Relationship Between Number of Intermediate/Large Drusen and Geographic Atrophy Lesion Growth Rate in the Sham Groups of the DERBY, OAKS, and FILLY Trials

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July 13–16, 2022
40th Annual Meeting of the American Society of Retina Specialists, NY, USA

Disclosures

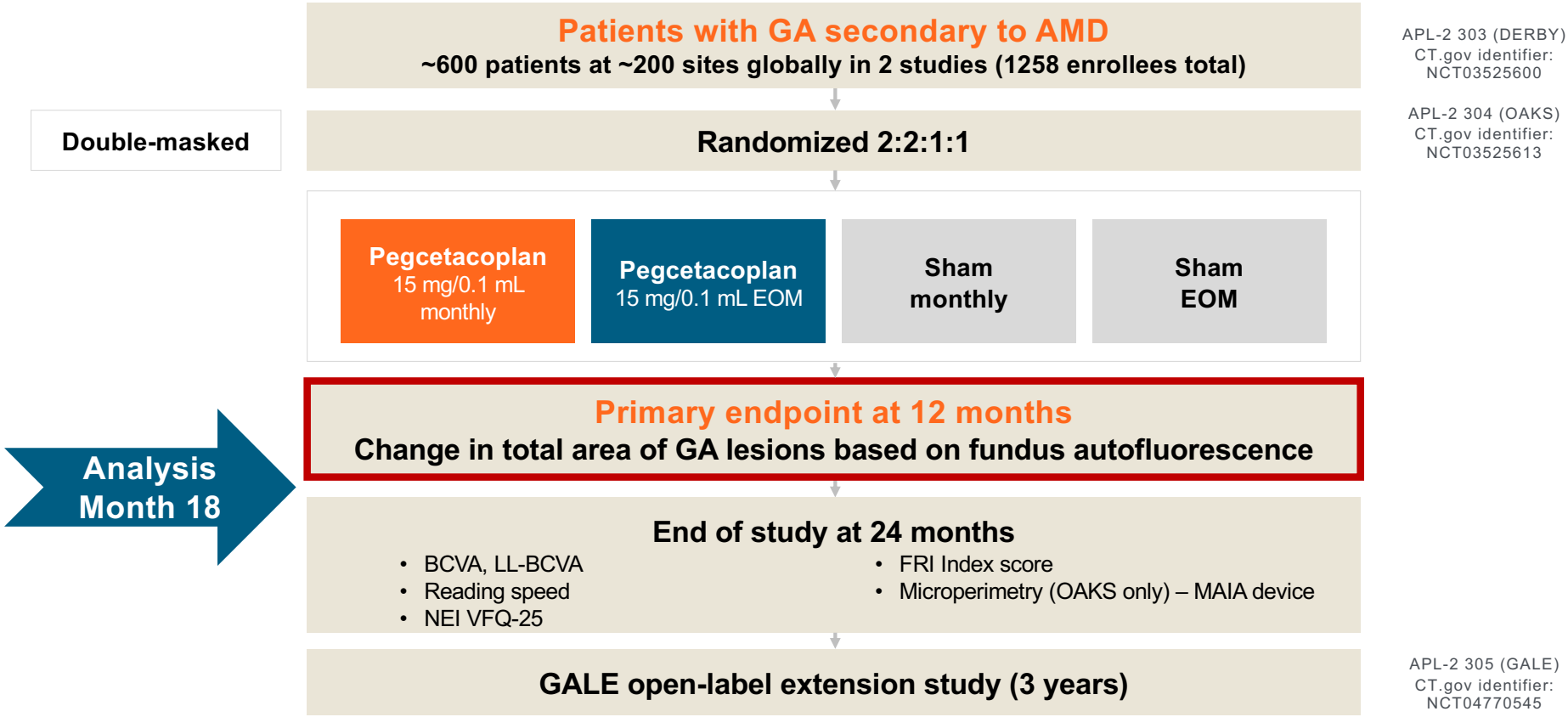
- **Scientific Advisor:**

  Apellis, Allegro, Alexion, Annexon, Galimedix, Gemini Therapeutics, IMI-2 Consortium, IVERIC Bio, Janssen, LumiThera, NGM Biopharmaceuticals, Nanoscope Therapeutics, Perceive Biotherapeutics, Novartis, Roche, Retrotope, Thea Laboratoires

- **Research Funding:**

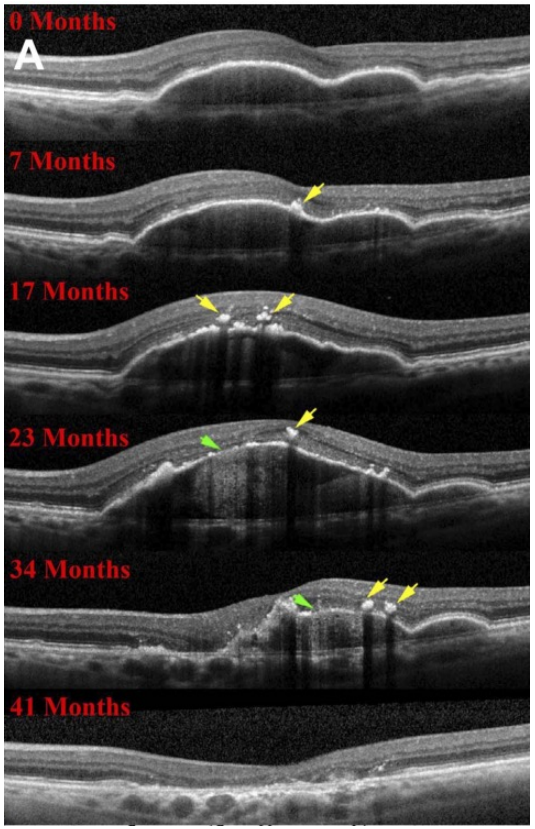
  Apellis, Alexion, Boehringer Ingelheim, Gemini Therapeutics, IVERIC Bio, LumiThera, Neurotech Research to Prevent Blindness, NIH/NEI K23, Novartis, Roche, VA CSR&D I01

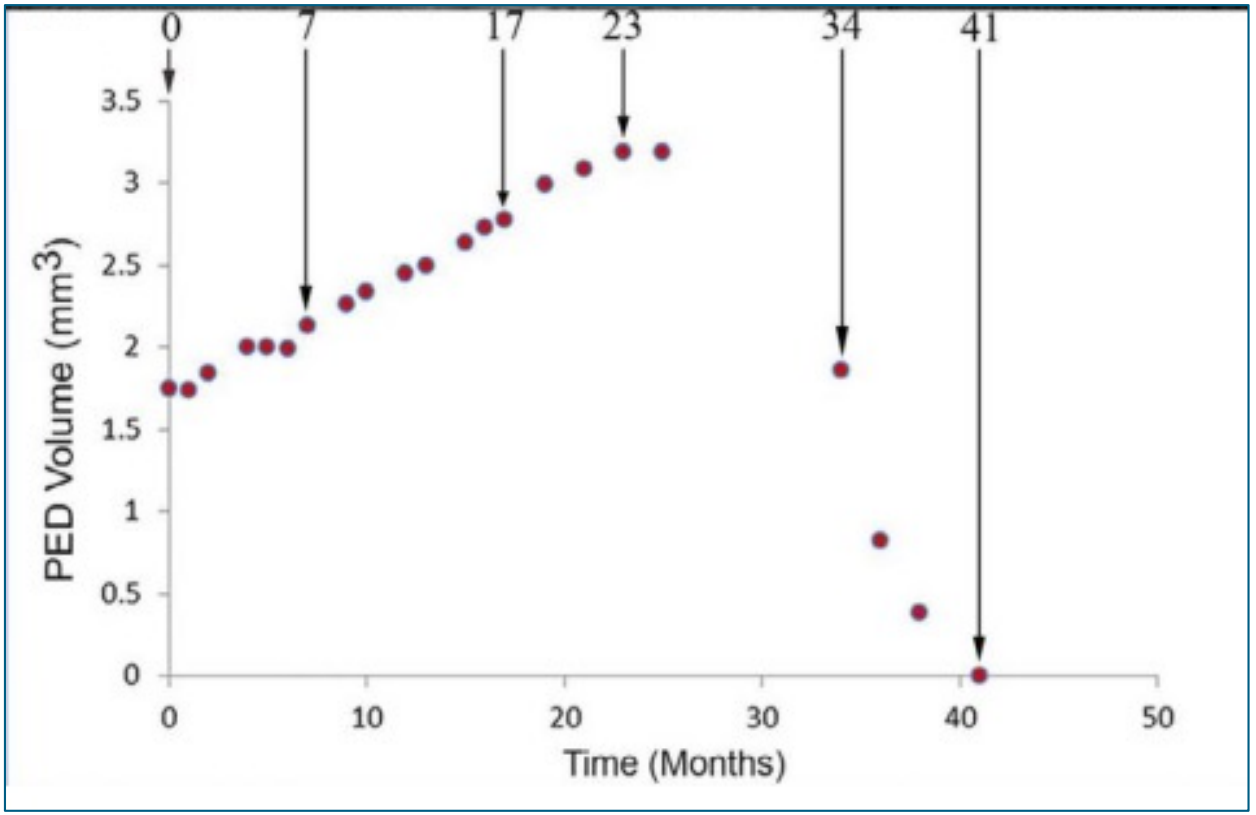
Global Phase 3 program: Design of studies (DERBY and OAKS)



AMD=age-related macular degeneration; BCVA=best-corrected visual acuity; EOM=every other month; FRI=functional reading independence; GA=geographic atrophy; LL=low luminance; MAIA=Macular Integrity Assessment; NEI-VFQ=National Eye Institute Visual Function Questionnaire-25.

RPE-drusen volume increases slowly but decreases rapidly as AMD progresses from early to advanced stage (GA)





Localized hyperreflective lesions arising from the RPE-BL band (yellow arrows); disruptions to the RPE-BL band (green arrows)
PED=pigment epithelial detachment.
Curcio CA. *Invest Ophthalmol Vis Sci* 2018;59:AMD160–81.

Are drusen number and size important in AMD and GA?

- Drusen are a prominent feature of AMD;[1] the number and size of drusen change as AMD progresses from early to advanced stages. RPE-drusen complex thinning is associated with progression to central GA.[2]

- **In DERBY**, there was an imbalance in the number of intermediate-large drusen at baseline. How did this imbalance affect the primary efficacy results?

	DERBY			
Baseline characteristic	PM (N=201)	PEOM (N=201)	Sham Pooled (N=195)	
Intermediate/large drusen **>20**, n (%)	78 (38.8%)	78 (38.8%)	98 (50.3%)	p=0.02

AMD=age-related macular degeneration; GA=geographic atrophy.

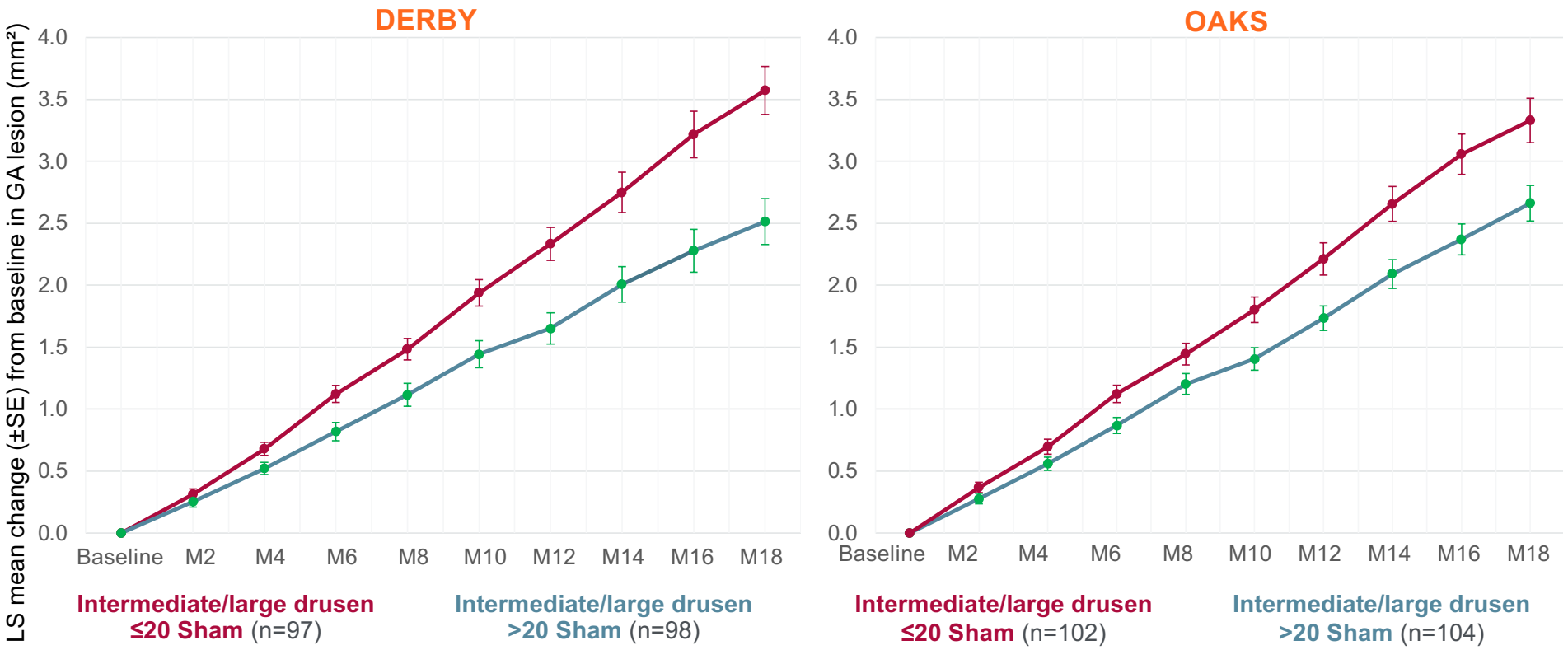
1. Fett AL et al. *Histol Histopathol* 2012;27:357–64; 2. Folgar FA et al. *Ophthalmology* 2016;123:39–50; 3. Friberg TR et al. *Invest Ophthalmol Vis Sci* 2012;53:1742–51.

Methods

- The sham arms of DERBY, OAKS, and FILLY were examined as natural history cohorts to assess the relationship between number and size of drusen with the growth rate of GA lesions
  - Post-hoc analysis
  - Total number of drusen was counted using a range: 0–5, 6–10, 10–20, over 20; 20 was closest to median
  - Stratified by >20 vs ≤20 intermediate/large drusen
  - Intermediate/large drusen were defined as drusen diameter ≥63 µm

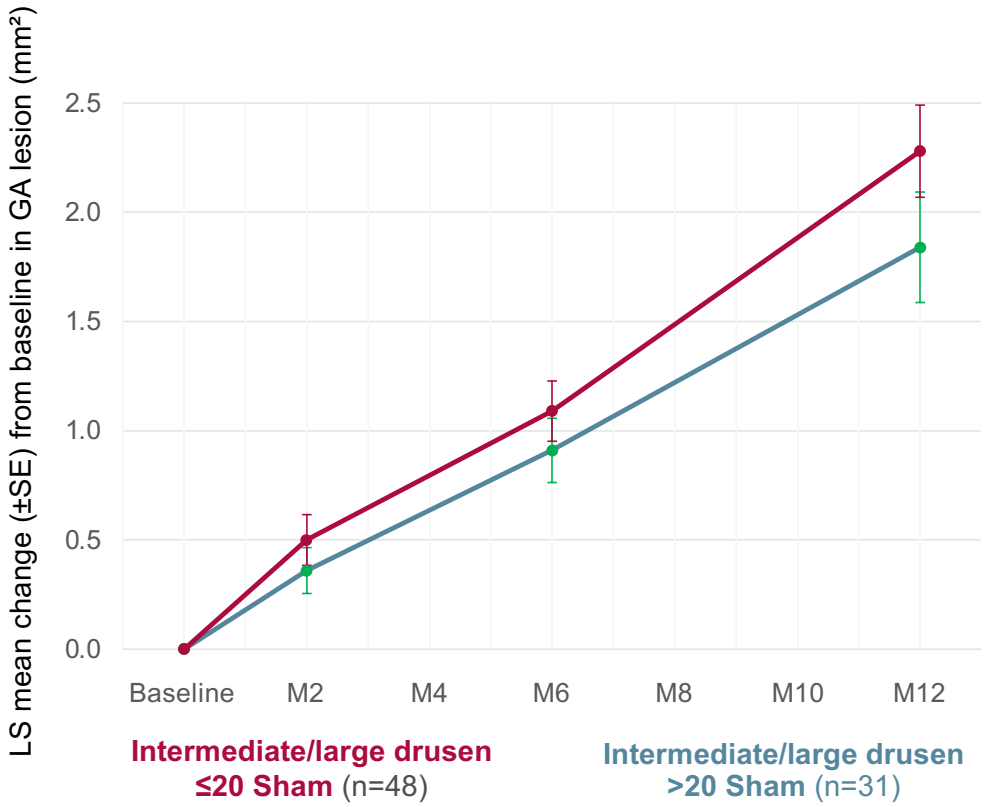
- **Hypothesis:** the presence of a greater number of intermediate/large drusen may indicate less baseline abnormal thinning of the RPE drusen complex volume (less pre-atrophic retina), therefore slower GA progression

DERBY and OAKS sham pooled arms
GA lesions grew more slowly in patients with more intermediate/large drusen



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; SE=standard error.

FILLY sham pooled arm
GA lesions grew more slowly in patients with more intermediate/large drusen



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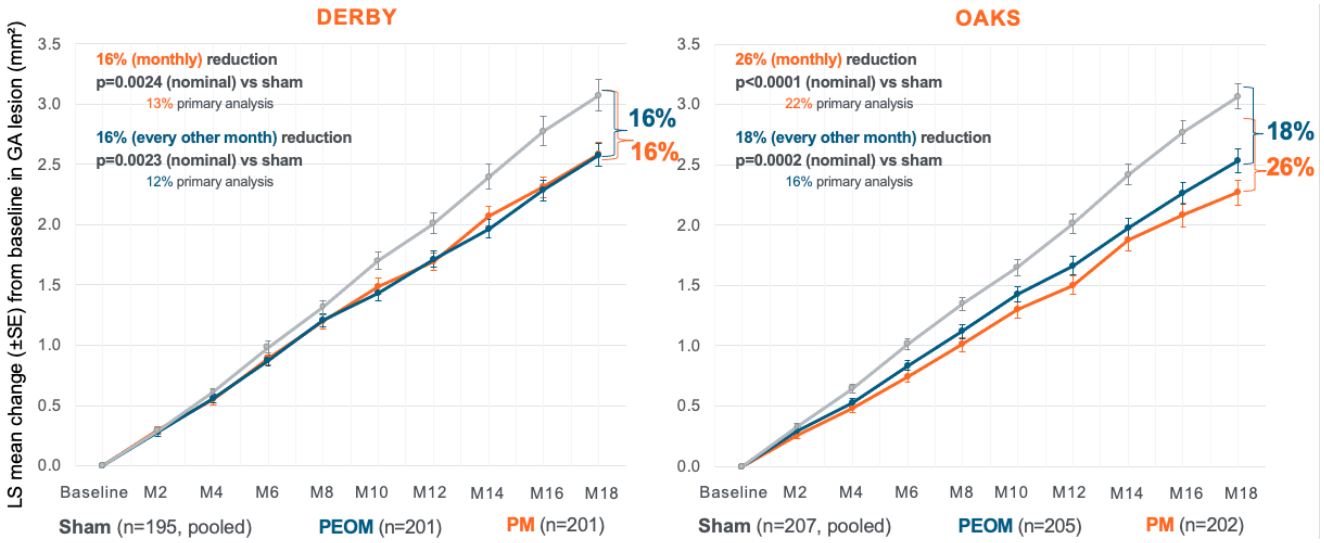
Conclusions and discussion

- In the sham arms of DERBY, OAKS, and FILLY, which represent the natural history of GA progression, the presence of **more intermediate/large drusen was associated with slower GA growth**
  - **Fewer drusen at this late stage of AMD may reflect a more atrophic retina that is progressing more quickly**[1,2]

- **In DERBY**, a larger proportion of patients in the sham arm had >20 intermediate/large drusen. This imbalance likely resulted in an **underestimation of the treatment effect and may partially explain the reduced treatment effect seen in DERBY compared with OAKS.**

Impact of pegcetacoplan on GA lesion growth over 18 months after adjusting for baseline imbalances



AMD=age-related macular degeneration; GA=geographic atrophy.1. Klein ML et al. *Ophthalmology* 2008;115:1026–31; 2. Ly A et al. *Ophthalmic Physiol Opt* 2016;36:303–16.

Thank you to all the patients and sites around the world