# 24-Month Safety Results From the OAKS and DERBY Trials With Further Characterization of Exudative Age-Related Macular Degeneration

Philip Ferrone

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# Disclosures

- Philip Ferrone has the following financial interests or relationships to disclose
  - Consultant/Advisor: Allergan, Apellis,  Genentech and Opthea
  - Research funding: Alexion, Apellis, Eyepoint, Genentech, Gyroscope, Opthea, Regeneron and REGENXBIO
  - ArcticDx: Stock

# Phase 3 OAKS and DERBY trials: Design and key criteria

OAKS DERBY

**Patients with GA secondary to AMD**
**1258** patients at **232** sites combined

**Randomized 2:2:1:1**

- **Pegcetacoplan Monthly**
- **Pegcetacoplan EOM**
- **Sham Monthly**
- **Sham EOM**

**12 month primary endpoint**
**Change in total GA lesion area on FAF**

**24 month secondary endpoint**
- BCVA[a]
- LLVA
- Reading speed[a]
- NEI VFQ-25
- FRI Index score[a]
- Microperimetry[a] (OAKS)
- Lesion growth

**GALE**
**3-year open-label extension study**

**Key inclusion criteria**

- Age ≥60 years
- BCVA ≥24 letters ETDRS (20/320 Snellen equivalent)
- GA lesion requirements:
  - Total size: ≥2.5 and ≤17.5 $mm^2$; If multifocal, at least 1 focal lesion must be ≥1.25 $mm^2$ (0.5 DA)
  - Presence of perilesional hyperautofluorescence
  - **GA lesions with or without subfoveal involvement allowed**

**Key exclusion criteria**

- GA secondary to a condition other than AMD, such as Stargardt disease, in either eye
- CNV in the study eye (active or history of), including presence of RPE tear (assessed by reading center)

CNV in the fellow eye was not exclusionary

OAKS, DERBY, GALE CT.gov identifiers: NCT03525613, NCT03525600, NCT04770545, respectively. [a]Key secondary endpoints. AMD=age-related macular degeneration; BCVA=best-corrected visual acuity; CNV=choroidal neovascularization; DA=disc area; EOM=every other month; ETDRS=Early Treatment Diabetic Retinopathy Study; FRI=Functional Reading Independence; GA=geographic atrophy; LL=low luminance; NEI-VFQ=National Eye Institute Visual Function Questionnaire; RPE=retinal pigment epithelium.

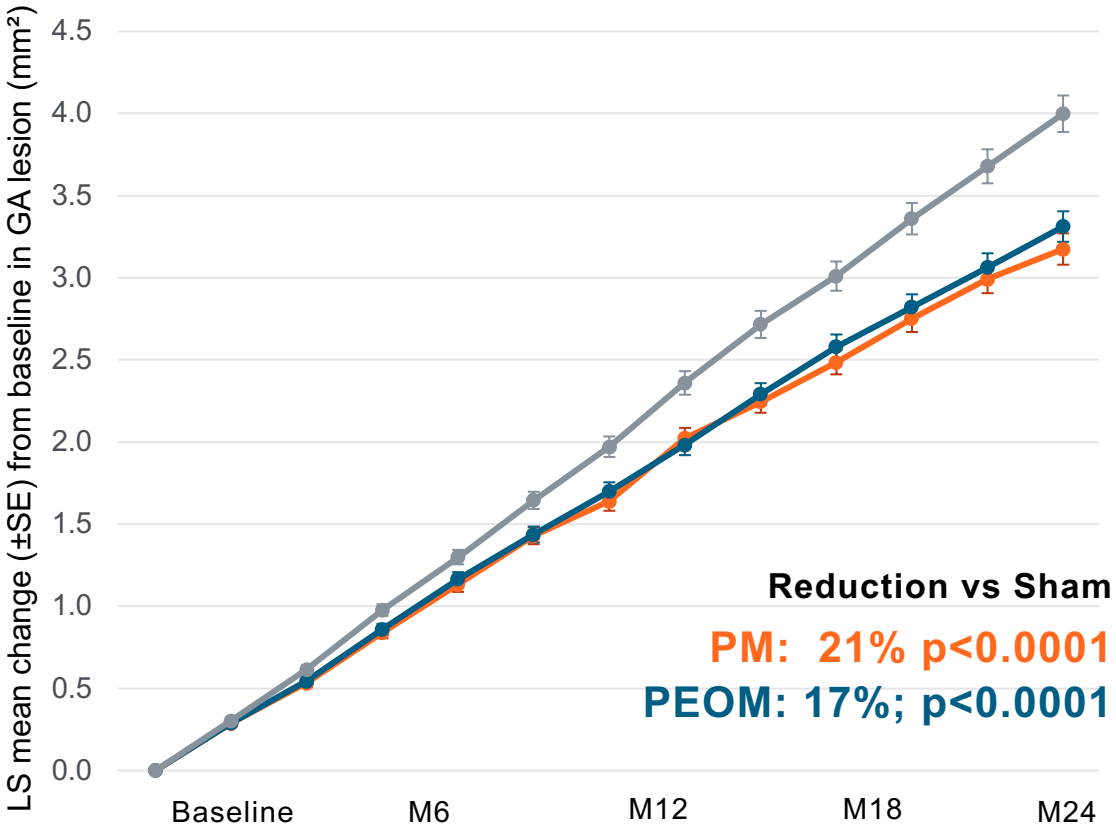
OAKS and DERBY combined

# Reductions in GA lesion growth at Month 24

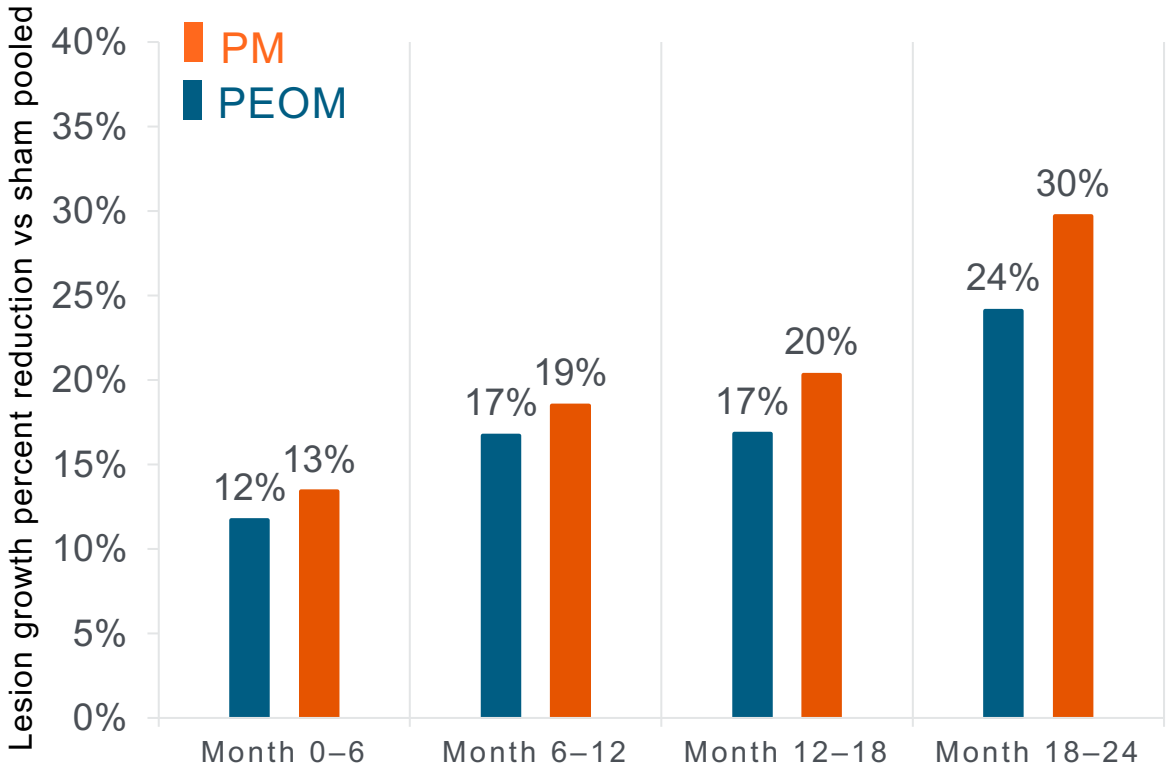
OAKS DERBY 24 MONTHS

*(all p-values are nominal)*

## MMRM primary analysis




## Reductions based on 6-month intervals




**Pegcetacoplan Monthly (n=403)** **Pegcetacoplan EOM (n=406)** **Sham (n=402)**

LS means estimated from MMRM analysis. The piecewise linear mixed-effects model evaluated mean rate of change in GA area between pegcetacoplan arms and sham arm from baseline to Month 24, with knots at Months 6, 12 and 18 allowing for the slope to be linear over each of the 6-month segments but to differ between segments (piecewise slope analysis). The mITT 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 one post-baseline value of GA lesion area in the study eye. GA=geographic atrophy; LS=least square; M=month; mITT=modified intent-to-treat; MMRM=mixed-effects model for repeated measures; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; SE=standard error.

OAKS and DERBY combined

# TEAEs in OAKS and DERBY over 24 months

OAKS DERBY 24 MONTHS

| | PM (N=419) | PEOM (N=420) | Sham pooled (N=417) |
|---|---|---|---|
| All TEAEs, n (%) | 370 (88.3) | 367 (87.4) | 344 (82.5) |
| Ocular TEAEs in study eye, patients, n (%) | 258 (61.6) | 231 (55.0) | 193 (46.3) |
| Non-ocular TEAEs, patients, n (%) | 337 (80.4) | 307 (73.1) | 300 (71.9) |
| Serious ocular TEAEs in the study eye, n (%) | | | |
| Endophthalmitis | 2 (0.5) | 3 (0.7) | 0 |
| Optic ischemic neuropathy | 3 (0.7) | 0 | 0 |
| Retinal detachment | 1 (0.2) | 1 (0.2) | 0 |
| Uveitis | 0 | 2 (0.5) | 0 |
| Vitritis | 2 (0.5) | 0 | 0 |
| Visual acuity reduced | 0 | 1 (0.2) | 1 (0.2) |
| Papilledema | 1 (0.2) | 0 | 0 |
| Iridocyclitis | 0 | 1 (0.2) | 0 |
| Retinal tear | 1 (0.2) | 0 | 0 |
| Dry AMD | 0 | 0 | 1 (0.2) |
| Macular hole | 0 | 0 | 1 (0.2) |
| Hyphema | 1 (0.2) | 0 | 0 |

No eAMD events were reported as SAEs in either trial

Safety set. The events of endophthalmitis include events of both infectious and non-infectious endophthalmitis. Sham patients do not receive injections. AMD=age-related macular degeneration; N/n=number of patients; M=number of events; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; TEAE=treatment-emergent adverse event.

# Evaluation of new-onset eAMD in the Phase 3 program

OAKS DERBY

- Events of new-onset eAMD include preferred terms of CNV and neovascular AMD
- During the study, if eAMD was suspected by an Investigator, prespecified imaging (CFP, OCT, FA, and OCTA [select sites]) was acquired and sent to reading center
- The decision to initiate anti-VEGF treatment for active CNV was solely at the discretion of the Investigator, regardless of reading center confirmation
- Patients who developed eAMD were treated with on-label anti-VEGF therapy while remaining on study treatment

AE=adverse event; AMD= age-related macular degeneration; CFP=color fundus photography; CNV=choroidal neovascularization; eAMD=exudative AMD; FA=fluorescein angiography; GA=geographic atrophy; OCT=optical coherence tomography; OCTA=OCT angiography; VEGF=vascular endothelial growth factor.

OAKS and DERBY combined

# New-onset investigator-determined eAMD[a]

| | PM | PEOM[b] | Sham Pooled |
|---|---|---|---|
| **eAMD, 0-12 months** | | | |
| **Study eye** - overall population, % (n/N) | **6.0%** (25/419) | **4.1%** (17/419) | **2.4%** (10/417) |
| **Study eye** - without fellow eye CNV at baseline, % (n/N) | **5.7%** (19/335) | **3.8%** (13/338) | **0.9%** (3/331) |
| **eAMD, 0-24 months** | | | |
| **Study eye** - overall population, % (n/N) | **12.2%** (51/419) | **6.7%** (28/419) | **3.1%** (13/417) |
| **Study eye -** without fellow eye CNV at baseline, % (n/N) | **11.0%** (37/335) | **5.6%** (19/338) | **1.5%** (5/330) |
| **Fellow eye*** % (n/N) | **4.2%** (14/335) | **4.1%** (14/339) | **4.5%** (15/330) |

**Fellow eye analysis includes subjects at risk for new onset eAMD*

[a]Events include preferred terms of CNV and neovascular AMD. [b]Number of patients at risk for new-onset eAMD in PEOM arms from OAKS and DERBY combined was 419. 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 every month; SD-OCT=spectral domain optical coherence tomography; VEGF=vascular endothelial growth factor.

# Reading center classification of CNV subtype*

OAKS DERBY 24 MONTHS

| CNV Type based in FA, n (%) | PM (N=35) | PEOM (N=23) | Sham Pooled (N=12) |
|---|---|---|---|
| No CNV | 1 (2.9%) | 1 (4.3%) | 0 |
| Active leakage with low likelihood of CNV | 5 (14.3%) | 0 | 1 (8.3%) |
| Classic | 1 (2.9%) | 1 (4.3%) | 0 |
| Occult | 28 (80.0%) | 21 (91.3%) | 11 (91.7%) |

**Table includes events with available reading center determination of CNV type on FA at time of eAMD study visit*

[a]Events include preferred terms of CNV and neovascular AMD.
Safety set. AE=adverse event; 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 every month.

OAKS and DERBY combined

# Anti-VEGF use and onset of eAMD[a] events

OAKS DERBY 24 MONTHS

## Anti-VEGF Use in Study Eye

| | PM (N=51) | PEOM (N=28) | Sham Pooled (N=13) |
|---|---|---|---|
| **Anti-VEGF use, n (%)** | 50 (98%) | 27 (96%) | 11 (85%) |
| **Injections/month following eAMD diagnosis** | 0.53 | 0.52 | 0.45 |

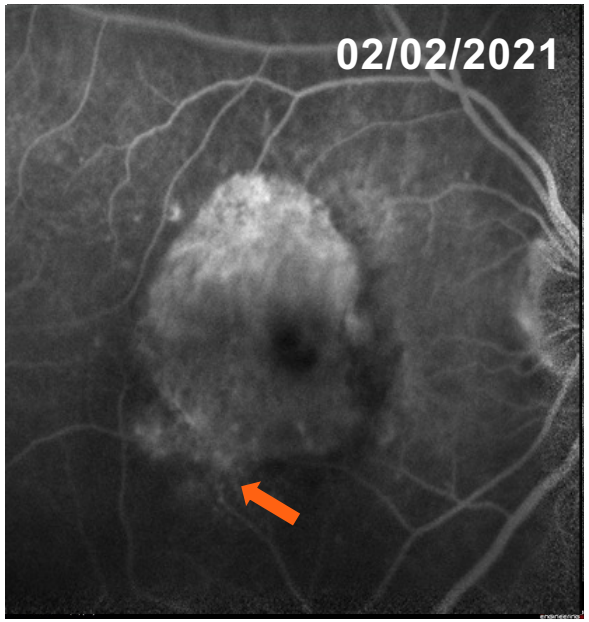
## Time to Development of eAMD

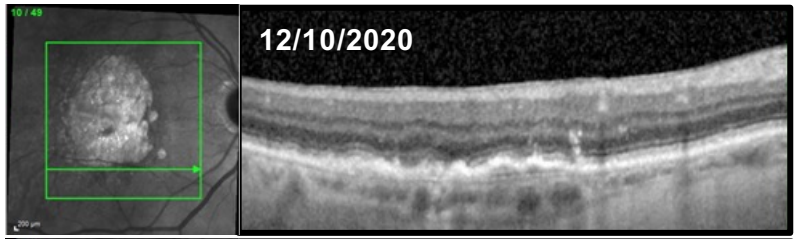
| | PM (N=51) | PEOM (N=28) | Sham pooled (N=13) |
|---|---|---|---|
| **Study eye,** mean days (SD) | 372 (198) | 282 (196) | 223 (193) |
| **Fellow eye,** mean days (SD) | 310 (185) | 296 (219) | 334 (223) |

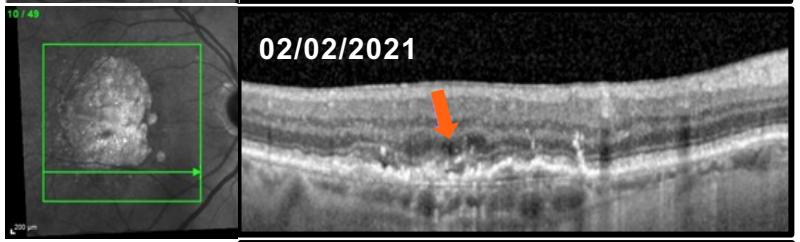
[a]Events include preferred terms of CNV and neovascular AMD.
CNV=choroidal neovascularization; eAMD=exudative AMD; N=number of patients; PEOM=pegcetacoplan every other month; PM=pegcetacoplan every month.

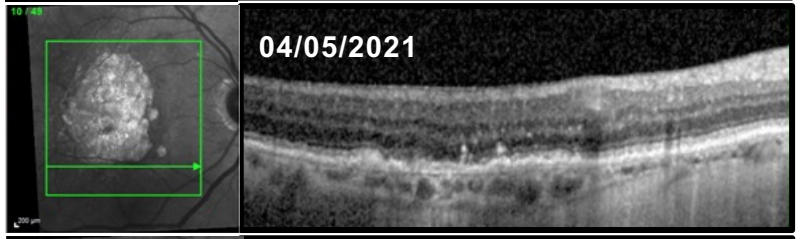
# Patient case: Occult neovascularization treated with anti-VEGF

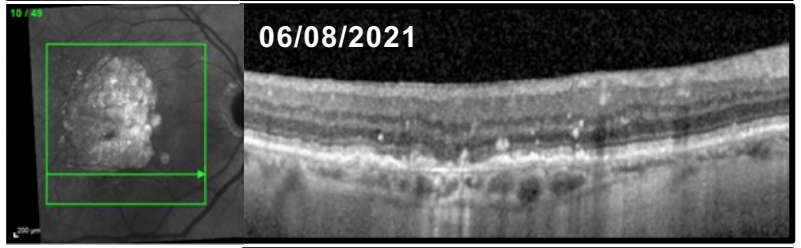
**FA on Day of Diagnosis**

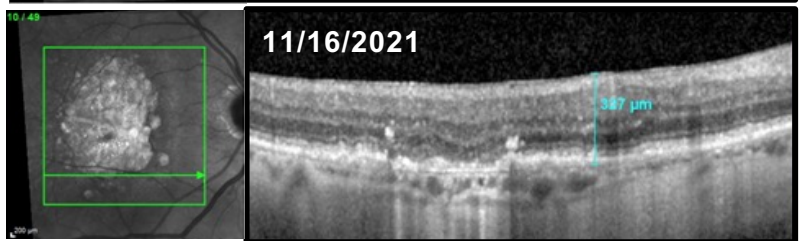



**Month 12**
BCVA 50

**Dx Visit - Month 14**
BCVA 50
1st anti-VEGF dose given 10 days after diagnosis

**Month 16**
BCVA 48
3 wks after 2nd monthly anti-VEGF

**Month 18**
BCVA 50
Same Day as 4th injection
2 mos after last loading dose

**Month 24 - End of study**
BCVA 49
3 mos after 5th injection

# Conclusions

- Safety data collected in a broad GA population of more than 1200 patients with nearly 12,000 injections studied for 2 years in OAKS and DERBY
  - Approximately **1,400 patient-years of exposure**
  - Overall, acceptable safety profile with 24 months treatment
  - eAMD rates higher with pegcetacoplan:  12.2%, 6.7%, and 3.1% over 24 months with PM, PEOM and sham respectively
  - eAMD rates in untreated fellow eyes were consistent across all arms, ranging between 4.1%-4.5%

- Pegcetacoplan is the first and only FDA-approved treatment for GA

eAMD=exudative age-related macular degeneration; PEOM=pegcetacoplan every other month; FDA=Food and Drug Administration; GA=geographic atrophy; PDUFA=Prescription Drug User Fee Act.