Geographic Atrophy

Consistent long-term efficacy and safety of pegcetacoplan were demonstrated in patients with GA secondary to AMD, with 5 years of treatment highlighting the importance of earlier treatment initiation

Earlier Treatment Yields Better Outcomes: 5 Years of Pegcetacoplan Treatment for Geographic Atrophy Secondary to AMD

Richard Gale[1], Dilsher S Dhoot[2], Maximilian Pfau[3], Sunir Garg[4], David Lally[5], Allen Hu[6], Andrew Chang[7-9], Laurentino Biccas[10], Nicole Eter[11], Jennifer Arnold[12], Chao Li[13], Felix Yemanyi[13], Michael Friedman[13a], Caroline R Baumal[13,14], Charles C Wykoff[15,16] on behalf of OAKS, DERBY, and GALE Investigators

[1]Hull York Medical School, University of York, Heslington, York, UK; [2]California Retina Consultants/Retina Consultants of America, Santa Barbara, CA, USA; [3]University of Bonn, Bonn, Germany; [4]MidAtlantic Retina, The Retina Service of Wills Eye Hospital, Thomas Jefferson University, Philadelphia, PA, USA; [5]New England Retina Consultants, Springfield, MA, USA; [6]Cumberland Valley Retina Consultants, Hagerstown, MD, USA; [7]Sydney Retina, Sydney, Australia; [8]The Save Sight Institute, The University of Sydney, Discipline of Ophthalmology, Sydney Medical School, Sydney, Australia; [9]University of New South Wales, Sydney, Australia; [10]Ocular Oftalmologia, Vitória, Espírito Santo, Brazil; [11]University of Münster, Münster, Germany; [12]Marsden Eye Specialists, Parramatta, NSW, Australia; [13]Apellis Pharmaceuticals, Waltham, MA, USA; [14]Retina Specialists of Boston and Wellesley, Wellesley, MA, USA; [15]Retina Consultants of Texas, Houston, TX, USA; [16]Blanton Eye Institute, Houston Methodist Hospital, Houston, TX, USA. [a]Employee of Apellis Pharmaceuticals at time of study

CONCLUSIONS

- Pegcetacoplan showed consistent long-term efficacy and favourable safety over 5 years in patients with GA secondary to AMD
- High completion rates in the OLE study support the tolerability and acceptability of long-term pegcetacoplan therapy
- Initiating treatment earlier led to slower GA progression and greater preservation of retinal tissue compared with delayed treatment
- Overall, findings emphasise the importance of early treatment to help slow GA progression

ACKNOWLEDGEMENTS

This study was funded by Apellis Pharmaceuticals. The authors and Apellis thank the patients, investigators, and staff who participated in this study. Professional medical writing support was provided by Matter and was funded by Apellis Pharmaceuticals.

REFERENCES

1. Heier JS, *et al. Lancet.* 2023;402:1434–1448. **2.** Goldberg RA, *et al. Ophthalmic Surg Lasers Imaging Retina.* 2025;56:398–406. **3.** Wykoff CC, *et al. Am J Ophthalmol.* 2025;276:350–364. **4.** Sunness JS, *et al. Ophthalmology.* 2007;114:271–277. **5.** Dreyhaupt J, *et al. Ophthalmic Epidemiol.* 2005;12(6):353–362. **6.** Holz FG, *et al. JAMA Ophthalmol.* 2018;136(6):666–677. **7.** Li C, *et al. Transl Vis Sci Technol.* 2023;12(3):26.

DISCLOSURES

Richard Gale: Consultant/Contractor: American Academy of Ophthalmology, Apellis, Bausch & Lomb, Boehringer Ingelheim, Coherus, Canadian Ophthalmological Society, Merck Manual, Physicians' Education Resource, Retina Fellows Forum, West Pharmaceuticals; Financial support: Alcon, American Academy of Ophthalmology, Apellis, Boehringer Ingelheim, Genentech, Kodiak Biosciences, NGM Bio, Regeneron. **Dilsher S Dhoot:** Consultant/Contractor: Apellis. **Maximilian Pfau:** Consultant/Contractor: Apellis, Johnson & Johnson; Employment: Roche; Financial Support: iCARE. **Sunir Garg:** Consultant/Contractor: Apellis; Financial Support: Apellis. **David Lally:** Consultant/Contractor: Apellis; Financial Support: Apellis. **Allen Hu:** Consultant/Contractor: Apellis; Financial Support: Apellis; Personal Financial Interest: Apellis. **Andrew Chang:** Consultant/Contractor: Apellis; Financial Support: Apellis. **Laurentino Biccas:** No Commercial Relationship. **Nicole Eter:** Consultant/Contractor: Apellis; Financial Support: Apellis. **Jennifer Arnold:** Consultant/Contractor: Apellis. **Chao Li:** Former Employment: Apellis. **Felix Yemanyi:** Employment: Apellis. **Michael Friedman:** Former Employment: Apellis. **Caroline R Baumal:** Employment: Apellis. **Charles C Wykoff:** Consultant/Contractor: Apellis; Financial Support: Apellis.

Data first presented at The Macula Society 49th Annual Meeting; February 25–28, 2026; Coronado, California, USA

Presented at Royal College of Ophthalmology Annual Meeting; May 18–21, 2026; Manchester, UK

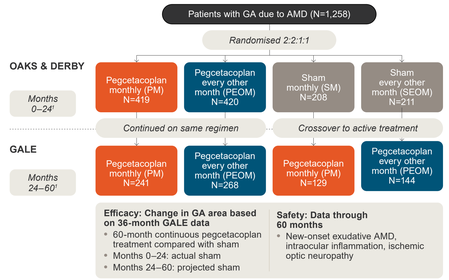
PURPOSE

- To assess the efficacy of early versus delayed treatment with intravitreal (IVT) pegcetacoplan for geographic atrophy (GA) secondary to age-related macular degeneration (AMD) after 5 years of continuous treatment

METHODS

- Following completion of the 24-month phase 3 OAKS and DERBY trials evaluating IVT pegcetacoplan versus sham,[1] patients were eligible to enter the 36-month GALE open-label extension (OLE) study[2,3] (**Figure 1**)
- Eyes receiving pegcetacoplan in OAKS/DERBY continued in GALE with the same dosing interval—monthly (PM) or every other month (PEOM)—forming the **Early Treatment** group
- Sham-observed eyes crossed over to active pegcetacoplan in GALE at the same dosing interval, forming the **Delayed Treatment** group
- A linear projected sham model was used as a comparator and validated using untreated fellow eyes with GA, which showed a consistent linear growth rate of ~2 mm²/year[2–6]
- Both subfoveal (SF) and nonsubfoveal (NSF) GA eyes were included
- Safety and efficacy outcomes over 5 years of continuous pegcetacoplan treatment were assessed

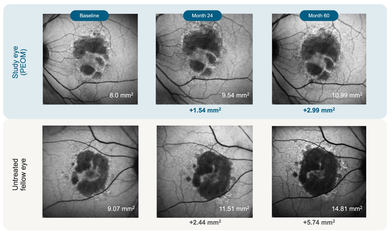
Figure 1: Study Design



RESULTS

- GALE case report of an 83-year-old female with bilateral NSF GA treated with pegcetacoplan for 60 months (**Figure 2**)
  - Pegcetacoplan-treated study eye (PEOM) showed slower GA growth, increasing from baseline by 1.54 mm² by Month 24 and 2.99 mm² by Month 60
  - Untreated fellow eye showed faster GA progression, increasing from baseline by 2.44 mm² by Month 24 and 5.74 mm² by Month 60, demonstrating greater GA enlargement compared with the treated eye
- This case demonstrates ~2 times greater growth of GA in the untreated eye as compared with the eye treated with pegcetacoplan

Figure 2: GALE Patient Case[2,3]



- Most (67%) patients completed 5 years (**Table 1**)
  - Excluding deaths, 74% of patients completed 5 years

Table 1: Patient Disposition

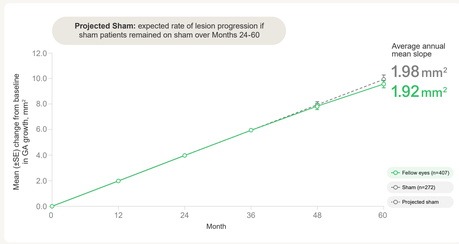
Number of patients	PM to PM	PEOM to PEOM	SM to PM	PEOM to PEOM	Overall
Enrolled in GALE	250	269	129	144	792
Included in modified full analysis set	241	267	129	143	780
Excluded from modified full analysis set					
No injection received in GALE	0	1	0	1	2
Enrolled from study other than OAKS or DERBY[a]	9	1	0	0	10
Completed 36 months in GALE, %	70.8	66.8	62.0	64.3	66.8
Discontinued prior to 36 months in GALE, %	29.2	33.2	38.0	35.7	33.2
Consent withdrawal	11.6	16.8	16.3	11.2	14.1
Death	6.0	7.1	6.2	8.4	6.8
Adverse event	4.0	3.7	4.7	3.5	3.9
Lost to follow-up	2.8	2.2	3.9	1.4	2.5
Physician's decision	2.8	0.7	3.1	2.1	2.0

[a]Enrolled in GALE from phase 1b study APL2-103, included in safety population.

- GA progression in untreated fellow eyes[a] and projected sham showed a consistent linear growth pattern, with average annual slopes of 1.98 mm² (projected sham) and 1.92 mm² (fellow eyes) (**Figure 3**)
- The close alignment between actual fellow eye growth and the projected sham model supports the use of a linear projected sham as a valid comparator for long-term GA progression analyses[2–6]

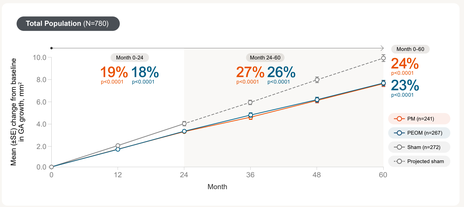
[a]Fellow eyes that would have met study inclusion criteria at OAKS/DERBY baseline: absence of exudative AMD in the medical history, GA area between 2.5 and 17.5 mm², presence of any pattern of hyperautofluorescence in the junctional zone of GA, and GA not confluent with any peripapillary atrophy.

Figure 3: GA Growth in Fellow Eye Compared With Projected Sham



- Between Months 24 and 60, pegcetacoplan reduced GA growth in the overall population (NSF and SF GA combined) by 27% with PM and 26% with PEOM (all p<0.0001; nominal) (**Figure 4**)
- Over 5 years, pegcetacoplan reduced GA growth in the overall population by 24% with PM and 23% with PEOM (all p<0.0001; nominal)

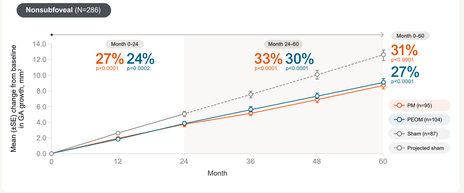
Figure 4: GA Growth in Pegcetacoplan-Treated Eyes vs Projected Sham Over 5 Years



[a]Mean rate of change in GA area between pegcetacoplan group and sham group from antecedent study baseline to Month 60, with knots at Months 12, 24, 36, and 48 allowing for the slope to be linear over each of the 12-month segments but to differ between segments using piecewise slope analysis. Mean rate of change of projected sham from Month 24 to Month 60 was estimated from the mean rate of change in each period from Month 0 to Month 24 in the sham group. The modified full analysis set was used for the analysis, defined as patients who were in the OAKS or DERBY antecedent study's ITT set, had not been enrolled in the phase 1b APL2-103 study, and received ≥1 injection of pegcetacoplan in GALE. All p-values are nominal. ITT, intention-to-treat.

- Between Months 24 and 60, pegcetacoplan reduced GA growth versus projected sham in NSF GA by 33% with PM and 30% with PEOM (all p<0.0001; nominal) (**Figure 5**)
- Over 5 years, pegcetacoplan reduced GA growth in NSF GA by 31% with PM and 27% with PEOM (all p<0.0001; nominal)

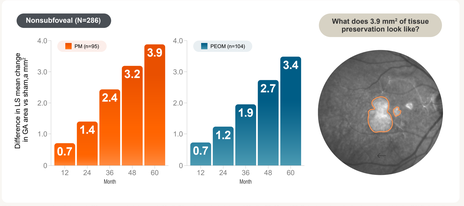
Figure 5: GA Growth in Pegcetacoplan-Treated Eyes vs Projected Sham Over 5 Years in Eyes With NSF GA



[a]Mean rate of change in GA area between pegcetacoplan group and sham group from antecedent study baseline to Month 60, with knots at Months 12, 24, 36, and 48 allowing for the slope to be linear over each of the 12-month segments but to differ between segments using piecewise slope analysis. Mean rate of change of projected sham from Month 24 to Month 60 was estimated from the mean rate of change in each period from Month 0 to Month 24 in the sham group. The modified full analysis set was used for the analysis, defined as patients who were in the OAKS or DERBY antecedent study's ITT set, had not been enrolled in the phase 1b APL2-103 study, and received ≥1 injection of pegcetacoplan in GALE. All p-values are nominal.

- In NSF GA, longer treatment with pegcetacoplan demonstrated increasing efficacy through 60 months and more tissue preservation (**Figure 6**)
- Specifically, through each year of the clinical program, more functional tissue was preserved, with up to 3.9 mm² of retinal tissue preserved at Month 60
- This represents >1.5 disc areas[4,7]

Figure 6: >1.5 Disc Areas of Retinal Tissue Preserved Through 5 Years of Pegcetacoplan Treatment



[a]Difference in mean rates of change in GA area vs pooled sham up to Month 24, and vs projected sham at Months 36, 48, and 60. Data shown for patients who continued into the GALE study after OAKS and DERBY. Projected sham during Months 24–60 was estimated from the mean rate of change in each period in Months 0–24. LS, least squares.

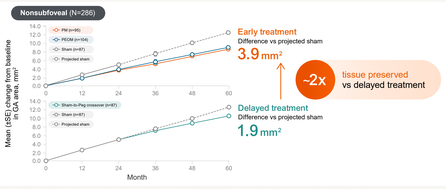
- Eyes with NSF GA in the:
  - Early Treatment group had GA growth reduced by 31% with PM, preserving 3.9 mm² (>1.5 disc areas)[4,7] of retinal tissue (**Figure 7**)
  - Delayed Treatment group had GA growth reduced by 26%, preserving 1.9 mm² of retinal tissue
- Earlier pegcetacoplan treatment led to ~2 times retinal tissue being preserved

KEY FINDINGS

5-year data from OAKS, DERBY, and GALE:

- Pegcetacoplan preserved 3.9 mm² of retinal tissue (**>1.5 disc areas**)[4,7]
- Earlier treatment initiation preserved **~2 times the retinal tissue** versus delayed treatment
- Pegcetacoplan treatment saved **~1.5 years** of disease progression
- Consistent safety profile with no new signals observed

Figure 7: Therapeutic Timing and Retinal Preservation



[a]Mean rate of change in GA area between pegcetacoplan group and sham group from OAKS/DERBY baseline to Month 60, with knots at Months 12, 24, 36, and 48 allowing for the slope to be linear over each of the 12-month segments but to differ between segments using piecewise slope analysis. Projected sham during Months 24–60 was estimated from the mean rate of change in each period in Months 0–24. The modified full analysis set was used for the analysis, defined as patients who were in the OAKS/DERBY ITT set, had not been enrolled in the phase 1b APL2-103 study, and received ≥1 injection of pegcetacoplan in GALE. Peg, pegcetacoplan.

- This corresponded to ~18.5 months (PM) and ~16.5 months (PEOM) of delayed disease progression with pegcetacoplan treatment (**Figure 8**)

Figure 8: Delays in Disease Progression With Pegcetacoplan Treatment

[a]Mean rate of change in GA area between pegcetacoplan group and sham group from OAKS/DERBY baseline to Month 60, with knots at Months 12, 24, 36, and 48 allowing for the slope to be linear over each of the 12-month segments but to differ between segments using piecewise slope analysis. Projected sham during Months 24–60 was estimated from the mean rate of change in each period in Months 0–24. The modified full analysis set was used for the analysis, defined as patients who were in the OAKS/DERBY ITT set, had not been enrolled in the phase 1b APL2-103 study, and received ≥1 injection of pegcetacoplan in GALE.

- The safety profile in GALE was consistent with OAKS and DERBY[1] (**Table 2**)
- From Months 0–60, the rates per injection were:
  - Infectious endophthalmitis: 0.04% per injection
  - Intraocular inflammation[a]: 0.22% per injection
  - Ischemic optic neuropathy: 0.02% per injection
- There were no study events of occlusive or non-occlusive retinitis or vasculitis in OAKS, DERBY, and GALE[1-3]
- An estimated ~900,000 pegcetacoplan injections (with an estimated ~133,000 first injections) have been administered to patients across clinical trials and real-world as of December 31, 2025
- The annual reporting rate of cases adjudicated as vasculitis has decreased by greater than 90%, from 0.013% in 2023, to 0.003% in 2024, and 0.001% in 2025

GALE 36 Months Mean incidence rate per year, %	PM to PM (n=250)	SM to PM (n=129)	PEOM to PEOM (n=268)	PEOM to PEOM (n=143)
Most common AEs in study eye				
New-onset exudative AMD[a]	6.6	3.6	2.3	2.6
Intraocular pressure increased	4.3	4.0	3.3	1.0
Vitreous floaters	2.9	3.8	1.0	2.8
Conjunctival haemorrhage	2.2	4.4	1.8	3.2
Cataract	3.1	1.4	1.8	2.4
Retinal haemorrhage	2.6	2.9	1.9	1.4
AEs of interest in study eye				
Infectious endophthalmitis	0.5	0.3	0.1	0.0
Intraocular inflammationa	1.8	1.7	0.5	0.5
Ischaemic optic neuropathy	0.2	0.4	0.0	0.3

[a]AEs calculated as the mean incidence rate per year through 36 months of GALE. The following terms were combined: new-onset exudative AMD included: neovascular AMD, choroidal neovascularization. Intraocular inflammation included: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, anterior chamber flare. AEs, adverse events.

Richard.Gale@york.ac.uk

Scan to download this poster