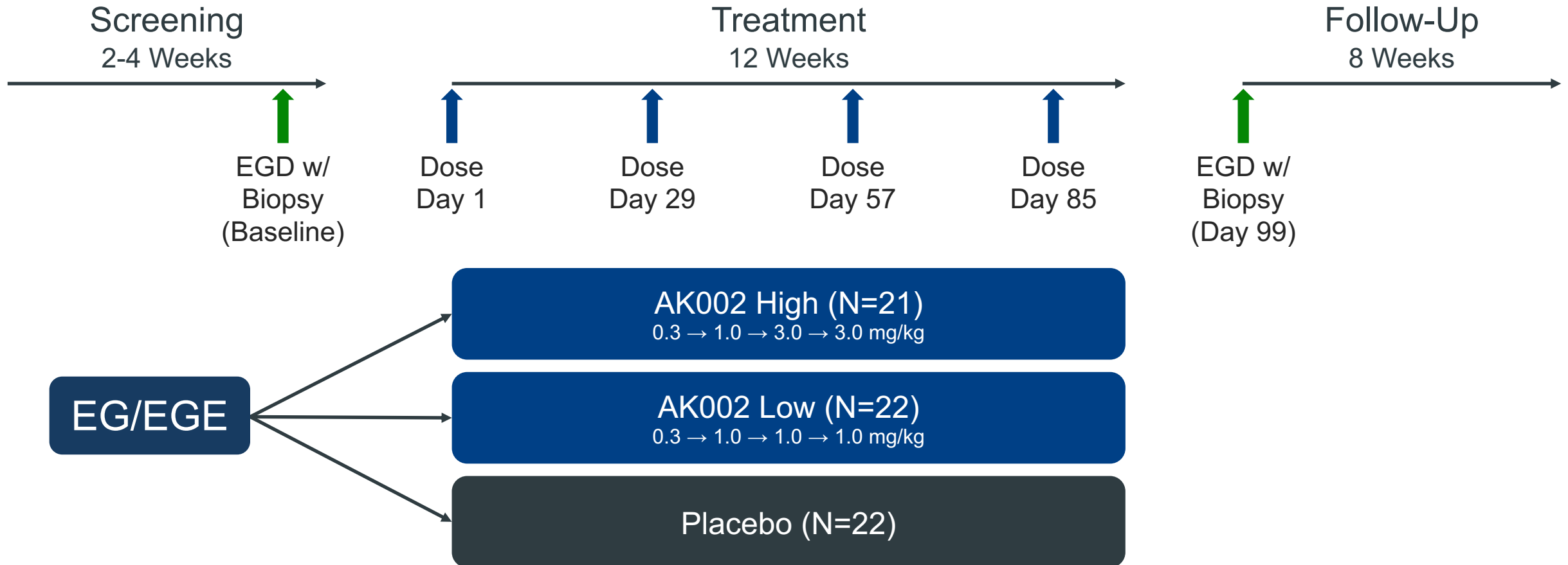
## Study Aim

- Determine safety and efficacy of AK002 for treatment of EG and/or EGE

## Key Inclusion Criteria

- Active moderate to severe symptoms<sup>1</sup> using the daily 8 symptom EG/EGE-SQ<sup>®</sup> Questionnaire
- Biopsy confirmed EG/EGE
  - Stomach:  $\geq 30$  eos/hpf in 5 hpfs
  - Duodenum:  $\geq 30$  eos/hpf in 3 hpfs

# ENIGMA Phase 2 Study Design





# Endpoints

## **Primary Endpoint**

- Mean percent change in gastrointestinal eosinophil counts from baseline

## **Symptoms Secondary Endpoint**

- Mean percent change in Total Symptom Score (TSS) from baseline

## **Responder Secondary Endpoint**

- Proportion of patients who have:
  - >75% decrease in tissue eosinophils AND >30% benefit in TSS

## **Primary analysis with a pre-specified hierarchical per protocol approach**

- Sensitivity analyses: ITT; subgroup with no steroid use

# Baseline Characteristics

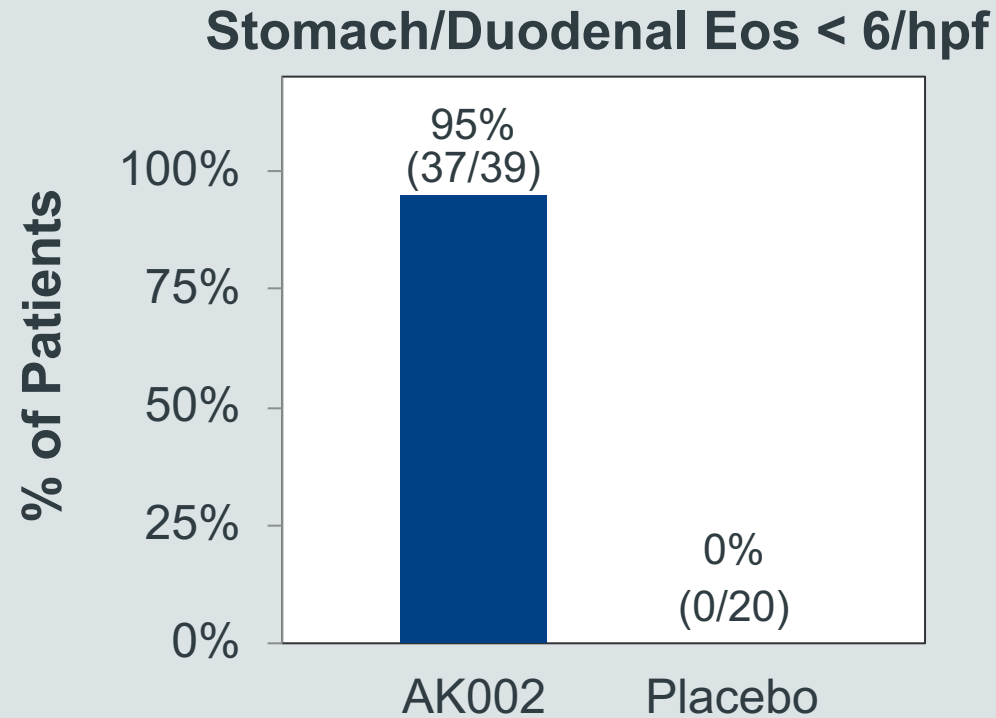
		AK002 Dose Groups			Placebo (n=20)	Total (N=59)
		High 0.3-3.0 mg/kg (n=20)	Low 0.3-1.0 mg/kg (n=19)	Combined High/Low (n=39)		
Age, Mean (Range)		42 (20-67)	43 (18-74)	42 (18-74)	40 (18-67)	41 (18-74)
Female		60%	84%	72%	50%	64%
White		85%	95%	90%	100%	93%
Mean Gastrointestinal <sup>1</sup> Eosinophils/hpf		76	80	78	75	77
Mean Gastrointestinal <sup>1</sup> Mast Cells/hpf		59	70	64	56	62
Mean Total Symptom Score (TSS) [0-80]		34.1	34.7	34.4	30.1	32.9
% of Patients (n) by AEC <sup>2</sup> /μL	<250	45% (9)	26% (5)	36% (14)	45% (9)	39% (23)
	250 to <500	35% (7)	42% (8)	38% (15)	15% (3)	31% (18)
	500 to <1500	20% (4)	21% (4)	21% (8)	35% (7)	25% (15)
	≥1500	0%	11% (2)	5% (2)	5% (1)	5% (3)

# Primary Endpoint – Mean % Change in Eosinophil Count

Treatment Arm	Baseline Eosinophil Counts / hpf	Mean %Δ in Eosinophil Counts	<i>p</i> - value
High Dose AK002 (n=20)	76	-97%	<b>&lt;0.0001</b>
Low Dose AK002 (n=19)	80	-92%	<b>&lt;0.0001</b>
Combined AK002 (n=39)	78	-95%	<b>&lt;0.0001</b>
Placebo (n=20)	75	+10%	-



# Tissue Eosinophil Depletion



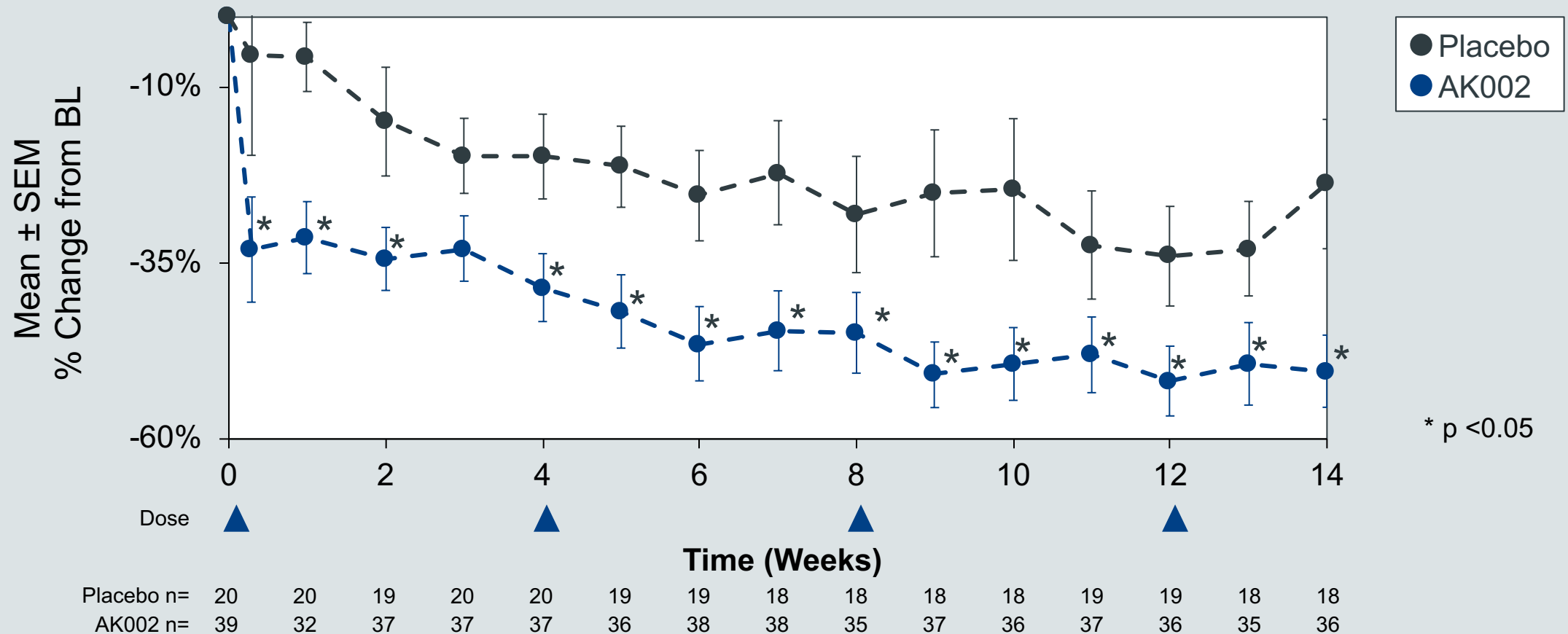
**37 of 39 patients had < 6 eos/hpf; 31/39 had 0 eos/hpf**

# Patient Reported Symptoms Secondary Endpoint

Treatment Arm	Baseline TSS	Mean % Change in TSS	<i>p</i> - value
High Dose AK002 (n=20)	34	-58%	<b>0.0012</b>
Low Dose AK002 (n=19)	35	-49%	<b>0.0150</b>
Combined AK002 (n=39)	34	-53%	<b>0.0012</b>
Placebo (n=20)	30	-24%	-

# Rapid & Sustained Improvement in Symptoms

EG/EGE-PRO Total Symptom Score

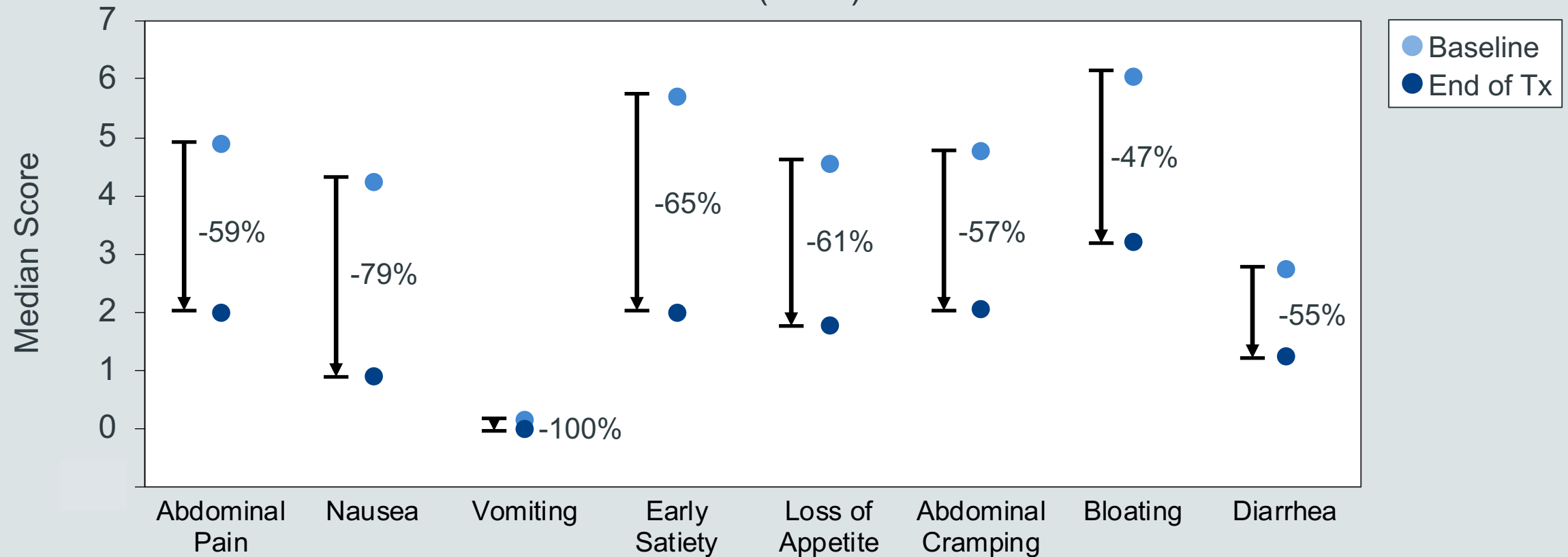


Placebo n=	20	20	19	20	20	19	19	18	18	18	18	19	19	18	18
AK002 n=	39	32	37	37	37	36	38	38	35	37	36	37	36	35	36

# Improvement Across All Symptoms

## EG/EGE-PRO Symptom Score

AK002 (n=39)



# Improvements in TSS Were Not Driven by Any Single Symptom

Mean Reduction in TSS	Combined AK002 (N=39)	Placebo (N=20)	<i>p</i> - value
<b><u>Total Score</u></b>	<b><u>-53.5%</u></b>	<b><u>-24.3%</u></b>	<b><u>0.0012</u></b>
Minus Abdominal Pain	-53.1%	-22.5%	0.0010
Minus Nausea	-53.2%	-23.9%	0.0009
Minus Vomiting	-53.0%	-24.9%	0.0018
Minus Satiety	-51.8%	-25.4%	0.0019
Minus Loss of Appetite	-53.0%	-24.9%	0.0009
Minus Abdominal Cramping	-53.0%	-22.4%	0.0011
Minus Bloating	-55.9%	-26.9%	0.0029
Minus Diarrhea	-54.9%	-24.0%	0.0010



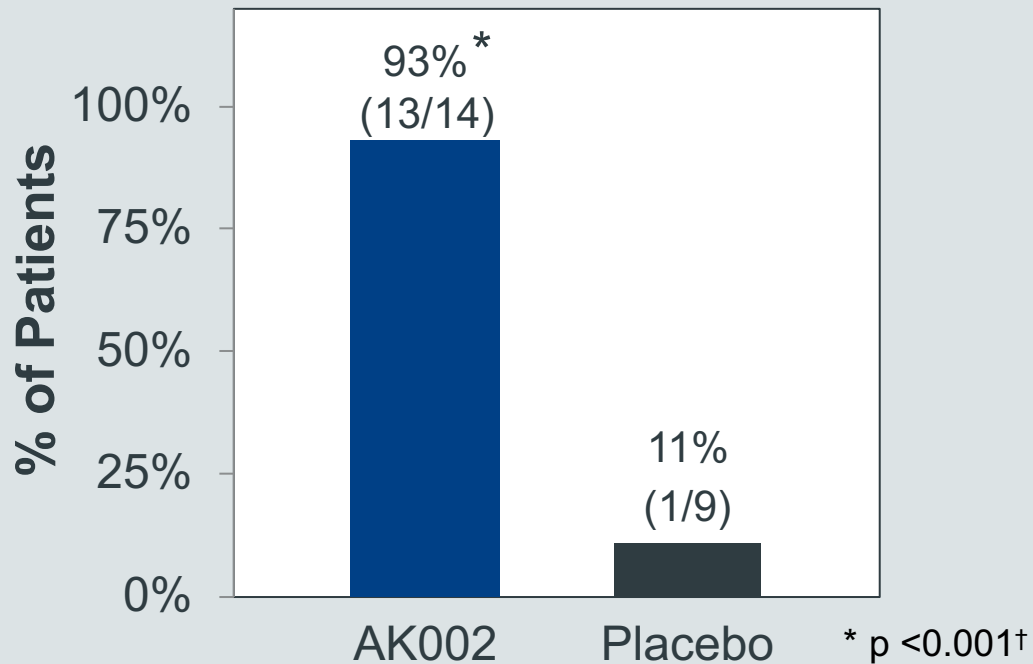
# AK002 Met Treatment Responder Secondary Endpoint

Treatment Arm	Treatment Responders	<i>p</i> - value
High Dose AK002 (n=20)	70%	<b>0.0009</b>
Low Dose AK002 (n=19)	68%	<b>0.0019</b>
Combined AK002 (n=39)	69%	<b>0.0008</b>
Placebo (n=20)	5%	-

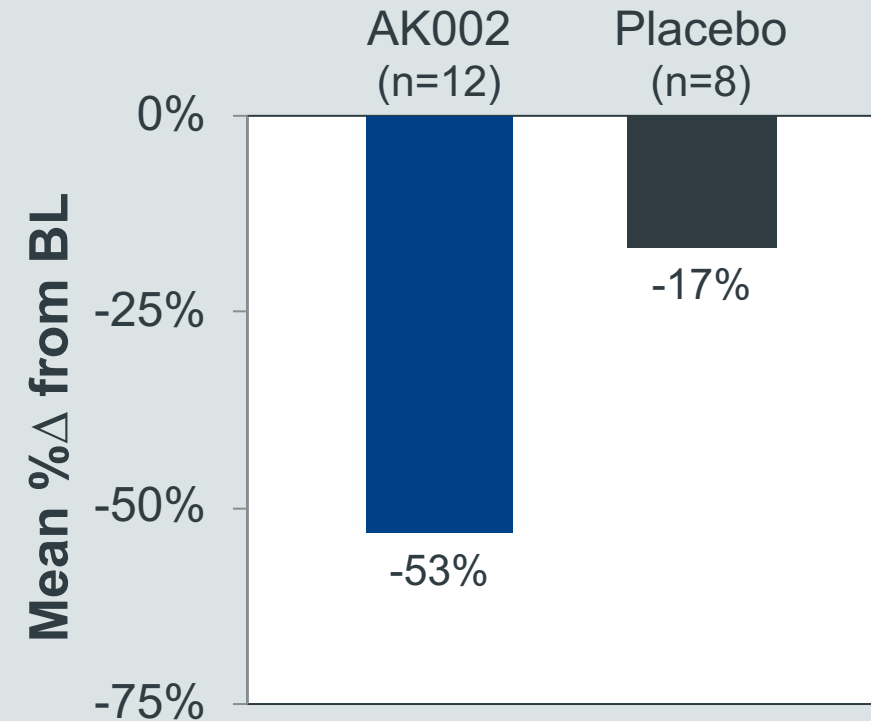
Treatment responder defined as: >75% reduction in tissue eosinophil counts AND >30% reduction in symptoms (TSS)

# Response in Concomitant EoE<sup>1</sup>

## Esophageal Eos $\leq$ 6/hpf<sup>2</sup>



## Severity of Dysphagia<sup>3</sup>



<sup>1</sup> 25 patients with concomitant EoE ( $\geq$ 15 eos/hpf or history of EoE) and baseline dysphagia

<sup>2</sup> Excludes patients with eos < 6/hpf at baseline. At end of treatment, 10/14 AK002 patients had 0 eos/hpf; 2/14 AK002 patients had 1 eos/hpf; 1/14 AK002 patients had 3 eos/hpf; 1/14 AK002 patients had 105 eos/hpf (biopsy occurred 6 weeks post last dose instead of 2 weeks per protocol); 1/9 placebo patients had 2 eos/hpf; 8/9 placebo patients had 19 – 200 eos/hpf

<sup>3</sup> All EoE patients with end of treatment dysphagia scores

† p = 0.00015

# Safety Summary

## Treatment-Emergent AEs in ≥5% of Patients

% of Patients, (n)	AK002 (n=43)	Placebo (n=22)
Infusion related reaction	60% (26)	23% (5)
Headache	9% (4)	9% (2)
Upper respiratory tract infection	9% (4)	9% (2)
Urinary tract infection	9% (4)	5% (1)
Nausea	7% (3)	14% (3)
Fatigue	7% (3)	9% (2)
Diarrhea	5% (2)	9% (2)
Nasopharyngitis	5% (2)	9% (2)
Abdominal pain	2% (1)	9% (2)
Dehydration	2% (1)	9% (2)
Gastroenteritis viral	2% (1)	9% (2)
Pyrexia	2% (1)	9% (2)
Sinusitis	2% (1)	9% (2)
Cough	0% (0)	9% (2)
Influenza	0% (0)	9% (2)
White blood cell count increased	0% (0)	9% (2)

- Generally well tolerated
- Most common AE was mild to moderate infusion related reactions (IRR)
  - 93% mild to moderate (flushing, feeling of warmth, headache, nausea, dizziness)
  - Mostly on first infusion, greatly reduced or does not occur on subsequent infusions
  - 1 drug-related serious adverse event, an IRR which recovered within 24 hours with no further sequelae
- Treatment-emergent SAEs: 9% on AK002, 14% on Placebo
- No other significant AEs

# ENIGMA Summary

- This was the first randomized study in EG/EGE
- Study met all primary and secondary endpoints, demonstrating significant histologic and symptom improvements in EG/EGE
- Strong histologic and symptom improvements in EoE
- Generally well-tolerated
- These results build on clinical activity of AK002 observed in other atopic and mast cell disorders (chronic urticaria, severe allergic conjunctivitis, asthma, atopic dermatitis, and indolent systemic mastocytosis)
- Further development of AK002 for EG/EGE is appropriate

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