

Avacincaptad pegol reduces progression of ellipsoid zone loss and degradation in eyes with the highest baseline ellipsoid zone burden

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KEY TAKEAWAYS

- ACP 2 mg slowed EZ loss over 12 months versus sham, with the greatest benefit seen in eyes with high baseline EZ burden and partial attenuation, highlighting an optimal treatment window before substantial photoreceptor structural loss
- EZ loss and degradation emerge as functionally relevant structural biomarkers

INTRODUCTION

- The EZ is an established imaging biomarker of photoreceptor integrity¹⁻⁴
- The integrity of the EZ may be a potential biomarker for GA progression rate⁵⁻⁷
- ACP is approved for the treatment of GA in the United States, Japan, and Australia⁸⁻¹⁰
- ACP reduced GA growth versus sham at a dose of 2 mg for up to 18 months in GATHER1 and 24 months in GATHER2¹¹⁻¹³
- A previous post hoc analysis demonstrated that ACP 2 mg treatment reduced GA lesion growth versus sham in eyes with the highest EZ burden at baseline (i.e., greatest EZ degradation/loss) over 12 months (**Figure 1**)¹⁴

OBJECTIVE

- This post hoc analysis of pooled GATHER1 and GATHER2 trial data assessed the impact of ACP 2 mg on the **progression of EZ attenuation** over 12 months in eyes with GA and the highest baseline EZ burden

METHODS

- GATHER1 (phase 2/3; NCT02686658) and GATHER2 (phase 3; NCT04435366) were multicenter, randomized, double-masked, sham-controlled trials that evaluated the efficacy and safety of ACP 2 mg in patients with non-center point involving GA^{12,15}
- Spectral-domain OCT scans were segmented using a machine-learning-enhanced multilayer retinal segmentation platform

METHODS (CONT'D)

- Parameters of EZ integrity in the macular cube included:
 - Partial EZ attenuation: Percentage of area with EZ–RPE thickness ≤20 μm (“EZ degradation”)
 - Total EZ attenuation: Percentage of area with EZ–RPE thickness = 0 μm (“EZ loss”)
- Eyes were stratified into quartiles based on baseline EZ integrity, from lowest (Q1) to highest (Q4) EZ burden (**Table 1**)
- Mean change in partial and total EZ attenuation over time was evaluated in eyes with the highest baseline EZ burden (Q4)

Table 1. Baseline EZ burden of pooled GATHER1 and GATHER2 data

	ACP 2 mg				Sham			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
n	73	72	72	73	83	83	83	83
Baseline partial EZ attenuation, % (SD)	22.3 (5.7)	38.4 (4.2)	53.6 (5.1)	76.1 (10.1)	23.2 (5.2)	39.4 (4.8)	52.7 (3.7)	74.7 (10.2)
Baseline total EZ attenuation, % (SD)	14.2 (3.2)	23.4 (2.5)	32.8 (2.8)	47.6 (7.0)	15.0 (3.1)	23.8 (2.5)	34.4 (3.3)	48.6 (9.4)

Q4: Eyes with highest baseline EZ attenuation

RESULTS

Highest partial EZ attenuation at baseline

- Compared with sham, ACP 2 mg slowed the progression of partial EZ attenuation in eyes with the greatest baseline partial EZ attenuation (Q4); demonstrating a 66.2% reduction in partial EZ attenuation (**Figure 2A**) and a 12.6% reduction in total EZ attenuation (**Figure 2B**) at month 12

Highest total EZ attenuation at baseline

- Compared to sham, ACP 2 mg slowed the progression of total EZ attenuation in eyes with the greatest baseline total EZ attenuation (Q4), demonstrating a 17.8% reduction in total EZ attenuation at month 12 (**Figure 3**)

Figure 1. GA lesion growth from a previous pooled post hoc analysis of GATHER1 and GATHER2¹⁴

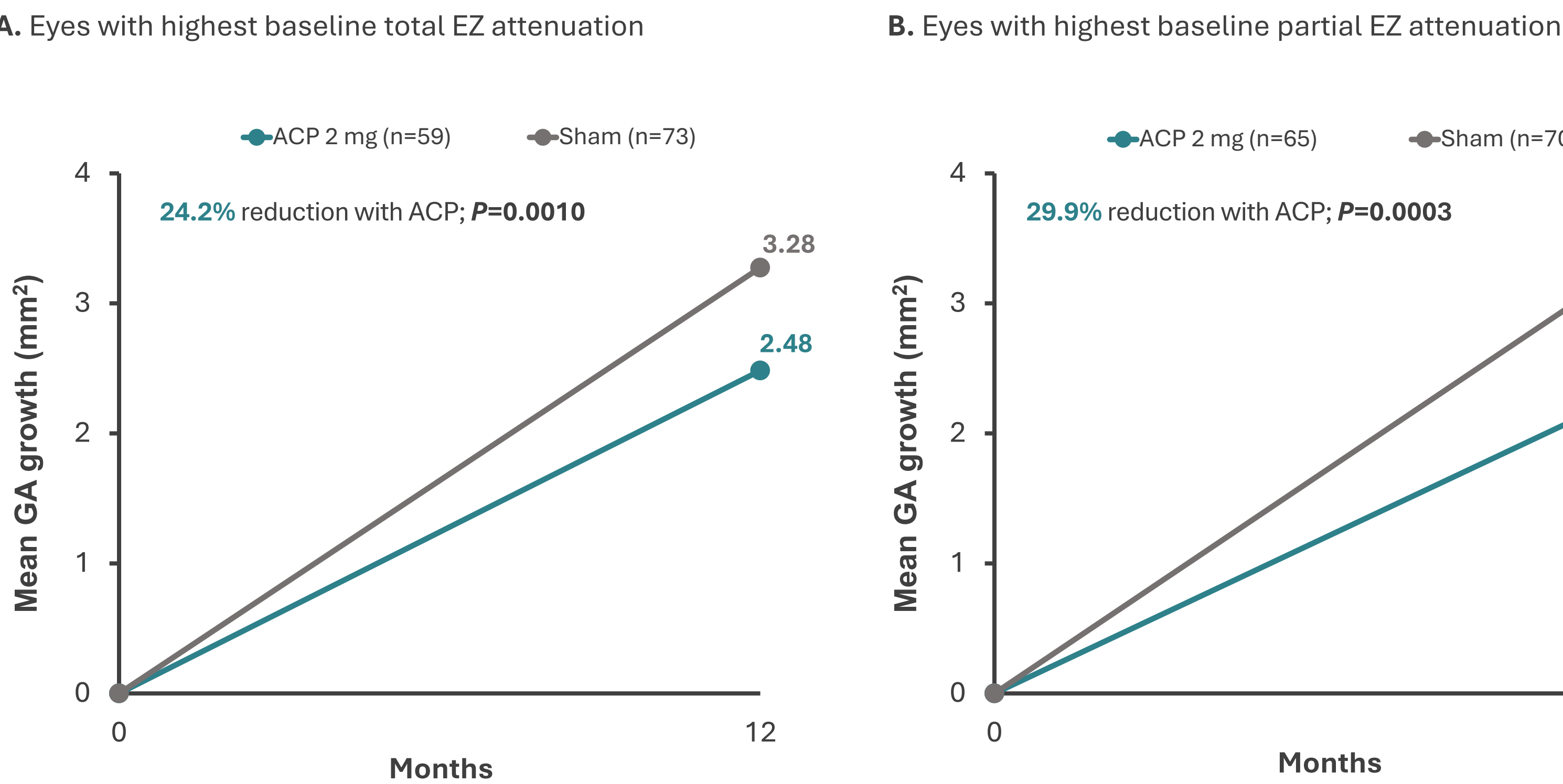


Figure 2. In eyes with the greatest baseline partial EZ attenuation (Q4), ACP 2 mg reduced progression of both (A) partial and (B) total EZ attenuation vs sham over 12 months

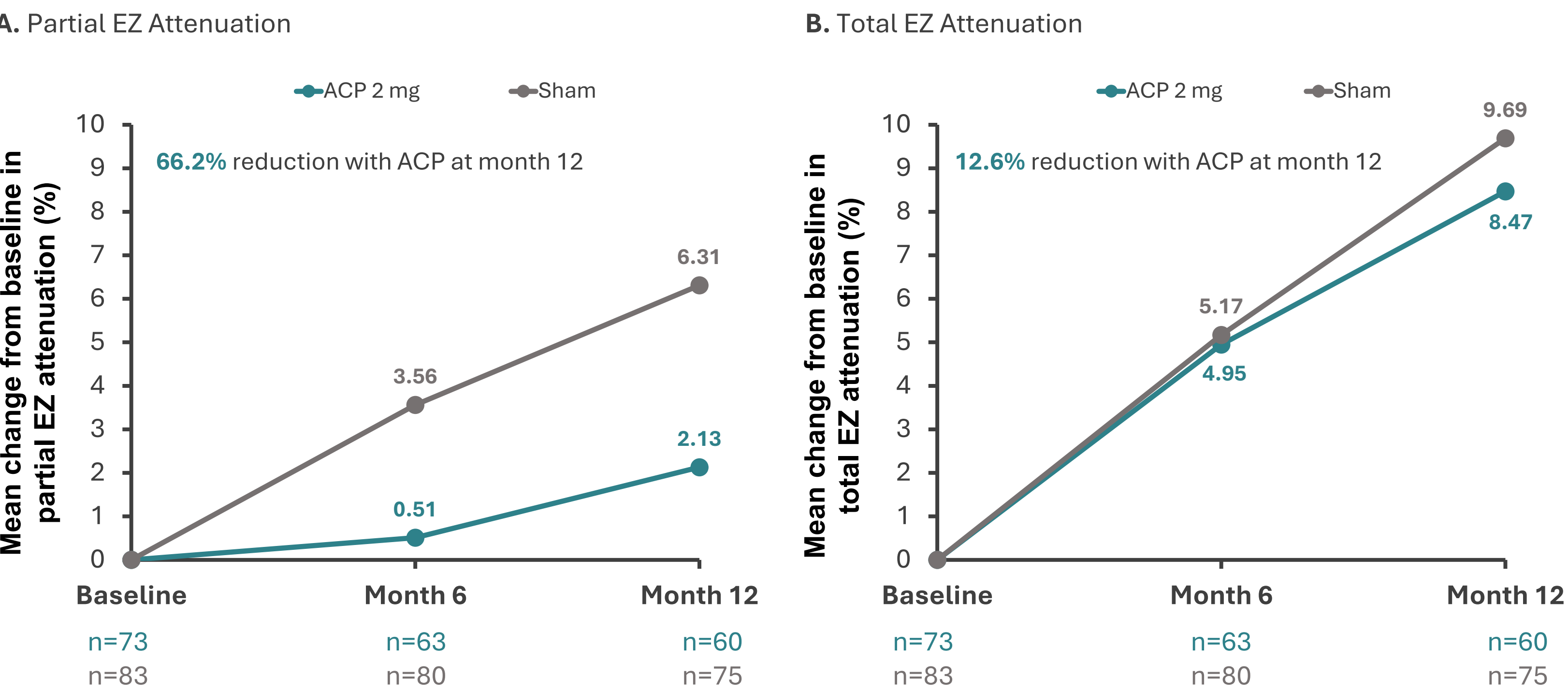
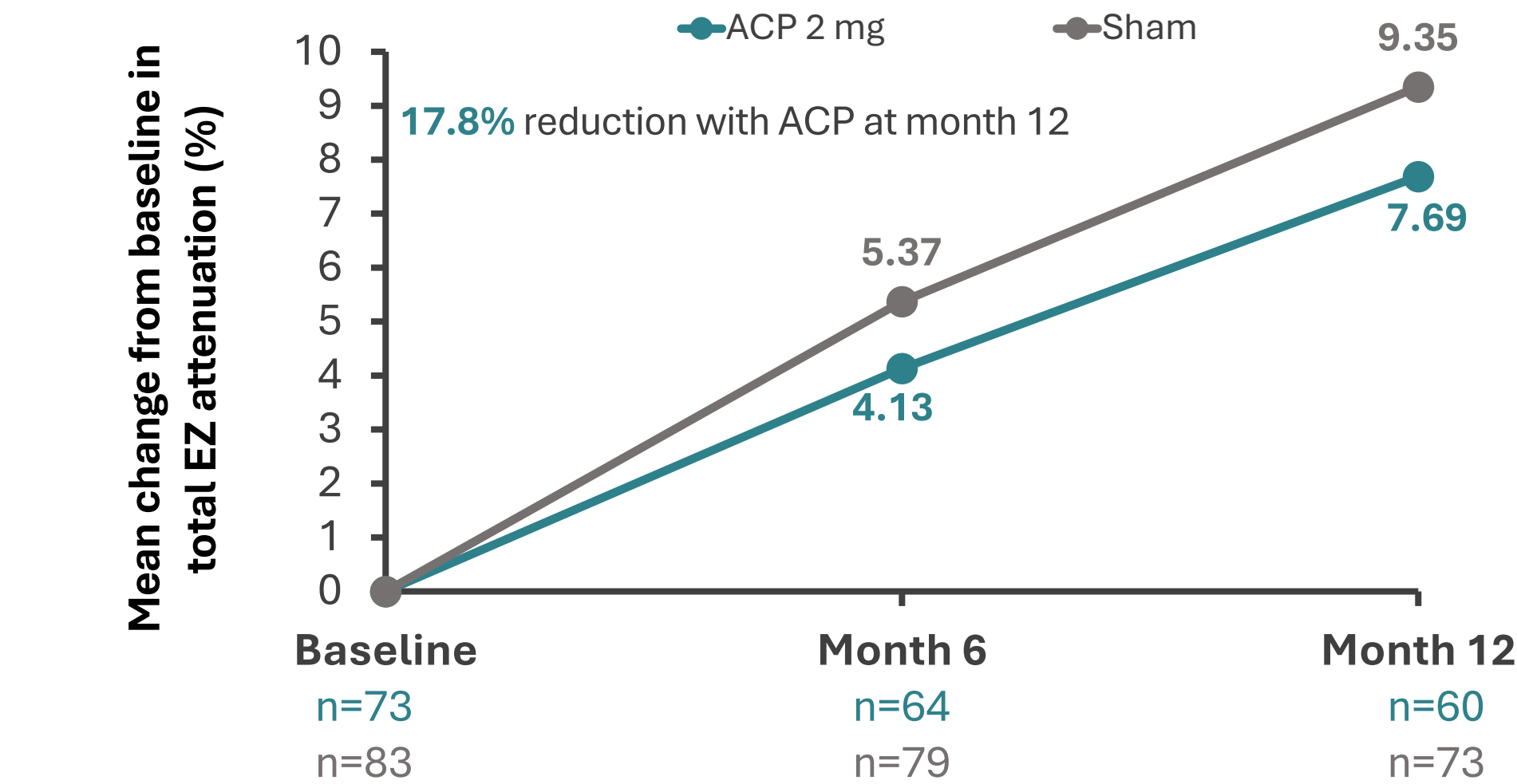


Figure 3. In eyes with the greatest baseline total EZ attenuation (Q4), ACP 2 mg reduced progression of total EZ attenuation vs sham over 12 months



CONCLUSIONS

- In eyes with the highest EZ burden at baseline, ACP 2 mg reduced the progression of EZ loss/degradation versus sham over 12 months
- This effect was most pronounced in reducing progression of EZ degradation in eyes with the highest baseline partial EZ attenuation
- ACP intervention may be an optimal strategy to slow EZ degradation in eyes with some degree of photoreceptor structure preservation
- Results support early EZ loss/degradation as important biomarkers to guide treatment decisions for individuals with GA who are at risk for high disease burden

Abbreviations: ACP, avacincaptad pegol; EZ, ellipsoid zone; GA, geographic atrophy; OCT, optical coherence tomography; Q, quartile; RPE, retinal pigmental epithelium; SD, standard deviation.

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