Safety of intravitreal pegcetacoplan in geographic atrophy: 24-month results from the OAKS and DERBY phase 3 trials

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Disclosures

- Rishi P. Singh has the following financial interests or relationships to disclose:
  - Consultant: Alcon, Bausch and Lomb, Genentech, Novartis, Regeneron Pharmaceuticals, and Zeiss
  - Contracted research: Aerie Pharmaceuticals, Apellis Pharmaceuticals, and Graybug
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Design of the Phase 3 OAKS and DERBY studies

OAKS DERBY

Patients with GA secondary to AMD
1258 patients at 232 sites in the combined studies

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

Prespecified secondary endpoints at 24 months

- BCVA[a], LL-BCVA
- Reading speed[a]
- NEI VFQ-25
- FRI Index score[a]
- Microperimetry (OAKS only)[a] – MAIA device
- Lesion growth

GALE 3-year open-label extension study

Primary analysis: MMRM methodology

Fixed effects:
- Treatment*, time, treatment × time interaction
- Baseline GA lesion and fellow eye CNV area strata
- Baseline GA lesion strata × time interaction

**Sham monthly and EOM were pooled for analysis*

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; EOM=every other month; FRI=Functional Reading Independence; GA=geographic atrophy; LL=low luminance; MAIA=macular integrity assessment; MMRM=mixed-effects model for repeated measures; NEI-VFQ=National Eye Institute Visual Function Questionnaire.

Key inclusion and exclusion criteria

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
  - GA lesions with or without subfoveal involvement allowed
  - If multifocal, at least 1 focal lesion must be ≥1.25 mm^2 (0.5 DA)
  - Presence of perilesional hyperautofluorescence

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

AMD=age-related macular degeneration; BCVA=best-corrected visual acuity; CNV=choroidal neovascularization; DA=disc area; ETDRS=Early Treatment Diabetic Retinopathy Study; GA=geographic atrophy; RPE=retinal pigment epithelium.

Patient disposition and exposure at Months 12 and 24

	OAKS			DERBY		
Completed study, ITT set	**PM (N=213)**	**PEOM (N=212)**	**Sham Pooled (N=212)**	**PM (N=206)**	**PEOM (N=208)**	**Sham Pooled (N=207)**
12 months, %	86.4%	89.6%	90.1%	88.8%	90.4%	86.5%
24 months, % (cumulative)	67.6%	79.7%	74.5%	71.4%	77.4%	77.8%

19% of study discontinuations over 24 months were attributed to COVID-19

Mean compliance, mITT set	**PM (N=202)**	**PEOM (N=205)**	**Sham Pooled (N=206)**	**PM (N=201)**	**PEOM (N=200)**	**Sham Pooled (N=194)**
12 months, %	88.6%	92.8%	89.0%	87.8%	90.8%	89.8%
24 months, % (cumulative)	87.4%	90.5%	87.9%	85.6%	89.0%	88.7%

Compliance % = injections administered/injections scheduled up to study completion or treatment discontinuation × 100

The ITT set includes all randomized patients. mITT = modified ITT, defined as all randomized patients who received at least one injection of pegcetacoplan or sham and have baseline and at least one post-baseline value of geographic atrophy lesion area in the study eye.
ITT=intent-to-treat; N=number of patients; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly.

TEAEs in OAKS over 24 months

	OAKS		
	PM (N=213)	**PEOM (N=212)**	**Sham pooled (N=211)**
All TEAEs, n (%)	192 (90.1%)	187 (88.2%)	175 (82.9%)
Ocular TEAEs in study eye			
Patients, n (%)	133 (62.4%)	123 (58.0%)	98 (46.4%)
Non-ocular TEAEs			
Patients, n (%)	174 (81.7%)	165 (77.8%)	154 (73.0%)
Serious ocular TEAEs in the study eye, n (%) M	5 (2.3%) 7	4 (1.9%) 4	1 (0.5%) 1
Optic ischemic neuropathy	2 (0.9%) 2	0	0
Retinal detachment	1 (0.5%) 1	1 (0.5%) 1	0
Papilledema	1 (0.5%) 1	0	0
Visual acuity reduced	0	0	1 (0.5%) 1
Endophthalmitis	2 (0.9%) 2	3 (1.4%) 3	0
Hyphema	1 (0.5%) 1	0	0

Safety set. Note that n indicates the number of patients. M indicates number of events.
The events of endophthalmitis include infectious and noninfectious endophthalmitis. Sham patients do not receive injections.
N=number of patients; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; TEAE=treatment-emergent adverse event.

TEAEs in DERBY over 24 months

	DERBY		
	PM (N=206)	PEOM (N=208)	Sham pooled (N=206)
All TEAEs, n (%)	178 (86.4%)	180 (86.5%)	169 (82.0%)
Ocular TEAEs in study eye			
Patients, n (%)	125 (60.7%)	108 (51.9%)	95 (46.1%)
Non-ocular TEAEs			
Patients, n (%)	163 (79.1%)	142 (68.3%)	146 (70.9%)
Serious ocular TEAEs in the study eye, n (%) M	4 (1.9%) 4	2 (1.0%) 4	2 (1.0%) 2
Uveitis	0	2 (1.0%) 2	0
Vitritis	2 (1.0%) 2	0	0
Iridocyclitis	0	1 (0.5%) 1	0
Optic ischemic neuropathy	1 (0.5%) 1	0	0
Retinal tear	1 (0.5%) 1	0	0
Visual acuity reduced	0	1 (0.5%) 1	0
Dry AMD	0	0	1 (0.5%) 1
Macular hole	0	0	1 (0.5%) 1

Safety set. Note that n indicates the number of patients. M indicates number of events. Sham patients do not receive injectio ns. AMD=age-related macular degeneration; N=number of patients; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly; TEAE=treatment-emergent adverse event.

Events of intraocular inflammation and infectious endophthalmitis in study eye at Months 12 and 24

OAKS DERBY

OAKS and DERBY combined

	PM (N=419)	PEOM (N=420)	Sham Pooled (N=417)
Intraocular inflammation			
12 months, n (%)	9 (2.1%)	4 (1.0%)	0
24 months – cumulative, n (%)	16 (3.8%)	9 (2.1%)	1 (0.2%)
Infectious endophthalmitis			
12 months, n (%)	1 (0.2%)	2 (0.5%)	0
24 months – cumulative, n (%)	2 (0.5%)	2 (0.5%)	0

- IOI rates include four events reported in 2018 and linked to drug impurity (including one event of noninfectious endophthalmitis)
- No reports of occlusive or nonocclusive retinitis or vasculitis
- Infectious endophthalmitis rate: ~1 per 3000 injections

Safety set. IOI=intraocular inflammation; N=number of patients; PEOM=pegcetacoplan every other month; PM=pegcetacoplan monthly.

Evaluation of new-onset eAMD in the Phase 3 program

- 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 responsibility to report eAMD-related AEs and to start anti-VEGF treatment was solely that 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, and GA lesion growth measurements were included in efficacy assessments

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.

New-onset eAMD in study eye at Months 12 and 24[a]

OAKS DERBY

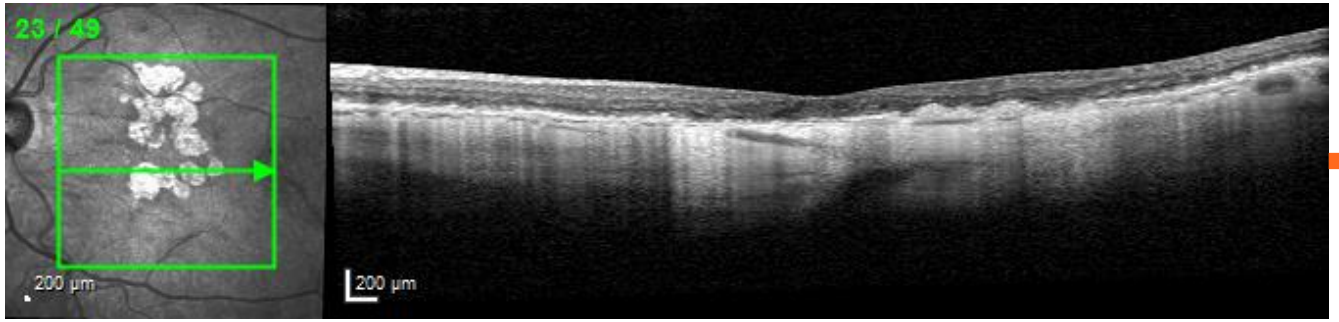
OAKS and DERBY combined

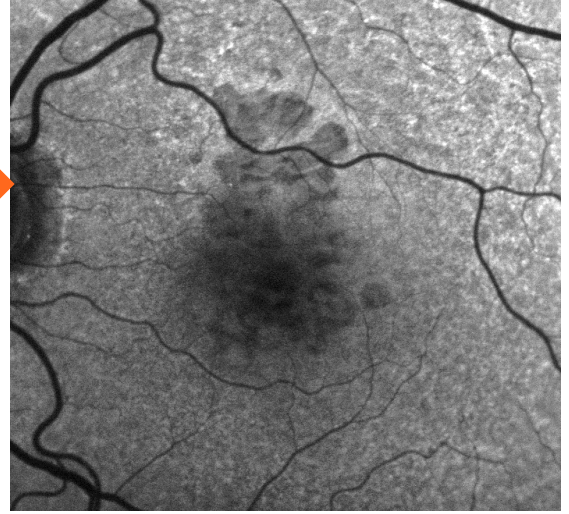
	PM (N=419)	PEOM (N=420)[b]	Sham Pooled (N=417)
New-onset investigator-determined eAMD 12 months, n (%)	25 (6.0%)	17 (4.1%)	10 (2.4%)
New-onset investigator-determined eAMD, 24 months – cumulative, n (%)	51 (12.2%)	28 (6.7%)	13 (3.1%)
Confirmed by reading center, 24 months, n (%) At time of investigator-reported eAMD, 100% of patients had available SD-OCT and 82% had available FA for reading center evaluation	37 (8.8%)	23 (5.5%)	11 (2.6%)

- The vast majority of CNV lesions that developed were occult lesions
- Patients who developed eAMD continued treatment with study drug and received on-label anti-VEGF therapy at the discretion of the investigator
- No patients in the pegcetacoplan study arms discontinued the studies due to eAMD

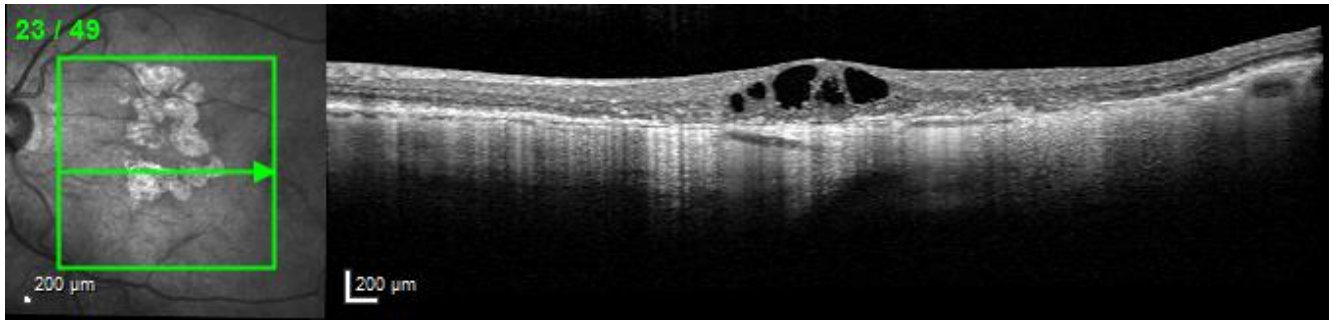
[a]Events include preferred terms of CNV and neovascular AMD. [b]Number of patients at risk for new-onset eAMD in PEOM arms from OAKS and DERBY combined was 419. AE=adverse event; AMD=age-related macular degeneration; CNV=choroidal neovascularization; eAMD=exudative AMD; FA=fluorescein angiography; N=number of patients; PEOM=pegcetacoplan every other month; PM=pegcetacoplan every month; SD-OCT=spectral domain optical coherence tomography; VEGF=vascular endothelial growth factor.

Baseline

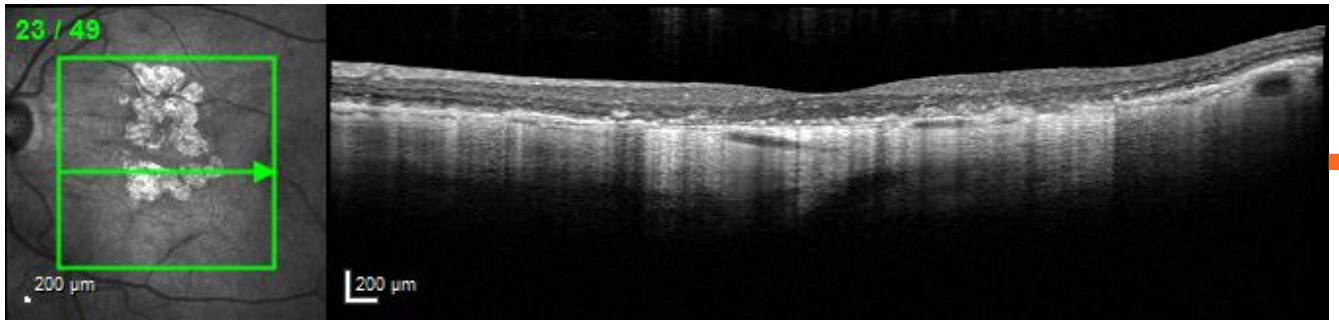


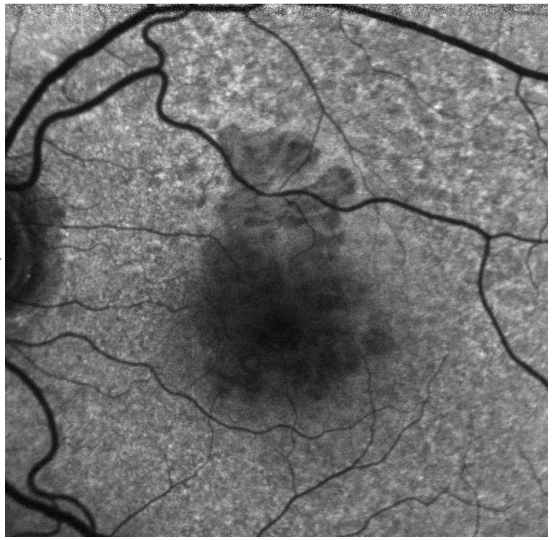


M10
(aVEGF that day)

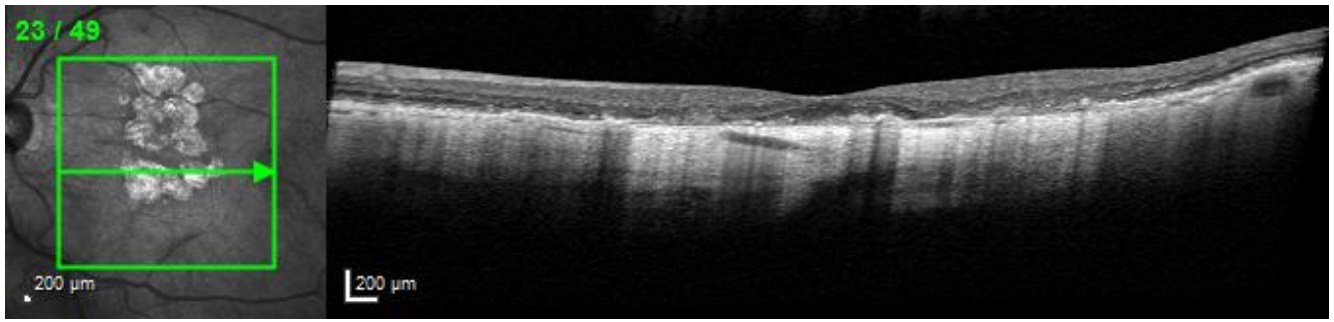


M12
(aVEGF that day)





M18
(aVEGF that day)



Graded as occult CNV at Month 10

Images from OAKS and DERBY. aVEGF=anti vascular endothelial growth factor.

Phase 3 OAKS and DERBY studies of pegcetacoplan in GA

- Pegcetacoplan slows GA progression with both every-other-month and monthly dosing, with effects increasing over time

- Safety data collected in real world population of more than 1200 patients with nearly 12,000 injections studied for 2 years
  - 12.2%, 6.7%, and 3.1% of patients in the combined monthly, EOM, and sham pooled groups experienced new-onset investigator-determined eAMD over 24 months
  - Overall safety profile in line with trials of intravitreal therapeutics

GA=geographic atrophy; eAMD=exudative age-related macular degeneration; EOM=every other month.