APL-2 (pegcetacoplan)
Geographic atrophy
Preliminary 18-month results

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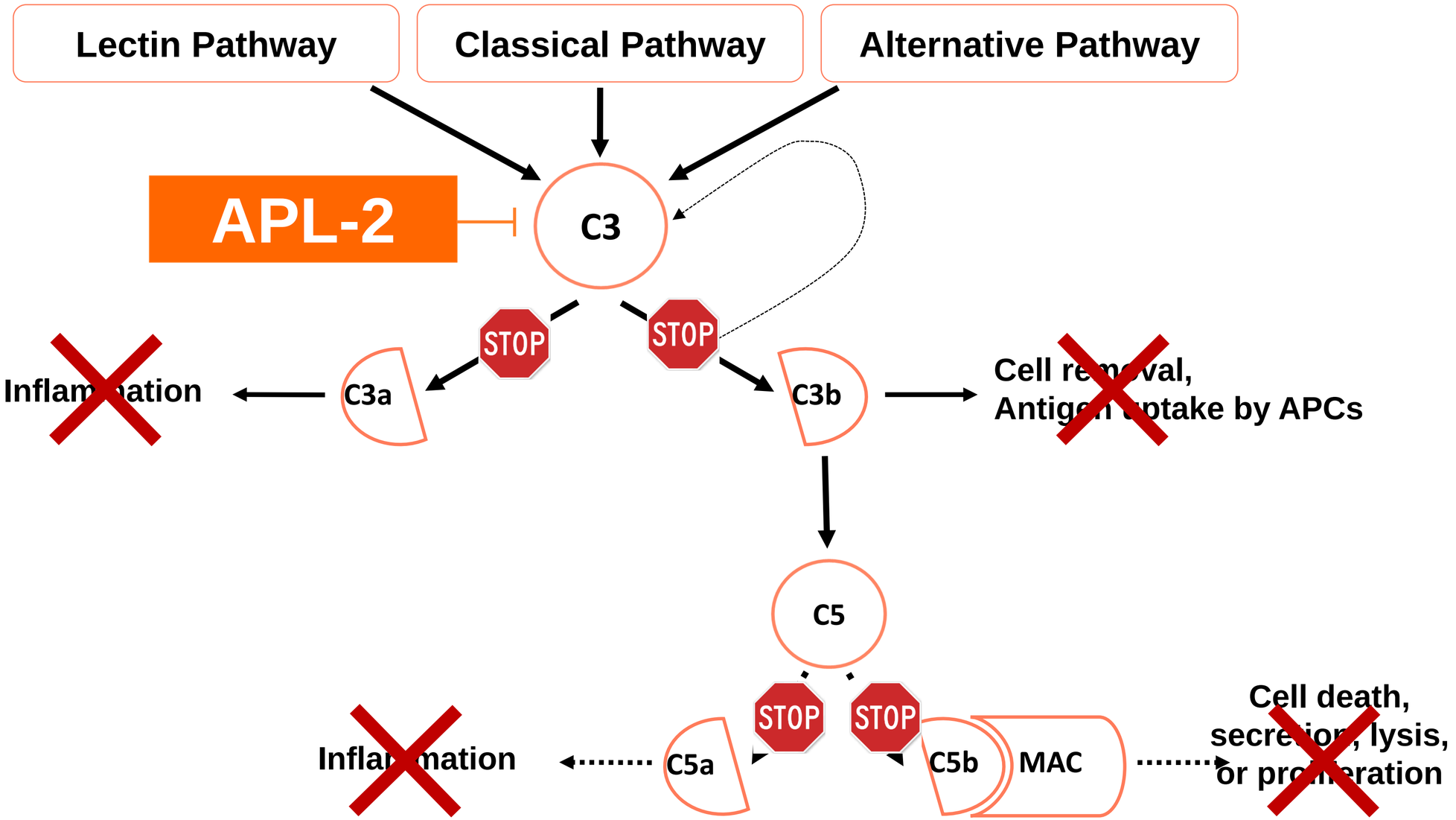
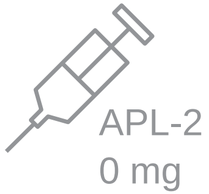
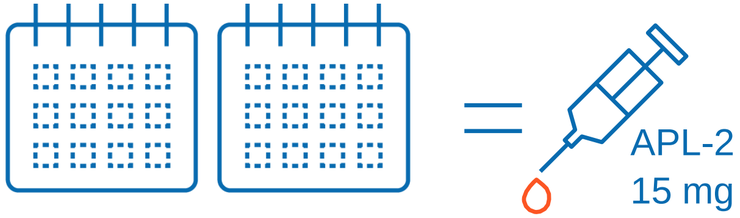
The Complement Pathway and Geographic Atrophy



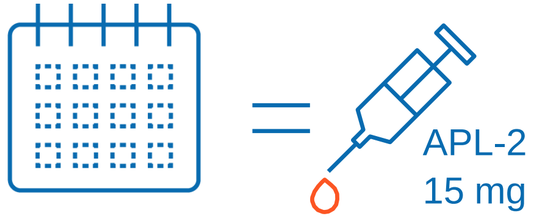
FILLY - Phase 2 study of APL-2 in Geographic Atrophy



Sham injections



APL-2 injections every other month



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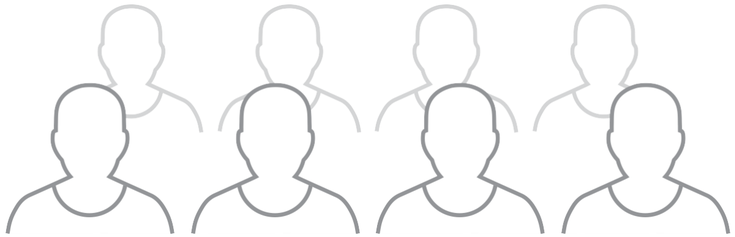
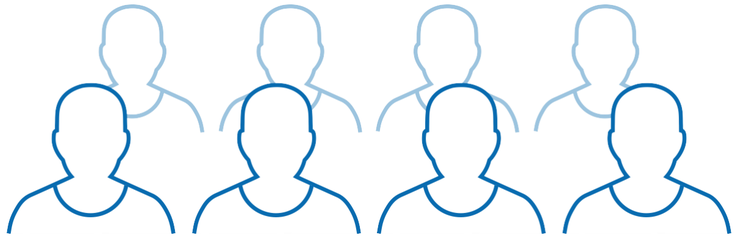
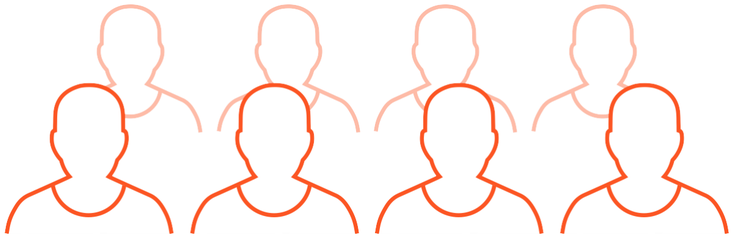


Sham group, n=81

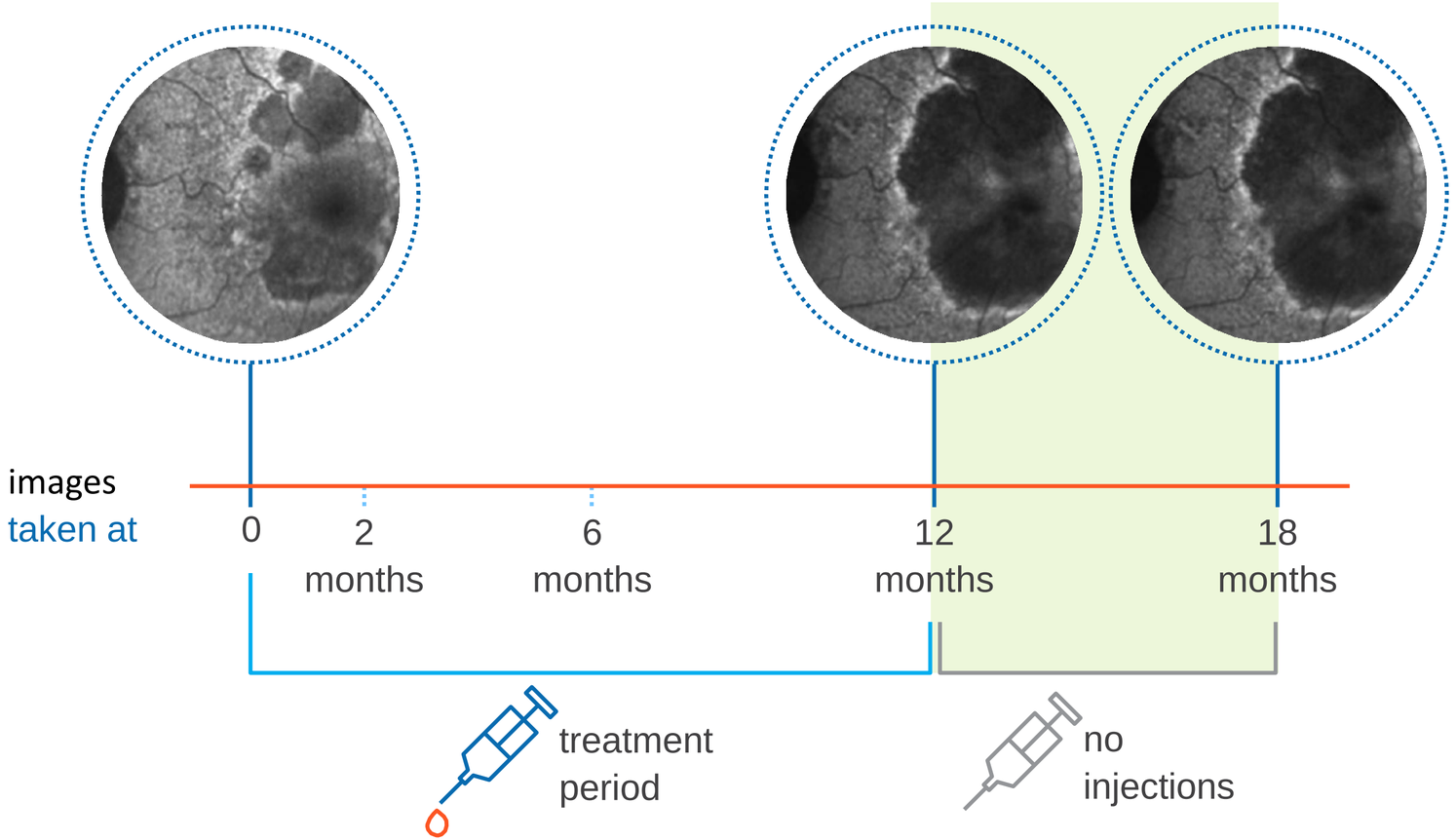


Active group 1, n=79



Active group 2, n=86

FILLY – timeline and endpoints



Primary efficacy endpoint is the primary registration endpoint

Change in geographic atrophy (GA) lesion size from baseline to month 12.

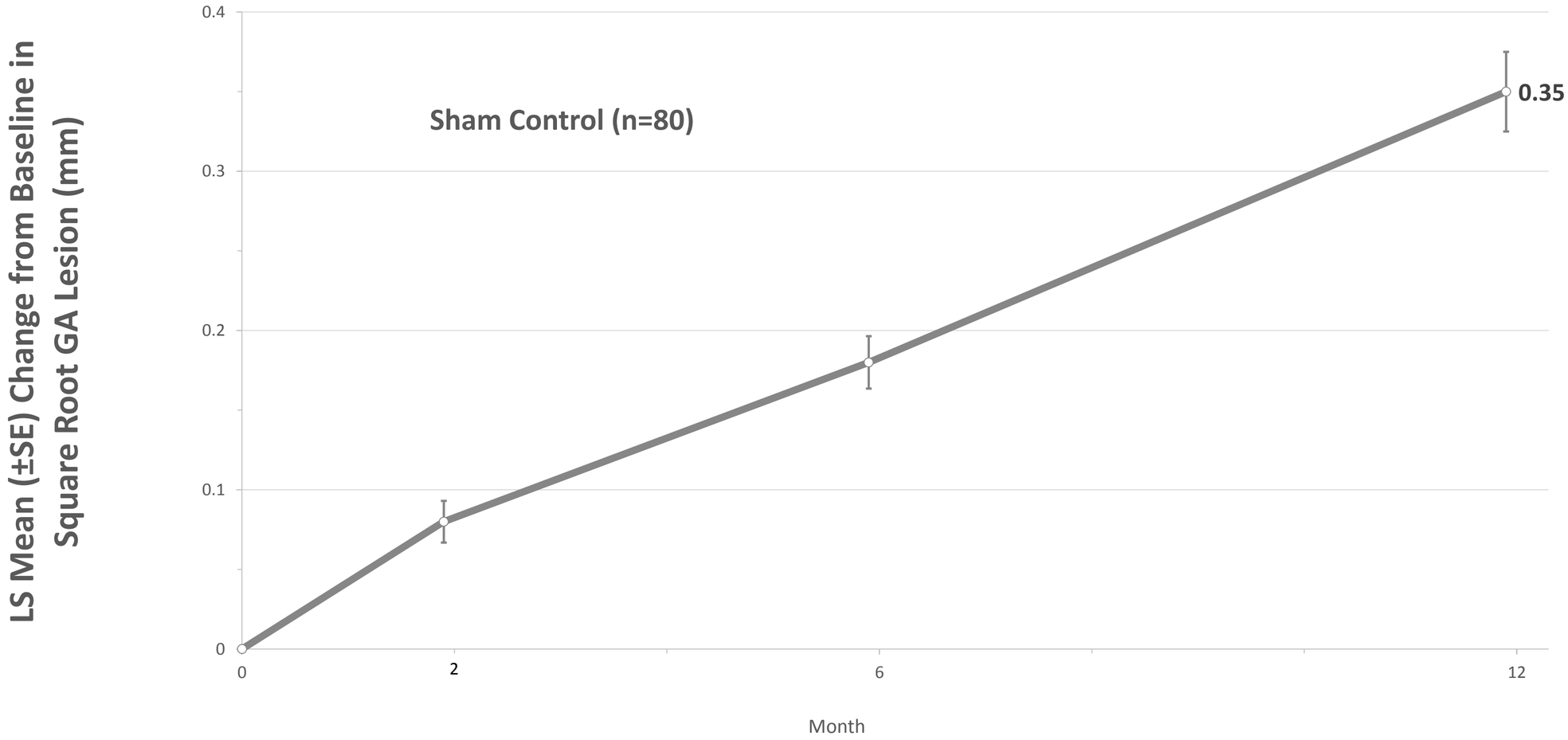
Primary safety endpoint

Number and severity of local and systemic treatment emergent adverse events (TEAEs).

Baseline Characteristics

	APL-2 Monthly N=86	APL-2 Every Other Month N=79	Sham Pooled N=81
Bilateral GA, n (%)	71 (85.5%)	64 (82.1%)	72 (90.0%)
History of CNV in Fellow Eye, n (%)	36 (41.9%)	28 (35.4%)	29 (35.8%)
GA lesion size, mean, mm^2 (SD)	8.0 (3.8)	8.9 (4.5)	8.2 (4.1)
BCVA score, mean letters (SD)	59.8 (15.7)	58.4 (16.0)	59.8 (17.2)
BCVA score (Snellen equivalent)	20/63	20/80	20/63
LL-BCVA score, mean letters (SD)	36.3 (16.6)	31.4 (17.1)	33.6 (17.8)

Primary Endpoint: GA Lesion Growth

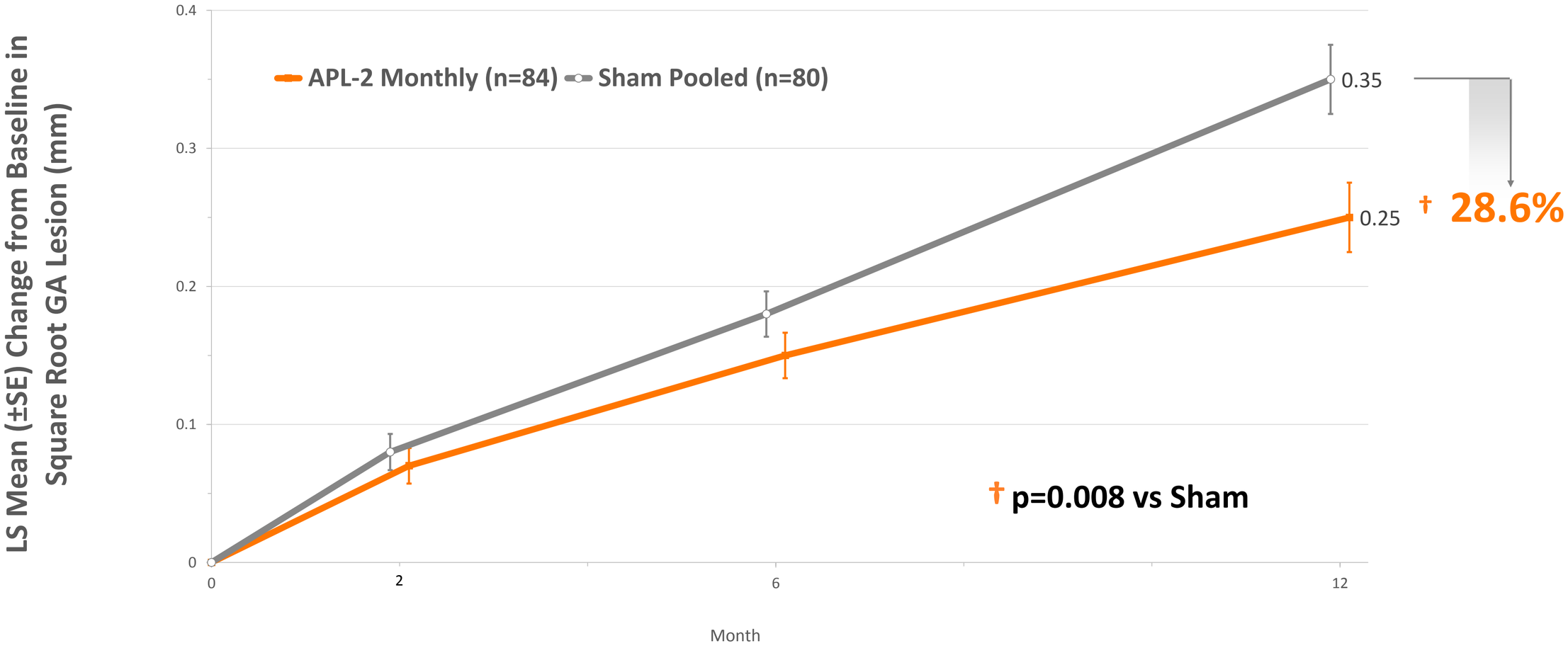


Modified Intent to Treat population (mITT), Observed, Mixed-Effect Model

A mixed effect model with main effects of treatment, visit and GA lesion at baseline, and interactions of treatment × visit, visit × baseline.

mITT = All subjects receiving at least one injection and having at least one FAF image after day 1

Primary Endpoint: GA Lesion Growth



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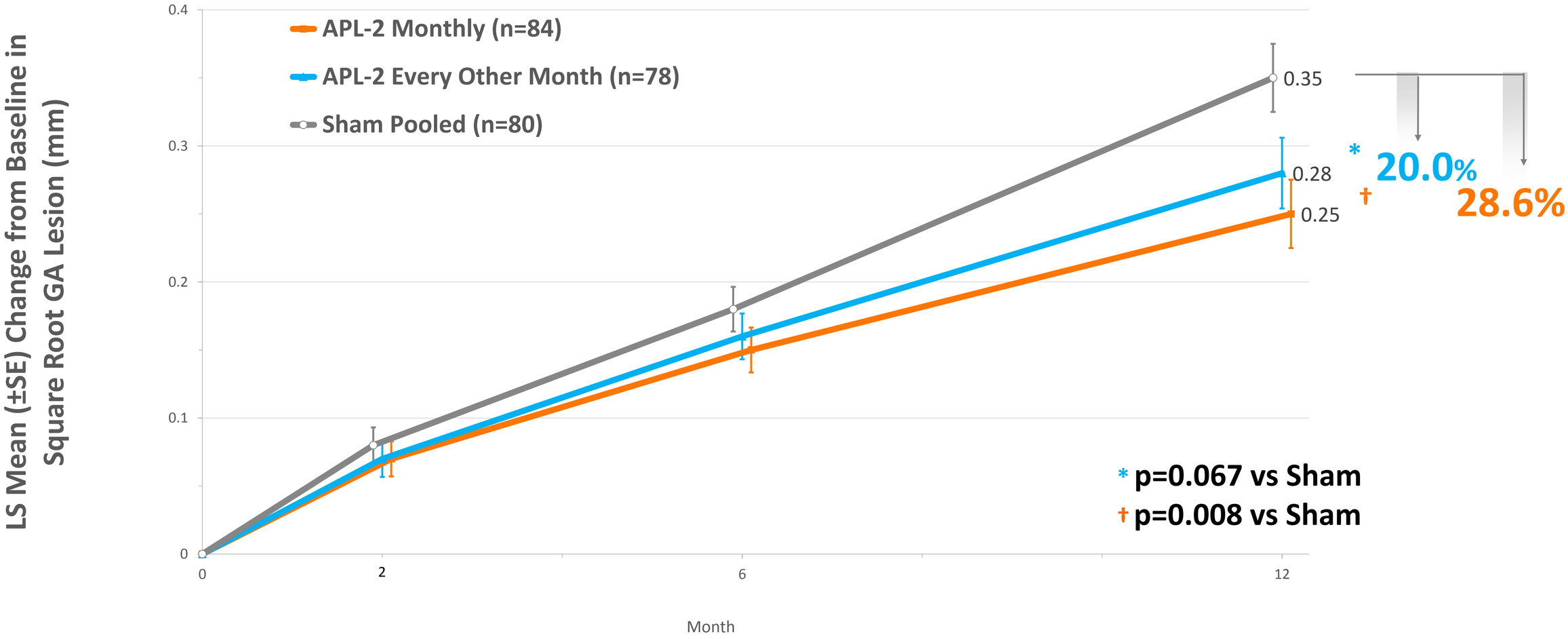

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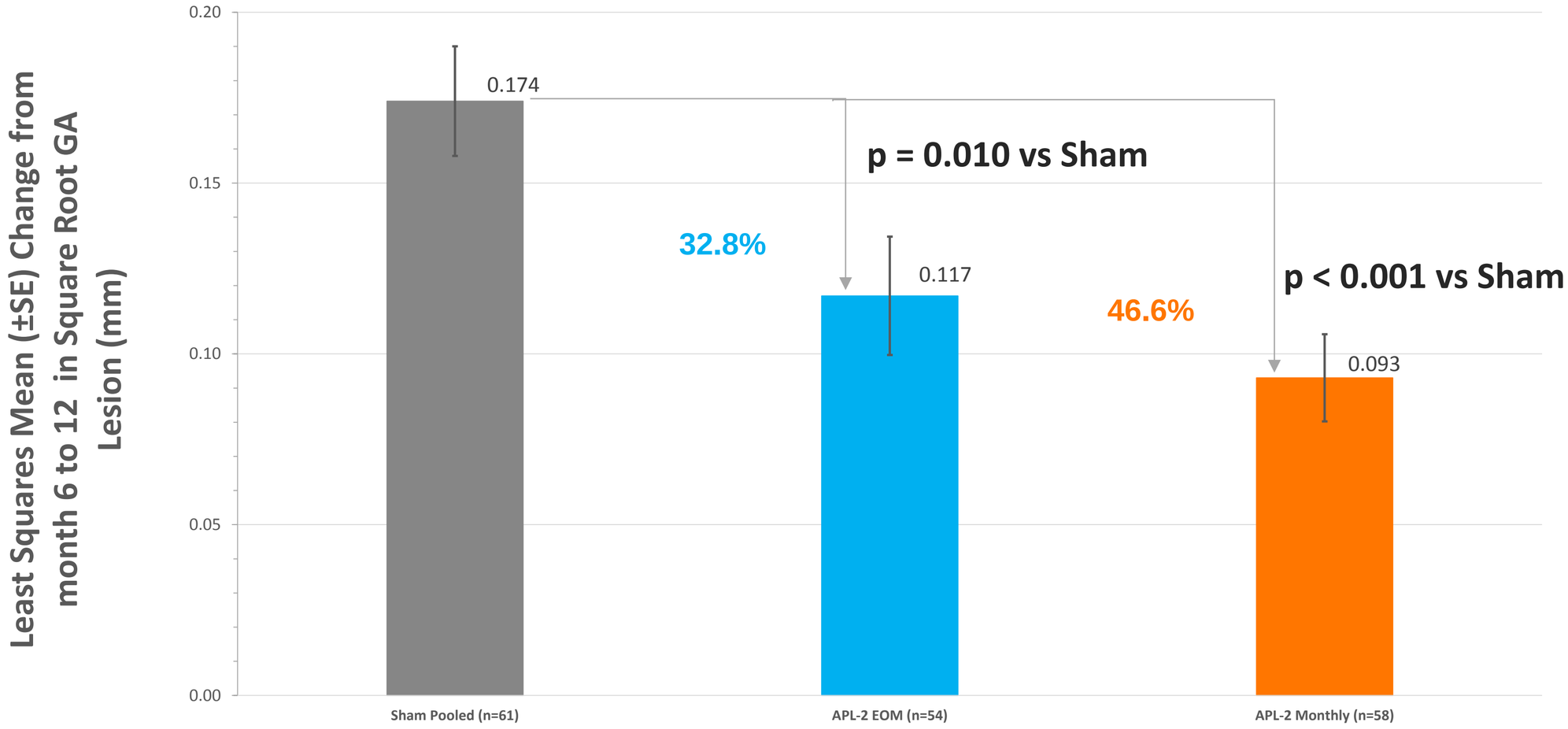
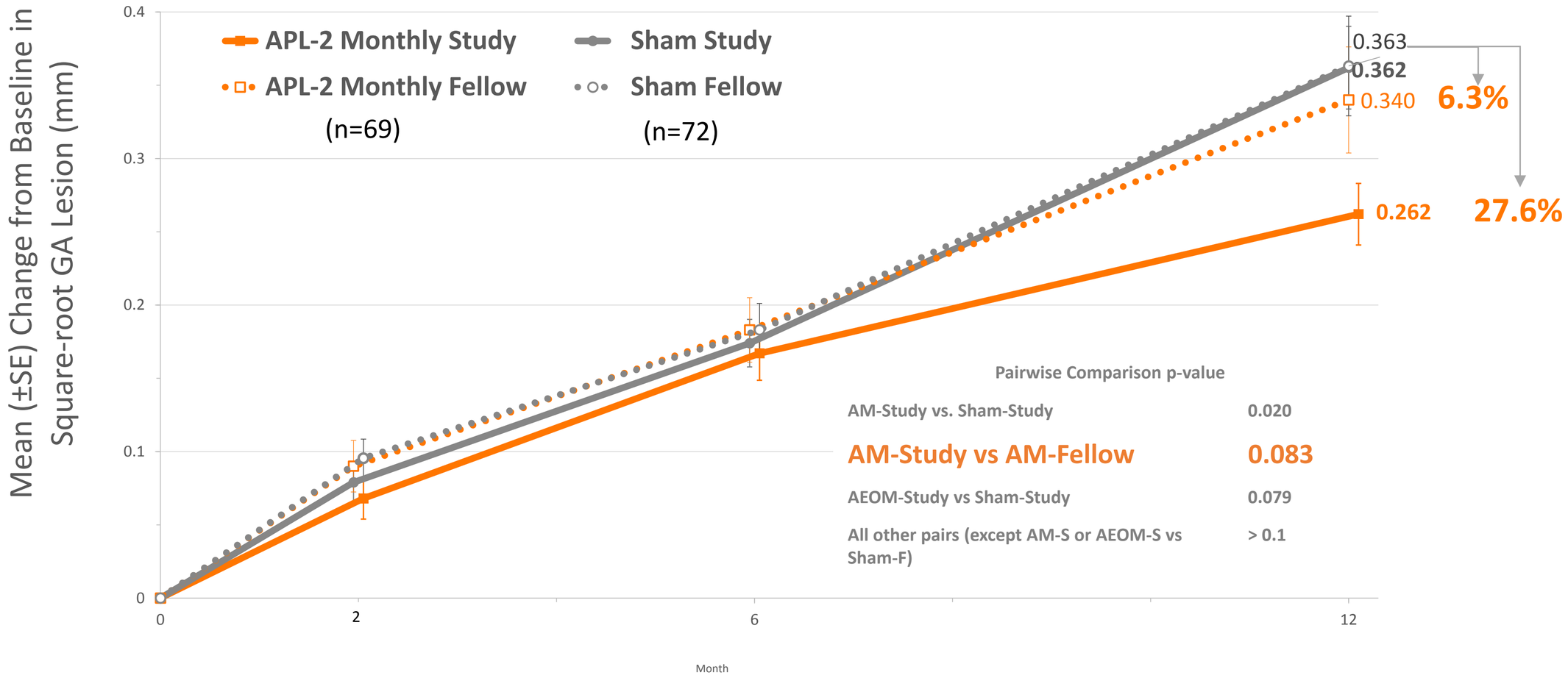
Post hoc analysis: greater reduction in GA lesion growth from month 6 to 12



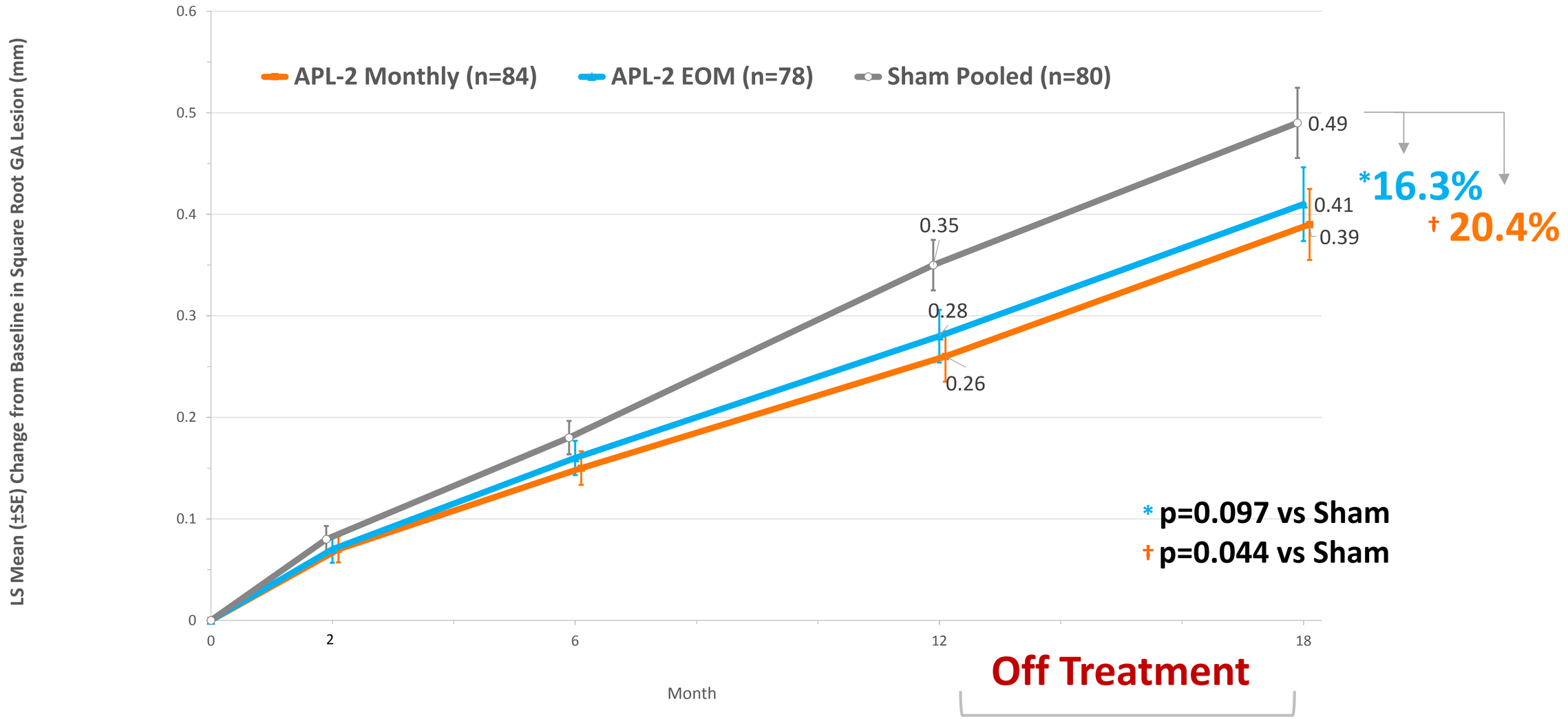
Data from subjects with a measurable GA lesion size at both Months 6 & 12. Data as of August 24, 2017

Post hoc analysis: in bilateral GA, monthly APL-2 reduced GA growth compared to contralateral eye



mITT-Bilateral GA, Observed, ANOVA at Month 12. Data as of August 24, 2017

GA Lesion Growth to 18 Months



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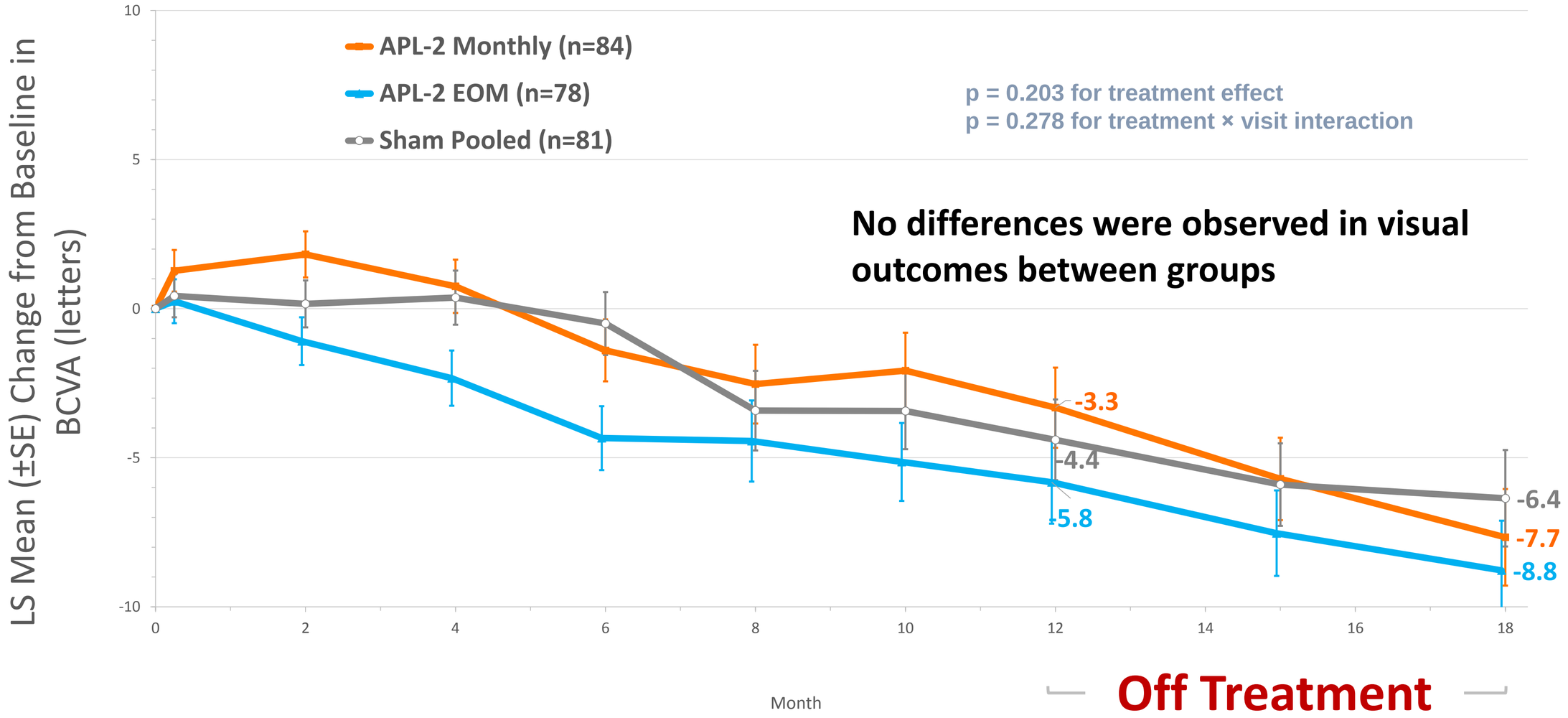
Best Corrected Visual Acuity



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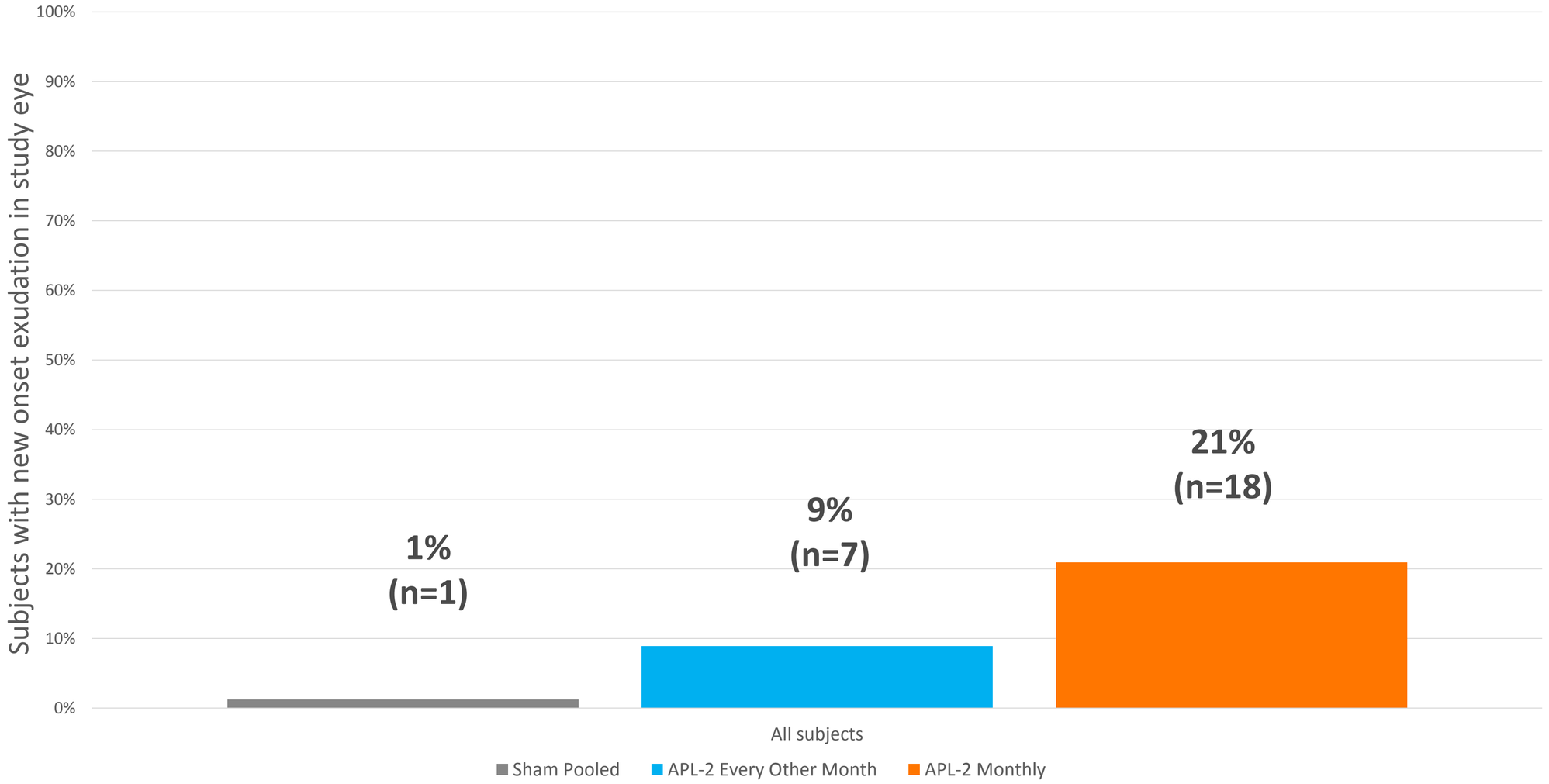
New Onset Exudation – 18 months



Adverse Event Profile

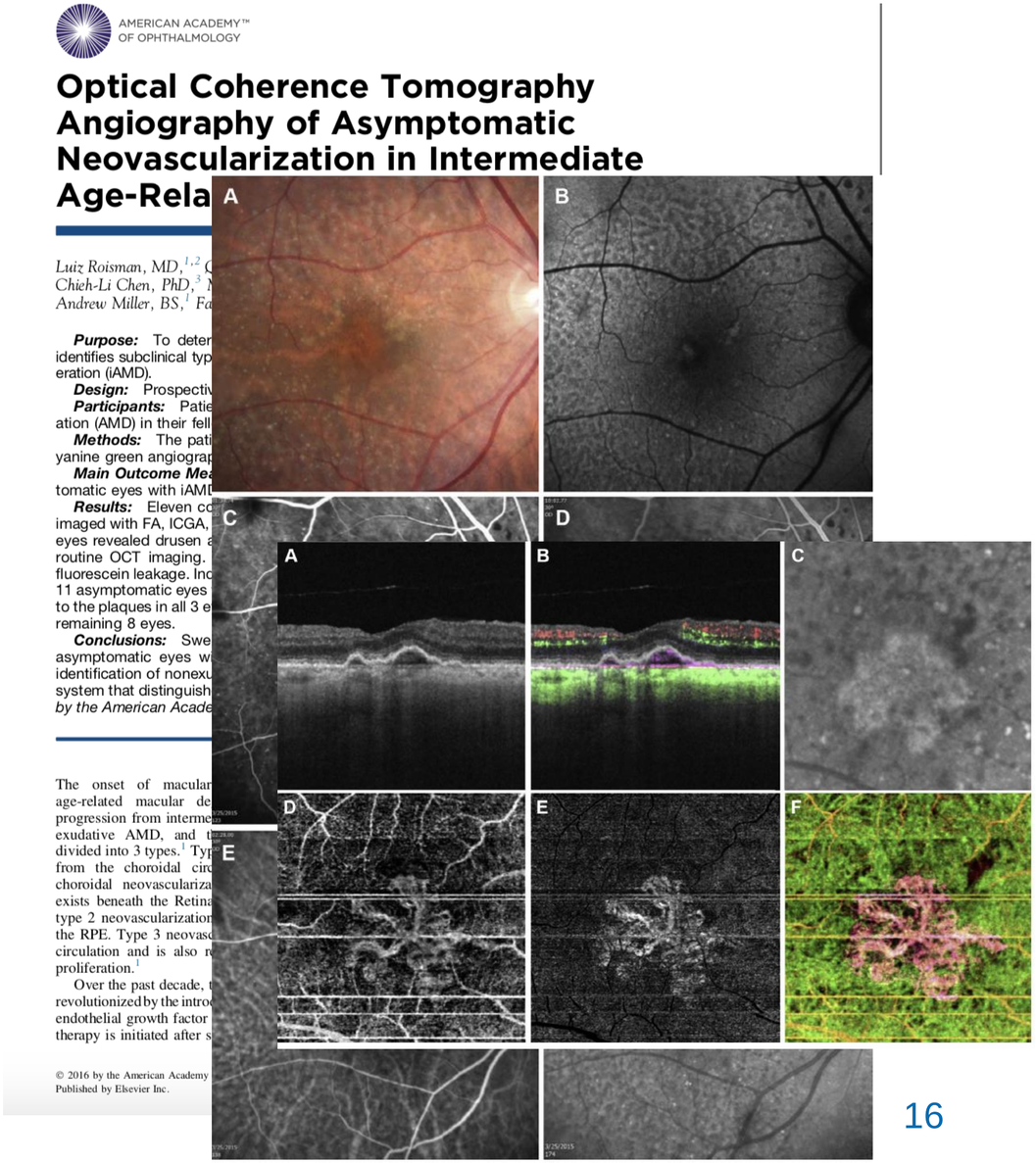
Adverse Event n (%) of subjects with events	APL-2 Monthly N=86	APL-2 Every Other Month N=79	Sham Pooled N=81
Ocular SAEs in study eye*	4 (4.7%)	2 (2.5%)	1 (1.2%)
Systemic (non-ocular) SAEs	19 (22.1%)	24 (30.4%)	23 (28.4%)
Treatment related ocular AEs in the study eye	22 (25.6%)	11 (13.9%)	0
↳ New onset exudation	18 (20.9%)	7 (8.9%)	1 (1.2%)
Treatment related systemic (non-ocular) 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

Possible explanations for APL-2 associated exudation

- APL-2 induces vascular exudation in the absence of neovascularization (VEGF-Like effect)
  - FA was not required on conversion to exudative AMD so no confirmation this was truly from CNV complex
- APL-2 induces neovascularization and exudation
- APL-2 induces exudation for pre-existing subclinical neovascularization
  - FA at baseline would have missed subclinical lesions
  - ICG angiography and OCT angiography were not performed in the study
  - Structural OCT was performed – double layer sign



Summary

- APL-2 inhibits C3 and the downstream effects of the complement cascade
- APL-2 when given monthly or every other month demonstrated statistically significant differences in GA growth over 18 months as compared to placebo patients despite no treatment for 6 months
- APL-2 slowed growth of GA independent of Complement Factor I genotype
- Upon discontinuation of APL-2 at month 12, the treatment effect declines
- The risk/benefit profile at 18 months supports the decision to move to Phase 3 testing