

Safety of Intravitreal Pegcetacoplan for Geographic Atrophy (GA): 18-Month Results from the DERBY and OAKS trials

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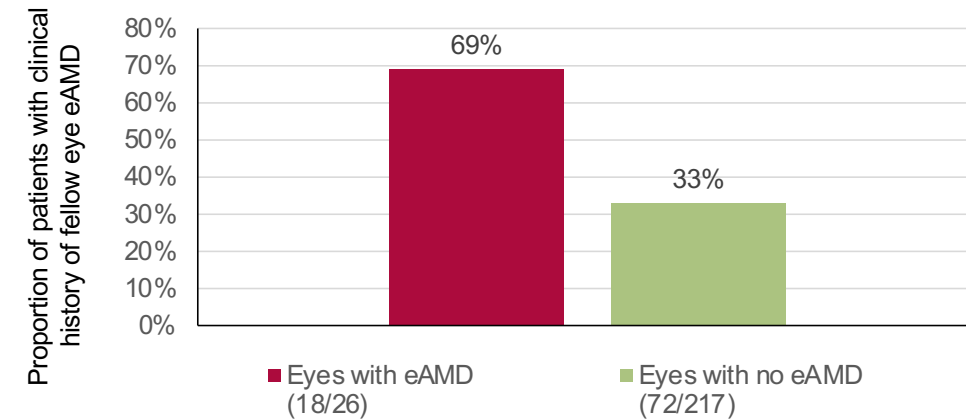
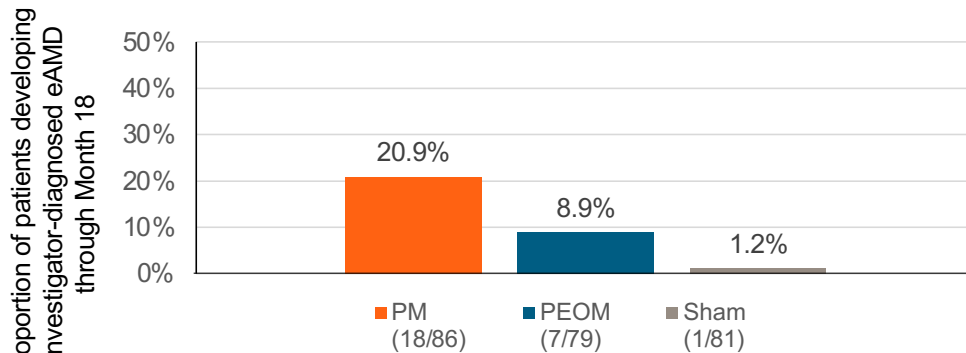
40th Annual Meeting of the American Society of Retina Specialists, NY, USA



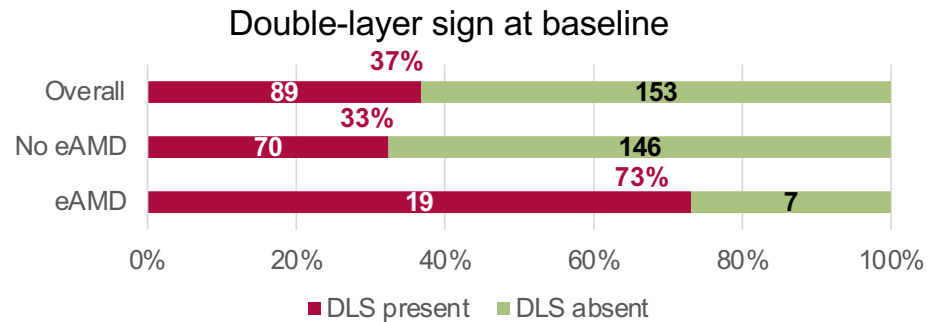
Disclosures

- Studies funded by Apellis Pharmaceuticals

Phase 2 FILLY trial: New-onset study eye eAMD



- An unexpected, dose-dependent difference in Investigator-determined study eye eAMD
- Associated with greater probability of eAMD development:
 - Fellow eye eAMD
 - DLS on SD-OCT



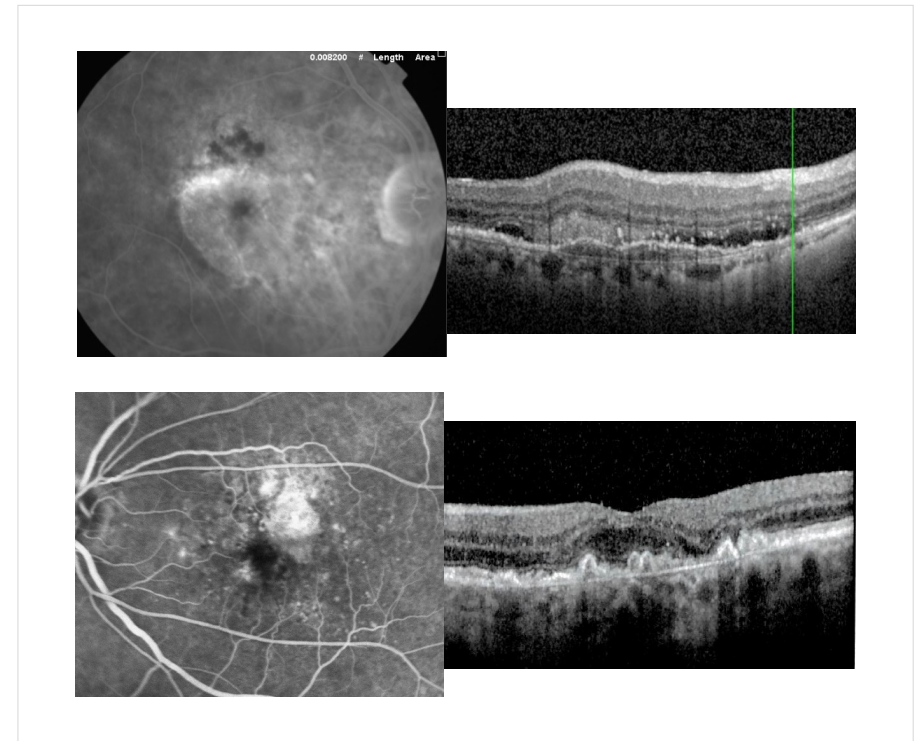
AMD=age-related macular degeneration; DLS=double-layer sign; eAMD=exudative AMD; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; SD-OCT=spectral domain optical coherence tomography.
 Wykoff CC et al. *Ophthalmology* 2021;128:1325-36.

FILLY post hoc analysis of CNV detected on FA at time of eAMD report

Fluorescein angiography:

Acquired in 17/26 (65%) eyes at the time of eAMD diagnosis

- 10 eyes had detectable CNV
 - All categorized as occult
- 7 eyes had no detectable CNV



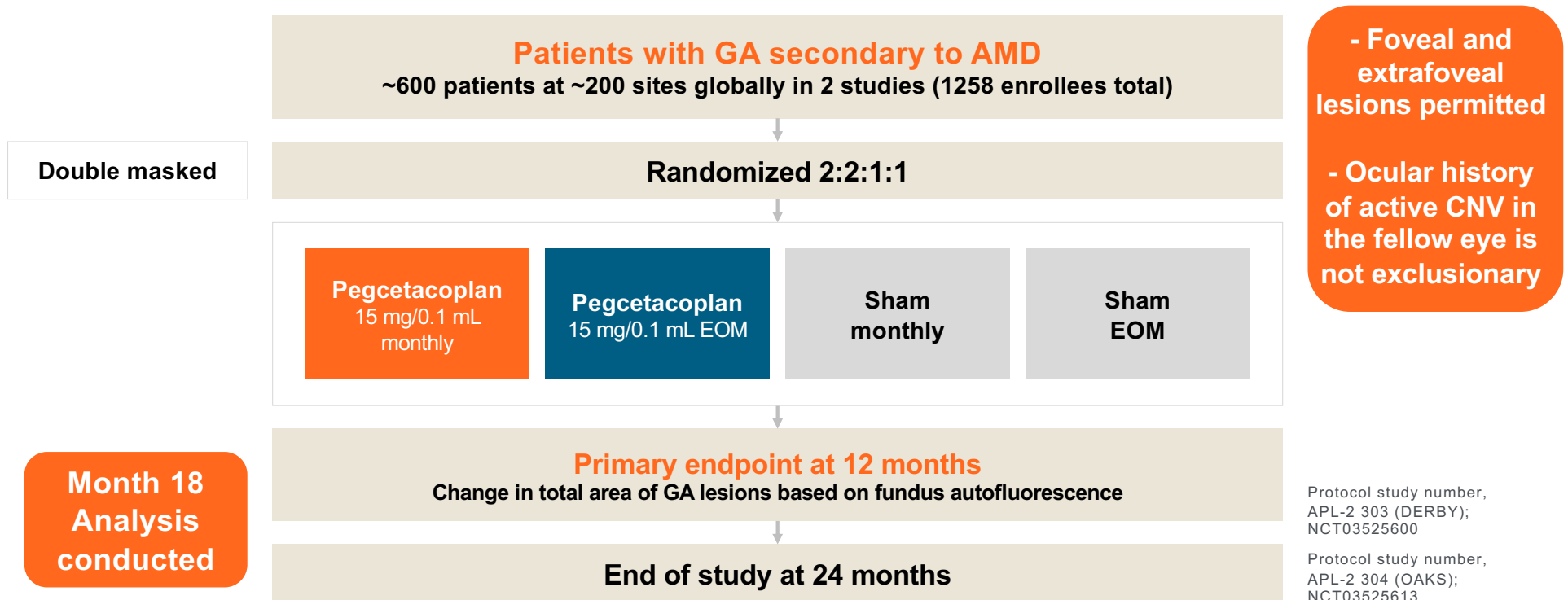
Images graded by DARC.

CNV=choroidal neovascularization; DARC=Digital Angiography Reading Center; eAMD=exudative age-related macular degeneration; FA=fluorescein angiography.
Wykoff CC et al. *Ophthalmology* 2021;128:1325–36.

eAMD findings from FILLY informed the design of the Phase 3 program

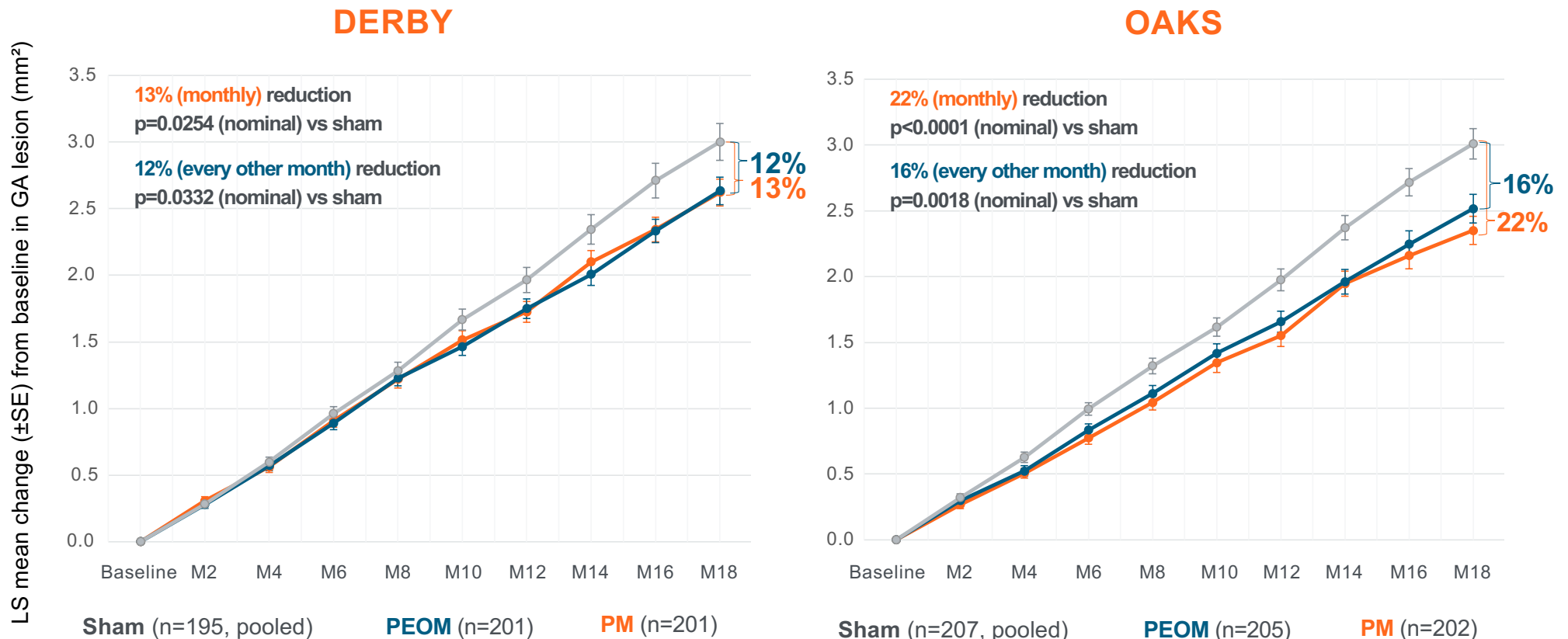
- If eAMD is suspected, prespecified imaging (CFP, OCT, FA and OCTA [select sites]) is captured
- Once eAMD is verified by masked reading center, patients remain on study treatment and should also be treated with on-label anti-VEGF pharmacotherapy
 - Initiation of anti-VEGF therapy for eAMD is at the discretion of the Investigator and is not reading-center determined
- Within the reporting from DERBY and OAKS
 - Reports of eAMD include all AEs reported by the Investigator falling within the preferred terms neovascular AMD or CNV

Global Phase 3 program: Design of DERBY and OAKS studies



AMD=age-related macular degeneration; CNV=choroidal neovascularization; EOM=every other month; GA=geographic atrophy.

Pegcetacoplan reduced GA lesion growth vs sham in **DERBY** and **OAKS** at Month 18



LS means estimated from a mixed-effects model for repeated measures. The modified intent-to-treat population was used for the analysis, defined as all randomized patients who received at least 1 injection of pegcetacoplan or sham and have baseline and at least 1 post-baseline value of GA lesion area in the study eye.
GA=geographic atrophy; LS=least squares; M=month; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; SE=standard error.

Investigator-reported events of eAMD through Month 18^a

	DERBY			OAKS		
	PM (N=206)	PEOM (N=208)	Sham Pooled (N=206)	PM (N=213)	PEOM (N=212 ^b)	Sham Pooled (N=211)
Patients with study eye Investigator-determined new-onset eAMD, n (%)	24 (11.7%)	11 (5.3%)	8 (3.9%)	16 (7.5%)	15 (7.1%)	4 (1.9%)
COMBINED STUDIES						
Investigator-determined new-onset eAMD, n (%)				40 (9.5%)	26 (6.2%)	12 (2.9%)

^aEvents include preferred terms of CNV and neovascular AMD.

^bOne patient in OAKS had CNV on medical history in study eye and is not counted in the denominator for this analysis; 211 patients were at risk of new-onset eAMD. AMD=age-related macular degeneration; CNV=choroidal neovascularization; eAMD=exudative AMD; n=number of patients; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly.

Investigator-reported events of eAMD through Month 18 by baseline fellow eye CNV and baseline study eye DLS status^a

COMBINED STUDIES	PM	PEOM	Sham Pooled
eAMD n/N (%), fellow eye CNV present	8/84 (9.5%)	8/81 (9.9%)	7/86 (8.1%)
eAMD n/N (%), fellow eye CNV absent	32/335 (9.6%)	18/338 (5.3%)	5/331 (1.5%)

COMBINED STUDIES	PM	PEOM	Sham Pooled
eAMD n/N (%), study eye DLS present	8/79 (10.1%)	6/73 (8.2%)	0/63 (0%)
eAMD n/N (%), study eye DLS absent	32/336 (9.5%)	20/345 (5.8%)	11/349 (3.2%)

^aEvents include preferred terms of CNV and neovascular AMD.

AMD=age-related macular degeneration; CNV=choroidal neovascularization; DLS=double-layer sign; eAMD=exudative AMD; n=number of patients; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly.

Characteristics of Investigator-reported eAMD events through Month 18^a

COMBINED STUDIES	PM (N=26)	PEOM (N=21)	Sham Pooled (N=11)
CNV type on FA at eAMD study visit			
Classic, n (%)	1 (3.8%)	1 (4.8%)	0
Occult, n (%)	22 (84.6%)	20 (95.2%)	10 (90.9%)
Classic + occult, n (%)	0	0	0
Active leakage with low likelihood of CNV, n (%)	3 (11.5%)	0	1 (9.1%)

- Table includes events with available reading center determination of CNV type on FA at time of eAMD study visit
- All patients had evaluable SD-OCT at time of eAMD study visit; majority of events showed no subretinal fluid

^aEvents include preferred terms of CNV and neovascular AMD. Events with no available reading center determination of CNV type on FA at time of eAMD are not included here. AMD=age-related macular degeneration; CNV=choroidal neovascularization; eAMD=exudative AMD; FA=fluorescein angiography; n=number of patients; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; SD-OCT=spectral domain optical coherence tomography.

Cases of eAMD in fellow eyes through 18 months^a

	OAKS			DERBY		
	PM (N=213)	PEOM (N=212)	Sham Pooled (N=211)	PM (N=206)	PEOM (N=206)	Sham Pooled (N=206)
Patients without baseline fellow eye CNV, N	168	173	167	167	166	164
Patients with new onset fellow eye eAMD, n (%)	8 (4.8%)	5 (2.9%)	7 (4.2%)	4 (2.4%)	8 (4.8%)	6 (3.7%)

COMBINED STUDIES	PM (N=419)	PEOM (N=420)	Sham Pooled (N=417)
Patients without baseline fellow eye CNV, N	335	339	331
Investigator-determined new-onset eAMD, n (%)	12 (3.6%)	13 (3.8%)	13 (3.9%)

^aEvents include preferred terms of CNV and neovascular AMD.

AMD=age-related macular degeneration; CNV=choroidal neovascularization; eAMD=exudative AMD; N=number of patients; PEOM=pegcetacoplan every other month; PM=pegcetacoplan every month;

Conclusions

- Pegcetacoplan was well tolerated through Month 18
- Definitions of eAMD were identical across FILLY, DERBY, and OAKS; all adverse events of eAMD are reported^a
- In DERBY and OAKS pooled, 9.5%, 6.2%, and 2.9% of patients in the combined PM, PEOM, and sham groups experienced new-onset Investigator-determined eAMD over 18 months
 - The majority of eAMD events with available images at time of exudation were classified as occult by the reading center
- IOI and endophthalmitis rates were low and consistent with those from other IVT studies
 - IOI: 2.1% at 18 months
 - 0.23% per injection (0.19% if excluding the 4 early cases attributed to drug impurity)
 - No reports of retinitis or vasculitis (occlusive or non-occlusive)
 - Infectious endophthalmitis: 0.5% over 18 months (0.044% per injection)

^aPreferred terms of neovascular AMD and CNV.

AMD=age-related macular degeneration; CNV=choroidal neovascularization; eAMD=exudative AMD; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly. IOI = intraocular inflammation