



The Efficacy of Avacincaptad Pegol in Geographic Atrophy: GATHER1 and GATHER2 Results

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Avacincaptad Pegol is an investigational product that has not been evaluated for safety and efficacy by the FDA

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Disclosures

Dr. Khanani

- **Consultant:**

Abbvie, Adverum Biotechnologies, AGTC, Alimera Sciences, Allergan, Apellis Pharmaceuticals, Arrowhead, Pharmaceuticals, AsclepiX Therapeutics, Aviceda Therapeutics, Bausch & Lomb , BroadWing Bio, Cholgene Therapeutics, 4D Molecular Therapeutics, Eyepoint Pharmaceuticals, Fronterra Therapeutics, Gemini Pharmaceuticals, Genentech, Graybug Vision, Gyroscope Therapeutics, **Iveric Bio**, Janssen Pharmaceuticals, Kato Pharmaceuticals, Kartos Therapeutics, Kodiak Sciences, Kriya Therapeutics, Ocular Therapeutix, Oculis, Ocuterra, Opthea, Oxurion, Novartis, Perfuse, PolyPhotonix, Ray Therapeutics, Recens Medical, Regeneron Pharmaceuticals, REGENXBIO, Roche, Stealth Biotherapeutics Therapeutics, Thea Pharma, UNITY Biotechnology, Vanotech

- **Research Support:**

Adverum Biotechnologies, Annexon Biosciences, Apellis Pharmaceuticals, AsclepiX Therapeutics, 4D Molecular Therapeutics, Gemini Pharmaceuticals, Genentech, Graybug Vision, Gyroscope Therapeutics, **Iveric Bio**, Janssen Pharmaceuticals, Kodiak, Neurotech, NGM Biopharmaceuticals, Novartis, Ocular Therapeutix, Oculis, Ocuterra, Opthea, Oxurion, Recens Medical, REGENXBIO, Roche, UNITY Biotechnology

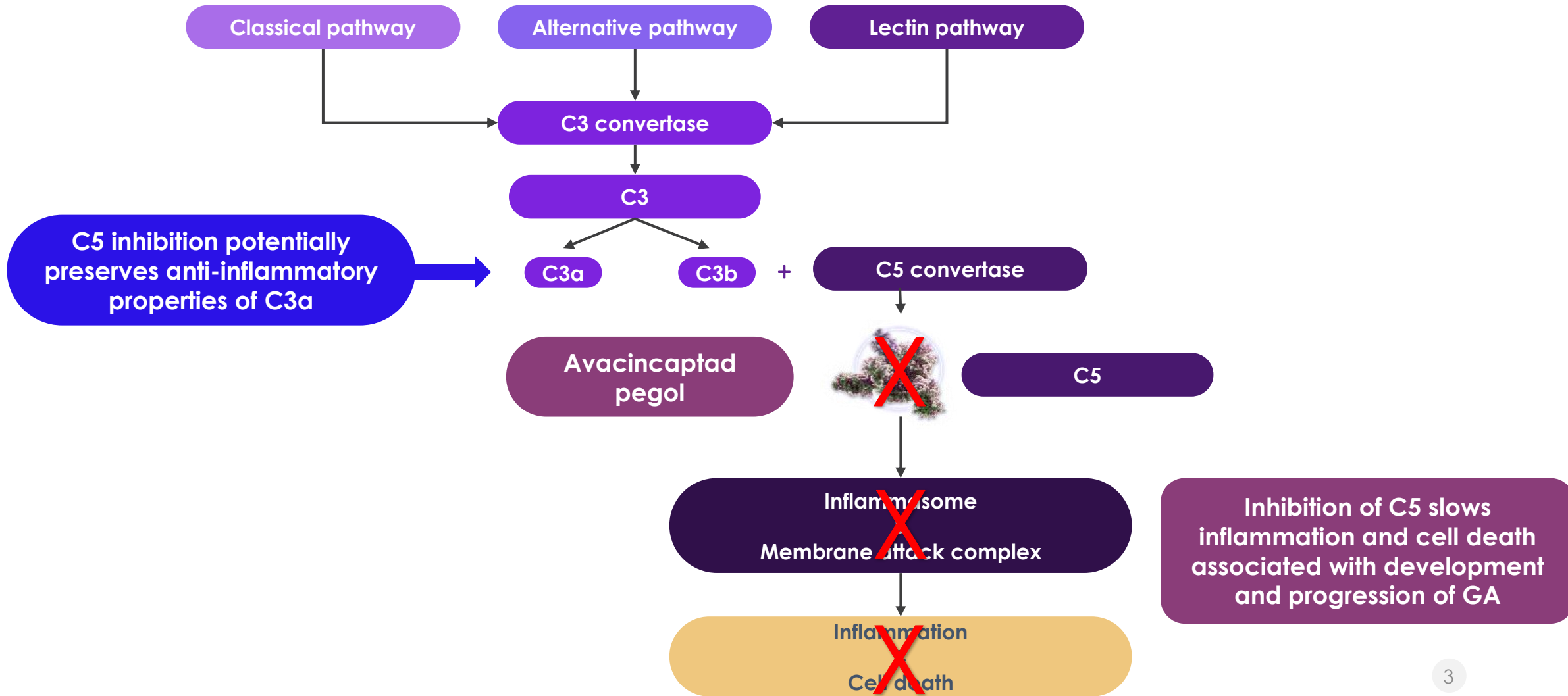
- **Speaker:**

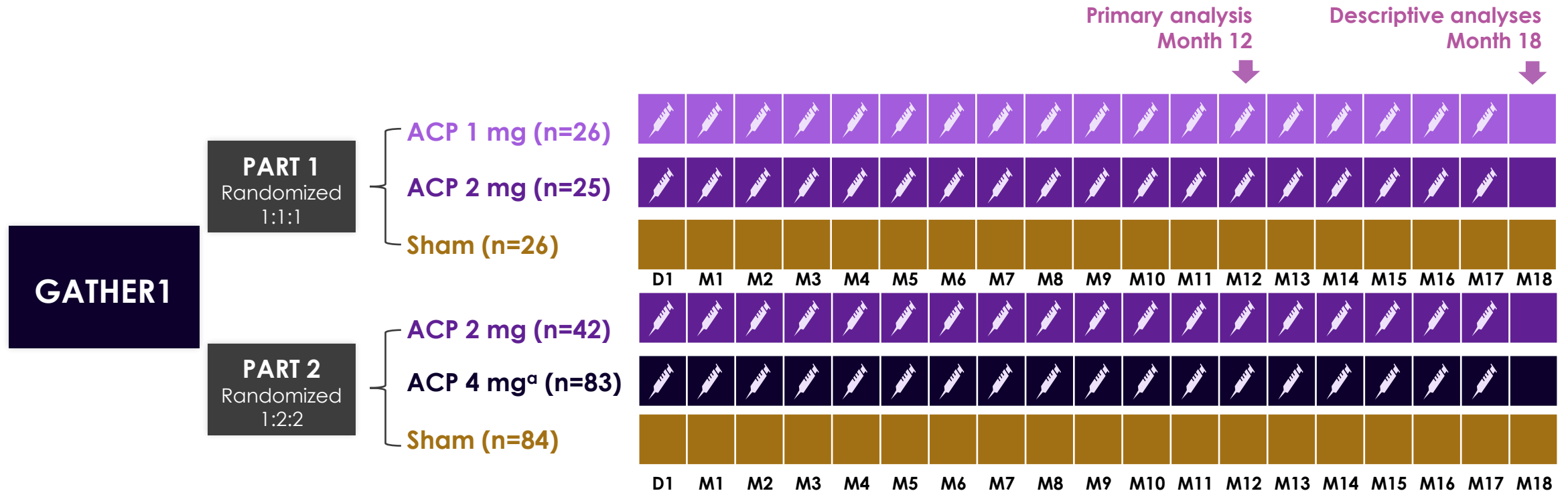
Abbvie, Apellis, Genentech, Novartis

- **Financial:**

Aviceda Therapeutics, PolyPhotonix, Recens Medical

Avacincaptad pegol is a pegylated RNA aptamer designed to be a specific inhibitor of complement C5

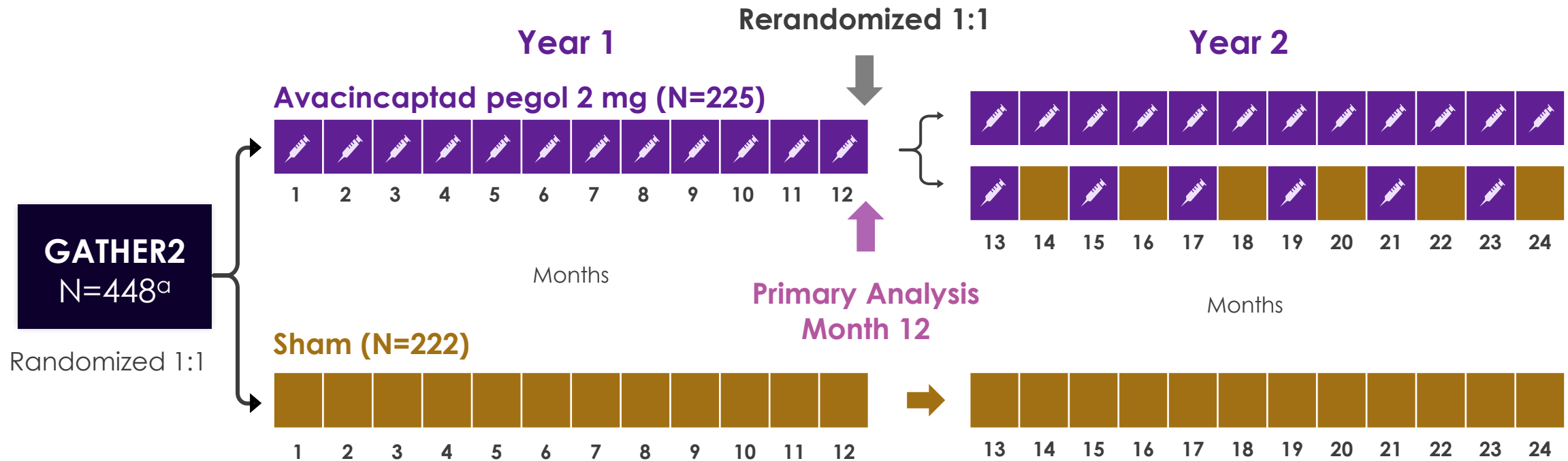




Primary Endpoint/Analysis

Mean change in GA area from baseline to Month 12 (square root transformation)

^a2 injections of 2 mg per eye.
ACP, avacincaptad pegol, D, day; FAF, fundus autofluorescence; GA, geographic atrophy; M, month.
1. Jaffe GJ, et al. Ophthalmology. 2021;128:576-586; 2. Data on file. IVERIC Bio.



Primary Endpoint/Analysis

Mean rate of growth (slope) in geographic atrophy area from baseline to month 12 (square root transformation)

^a448 randomized, with 447 treated (one patient in sham not receiving treatment after randomization).
Khanani AM, et al. Presented at: AAO; September 30-October 3, 2022.

Inclusion Criteria

- Age ≥ 50 years
- BCVA between 20/25 and 20/320
- GA lesion:
 - Non-center point involving
 - GA in part within 1500 μm from the foveal center
 - Total area between 2.5 mm^2 and 17.5 mm^2 (1 – 7 DA, respectively)
 - If multifocal lesions, at least 1 lesion had to be $\geq 1.25 \text{ mm}^2$ (0.5 DA)

Exclusion Criteria

- Evidence of CNV in either eye at baseline
- GA secondary to any condition other than AMD in either eye
- Any prior treatment for AMD or any prior intravitreal treatment for any indication in either eye (except oral vitamin or mineral supplements)
- Any ocular condition in study eye that could progress during the study and potentially affect central vision or otherwise act as a confounding factor
- Any sign of diabetic retinopathy in either eye

GA had to be in part within 1500 μm , but not involving the center point

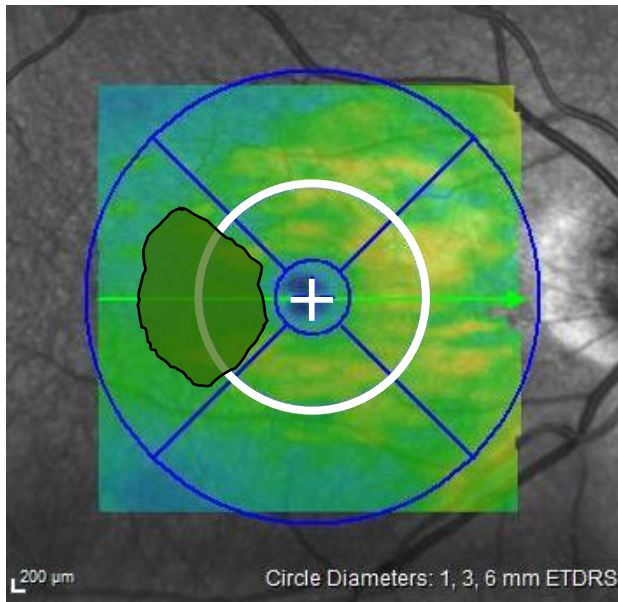
Center point involvement was determined by the Duke Reading Center using multimodal imaging

✓ **Included**

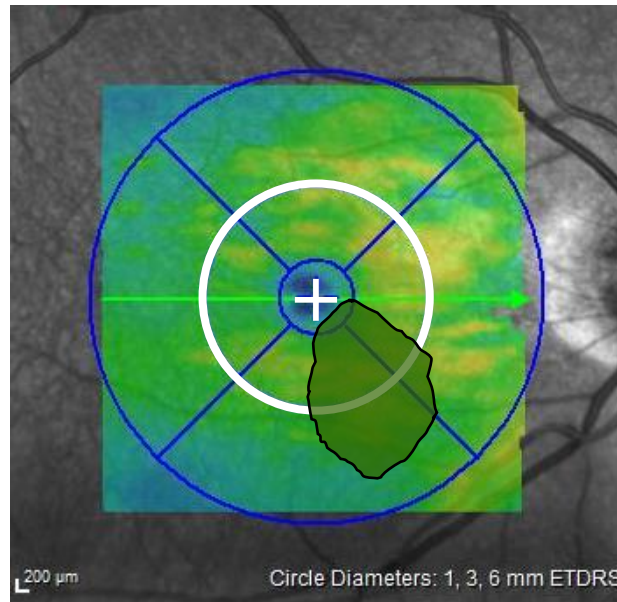
✓ **Included**

✗ **Excluded**

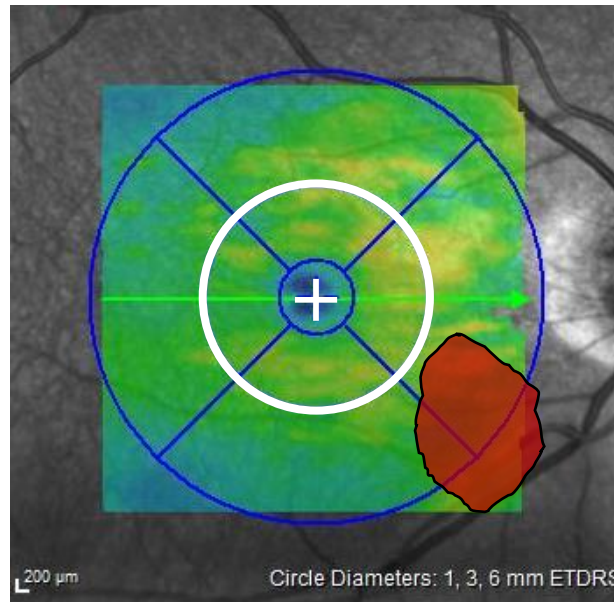
✗ **Excluded**



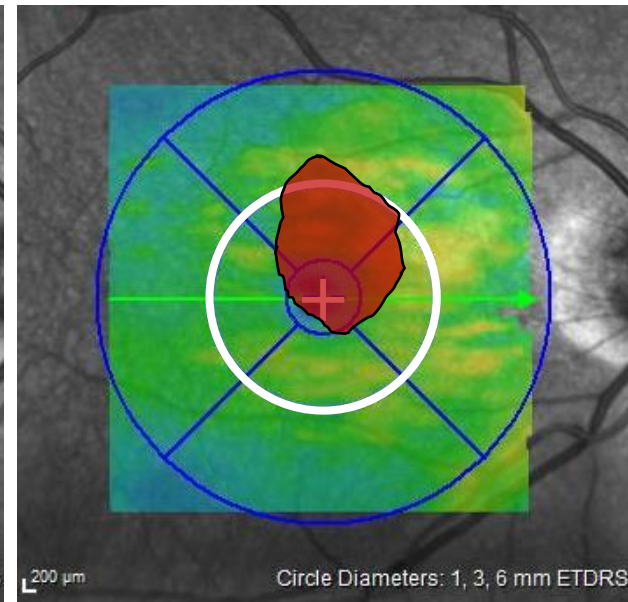
Within 1500 μm of, but not involving the foveal center point



Within 1500 μm of, but not involving the foveal center point



Outside of 1500 μm from the foveal center point



Foveal center point involvement

NOTE: unifocal lesion for example only, patients could have had multi-focal lesions

Treatment fidelity through year one was high in both studies^{1,2}



*Injection fidelity rate is calculated by dividing the total number of administered injections by the total number of expected injections based on the number of enrolled patients

Baseline characteristics were balanced between the two groups in both studies^{1,2}

	GATHER 1		GATHER 2	
	ACP 2 mg (N=67)	Sham (N=110)	ACP 2 mg (N=225)	Sham (N=222)
Mean age, years (SD)	78.8 (10.2)	78.2 (8.8)	76.3 (8.6)	76.7 (8.8)
Female, n (%)	45 (67.2)	79 (71.8)	154 (68.4)	156 (70.3)
Caucasian, n (%)	67 (100)	107 (97.3)	182 (80.9)	186 (83.8)
Active smoker, n (%)	25 (37.3)	36 (32.7)	106 (47.1)	107 (48.2)
Mean total GA area, mm² (SD)^a	7.33 (3.79)	7.42 (3.84)	7.48 (4.01)	7.81 (3.89)
Mean square root GA area, mm (SD)^a	2.62 (0.70)	2.63 (0.70)	2.64 (0.71)	2.71 (0.70)
Bilateral GA, n (%)	67 (100)	108 (98.2)	212 (94.2)	210 (94.6)
Mean BCVA, letters (SD)^a	70.2 (10.0)	69.0 (10.4)	70.9 (8.9)	71.6 (9.4)
Mean LL-BCVA, letters (SD)^a	36.7 (21.1)	34.5 (19.3)	41.0 (19.7)	39.6 (19.6)

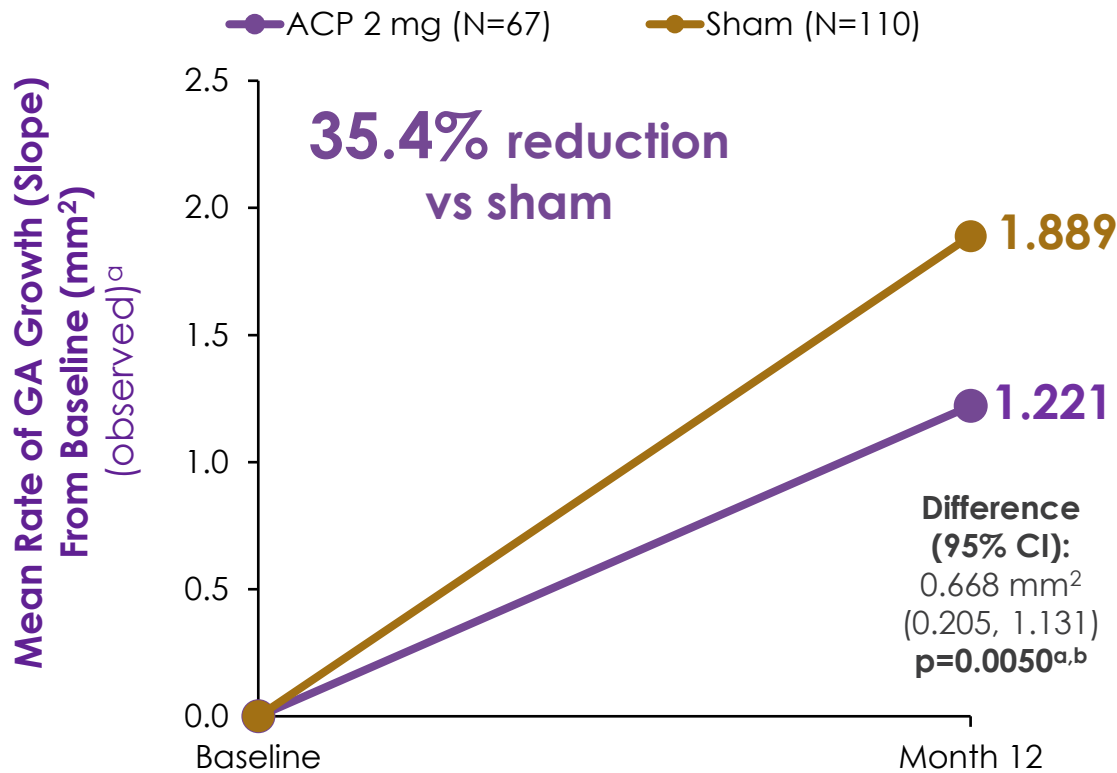
^aStudy eye.

ACP, avacincaptad pegol; BCVA, best-corrected visual acuity; GA, geographic atrophy, LL-BCVA, low luminance best-corrected visual acuity; SD, standard deviation.

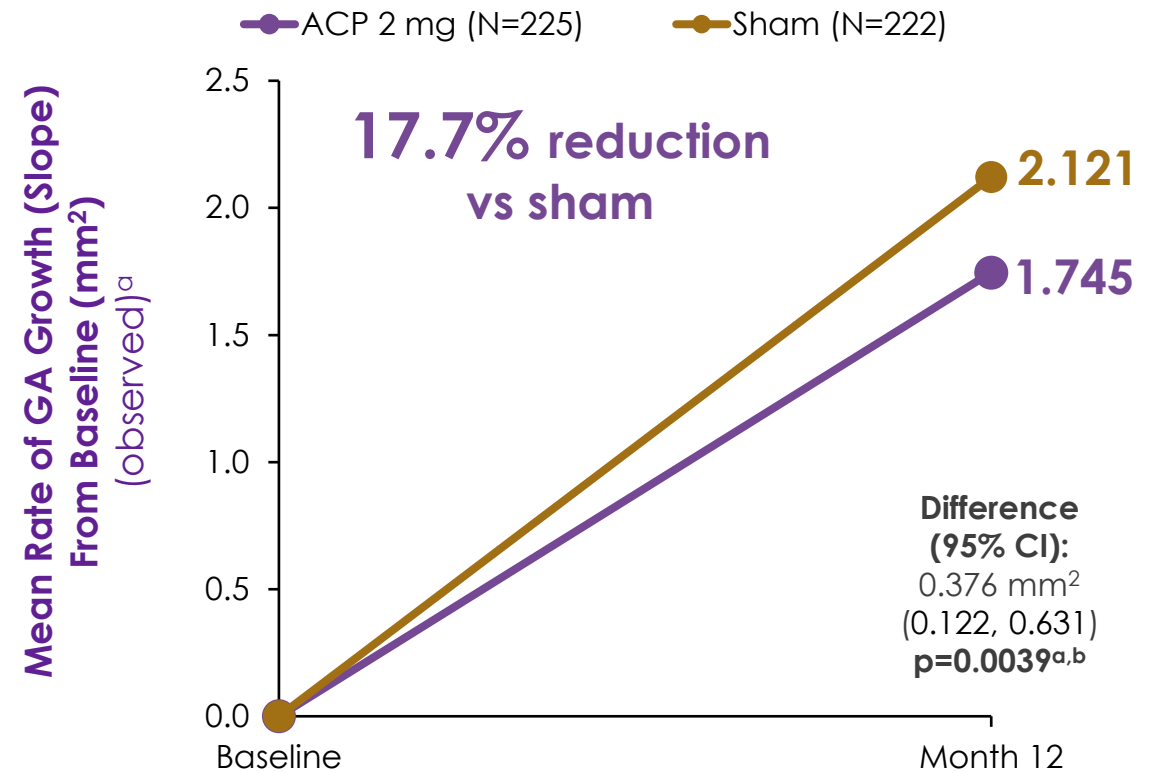
1. Jaffe GJ, et al. Ophthalmology. 2021;128:576-586; 2. Khanani AM, et al. Presented at: AAO; September 30-October 3, 2022.

Mean rate of observed GA growth (slope analysis) demonstrated consistent efficacy results between the two studies

GATHER 1



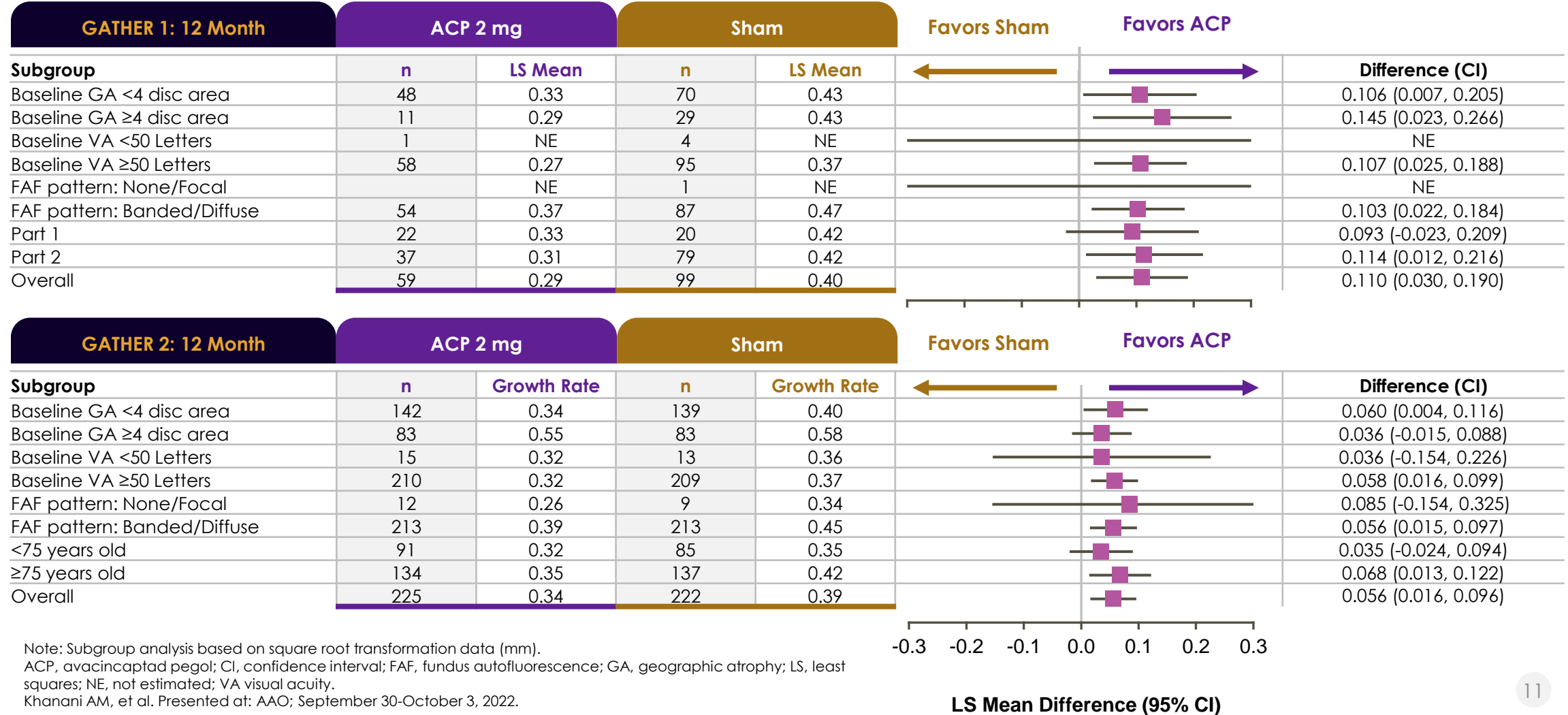
GATHER 2



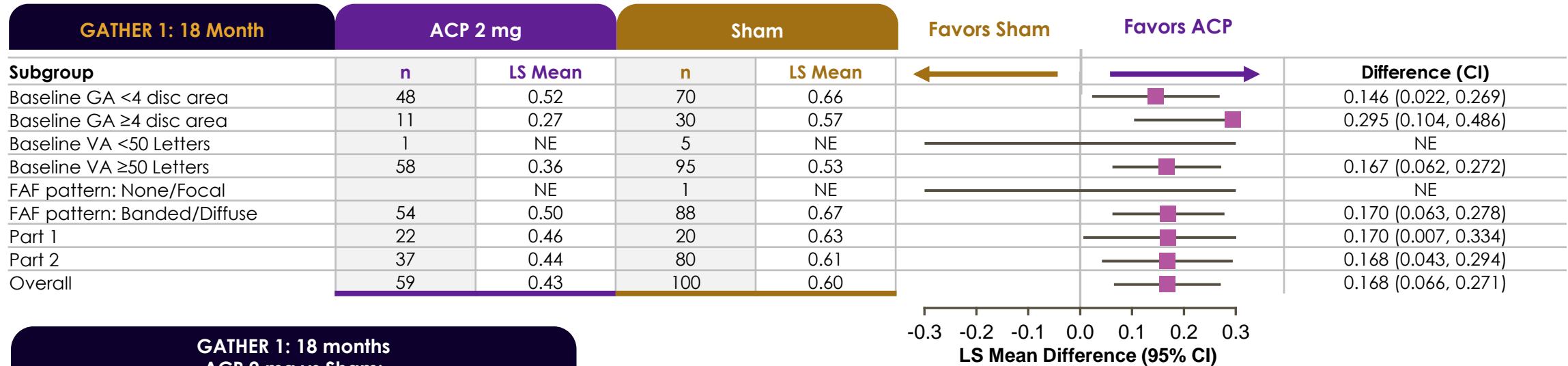
Note: The primary analysis for GATHER 1 (mean change in square root transformed GA area from baseline to month 12 [mm]) is consistent with the slope analysis utilizing observed data. The estimates for the GATHER 1 ACP 2 mg group vs sham are from the MMRM model, drawing on all available data, including data from groups with different randomization ratios in Part 1 and Part 2 of the trial, and should not be interpreted as directly observed data. ^aNon-square root transformation; ^bDescriptive p-value.

ACP, avacincaptad pegol; CI, confidence interval; GA, geographic atrophy.
Data on file. IVERIC bio.

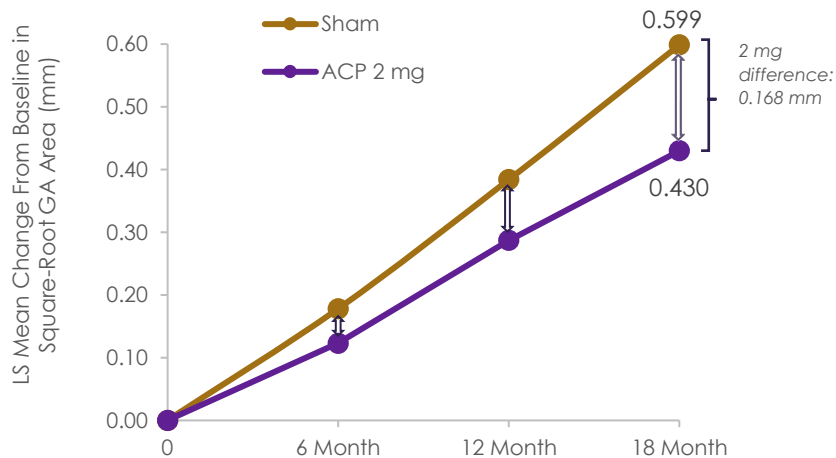
Benefit across subgroups is consistent among the pivotal GATHER1 and GATHER2 studies



Benefit across subgroups seen in GATHER 1 increases with duration of therapy over 18 months



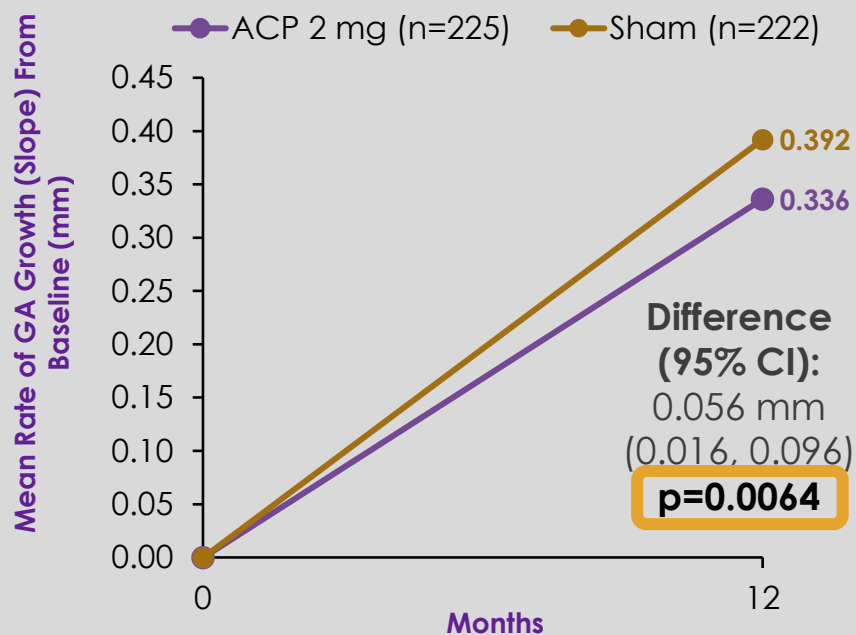
**GATHER 1: 18 months
ACP 2 mg vs Sham:**



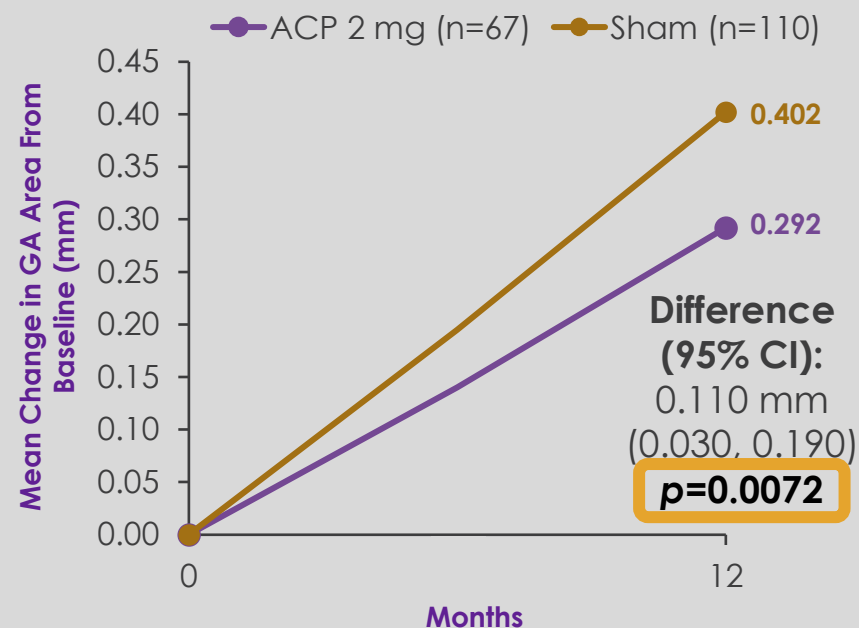
Note: Subgroup analysis based on square root transformation data (mm).
 ACP, avacincaptad pegol; CI, confidence interval; FAF, fundus autofluorescence; GA, geographic atrophy; LS, least squares; NE, not estimated; VA visual acuity.
 Khanani AM, et al. Presented at: AAO; September 30-October 3, 2022.

Avancincaptad pegol is the first investigational therapy in GA to achieve the 12-month prespecified, primary endpoint, in two pivotal, phase 3 studies

GATHER 2



GATHER 1



Thank you to the GATHER program
investigators, research staff, and patients

