IVERIC BIO

DEVELOPING TRANSFORMATIVE THERAPIES
FOR RETINAL DISEASES

June 2022
NASDAQ: ISEE

Forward-looking statements

Any statements in this presentation about IVERIC bio (the Company)'s future expectations, plans and prospects constitute forward-looking statements for purposes of the safe harbor provisions under the Private Securities Litigation Reform Act of 1995. Forward-looking statements include statements about the strategy, operations and future expectations and plans and prospects for the Company, and any other statements containing the words "anticipate," "believe," "estimate," "expect," "intend", "goal," "may", "might," "plan," "predict," "project," "seek," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions.

In this presentation, the Company's forward-looking statements include statements about the hypotheses underlying, the results of and the implications of post-hoc analyses of the Company's GATHER1 clinical trial evaluating Zimura (avacincaptad pegol or ACP) for the treatment of geographic atrophy, and the potential utility of Zimura. Such forward-looking statements involve substantial risks and uncertainties that could cause the Company's research and development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the progress and results of clinical trials and other research and development programs, developments from the scientific and medical community and from the Company's competitors, and other factors discussed in the "Risk Factors" section contained in the quarterly and annual reports that the Company files with the Securities and Exchange Commission.

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Exploration of Machine Learning–Enhanced Compartmental Retinal Integrity Assessment for Progression Risk and Treatment Response in the GATHER1 Study

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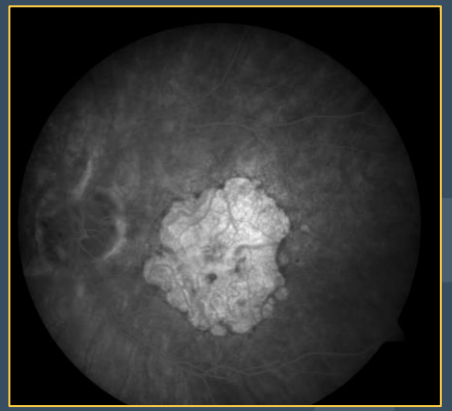
Advanced AMD and Compartmental Assessment with OCT

- There are no approved therapies to slow the progression of geographic atrophy (GA); however, several are under investigation.
- Identifying optimal imaging and image analysis strategies will be important for future therapeutic decision-making.
- Fundus autofluorescence (FAF) is the traditional gold standard to measure area of GA.[1,2]
- However, OCT availability is more widespread throughout practices.
- Compartmental OCT analysis may provide important biomarkers for therapeutic response and enable measurement of specific features, such as GA area and ellipsoid zone (EZ) integrity.



AMD, age-related macular degeneration.

1. Jaffe GJ, et al. *Ophthalmology*. 2021;128(4):576-586; 2. Liao DS, et al. *Ophthalmology*. 2020;127(2):186-195.

Ellipsoid Zone Integrity as Biomarker for GA progression

- The EZ is a hyperreflective outer retinal band observed on OCT associated with a mitochondrial rich area of the photoreceptors.[1]
- EZ integrity has been found to be a predictor of GA progression and linked to visual function.[2]
- Emerging technology now enables quantitative EZ integrity assessment.[2]
- In eyes with AMD, progression to subfoveal GA over 2 and 5 years was associated with[2]:
  - Multiple EZ parameters, including total EZ attenuation and progressive loss of EZ preservation.

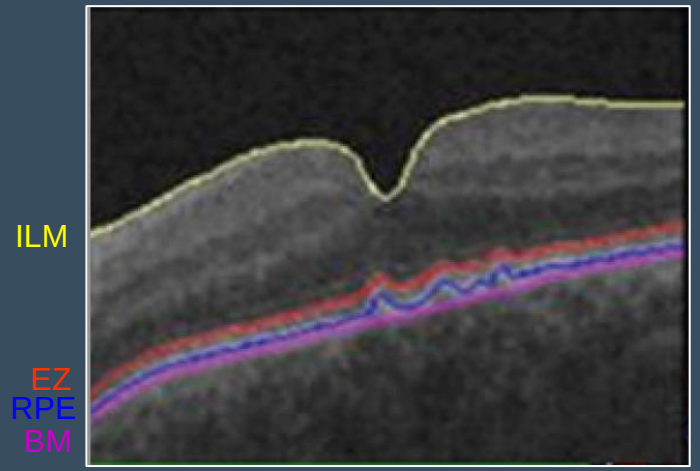


Image from Sarici K, et al. *Ophthalmic Surg Lasers Imaging Retina*. 2022;53(1):31-39.

AMD, age-related macular degeneration; BM, Bruch's membrane; EZ, ellipsoid zone; GA, geographic atrophy; ILM, internal limiting membrane; RPE, retinal pigment epithelium.

1. Litts KM, et al. *Retina*. 2018;38(3):445-461; 2. Sarici K, et al. *Ophthalmic Surg Lasers Imaging Retina*. 2022;53(1):31-39.

Longitudinal Assessment with Minimal EZ Attenuation

B scans

En face EZ-RPE thickness map

En face sub-RPE thickness map

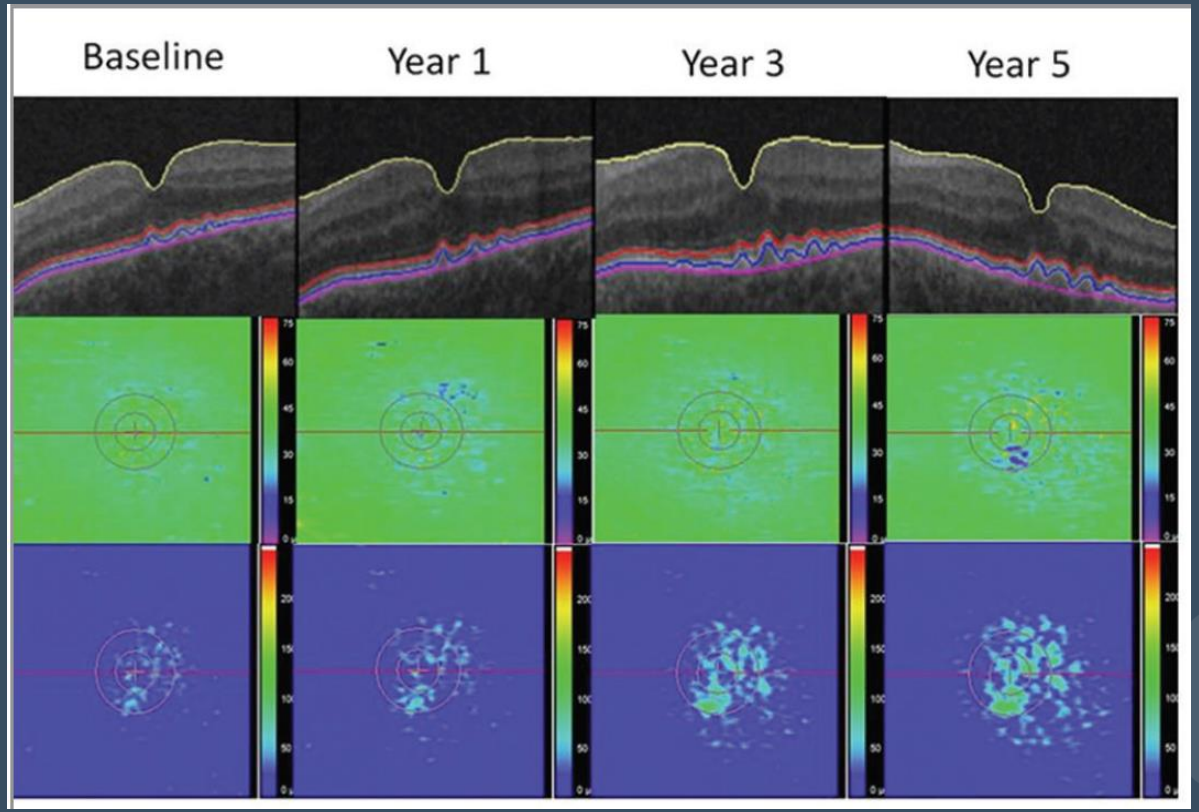


Image from Sarici K, et al. *Ophthalmic Surg Lasers Imaging Retina*. 2022;53(1):31-39.

EZ, ellipsoid zone; RPE, retinal pigment epithelium.

Longitudinal Assessment with Significant EZ attenuation

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En face EZ-RPE thickness map

En face sub-RPE thickness map

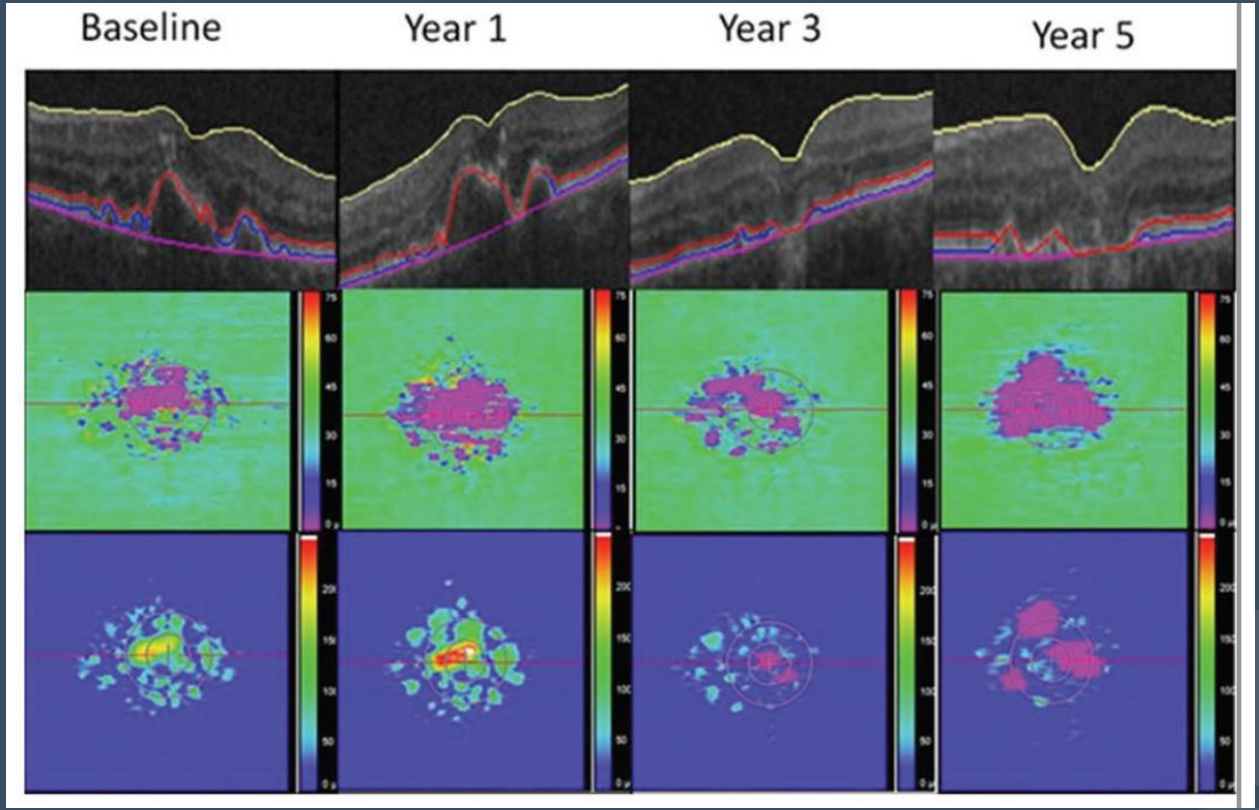


Image from Sarici K, et al. *Ophthalmic Surg Lasers Imaging Retina*. 2022;53(1):31-39.

EZ, ellipsoid zone; GA, geographic atrophy; RPE, retinal pigment epithelium.

GATHER1 study design

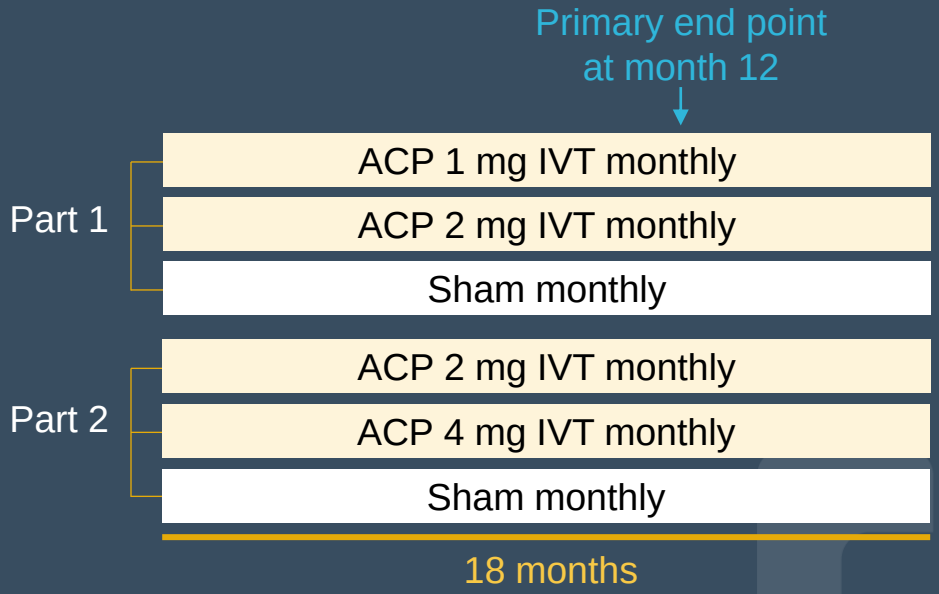
GATHER1 was a randomized, double-masked, phase 2/3 study that examined efficacy and safety of avacincaptad pegol (ACP) , an investigational complement C5 inhibitor, in eyes with GA.[1]

Key inclusion criteria:

- Nonfoveal[a] GA
- Total GA area ≥2.5 and ≤17.5 mm^2

Key exclusion criteria:

- Evidence of CNV in either eye

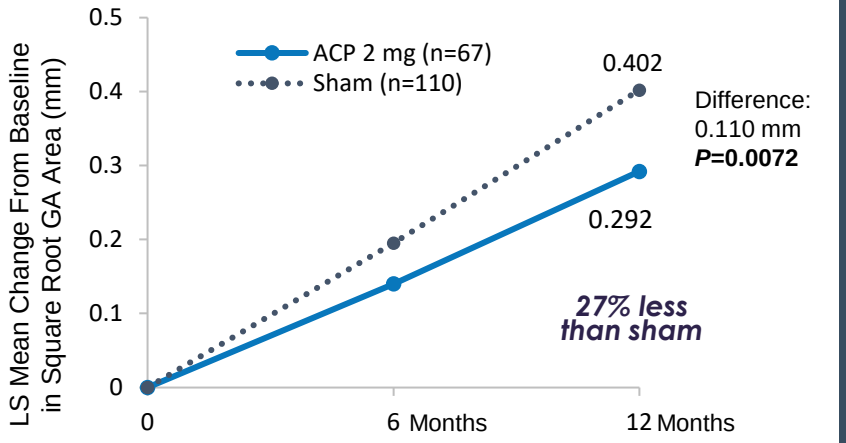


[a]Nonfoveal GA included lesions inside and outside the 1.5-mm diameter area of the fovea but not the foveal center point.
ACP, avacincaptad pegol; CNV, choroidal neovascularization; GA, geographic atrophy; IVT, intravitreal.
1. Jaffe GJ, et al. *Ophthalmology*. 2021;128(4):576-586.

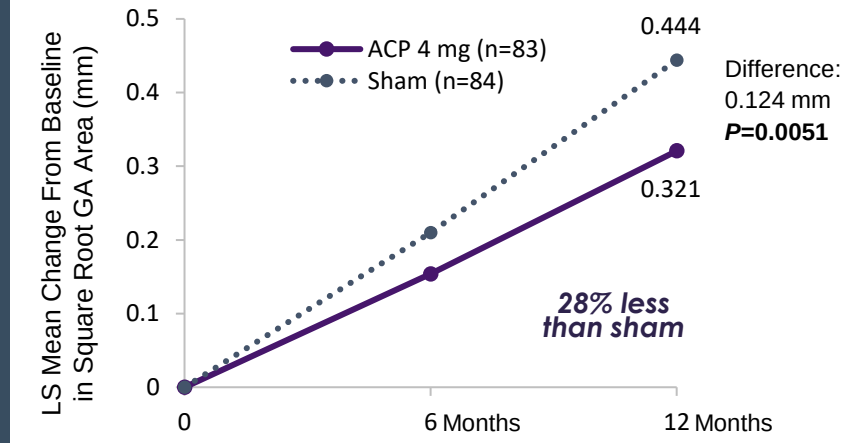
GATHER1 Met Primary End Point: ACP significantly reduced growth of GA area over 12 months[1]

Change in square-root GA area

Avacincaptad pegol 2 mg vs sham[1]



Avacincaptad pegol 4 mg vs sham[1]



Note: Based on LS means from MMRM model; ITT population Hochberg procedure was used for significance testing. These LS means are estimates from the MMRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2, and should not be interpreted as directly observed data.

ACP, avacincaptad pegol; GA, geographic atrophy; ITT, intention to treat; LS, least squares; MMRM, mixed model repeated measures.

1. Jaffe GJ, et al. *Ophthalmology*. 2021;128(4):576-586.

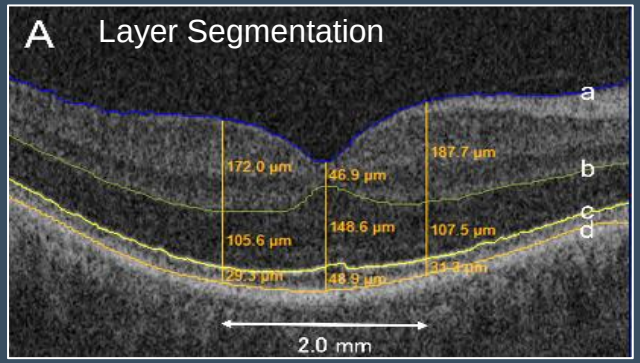
GATHER1 Post-hoc Analysis Objectives

- Primary objectives:
  - To examine the effect of ACP on EZ integrity change and OCT-measured GA growth in the GATHER1 study.[1]
  - To examine the relationship between EZ integrity and GA growth.
- Secondary objective:
  - To examine the correlation between FAF-measured and OCT-measured GA progression.

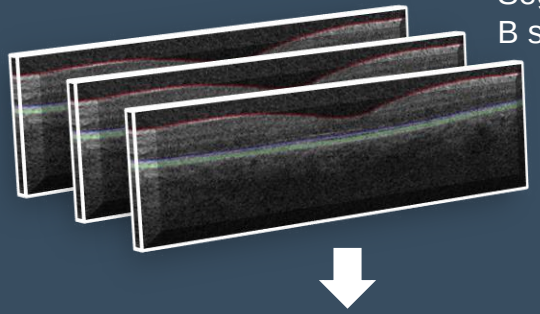
EZ, ellipsoid zone; FAF, fundus autofluorescence; GA, geographic atrophy.

Machine Learning-Enhanced OCT Analysis with EZ Mapping

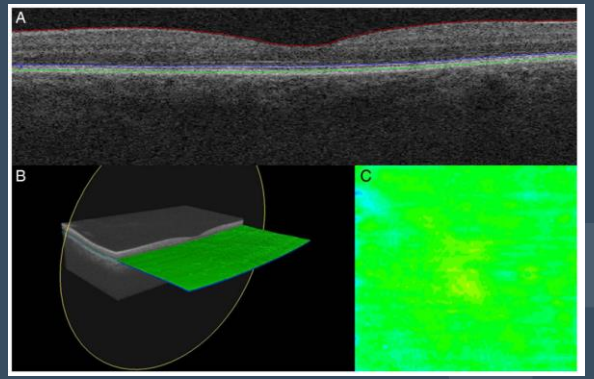
- Macular cube OCT scans from the ACP 2 mg, ACP 4 mg, and sham groups were loaded into an OCT mapping software.
- Key outer retinal layers identified included:
  - Ellipsoid zone (EZ)
  - Retinal pigment epithelium (RPE)
  - Bruch's membrane (BM)



EZ
RPE



Segmented
B scans



3D reconstruction of macular cube

En face view

ACP, avacincaptad pegol.

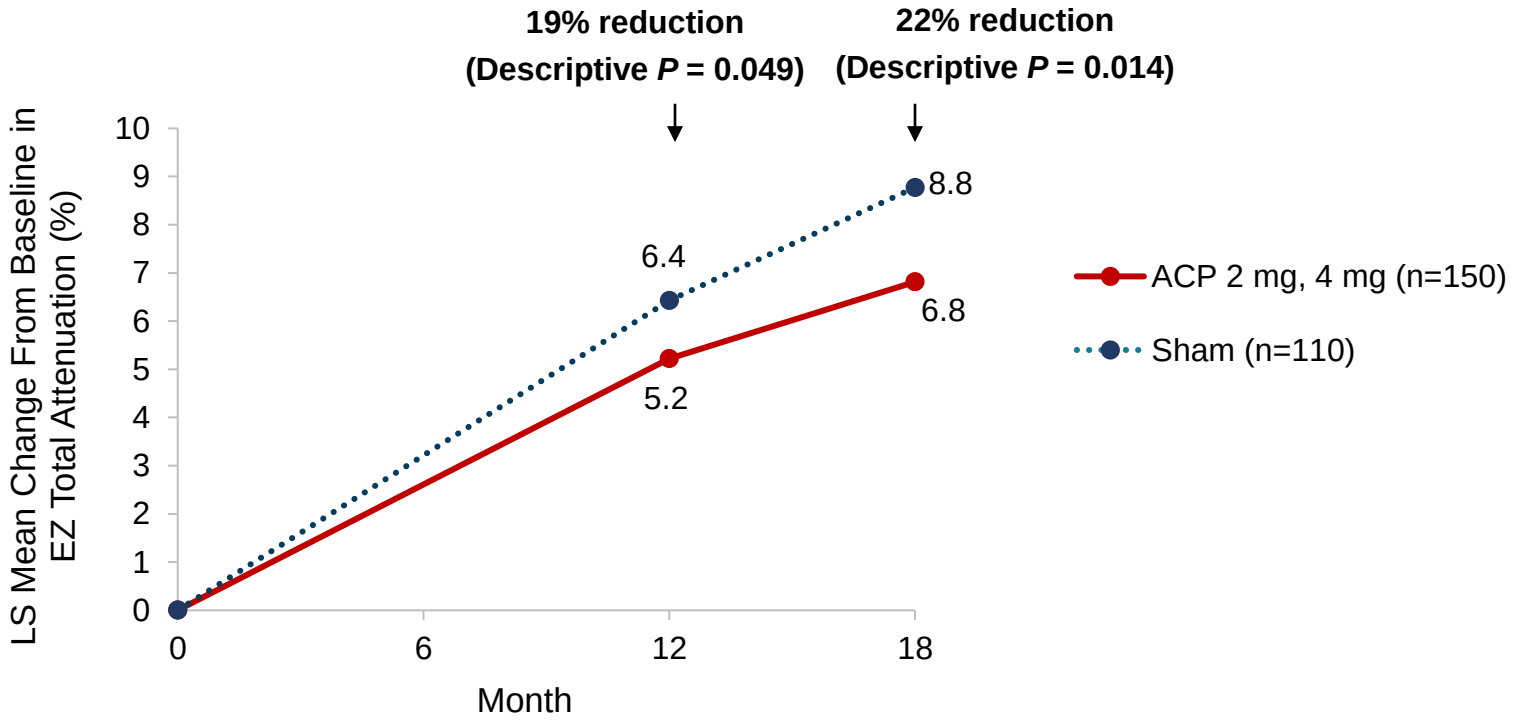
Various OCT measures of outer retinal atrophy were exported

OCT Measure	Description
EZ total attenuation (%)	**Percentage of macular cube with EZ-RPE thickness = 0 µm**
RPE total attenuation (%)	**Percentage of macular cube with RPE-BM thickness = 0 µm**
GA area (mm^2)	**Area of macular cube with RPE-BM thickness = 0 µm**
EZ partial attenuation (%)	Percentage of macular cube with EZ-RPE thickness ≤ 20 µm
EZ/GA Ratio	Total EZ loss / OCT-based GA
EZ-GA Gap (%)	EZ Loss Excess relative to GA (i.e., EZ total attenuation – GA)
EZ-GA Gap Index	(EZ-GA Gap)/OCT based

BM, Bruch's membrane; EZ, ellipsoid zone; GA, geographic atrophy; RPE, retinal pigment epithelium.

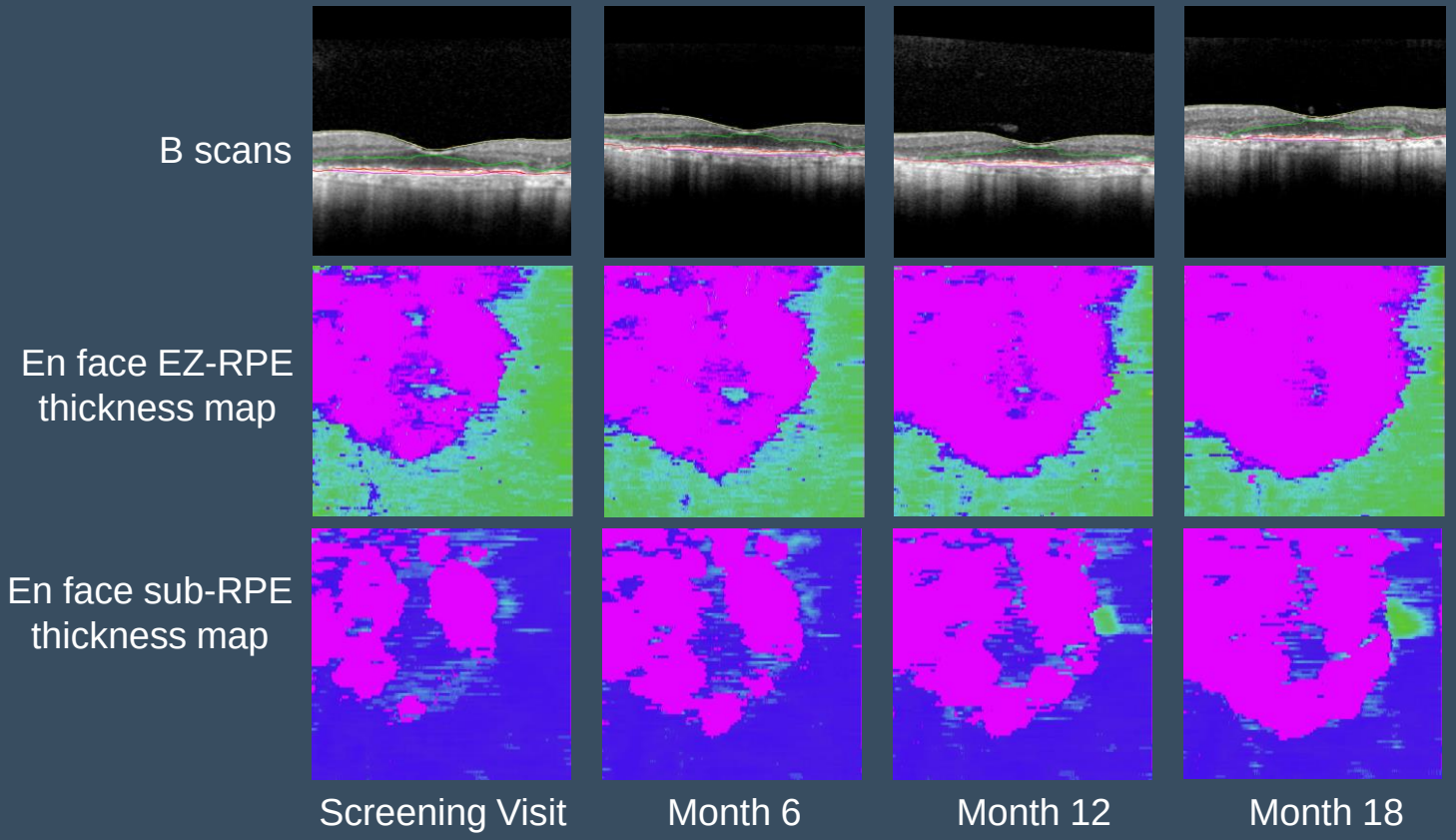
EZ Integrity Results

ACP Demonstrated Reduction in Progressive Total EZ Attenuation



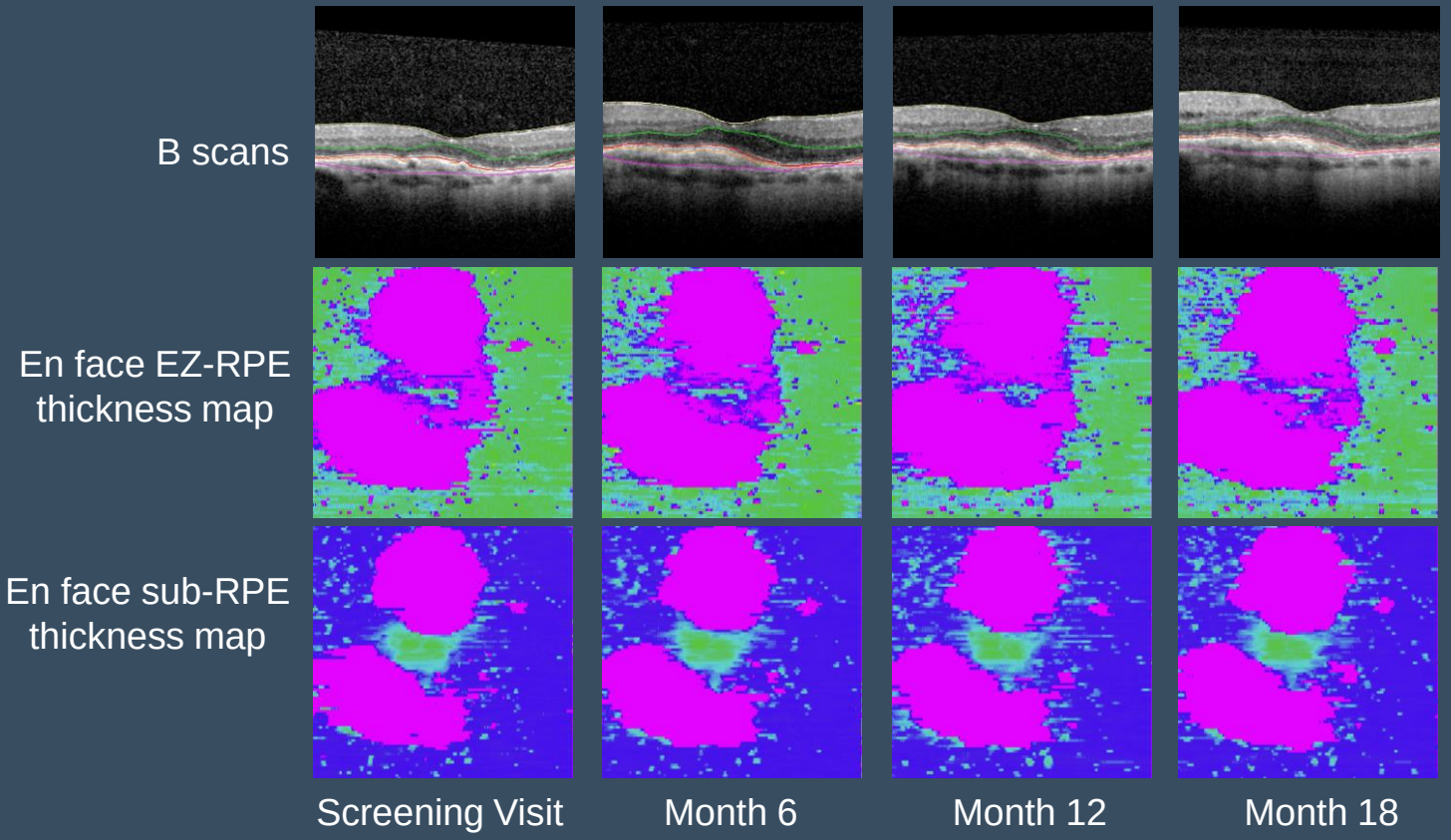
Note: Based on LS means from model for repeated measures.
ACP, avacincaptad pegol; BL, baseline; EZ, ellipsoid zone; LS, least squares.

Representative Example: Sham-treated Eye



EZ, ellipsoid zone; RPE, retinal pigment epithelium.

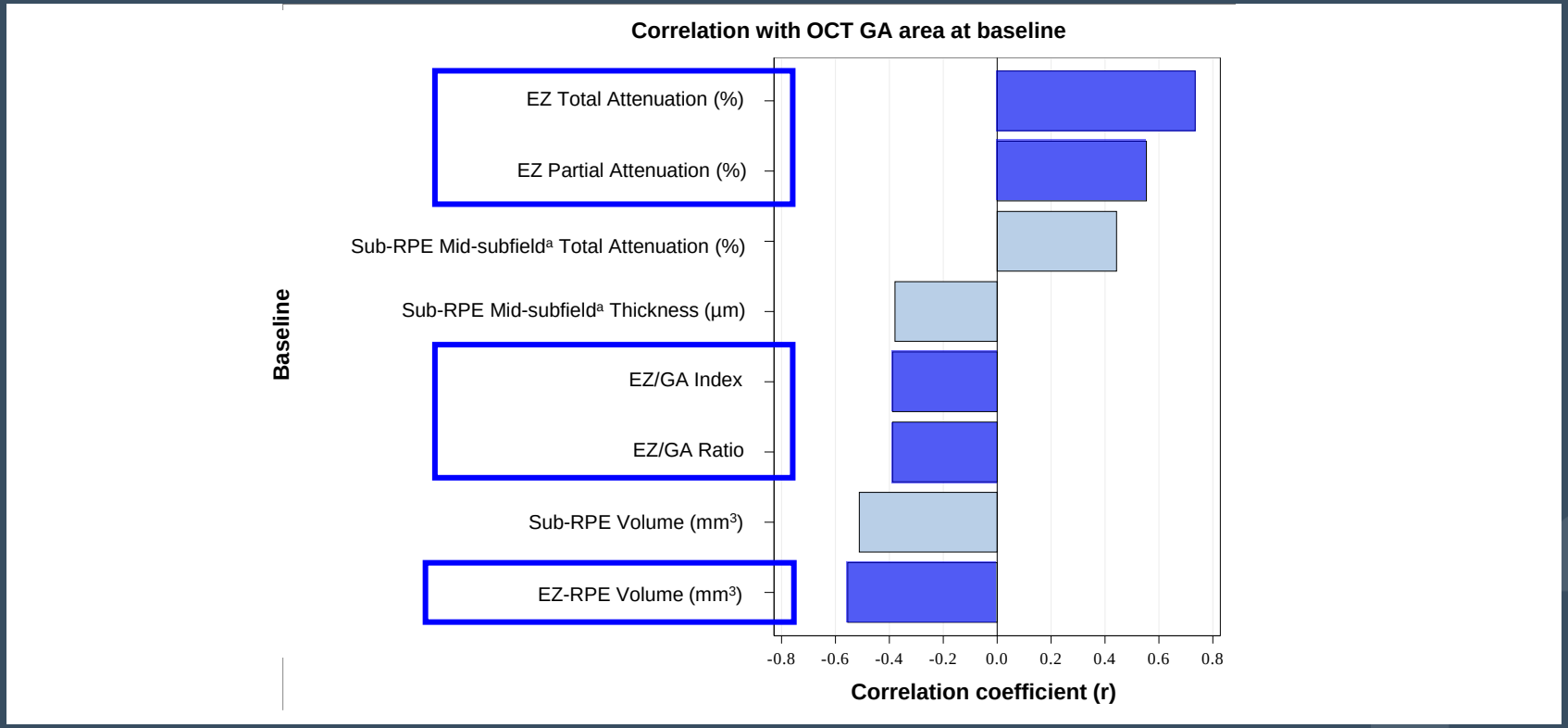
Representative Example: ACP-treated Eye



ACP, avacincaptad pegol; EZ, ellipsoid zone; RPE, retinal pigment epithelium.

EZ – GA Associations

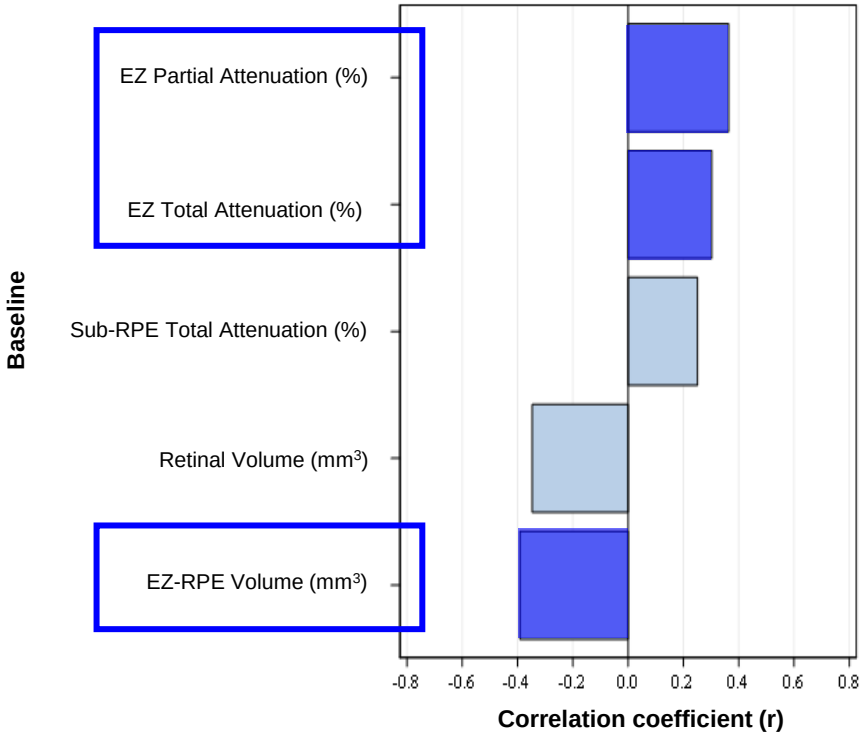
Association of Baseline EZ Measures with OCT-based GA Area



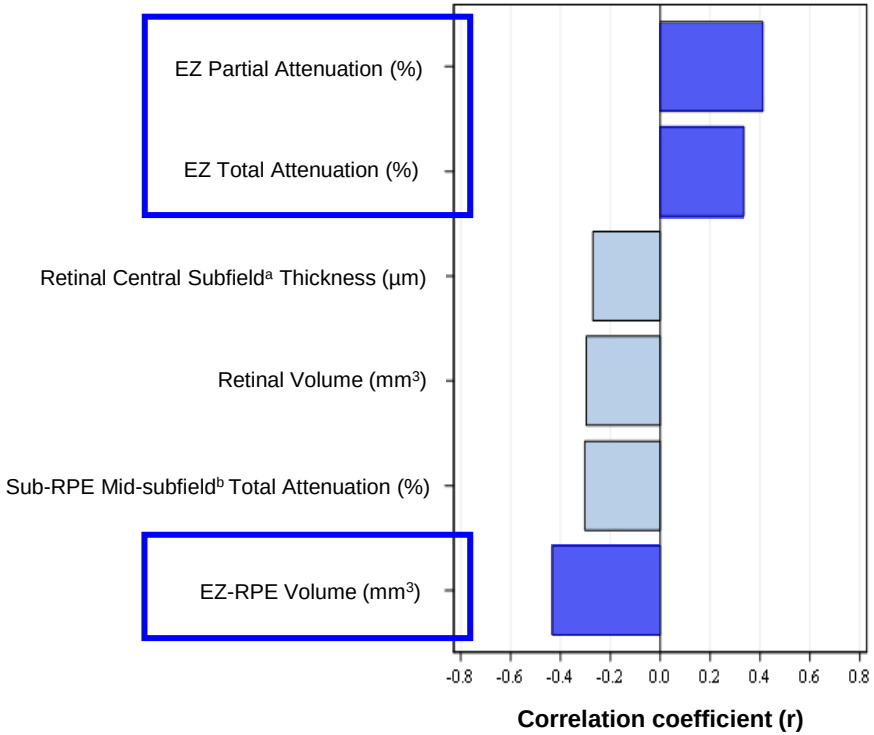
Note: Parameters with absolute value of correlation coefficient ≥0.3 are displayed. [a]Mid-subfield refers to the 2-mm diameter area centered on the fovea.
EZ, ellipsoid zone; GA, geographic atrophy; RPE, retinal pigment epithelium.

Baseline EZ Integrity and Association with GA Growth

Correlation with change from baseline in OCT GA at month 12 for sham

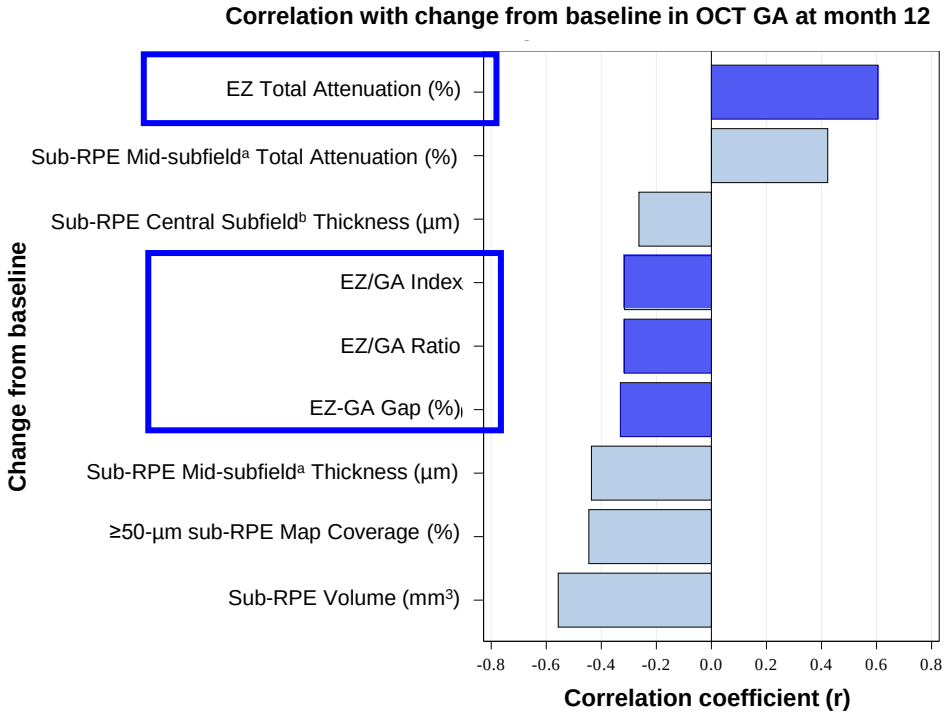


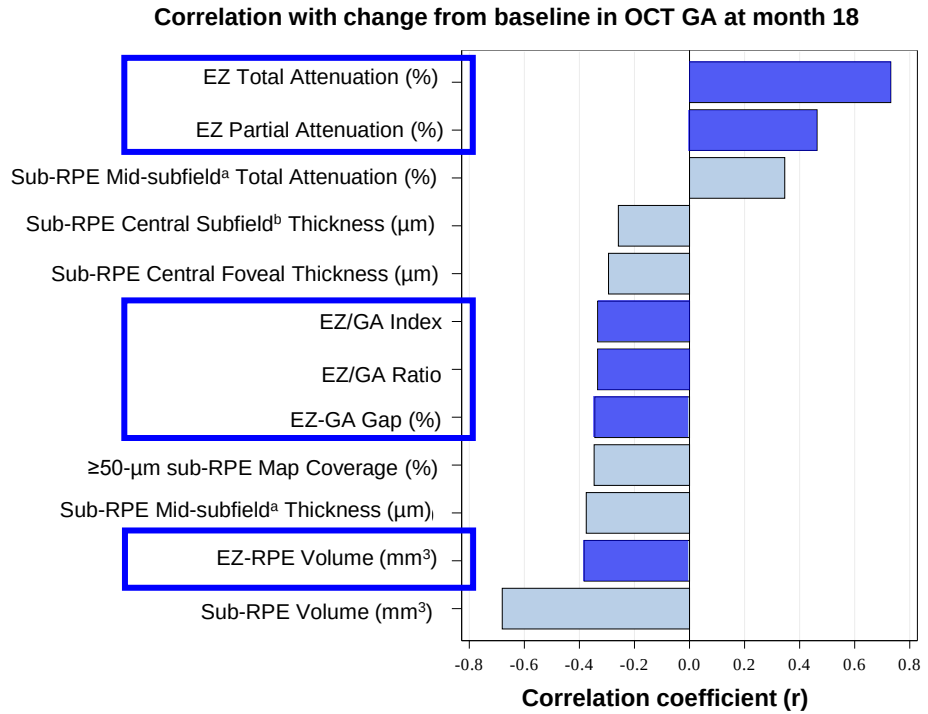
Correlation with change from baseline in OCT GA at month 18 for sham



Note: Parameters with absolute value of correlation coefficient ≥0.25 are displayed. [a]Central subfield refers to the 1-mm diameter area centered on the fovea. [b]Mid-subfield refers to the 2-mm diameter area centered on the fovea.
EZ, ellipsoid zone; GA, geographic atrophy; RPE, retinal pigment epithelium.

Association of Change in EZ Parameters with Change in GA

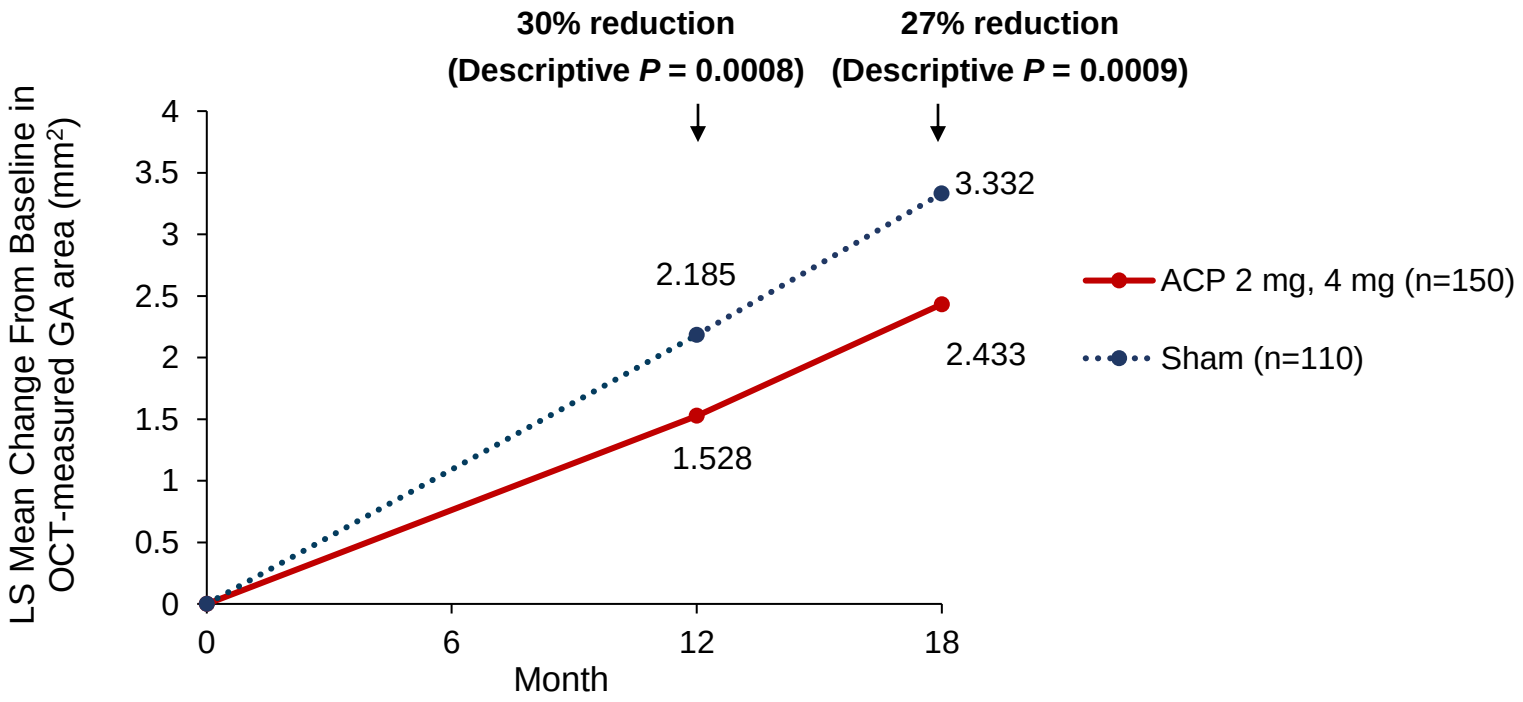




Note: Parameters with absolute value of correlation coefficient ≥0.25 are displayed. [a]Mid-subfield refers to the 2-mm diameter area centered on the fovea. [b]Central subfield refers to the 1-mm diameter area centered on the fovea.
EZ, ellipsoid zone; GA, geographic atrophy; RPE, retinal pigment epithelium.

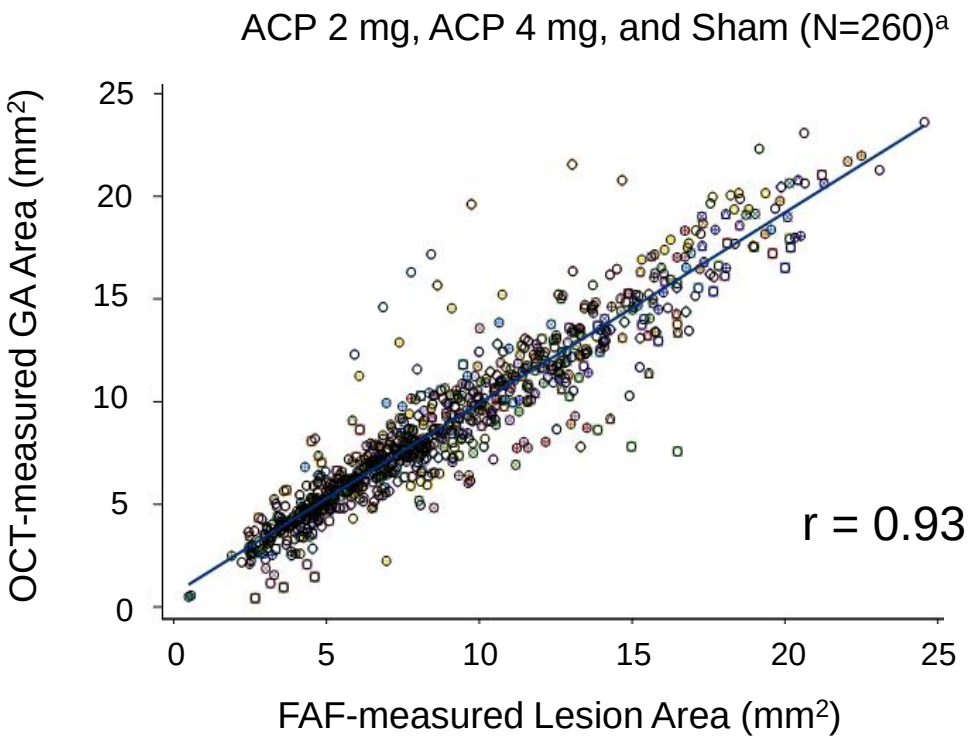
OCT-based GA Results

ACP demonstrated reduction in OCT-based GA Growth



Note: Based on LS means from model for repeated measures.
ACP, avacincaptad pegol; GA, geographic atrophy; LS, least squares.

Correlation Between FAF and OCT-based GA Measurements



[a]Multiple timepoints were included in the correlation.
ACP, avacincaptad pegol; FAF, fundus autofluorescence; GA, geographic atrophy.

Mean GA Area Difference between OCT and FAF was Minimal

Month	Mean (SD) Difference Between OCT- and FAF-Measured GA Area (mm^2)
0	0.07 (1.33)
6	0.04 (1.61)
12	-0.16 (1.80)
18	-0.01 (1.74)

FAF, fundus autofluorescence; GA, geographic atrophy.

Conclusions and Future Directions

- ACP reduced progressive EZ degradation by 22% compared with sham.
- EZ integrity measures correlated with GA features, including lesion size.
- OCT-measured GA growth was reduced by 30% with ACP compared to sham at 12 months, consistent with FAF findings.
- OCT-measured GA area strongly correlated with FAF-measured GA area, demonstrating the consistency between measures for consideration of future clinical trial design.
- Ongoing exploration of the role of EZ integrity as a biomarker for GA progression, functional correlation, and potential for future clinical trial enrichment is underway.

ACP, avacincaptad pegol; BM, Bruch's membrane; EZ, ellipsoid zone; FAF, fundus autofluorescence; GA, geographic atrophy; RPE, retinal pigment epithelium.

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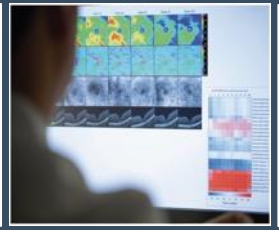
- Conor McConville
- Hannah Yates



Thank you