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Financial Disclosures
GSR: RetInSight (F)
WDV, AS: RetInSight (E)
HB: Heidelberg Engineering, Apellis, RetInSight (F); Bayer, Apellis (R)
USE: Genentech, Kodiak, Novartis, Apellis, RetInSight (F); Apellis (C); RetInSight (P)

317 - C0154

Disease Activity of Geographic Atrophy in Fellow Eyes of the Pegcetacoplan phase III Studies measured by automated AI-based OCT Biomarker Quantifications

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Objective

Geographic atrophy (GA) secondary to age-related macular degeneration (AMD) is characterized by the degeneration of retinal pigment epithelium (RPE), photoreceptors (PR) and the choriocapillaris.

Fellow eyes with GA in the **pegcetacoplan phase III** studies provide a **large scale reference** for the analysis of the **natural progression of GA**.

Our study aimed to measure disease progression of GA in untreated fellow eyes from two large phase III clinical studies (OAKS, NCT03525613 and DERBY, NCT03525600) using **automated AI-based quantifications** of the outer retina on optical coherence tomography (OCT).

Patients and Methods

Untreated fellow eyes presenting with GA from OAKS and DERBY were analyzed. To detect eyes with GA, all fellow eyes were manually graded for early/intermediate AMD, GA or nAMD including scans with fibrosis. Only eyes presenting with GA and without signs of exudation were included in the analysis.

Loss of **PR and RPE integrity** were quantified on **Spectralis OCT** using fully automated AI-based algorithms.

Longitudinal **PR/RPE integrity loss ratios** were calculated and investigated over time. To reduce the influence of baseline lesion size, PR and RPE loss growth rates were calculated for each study year after performing a square root transformation and were assessed in mm/year.

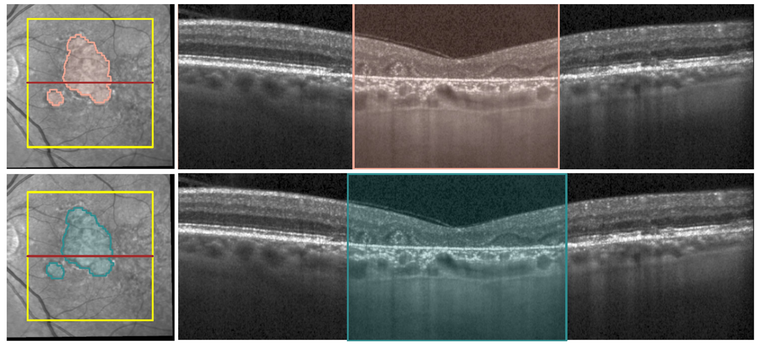

Figure 1. Examples of AI-based quantifications of the loss of RPE (top) and PR integrity (bottom).

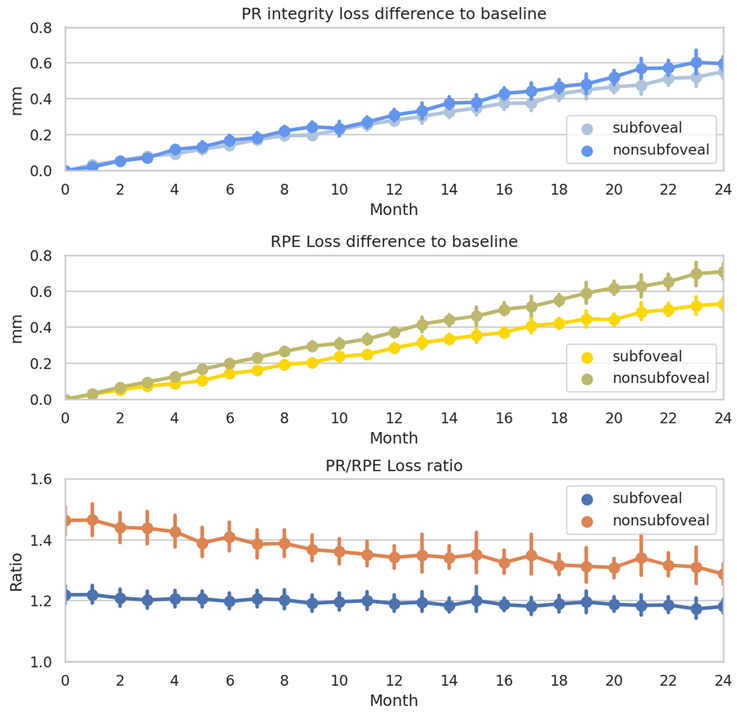

Figure 2. AI-quantified OCT markers of GA during the 2 year follow-up period split between eyes with and without subfoveal atrophy. Squareroot transformed area of Photoreceptor (PR) integrity loss (top), Retinal pigment epithelium loss (middle).Ratio of PR/RPE integrity loss (bottom).

Results

753 fellow eyes from OAKS and DERBY combined were included. 369 eyes presented with and 384 eyes without subfoveal atrophy, respectively.

At baseline, mean (SD) area of **PR integrity loss** was similar between eyes with and without subfoveal GA with 11.80 (7.03) vs. 11.67 (6.47) mm^2, respectively.

Furthermore, no significant difference of the increase of PR integrity loss could be observed between eyes with/without subfoveal GA (p=0.079).

Eyes without subfoveal GA at baseline had a significantly smaller mean **RPE loss** area (6.49 (4.5) vs 8.33 (4.89) mm^2). PR/RPE loss ratios were consistently and significantly larger in patients without subfoveal GA for the complete study period of 24 months (p<0.001).

Nonetheless, a convergence of **PR/RPE integrity loss ratios** between eyes with and without subfoveal involvement can be observed as the PR/RPE integrity loss ratio was significantly larger during the first study year compared to the second study year (p<0.001).

This can be explained by a significantly faster progression (p<0.01) of RPE loss during the first (0.387 (0.205) vs 0.297 (0.183) mm/year (SD)) and second year (0.34 (0.179) vs. 0.269 (0.148) mm/year (SD)) in patients without subfoveal GA.

Discrepancies in the field of view between FAF and OCT could explain that effects detected in the periphery are less likely to be captured by OCT.

Conclusion

- Automated quantification of the outer retina layers with advanced OCT-based AI tools enables personalized patient monitoring of disease activity over time.
- PR/RPE loss ratios decrease in patients without subfoveal GA, suggesting decelerating RPE degeneration over time in this subgroup.

References and further readings

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