Assessment of Geographic Atrophy Progression in the FILLY Study

Allen Chiang, MD[1] and David R. Lally, MD[2]

[1]Mid-Atlantic Retina; Wills Eye Hospital
[2]New England Retina Consultants

Financial Disclosures

AC:
Consultant: Apellis, Genentech, Orbit Biomedical - Gyroscope
Grant Support: Apellis, Genentech, Regeneron

DL:
Consultant: Alimera Sciences, Allergan, Genentech, Kubota Vision, Novartis
Speaker: Alimera Sciences, Allergan, Apellis, Novartis
Grant Support: Aldeyra Therapeutics, Apellis, Canon, Chengdu Hangkong, Genentech, Iveric Bio, Kodiak Sciences, EMMES/Mac Tel Project, Neurotech, Notal Vision, Novartis, Optos, Ora

Summary

- Consistent with the overall results, proportion of patients with relatively smaller change in GA lesion size was higher in the APL-2 treatment arms compared to the sham control group, suggestive of APL-2's effect over reducing disease progression

  - Quartile evaluation within treatment groups further supports these findings

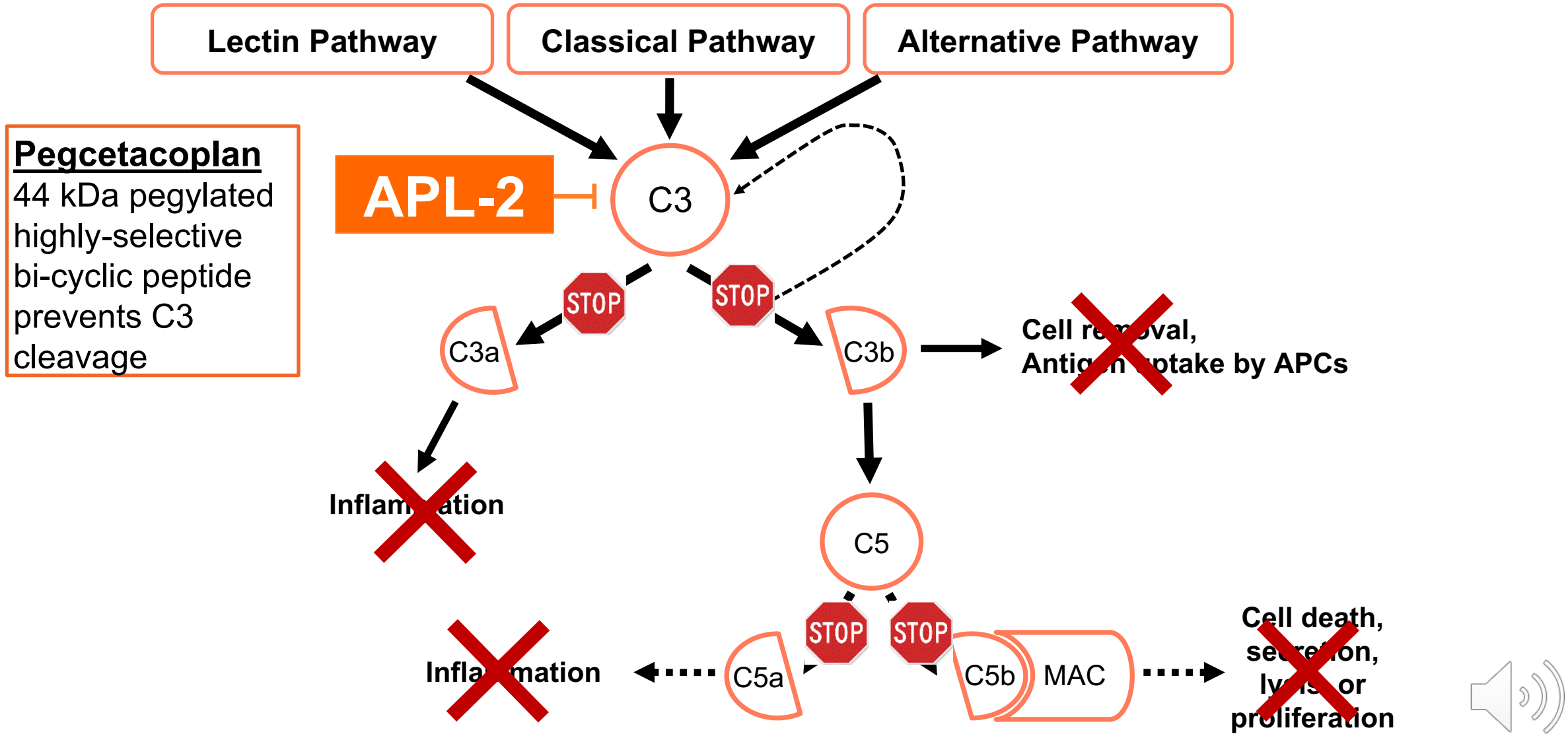
- In general, foveal lesions had slower GA progression compared to extrafoveal lesions across all treatment groups

Disclaimer

- Pegcetacoplan (APL-2) is an investigational product

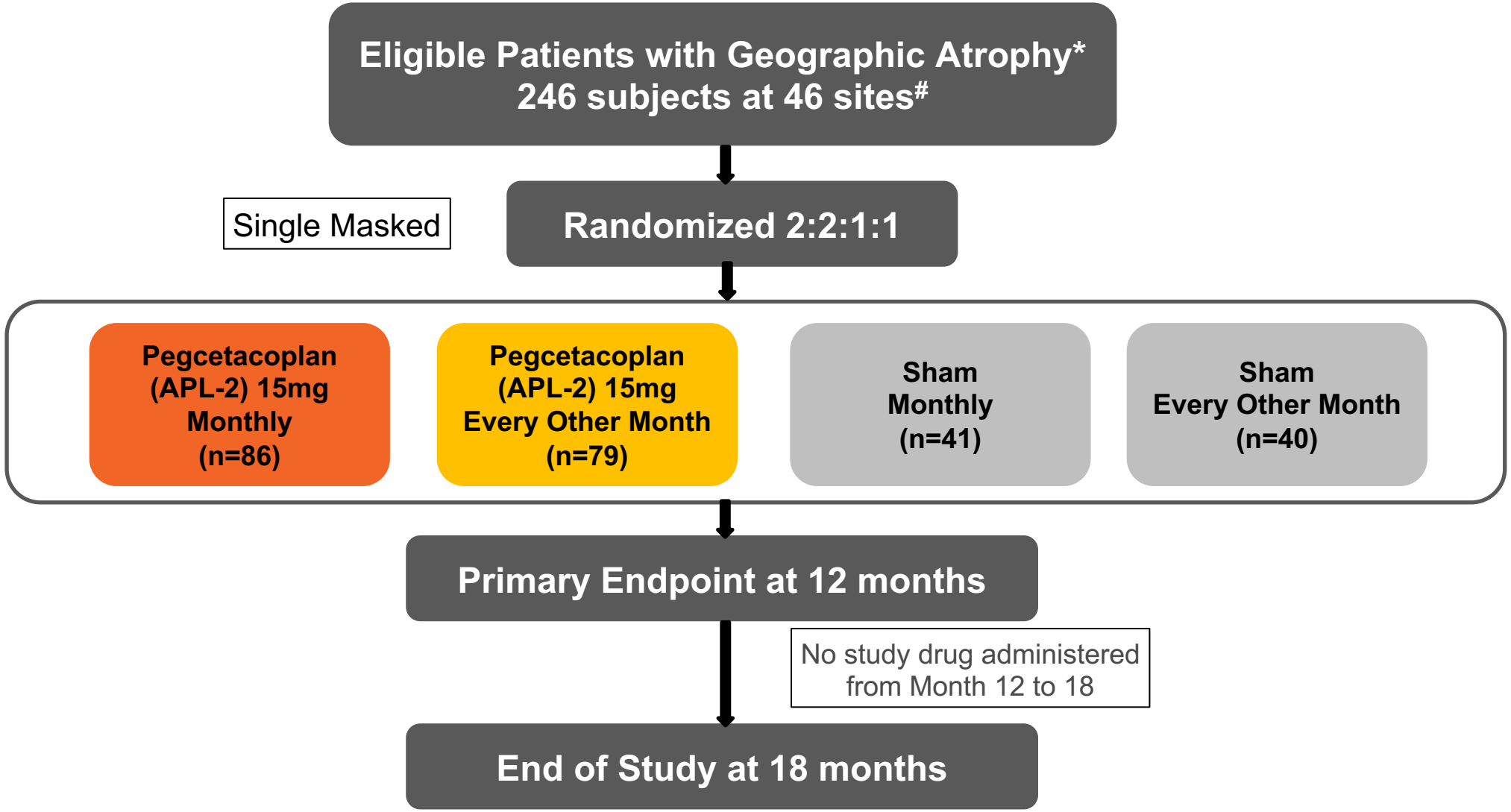
- The safety and effectiveness of pegcetacoplan have not been determined, nor has pegcetacoplan been approved by the FDA or any other regulatory authority

Pegcetacoplan (APL-2): C3 Inhibitor



Berger, N et al. J Med Chem. 2018 26;61(14):6153-6162

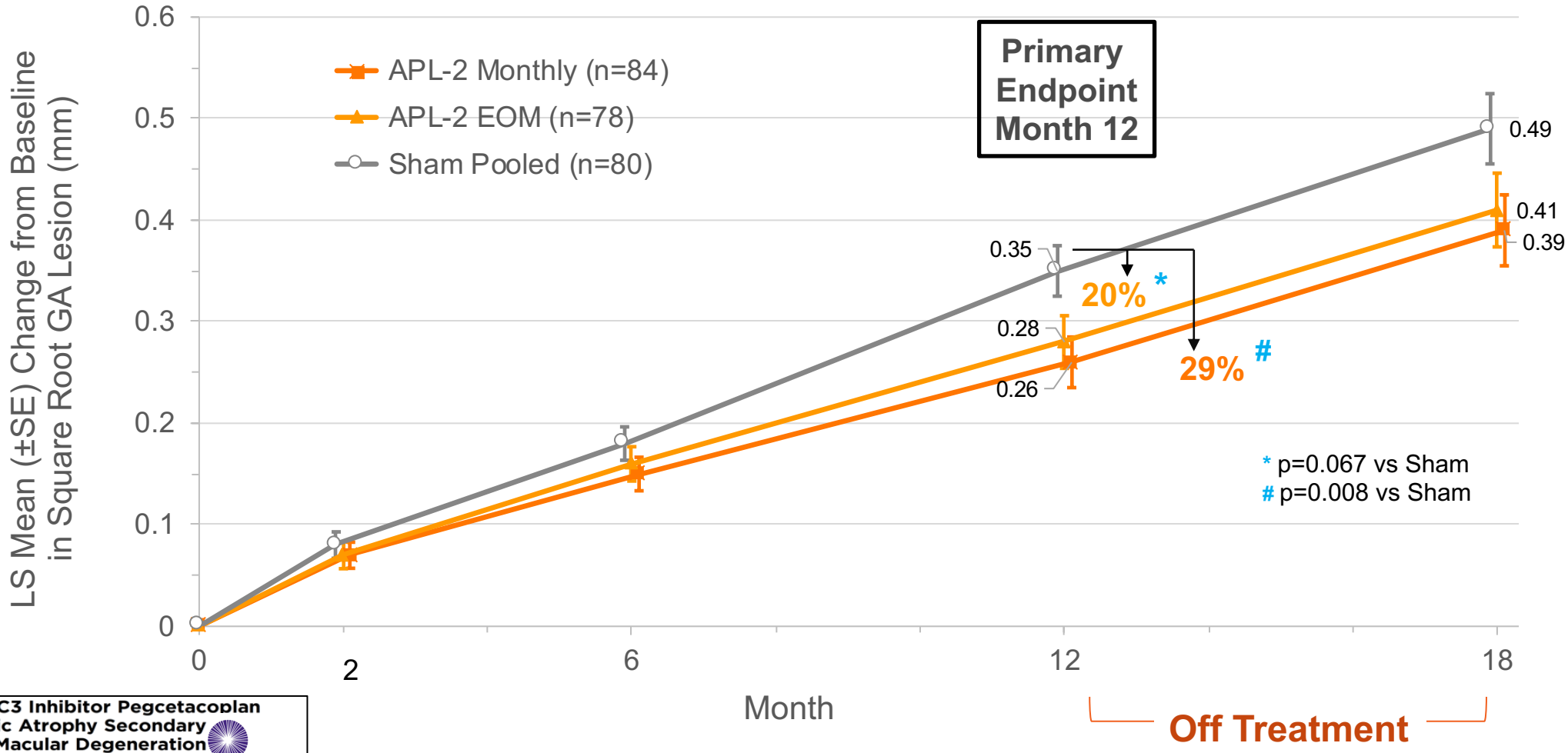
Phase 2 Trial Design



* Confirmed by the central reading center using FAF images
\# Not counting the 3 satellite sites

Liao, D et al. Ophthalmology. 2019. pii: S0161-6420(18)33132-4. [Epub ahead of print]
Protocol study number, POT-CP121614 (FILLY); NCT02503332

Pegcetacoplan (APL-2) Slows GA Lesion* Growth



Complement C3 Inhibitor Pegcetacoplan for Geographic Atrophy Secondary Age-Related Macular Degeneration

A Randomized Phase 2 Trial *Ophthalmology* 2019

David S. Liao, MD,[1] Federico V. Grossi, MD, PhD,[2] Delphine El Mehdi, PhD,[2] Monica R. Gerber, MD, PhD,[2] David M. Brown, MD,[3] Jeffrey S. Heier, MD,[4] Charles C. Wykoff, MD, PhD,[5] Laurence J. Singerman, MD,[6] Prema Abraham, MD,[7] Felix Grassmann, PhD,[8,9] Peter Nuernberg, PhD,[10] Bernhard H.F. Weber, PhD,[8] Pascal Deschatelets, PhD,[2] Robert Y. Kim, MD,[2] Carol Y. Chung, PhD,[2] Ramiro M. Ribeiro, MD, PhD,[2] Mohamed Hamdani, MS,[2] Philip J. Rosenfeld, MD, PhD,[11] David S. Boyer, MD,[12] Jason S. Slakter, MD,[13,14] Cedric G. Francois, MD, PhD[2]

*Square root. Modified intention-to-treat (mITT) population was used for the efficacy analysis; defined as all patients who received at least 1 injection and underwent at least 1 follow-up examination at month 2 or later at which primary efficacy data were collected. 2-sided t tests at the alpha = 0.1 level

Protocol study number, POT-CP121614 (FILLY); NCT02503332

Adverse Event Profile

Adverse Event n (%) of subjects with events	APL-2 Monthly N=86	APL-2 EOM N=79	Sham Pooled N=81
Ocular SAEs in study eye*	4 (4.7%)	2 (2.5%)	1 (1.2%)
Systemic SAEs	19 (22.1%)	24 (30.4%)	23 (28.4%)
Treatment related ocular AEs in the study eye	22 (25.6%)	11 (13.9%)	0
Treatment related systemic AEs	0	0	0

Ocular SAEs	APL-2 Monthly N=86	APL-2 EOM N=79	Sham Pooled N=81
Endophthalmitis*	2 (2.3%)	1 (1.3%)	0
IOP increased	1 (1.2%)†	1 (1.3%)	0
Retinal detachment	1 (1.2%)	0	0
Visual impairment	0	0	1 (1.2%)

*2 culture positive for coagulase-negative Staphylococcus. 1 culture negative in the monthly group. †2 events in a subject

Liao, D et al. Ophthalmology. 2019. pii: S0161-6420(18)33132-4. [Epub ahead of print]
Protocol study number, POT-CP121814 (FILLY); NCT02503332

Post hoc Analysis: *Objective*

To further assess progression of geographic atrophy (GA) by categories of change in GA lesion size in eyes receiving treatment with pegcetacoplan (APL-2) or sham

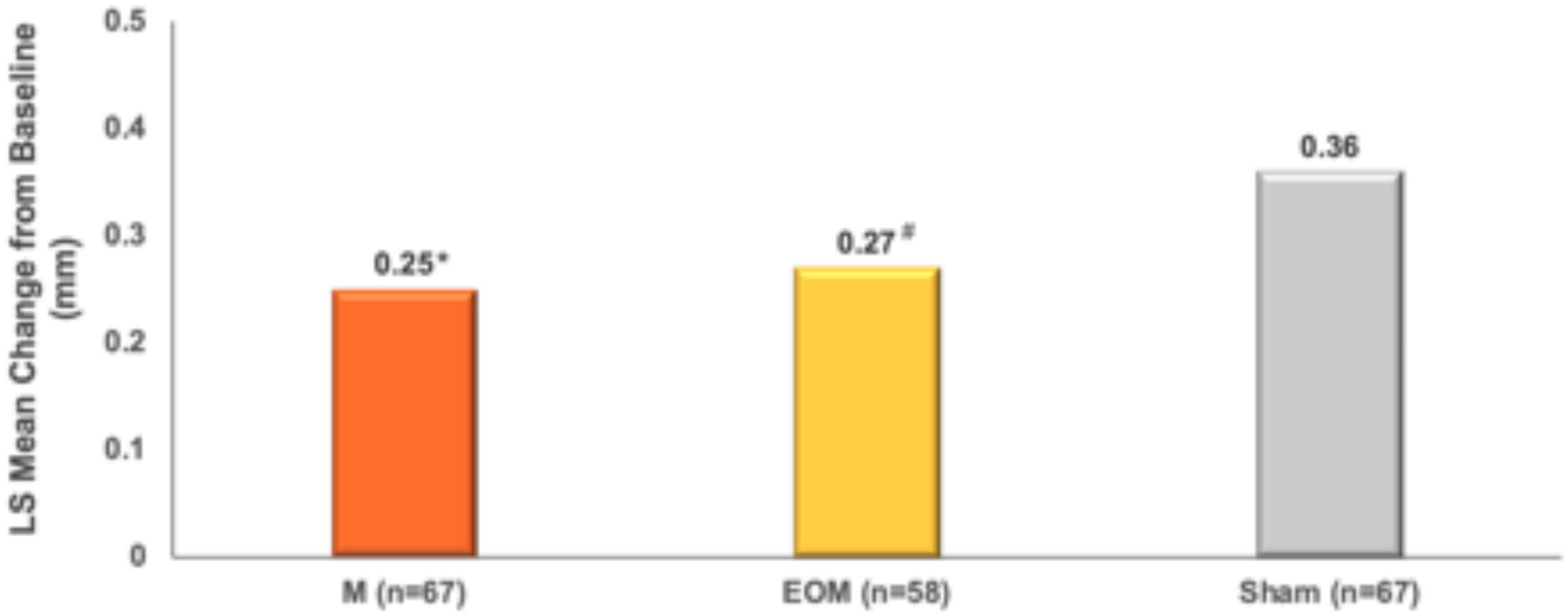
Post hoc Analysis: *Methods*

GA progression: Change in square root lesion size from baseline to Month 12

- GA progression **by quartiles** assessed in:
  - Overall patient population
  - By treatment group:
    - Pegcetacoplan monthly (M)
    - Pegcetacoplan every-other month (EOM)
    - Sham

- Only patients with observed data at Month 12 were included (n=192)

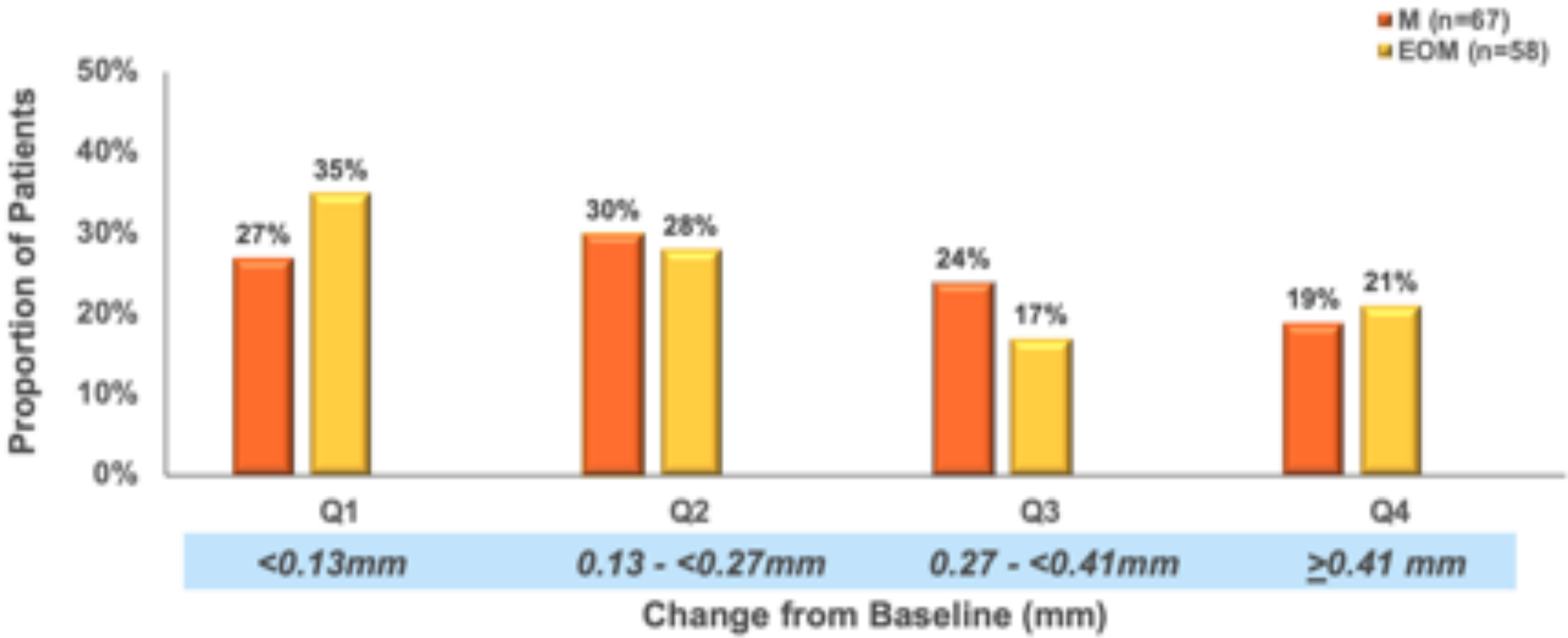
Mean Change in GA Lesion Size
Overall



* *p = 0.004 vs sham*
\# *p = 0.023 vs sham*

Data on File
Observed Data (n=192)

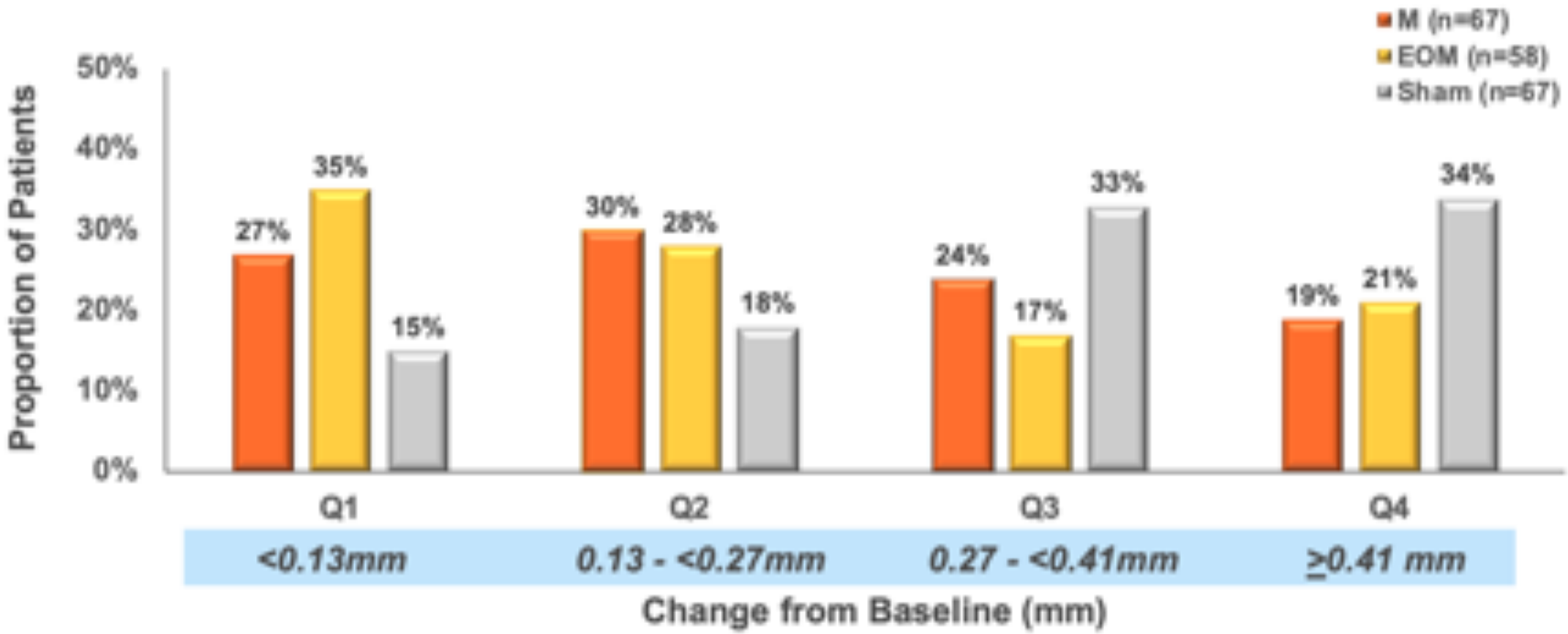
Quartile Distribution (GA Lesion Growth)
Overall



Higher proportion of eyes treated with APL-2 in Q1 (slow progressors)

Data on File
Observed Data (n=192)

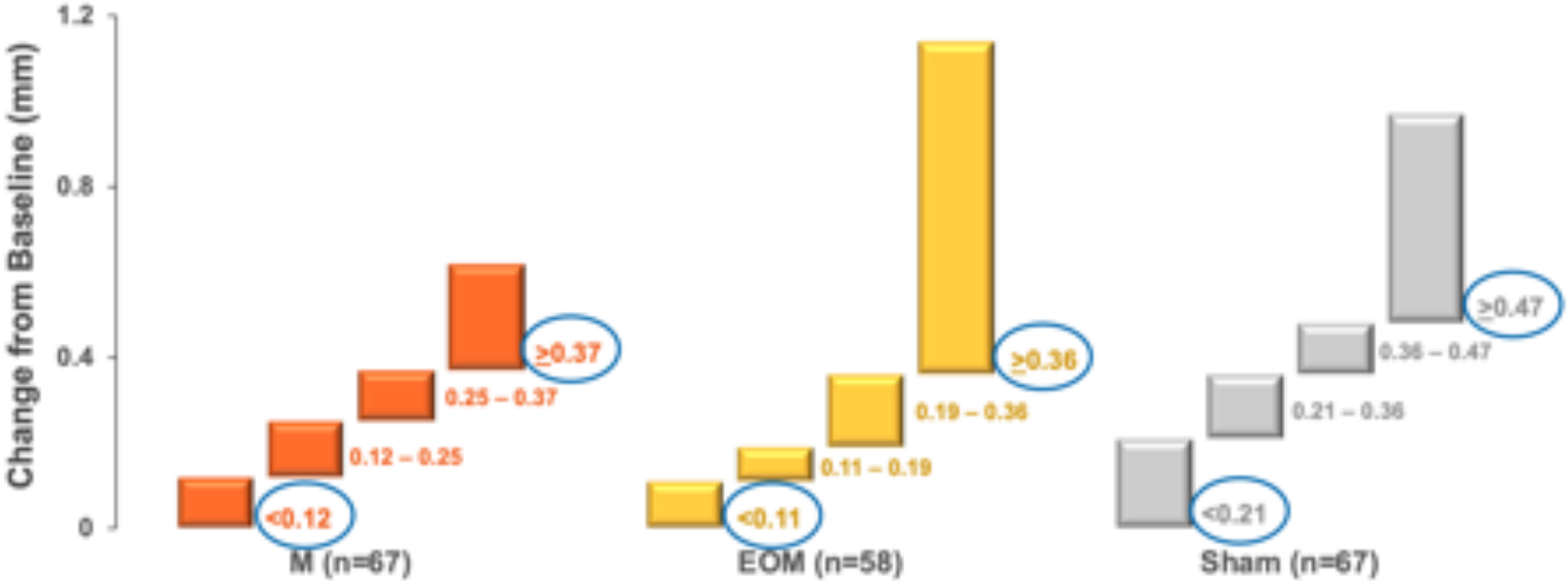
Quartile Distribution (GA Lesion Growth)
Overall



Higher proportion of eyes treated with APL-2 in Q1 (slow progressors)
Higher proportion of eyes in sham group in Q4 (fast progressors)

Data on File
Observed Data (n=192)

Quartile Distribution (GA Lesion Growth)
By Treatment Group



Shift in the APL-2 groups compared to sham group indicates slower progression

Data on File
Observed Data (n=192)

Baseline Characteristics by Quartiles
Overall

	Q1 *(<0.13mm)*	Q2 *(0.13 - <0.27mm)*	Q3 *(0.27 - <0.41mm)*	Q4 (≥0.41 mm)
Mean Lesion Size, mm^2	8.55	9.11	8.03	7.51
Lesion Focality, n (%)				
Unifocal	18 (37.5%)	14 (29.2%)	19 (39.6%)	14 (29.2%)
Multifocal	30 (62.5%)	34 (70.8%)	29 (60.4%)	34 (70.8%)
Lesion Location, n (%)				
Foveal	36 (75.0%)	33 (68.8%)	28 (58.3%)	18 (37.5%)
Extrafoveal	12 (25.0%)	15 (31.3%)	20 (41.7%)	30 (62.5%)

Data on File
Observed Data (n=192)

Baseline Characteristics by Quartiles *Within Treatment Groups*

	Q1 *(<0.13mm)*			Q2 *(0.13 - <0.27mm)*		
	M (n=18)	EOM (n=20)	Sham (n=10)	M (n=20)	EOM (n=16)	Sham (n=12)
Mean Lesion Size, mm^2	8.32	9.00	8.04	8.95	8.88	9.67
Lesion Focality, n (%)						
Unifocal	5 (27.8%)	9 (45.0%)	4 (40.0%)	5 (25.0%)	7 (43.8%)	2 (16.7%)
Multifocal	13 (72.2%)	11 (55.0%)	6 (60.0%)	15 (75.0%)	9 (56.3%)	10 (83.3%)
Lesion Location, n (%)						
Foveal	13 (72.2%)	15 (75.0%)	8 (80.0%)	13 (65.0%)	13 (81.3%)	7 (58.3%)
Extrafoveal	5 (27.8%)	5 (25.0%)	2 (20.0%)	7 (35.0%)	3 (18.8%)	5 (41.7%)

	Q3 *(0.27 - <0.41mm)*			Q4 (≥0.41 mm)		
	M (n=16)	EOM (n=10)	Sham (n=22)	M (n=13)	EOM (n=12)	Sham (n=23)
Mean Lesion Size, mm^2	7.60	9.83	7.53	6.45	6.58	8.61
Lesion Focality, n (%)						
Unifocal	6 (37.5%)	4 (40.0%)	9 (40.9%)	3 (23.1%)	2 (16.7%)	9 (39.1%)
Multifocal	10 (62.5%)	6 (60.0%)	13 (59.1%)	10 (76.9%)	10 (83.3%)	14 (60.9%)
Lesion Location, n (%)						
Foveal	10 (62.5%)	5 (50.0%)	13 (59.1%)	4 (30.8%)	5 (41.7%)	9 (39.1%)
Extrafoveal	6 (37.5%)	5 (50.0%)	9 (40.9%)	9 (69.2%)	7 (58.3%)	14 (60.9%)

Consistent with overall population, foveal lesions progressed slowly within all treatment groups

Data on File; Observed Data (n=192)

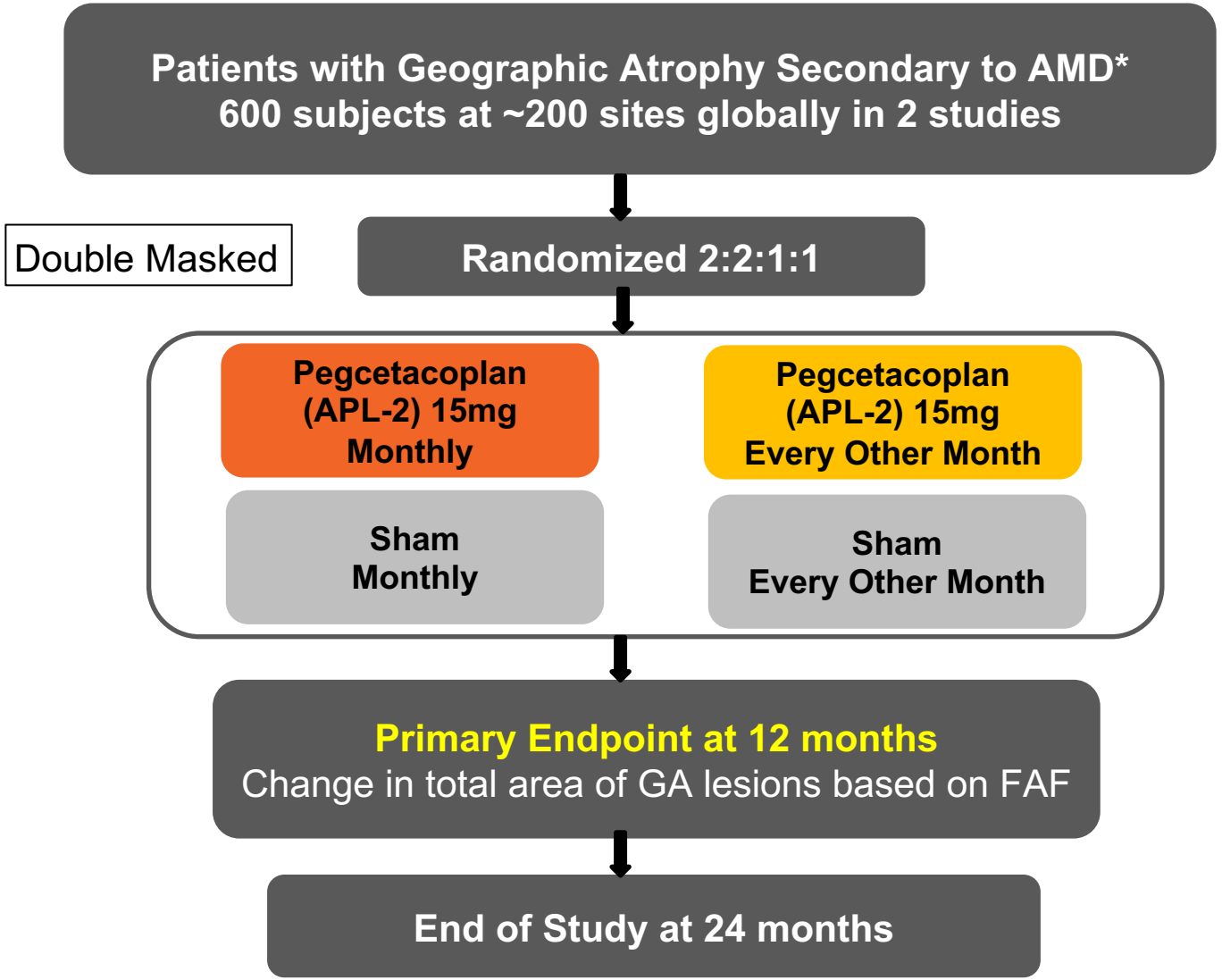
Summary

- Consistent with the overall results, proportion of patients with relatively smaller change in GA lesion size was higher in the APL-2 treatment arms compared to the sham control group, suggestive of APL-2's effect over reducing disease progression

  - Quartile evaluation within treatment groups further supports these findings

- In general, foveal lesions had slower GA progression compared to extrafoveal lesions across all treatment groups

Global Phase 3 Program



Protocol study number, APL-2 303 (DERBY); NCT03525600
Protocol study number, APL-2 304 (OAKS); NCT03525613