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

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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

- Proportion of patients developing Investigator-diagnosed eAMD through Month 18

- Proportion of patients with clinical history of fellow eye eAMD

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.

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.
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

AE=adverse event; AMD=age-related macular degeneration; CFP=color fundus photography; CNV=choroidal neovascularization; eAMD=exudative AMD; FA=fluorescein angiography; OCT=optical coherence tomography; OCTA=OCT angiography; VEGF=vascular endothelial growth factor.
Global Phase 3 program: Design of DERBY and OAKS studies

Patients with GA secondary to AMD
~600 patients at ~200 sites globally in 2 studies (1258 enrollees total)

Double masked
Randomized 2:2:1:1

- Pegcetacoplan 15 mg/0.1 mL monthly
- Pegcetacoplan 15 mg/0.1 mL EOM
- Sham monthly
- Sham EOM

Primary endpoint at 12 months
Change in total area of GA lesions based on fundus autofluorescence

Month 18 Analysis conducted
End of study at 24 months

- Foveal and extrafoveal lesions permitted
- Ocular history of active CNV in the fellow eye is not exclusionary

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

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

<table>
<thead>
<tr>
<th></th>
<th>DERBY</th>
<th>OAKS</th>
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<tbody>
<tr>
<td></td>
<td>PM (N=206)</td>
<td>PEOM (N=208)</td>
</tr>
<tr>
<td>Patients with study eye Investigator-determined new-onset eAMD, n (%)</td>
<td>24 (11.7%)</td>
<td>11 (5.3%)</td>
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<tr>
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<th>COMBINED STUDIES</th>
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<tbody>
<tr>
<td></td>
<td>PM (N=419)</td>
<td>PEOM (N=420\textsuperscript{b})</td>
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<tr>
<td>Investigator-determined new-onset eAMD, n (%)</td>
<td>40 (9.5%)</td>
<td>26 (6.2%)</td>
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</table>

\textsuperscript{a}Events include preferred terms of CNV and neovascular AMD.  
\textsuperscript{b}One 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

<table>
<thead>
<tr>
<th>COMBINED STUDIES</th>
<th>PM</th>
<th>PEOM</th>
<th>Sham Pooled</th>
</tr>
</thead>
<tbody>
<tr>
<td>eAMD n/N (%), fellow eye CNV present</td>
<td>8/84 (9.5%)</td>
<td>8/81 (9.9%)</td>
<td>7/86 (8.1%)</td>
</tr>
<tr>
<td>eAMD n/N (%), fellow eye CNV absent</td>
<td>32/335 (9.6%)</td>
<td>18/338 (5.3%)</td>
<td>5/331 (1.5%)</td>
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<tbody>
<tr>
<td>eAMD n/N (%), study eye DLS present</td>
<td>8/79 (10.1%)</td>
<td>6/73 (8.2%)</td>
<td>0/63 (0%)</td>
</tr>
<tr>
<td>eAMD n/N (%), study eye DLS absent</td>
<td>32/336 (9.5%)</td>
<td>20/345 (5.8%)</td>
<td>11/349 (3.2%)</td>
</tr>
</tbody>
</table>

Events 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

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

- 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

*Events 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

<table>
<thead>
<tr>
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<tbody>
<tr>
<td></td>
<td>PM (N=213)</td>
<td>PEOM (N=212)</td>
<td>Sham Pooled (N=211)</td>
<td>PM (N=206)</td>
</tr>
<tr>
<td>Patients without baseline fellow eye CNV, N</td>
<td>168</td>
<td>173</td>
<td>167</td>
<td>167</td>
</tr>
<tr>
<td>Patients with new onset fellow eye eAMD, n (%)</td>
<td>8 (4.8%)</td>
<td>5 (2.9%)</td>
<td>7 (4.2%)</td>
<td>4 (2.4%)</td>
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**COMBINED STUDIES**

<table>
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<th>Sham Pooled (N=417)</th>
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<tbody>
<tr>
<td>Patients without baseline fellow eye CNV, N</td>
<td>335</td>
<td>339</td>
<td>331</td>
</tr>
<tr>
<td>Investigator-determined new-onset eAMD, n (%)</td>
<td>12 (3.6%)</td>
<td>13 (3.8%)</td>
<td>13 (3.9%)</td>
</tr>
</tbody>
</table>

*Events 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

• 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)

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*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