Retinal Pigment Epithelium Cell Therapy in Geographic Atrophy Secondary to Age-related Macular Degeneration: 3-Year Results from the Phase 1/2a Study

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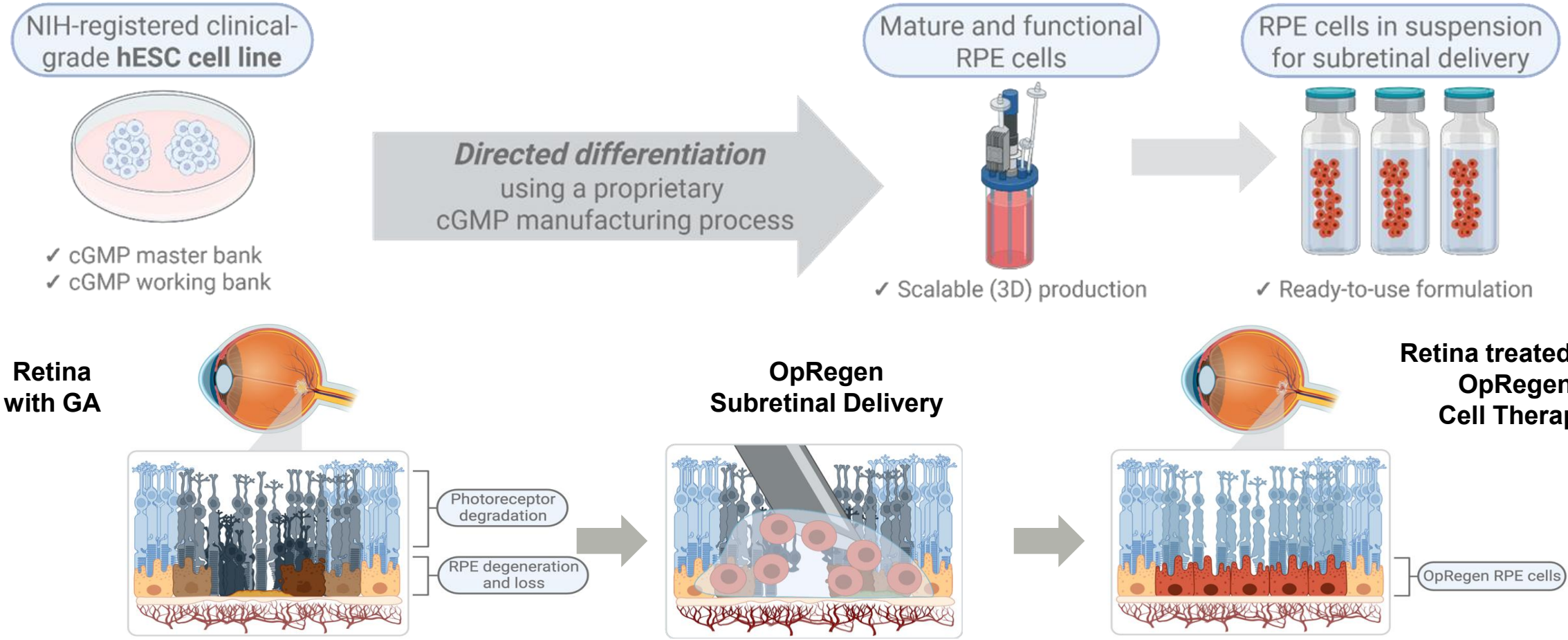
Disclosures

- Grants or Contracts (Past 36 months):
  - CellCure Neurosciences: Sponsored the translational research and the clinical trial
  - Lineage Cell Therapeutics: Research Grant (2019-2022) held jointly with B. Reubinoff
- Royalties or Licenses (Past 36 months):
  - Lineage Cell Therapeutics & Genentech: Inventor on patents licensed by Hadasit (institution IP arm) to Lineage and sublicensed to Genentech; receives a share of sublicense fees, milestone payments, and royalties through Hadasit
- Consulting Fees (Past 36 months):
  - CellCure Neurosciences: Receives monthly consulting fees through Hadasit
- Patents Planned, Issued, or Pending (Past 36 months):
  - Lineage Cell Therapeutics & Genentech: Inventor on multiple patents regarding the derivation of RPE cells from hESCs (licensed to Lineage and sublicensed to Genentech)
- Stock or Stock Options (Past 36 months):
  - Lineage Cell Therapeutics: Hold a small number of stock options
- Receipt of Equipment, Materials, Medical Writing, or Other Services (Past 36 months):
  - Genentech: Provided clinical data analysis, medical writing, manuscript preparation, and article processing charges

OpRegen Cell Therapy – A Suspension of Allogeneic RPE Cells
With the Potential to Counteract RPE Cell Dysfunction & Loss in GA



cGMP, current Good Manufacturing Practice; hESC, human embryonic stem cell.
NIH registry for hESC cell line HAD-C 102 available at https://grants.nih.gov/stem_cells/registry/current.htm?id=428. Figures created with BioRender.com.

Phase I/IIa Study Design (NCT02286089; Active)
An Open-Label, Single-Arm, Multi-Center, Dose-Escalation Trial

Key Enrollment Criteria

Patients with bilateral GA secondary to AMD

Cohorts 1-3 (n=12):

- Legally blind (BCVA: ≤20/200)
- GA area: 1.25–17 mm^2

Cohort 4 (n=12):

- **Impaired vision (BCVA: ≥20/250 and ≤20/64)**
- **GA area: ≥4 and ≤11 mm^2**

Single OpRegen Administration

- **Cohort 1 (n=3)** 50,000 cells
- **Cohort 2 (n=3)** Up to 200,000 cells
- **Cohort 3 (n=6)** Up to 200,000 cells
- **Cohort 4 (n=12)** Up to 200,000 cells

Subretinal Delivery

- Transvitreal (n=5)
- Transchoroidal using Orbit® SDS (Gyroscope Therapeutics) in Cohort 4 only (n=7)

Perioperative Immunosuppressive Regimen
Tacrolimus 0.01 mg/kg daily up to 6 weeks after surgery
Mycophenolate up to 2.0 g daily at least 3 months after surgery

Primary Objective:
To evaluate the safety and tolerability of OpRegen cell therapy

Secondary Objective:
To evaluate the potential activity of OpRegen cell therapy via changes in retinal structure and visual function

AMD, age-related macular degeneration; BCVA, best corrected visual acuity; GA, geographic atrophy; SDS, subretinal delivery system.

Baseline Characteristics and Safety Summary[a]

Baseline Characteristic	Cohorts 1-3 (n=12) Legally Blind	Cohort 4 (n=12) Impaired Vision
Age, years, mean (SD, min–max)	78.1 (±8.2, 64.8–92.2)	75.7 (±8.0, 60.1–87.6)
Sex, female | male, n	7 | 5	6 | 6
Study Eye BCVA[b], letters, mean (SD, min–max)	23.5 (±11.7, 0–39) [24 letters ≈ 20/320]	44.8 (±7.5, 28–54) [45 letters ≈ 20/125]
Study Eye GA Area[c], mm^2, mean (SD, min–max)	12.7 (±6.7, 6–30)	7.4 (±2.9, 1.6–10.9)

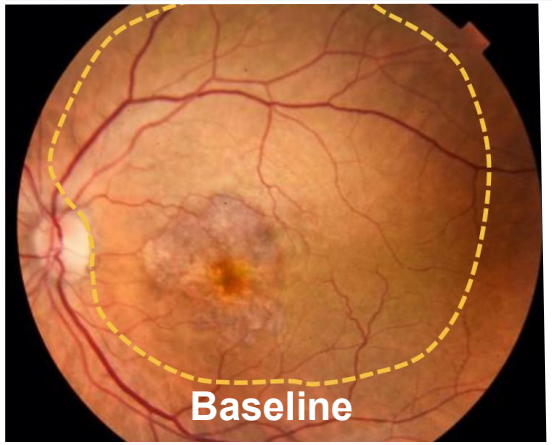
- The most frequent ocular AEs reported in all patients on study were conjunctival hemorrhage/hyperemia (71%) and ERM (67%)[d]
- Most AEs reported following OpRegen administration were mild (87%)
- No reported cases of:
  - Rejection following OpRegen delivery
  - Acute or delayed intraocular inflammation
  - Discontinuation due to a related AE
- No cluster of AEs related to immunosuppressive regimen were reported

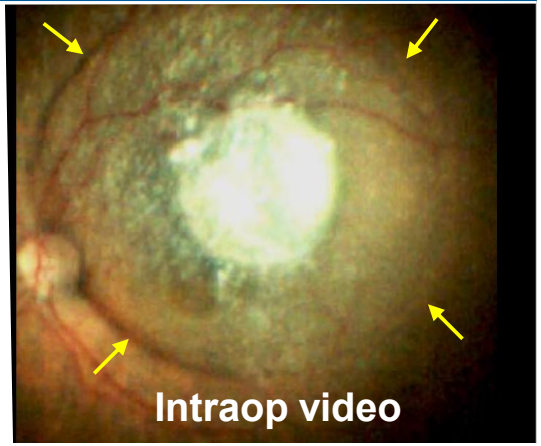
[a]Safety data previously presented (Ho AC et al. ARVO 2022. https://iovs.arvojournals.org/article.aspx?articleid=2780049)
[b]The worse eye based on BCVA was selected for OpRegen subretinal delivery.
[c]Based on central grading of fundus autofluorescence imaging.
[d]Three patients had clinically significant ERM requiring surgical intervention.

ERM, epiretinal membrane. Data cutoff: 30 Oct 2023.

Subgroup Analysis in Cohort 4: Functional and Anatomic Outcomes in Eyes With and Without Delivery of OpRegen Cell Therapy to Central GA

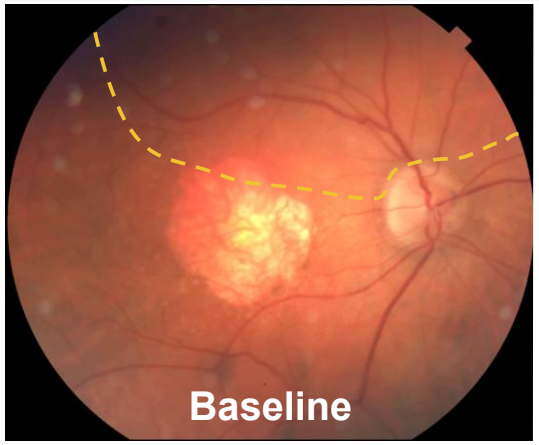
Extensive bleb coverage (n=5)
Extensive bleb coverage of GA (including fovea)

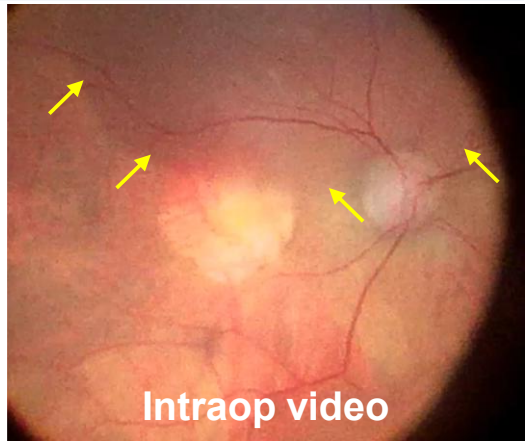




Case #14

Limited bleb coverage (n=7)
Minimal to no bleb coverage of GA

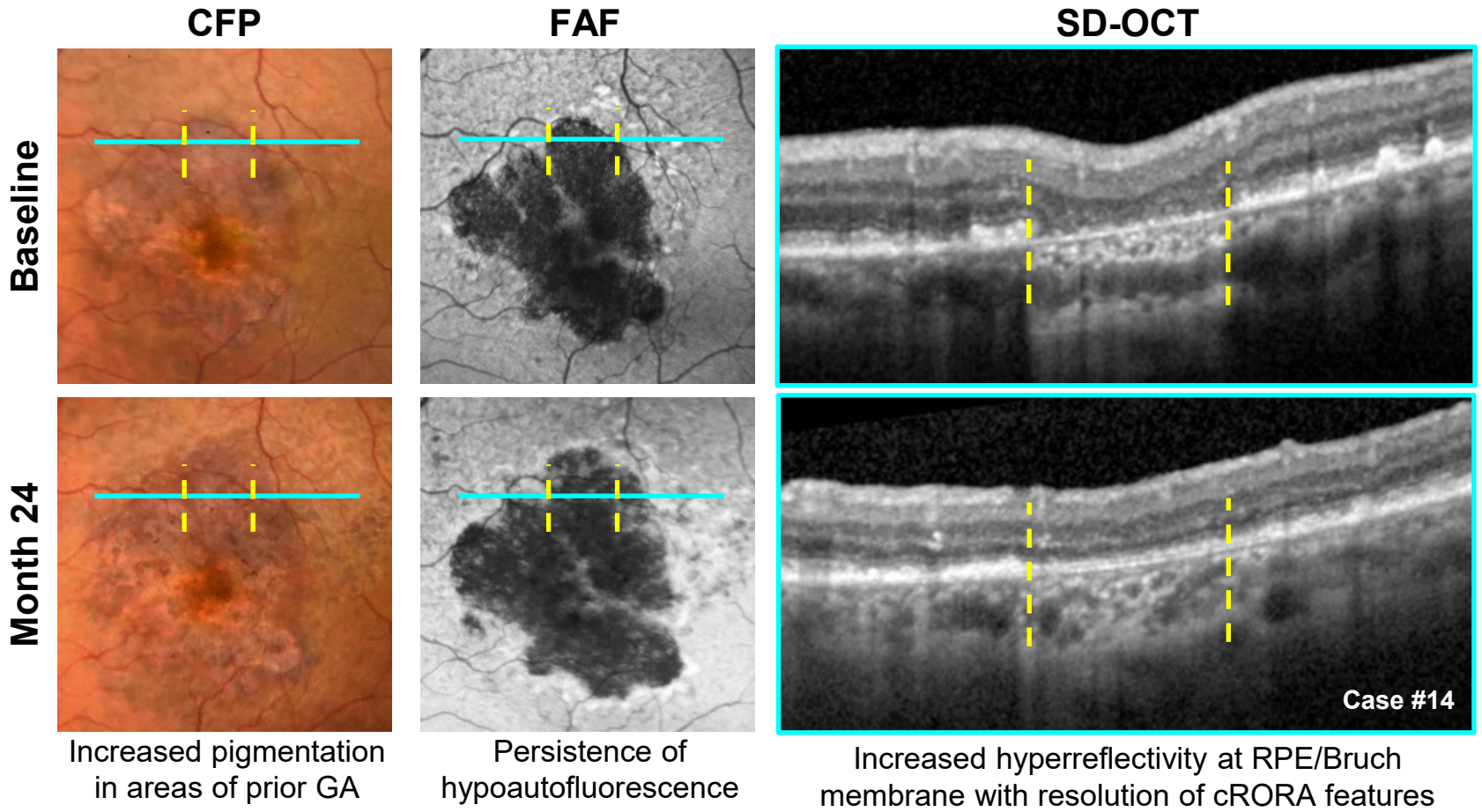




Case #18

OpRegen bleb coverage of GA determined by surgical video for all Cohort 4 cases (n=12)

SD-OCT May be More Suitable than FAF for Defining an Area of GA in the Setting of RPE Cell Therapy



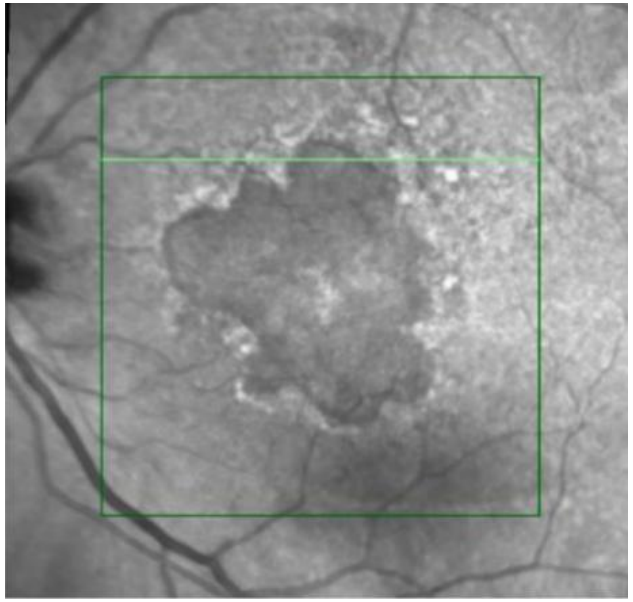
- The allogeneic hESC-derived RPE cells in OpRegen are young and have low lipofuscin content
- Therefore, OpRegen RPE cells are not expected to be readily detectable by standard FAF following subretinal delivery
- OCT imaging may thus be better suited to study retinal structure and define atrophy following subretinal delivery

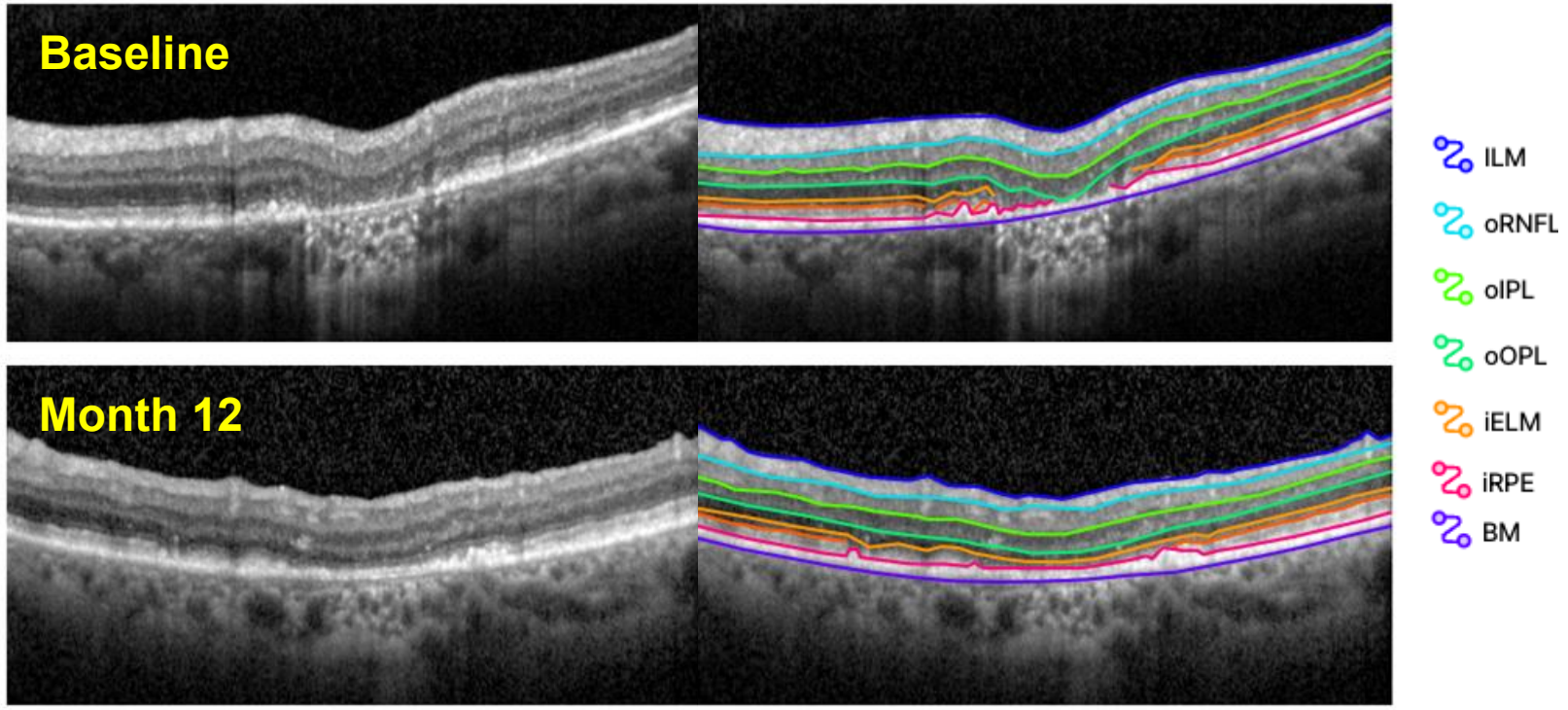
CFP, color fundus photography; cRORA, complete RPE and outer retinal atrophy; FAF, fundus autofluorescence; GA, geographic atrophy; hESC, human embryonic stem cells; RPE, retinal pigment epithelium; SD-OCT, spectral domain optical coherence tomography.

Banin E, et al. Presented at the the Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting. New Orleans, LA, USA. April 23-27, 2023.

Resolution of cRORA Near Borders of Baseline GA

In Cases With Extensive OpRegen Bleb Coverage of Area of GA





- Features of cRORA no longer present
- Greater hyperreflectivity at the level of RPE/BM
- Less choroidal hypertransmission

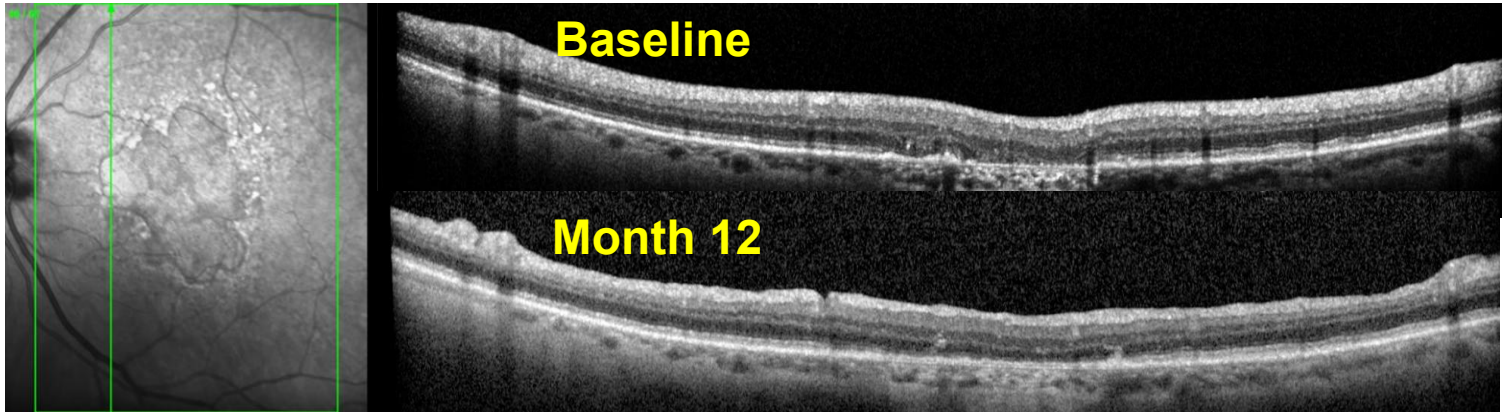
- Resolution of retinal subsidence, with greater continuity of outer retinal layers
- Similar features also seen at nasal, superior, and inferior borders of GA

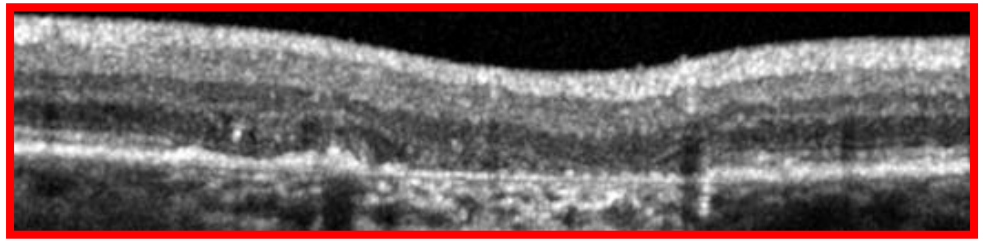
cRORA, complete RPE and outer retinal atrophy; i-, inner boundary of layer; ILM, internal limiting membrane; IPL, inner plexiform layer; o-, outer boundary of layer; OPL, outer plexiform layer; RNFL, retinal nerve fiber layer.

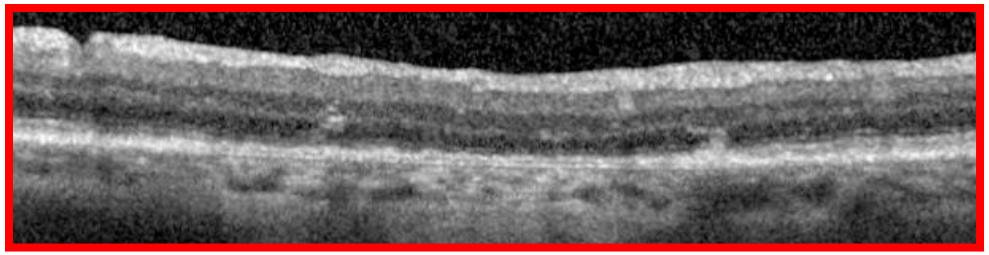
Case #14

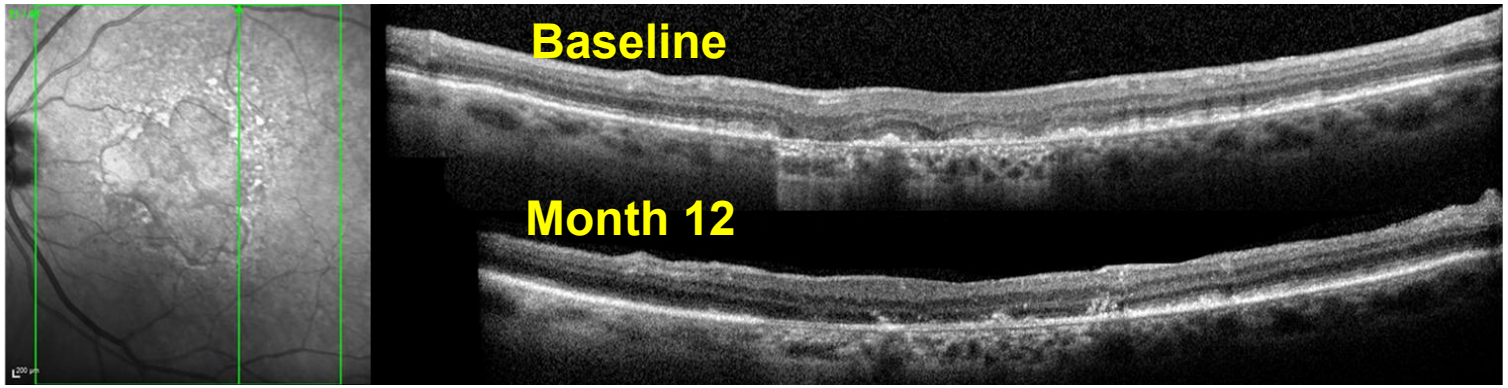
Resolution of cRORA/iRORA Near Borders of Baseline GA

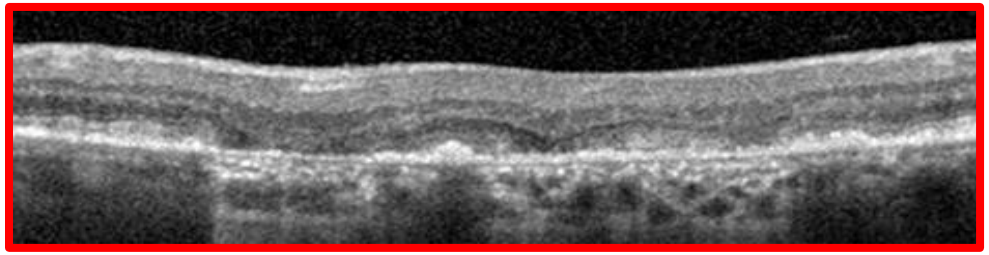
In Cases With Extensive OpRegen Bleb Coverage of Area of GA

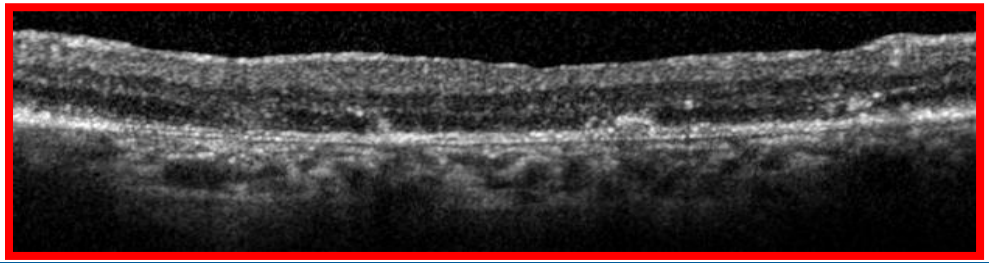








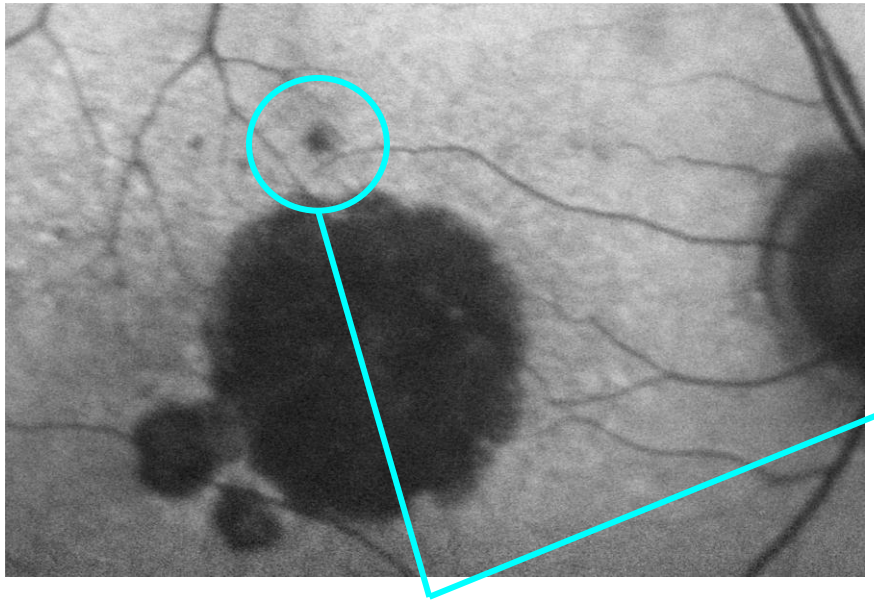


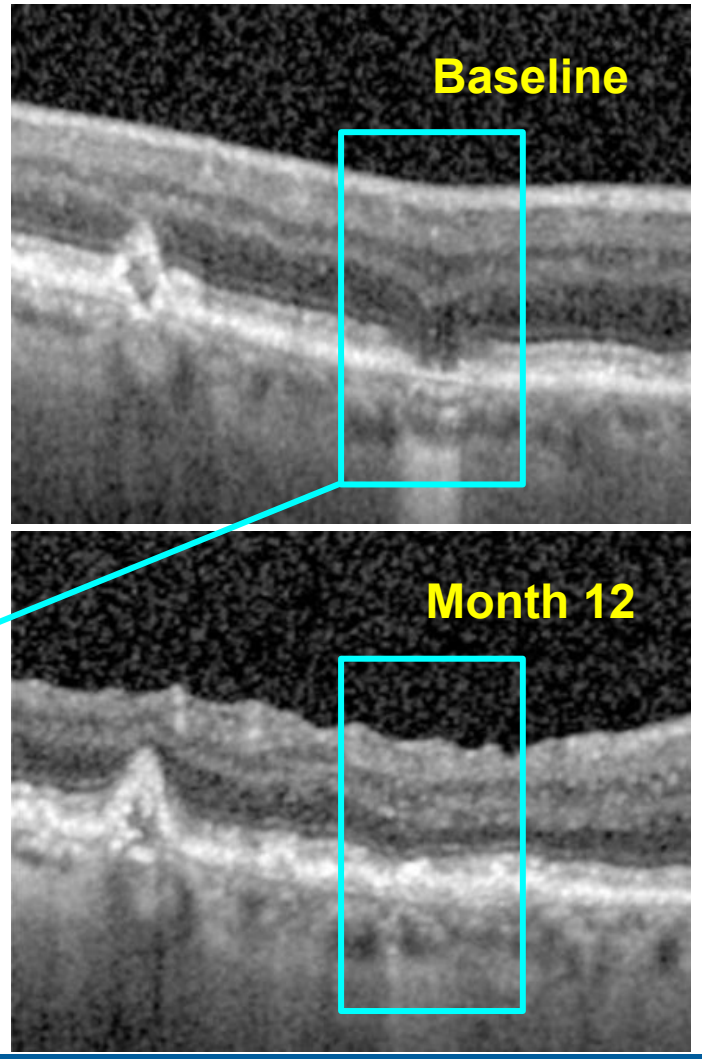


Case #14

Resolution of iRORA After OpRegen Treatment

In Cases With Extensive OpRegen Bleb Coverage of Area of GA





Area of hypoautofluorescence on FAF at baseline with features of iRORA on SD-OCT

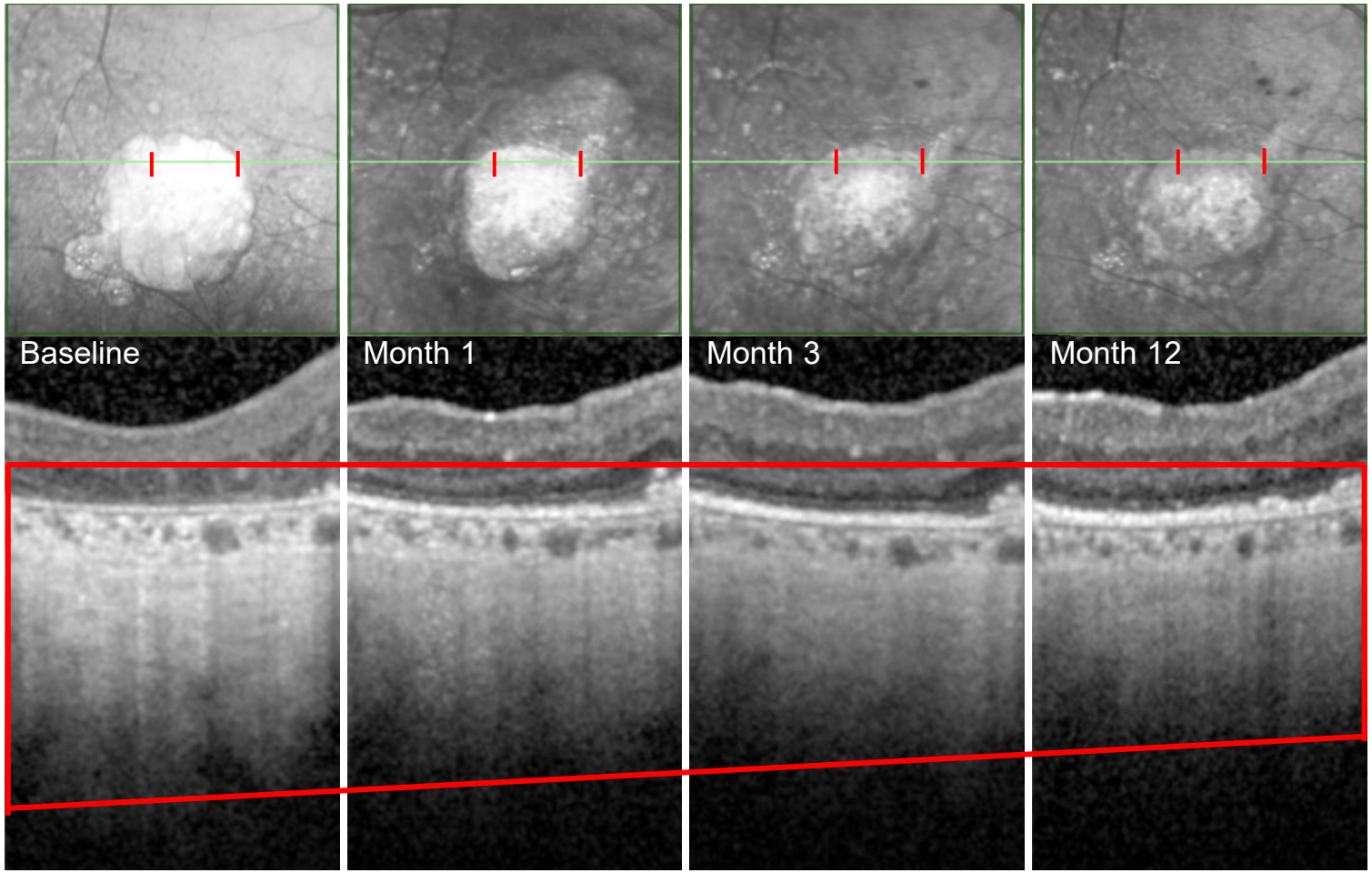
- Focal disruption of the RPE layer, choroidal hypertransmission, and outer retinal subsidence at baseline are no longer present at Month 12
- Registration of scans is confirmed by presence of a prominent druse and by choroidal vascular markings

Case #21

iRORA, incomplete RPE and outer retinal atrophy.

SD-OCT Imaging Suggests OpRegen Presence in Areas of Former GA

Greater Hyperreflectivity Visible at RPE/BM & Weaker Choroidal Hypertransmission



← Reappearance of ONL and ELM

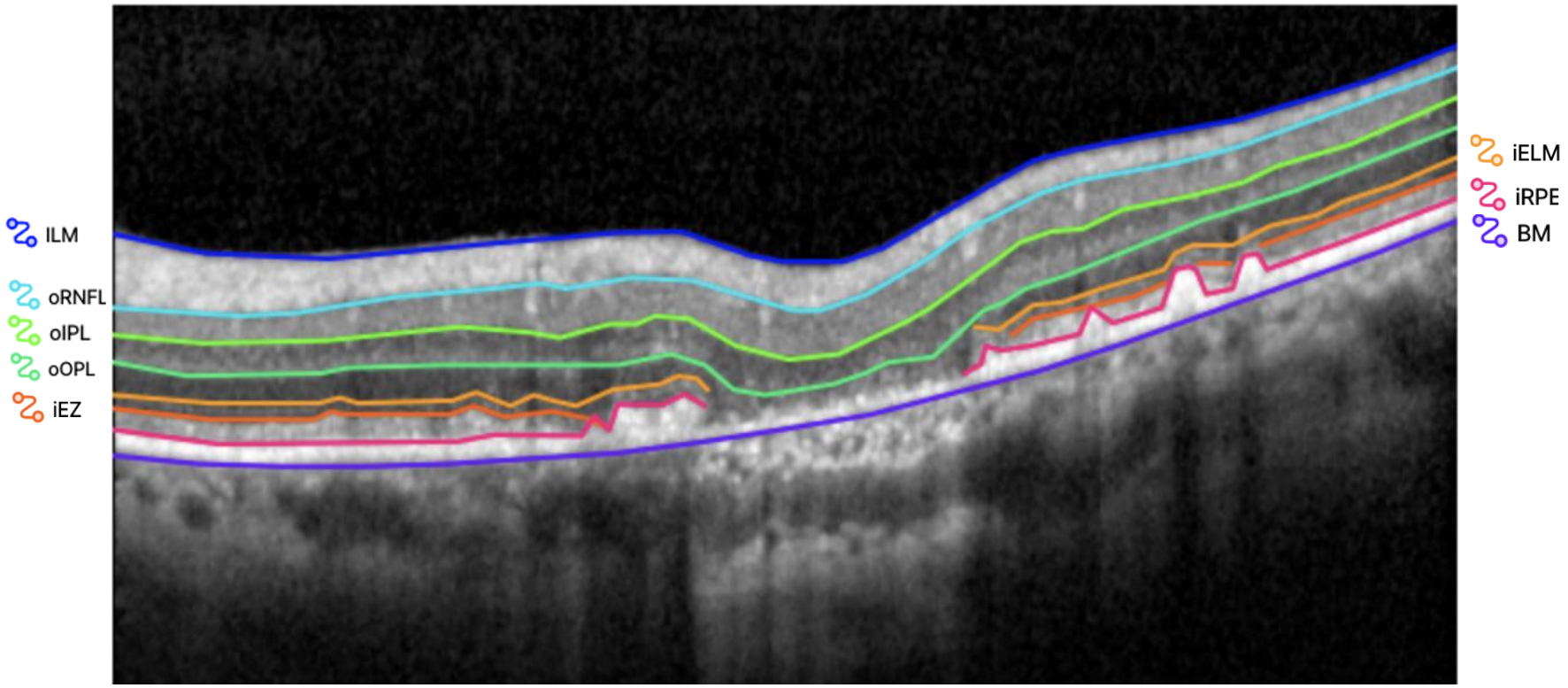
← Greater hyperreflectivity visible at RPE/BM

← Weaker choroidal hypertransmission

Case #21

BM, Bruch's membrane; ELM, external limiting membrane; ONL, outer nuclear layer; SD-OCT, spectral domain optical coherence tomography.

Outer Retinal Structure Analyzed Using EyeNotate OCT Segmentation Algorithm in Cohort 4 Patients



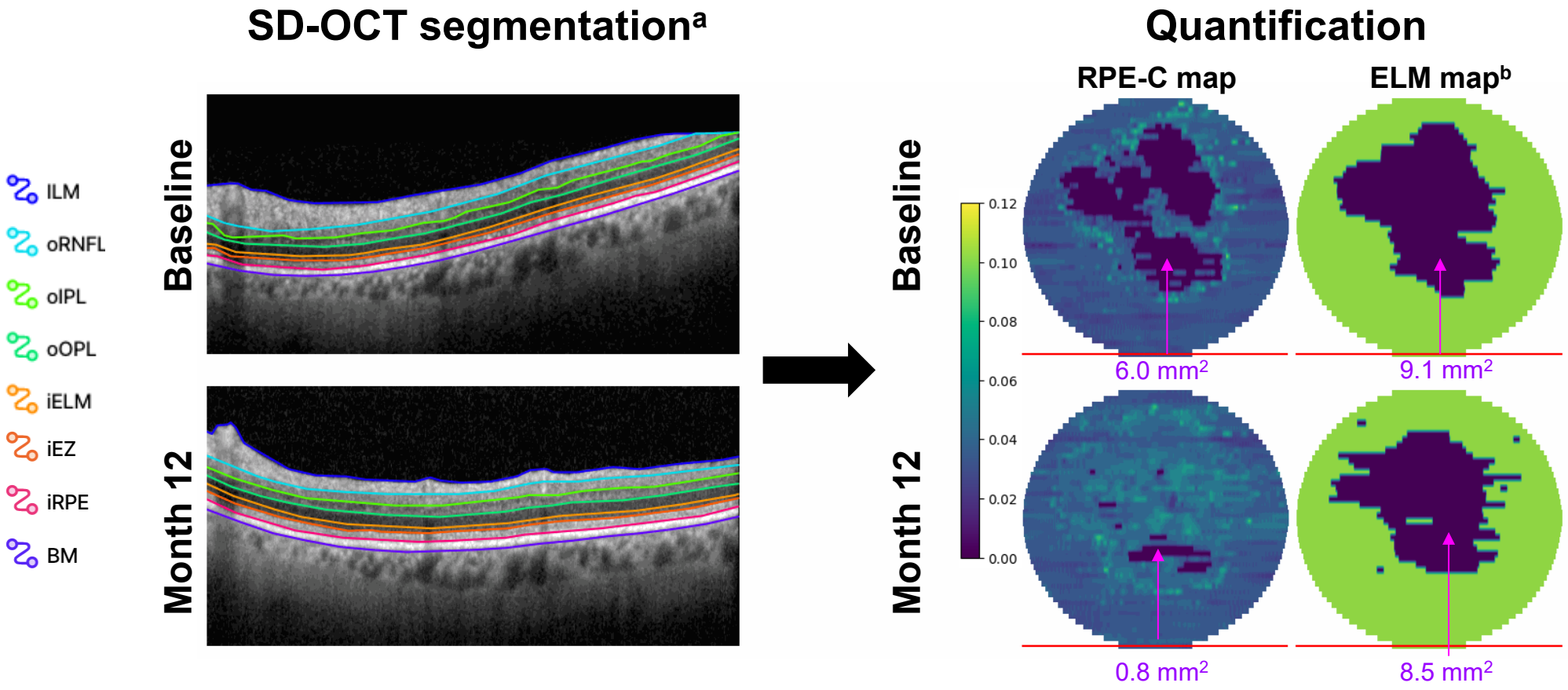
ELM (external limiting membrane):
Graded as present or absent (orange line).

RPE-C (retinal pigment epithelium complex):
The thickness between the hyper-reflective bands representing inner border of RPE (red line) and **BM (purple line)** when RPE is present.

Segmentation result generated by Genentech EyeNotate OCT segmentation algorithm, reviewed and corrected by a single masked expert grader.

BM, Bruch's membrane; EZ, ellipsoid zone; i-, inner boundary of layer; ILM, internal limiting membrane; IPL, inner plexiform layer; o-, outer boundary of layer; OPL, outer plexiform layer; RNFL, retinal nerve fiber layer.

Quantitation of RPE-C and ELM Area Shows Cases of Improvement Between Baseline and Month 12

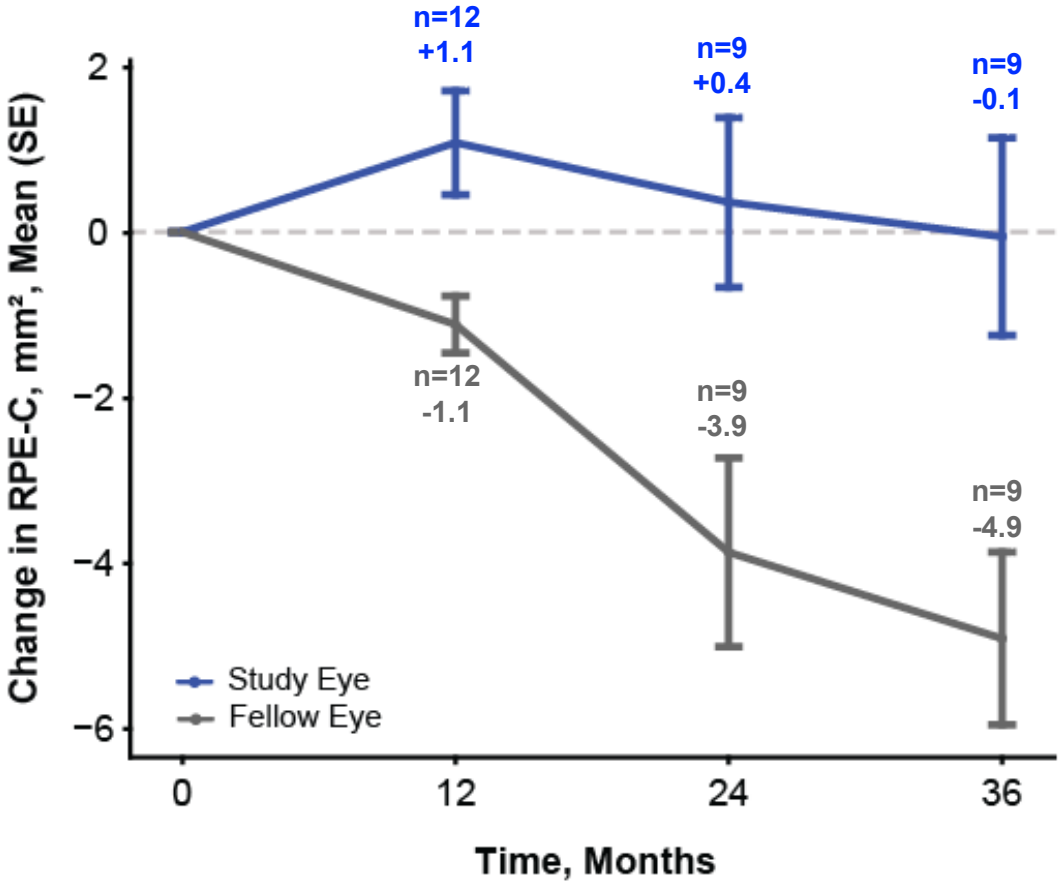


ELM, external limiting membrane; RPE-C, retinal pigment epithelium complex.
[a]Segmentation result is generated by Genentech EyeNotate OCT segmentation algorithm, reviewed and corrected by a single masked expert grader.
[b]ELM map, binary external limiting membrane presence/absence map, green when ELM is present, dark blue when ELM is absent.

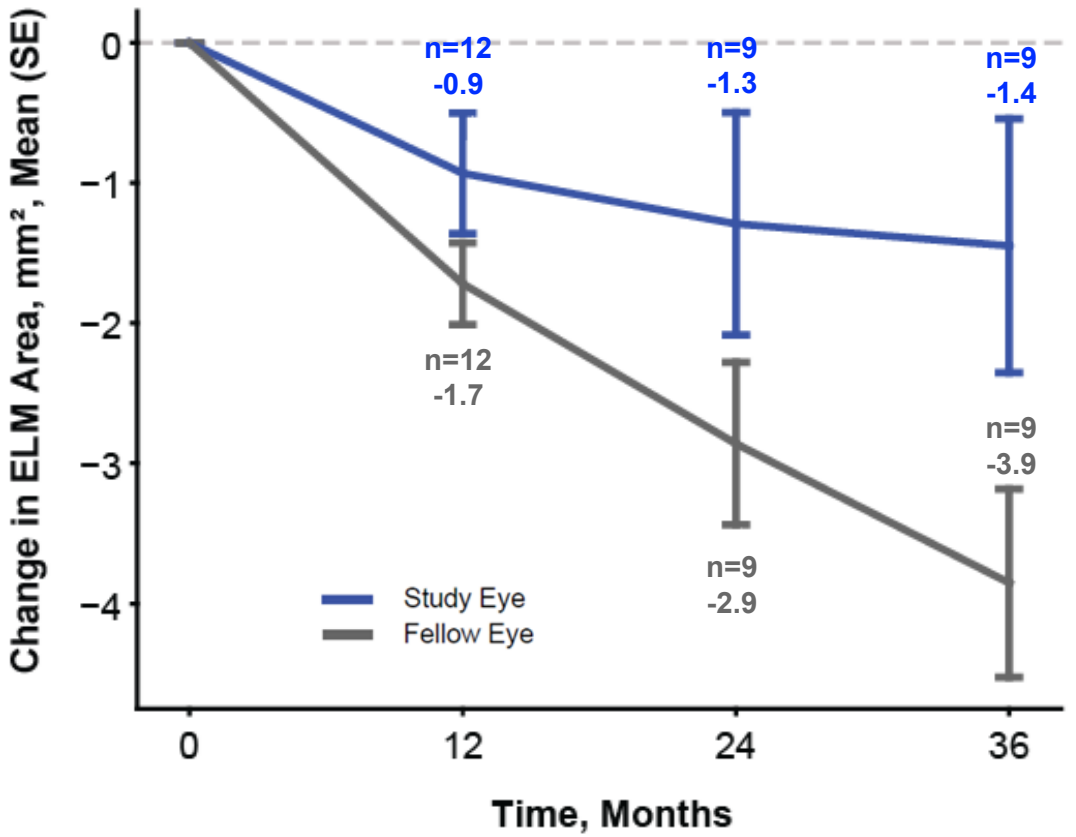
Case #14

Study Eyes of Cohort 4 Patients (Less Advanced GA) Show Sustained Evidence of Retinal Structural Support by Quantitative OCT Analysis Through Month 36

RPE Complex (RPE-C)
Cohort 4 (n=12)

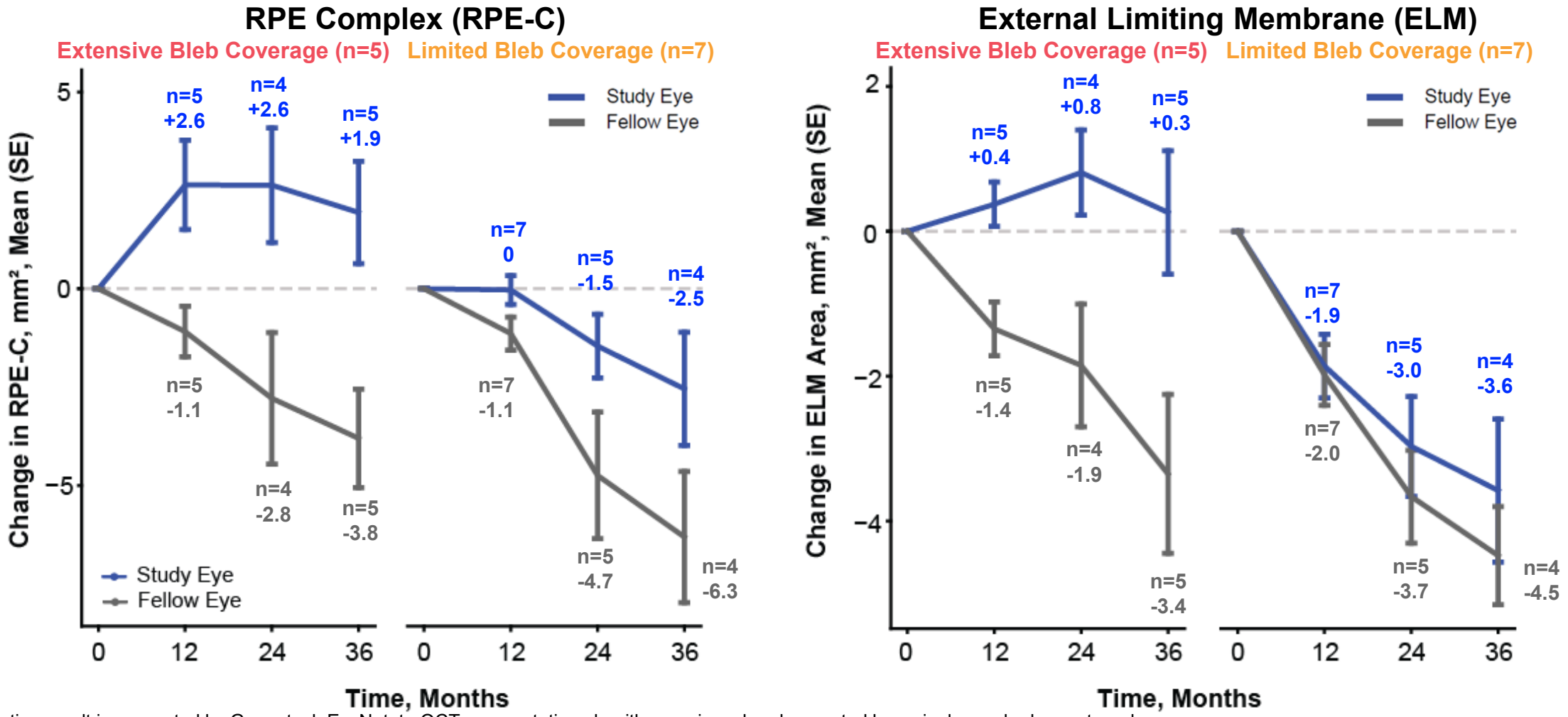


External Limiting Membrane (ELM)
Cohort 4 (n=12)



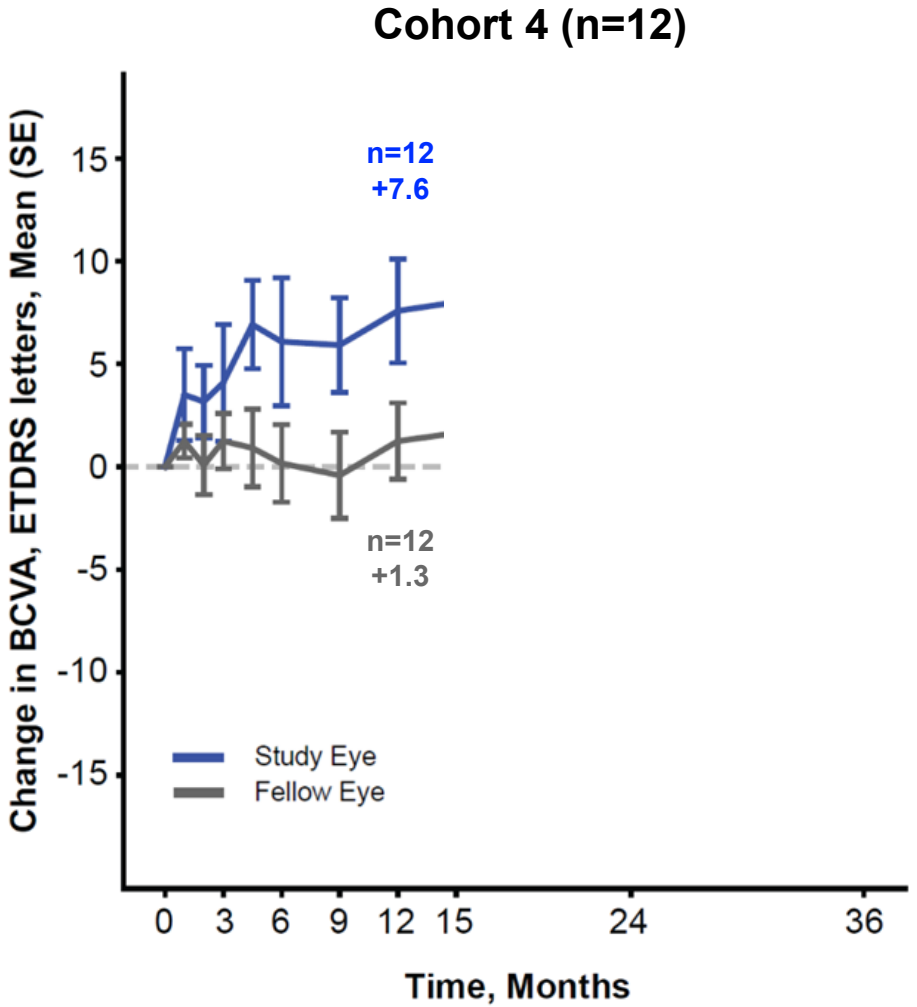
Segmentation result is generated by Genentech EyeNotate OCT segmentation algorithm, reviewed and corrected by a single masked expert grader.

The Beneficial Supportive Effect is Most Evident Among Eyes with Extensive Coverage of GA by the Surgical Bleb



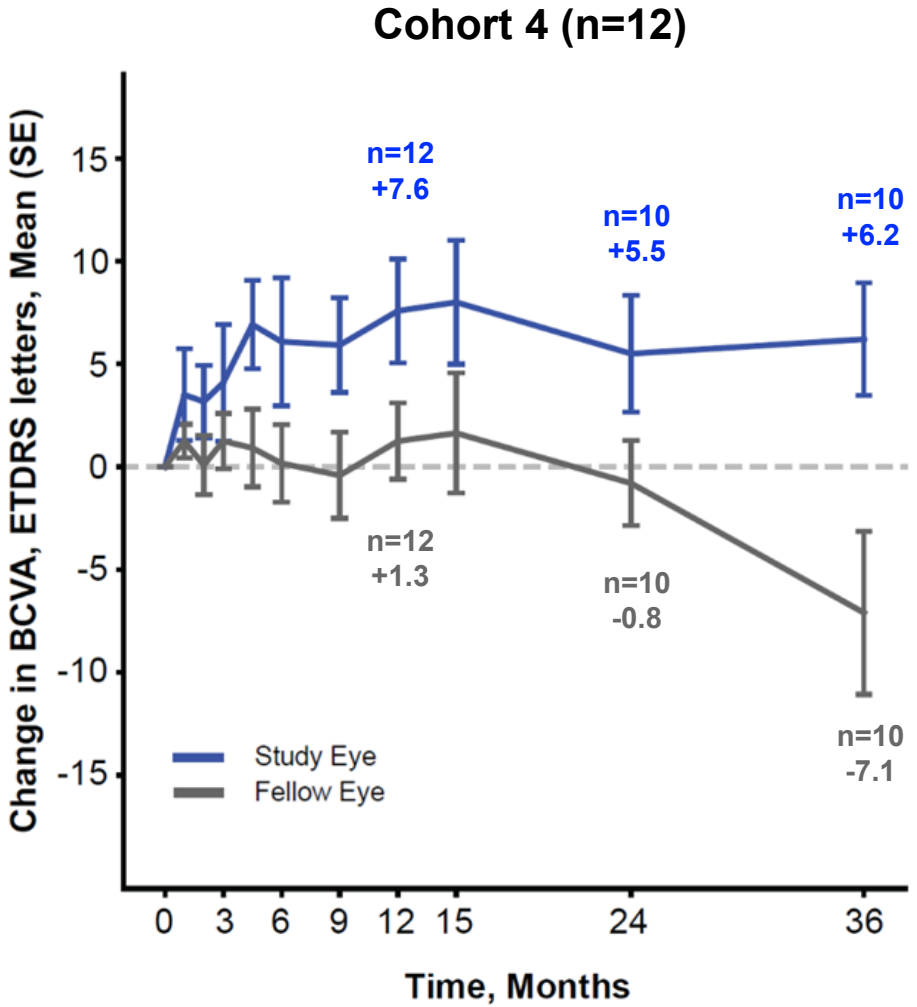
Segmentation result is generated by Genentech EyeNotate OCT segmentation algorithm, reviewed and corrected by a single masked expert grader.

The Structural Support in Cohort 4 Patients is Accompanied by Sustained BCVA Gains Through Month 36, with Greater Gains Among Eyes with Extensive Coverage of GA



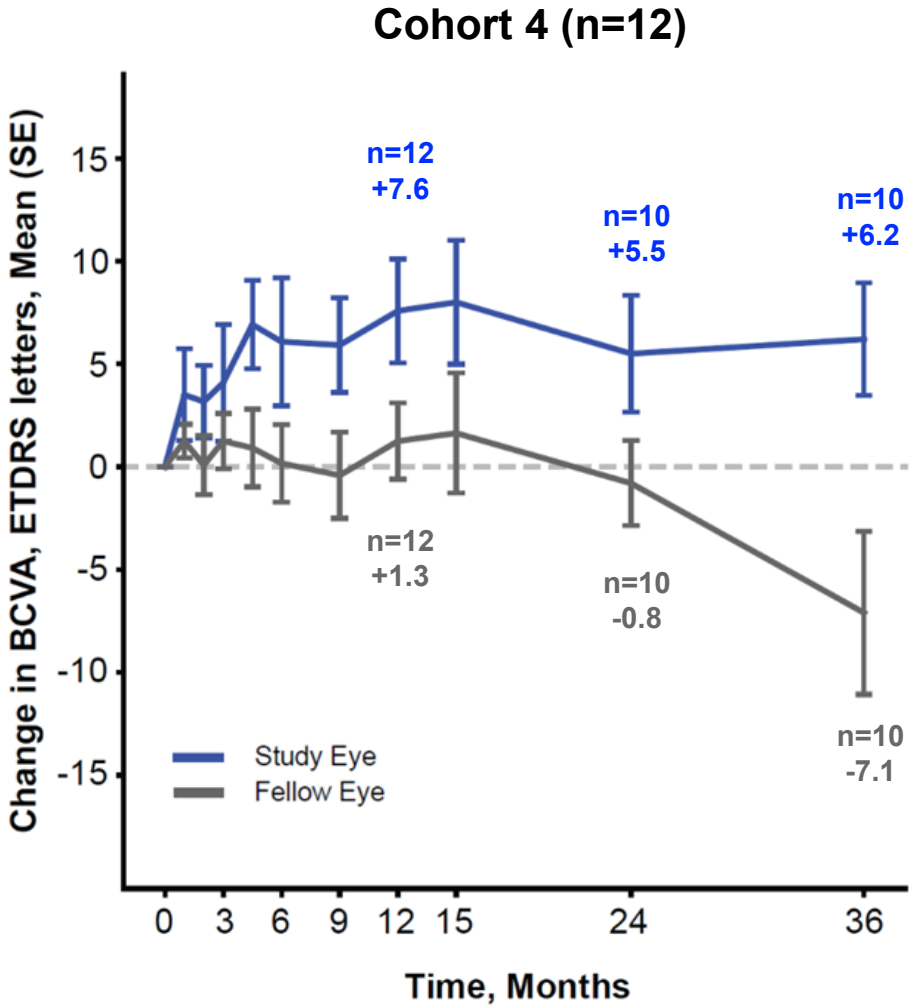
ETDRS, Early Treatment Diabetic Retinopathy Study.

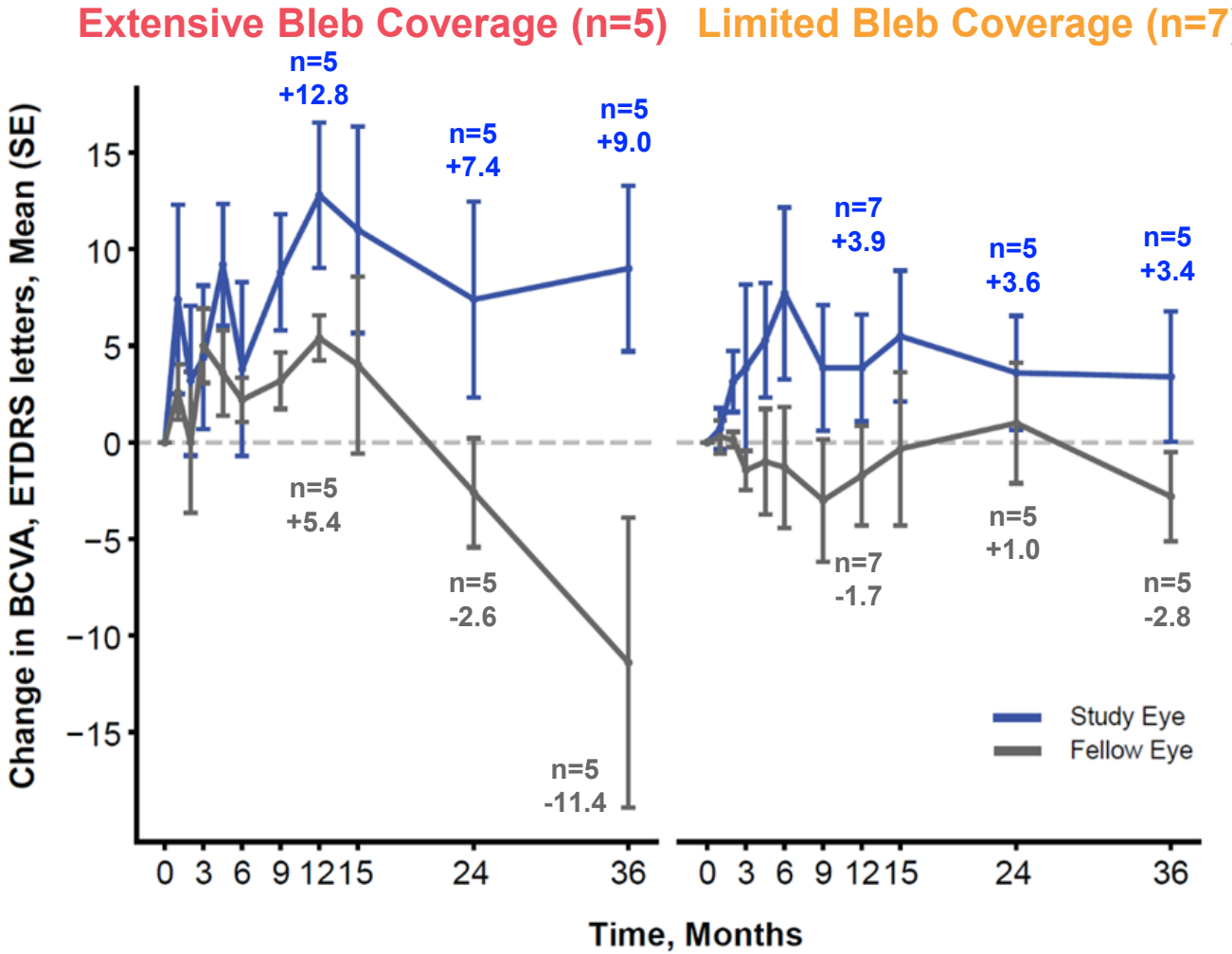
The Structural Support in Cohort 4 Patients is Accompanied by Sustained BCVA Gains Through Month 36, with Greater Gains Among Eyes with Extensive Coverage of GA



ETDRS, Early Treatment Diabetic Retinopathy Study.

The Structural Support in Cohort 4 Patients is Accompanied by Sustained BCVA Gains Through Month 36, with Greater Gains Among Eyes with Extensive Coverage of GA





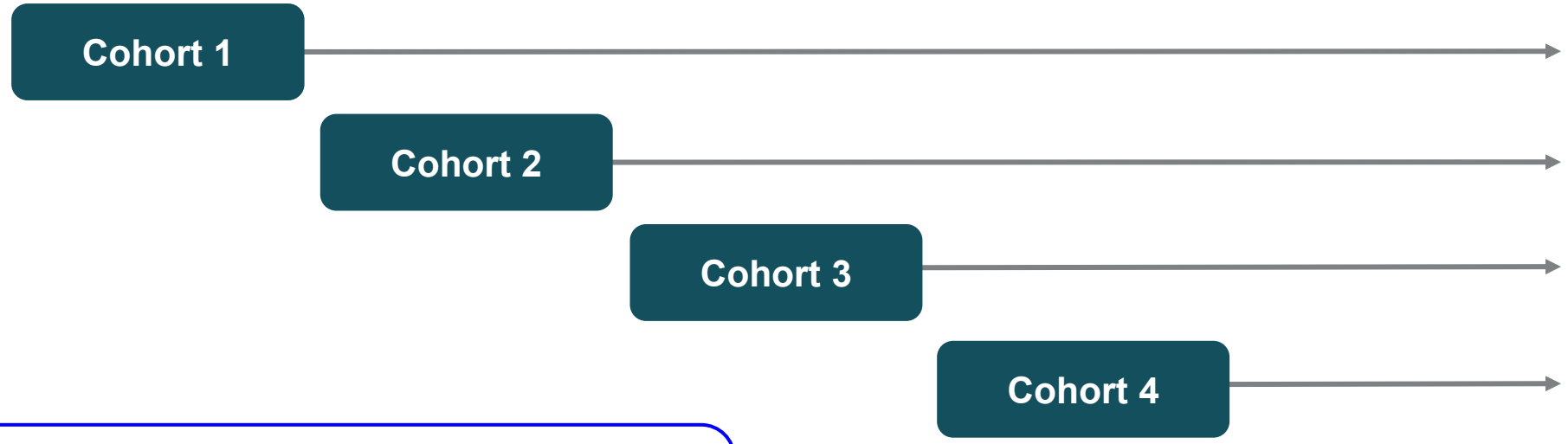
ETDRS, Early Treatment Diabetic Retinopathy Study.

GAlette: A Phase 2a Multicenter, Open-Label, Single-Arm Study to Optimize the Subretinal Delivery of OpRegen Cell Therapy In GA (NCT05626114; Recruiting)[1]

Key Enrollment Criteria

- Age ≥50 years
- Diagnosis of GA secondary to AMD
- BCVA score ≥29 letters and ≤60 letters in the study eye as assessed by ETDRS
- Pseudophakic (study eye)
- Ability to undergo vitreoretinal surgical procedure under sedation or general anesthesia

Up to ~60 patients
3-10 patients per cohort
Up to 200,000 cells



Primary Endpoints

- Success of OpRegen subretinal surgical delivery to target GA regions
- Safety of OpRegen surgical delivery at 3 months

ClinicalTrials.gov Identifier: NCT05626114. Accessed 05/2025 from https://clinicaltrials.gov/study/NCT05626114.

Conclusions

- Imaging evidence of structural benefit and greater gains in visual acuity were seen in study eyes in Cohort 4 patients (less advanced GA) at Month 12, continuing through Month 36
  - Differences as compared with fellow eyes increased over time, suggesting possible modification of the course of disease
  - Effects were more prominent in patients with extensive compared with limited OpRegen bleb coverage of GA
- Quantitative analysis of OCT imaging revealed areas with partial restoration of outer retinal structure including re-appearance of an RPE layer as well as features associated with recovery of photoreceptors
- These data suggest that OpRegen cell therapy may counteract RPE cell dysfunction and loss in GA by providing support to remaining retinal cells, and these effects appear durable through at least 36 months after a single administration
- The Phase IIa GAlette study evaluating the success of subretinal delivery of OpRegen cell therapy to target areas of GA is currently enrolling (NCT05626114)

Thank You to All Participating Ph1/2a Investigators, Sites, and Patients

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Trial Conduct

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*Former Lineage employee; Gary Hogge contributed to this work while at Lineage Cell Therapeutics, Inc.


THANK YOU!