

# Retinal Structure Improvements With OpRegen<sup>®</sup> RPE Cell Therapy in a Phase I/IIa Study in Geographic Atrophy

**Allen Ho, MD**, *on behalf of the OpRegen Phase I/IIa Study Investigators*  
Mid Atlantic Retina, Philadelphia, PA, USA

# Investigators, Sites, and Support

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# Disclosures

4DMT S

Aavantgarde Bio: C

AcuSurgical: C

Adverum: C, S

Aerie: C, S

Alcon Laboratories, Inc: C, S

Aldeyra: C, S

Allergan: C, S

Apellis: C, S

Astellas: C

Atsena: C, S

Beaver-Visitec International, Inc.: C

Chengdu Kanghong Biotechnology: C, S

Clearside: C

Covalent Medical, LLC: PS

Dompe: C

EyePoint: C

Eyevensys: C

Genentech: C, S

Gyroscope: C, P, S

Iveric: C, S

Janssen / Johnson & Johnson: C, S

Kiora: C, PS

Lineage: C, S

Lumithera: S

Nanoscope: C

National Eye Institute: S

Notal: C, S

Novartis: C, S

Ocular Therapeutics: C

ONL: C, PS

Oxular: C

ProQR: S

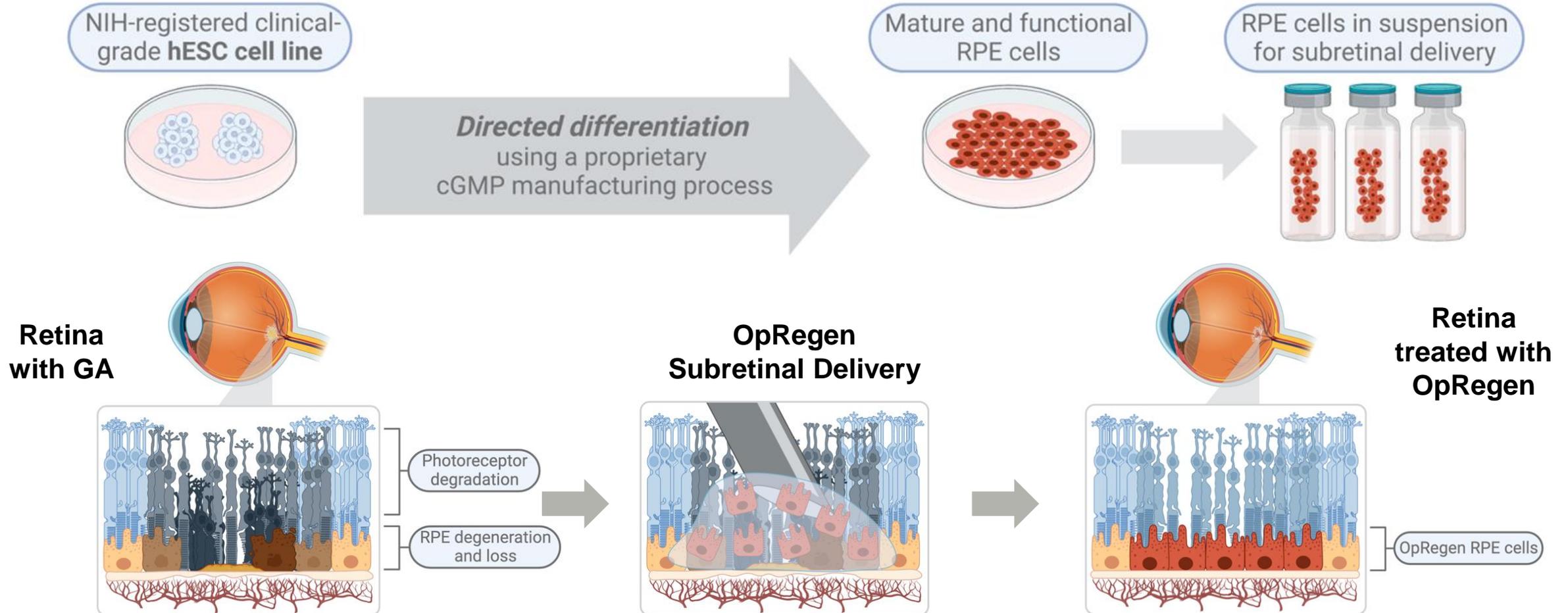
Regeneron Pharmaceuticals, Inc.: C, S

RegenXBio: C, S

Stealth: C

Vanotech: C

# OpRegen – 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; RPE, retinal pigment epithelium.

NIH registry for hESC cell line HAD-C 102 available at [https://grants.nih.gov/stem\\_cells/registry/current.htm?id=428](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:  $\leq 20/200$ )
- GA area: 1.25–17 mm<sup>2</sup>

#### Cohort 4 (n=12):

- Impaired vision (BCVA:  $\geq 20/250$  and  $\leq 20/64$ )
- GA area:  $\geq 4$  and  $\leq 11$  mm<sup>2</sup>

### 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

### 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

### Subretinal Delivery

Vitrectomy/retinotomy (n=17)

Suprachoroidal cannula using Orbit SDS<sup>®</sup>  
(Gyroscope Therapeutics) in Cohort 4 only (n=7)

### Key Study Endpoints

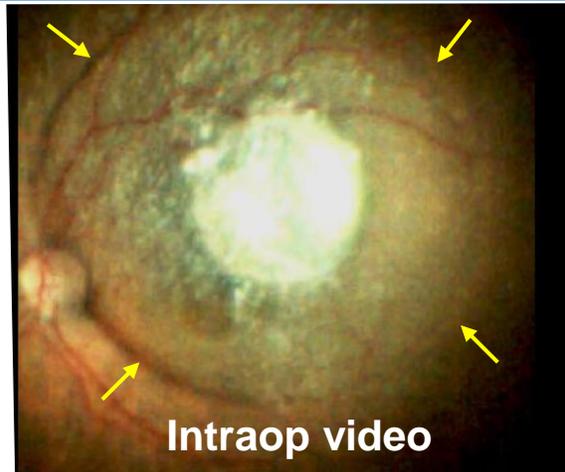
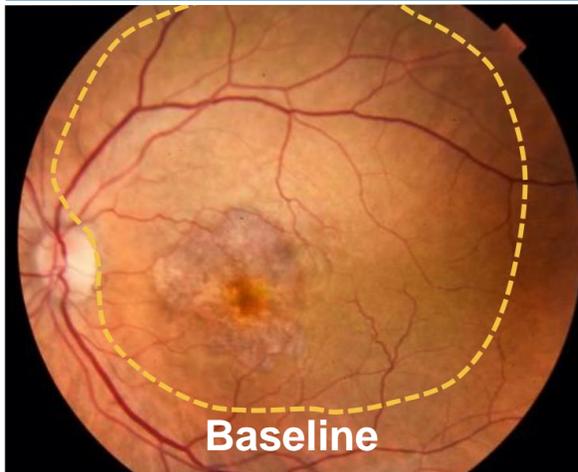
Assessed **12 months** post OpRegen subretinal delivery; patients followed for up to 5 years

- **Primary:** safety and tolerability of OpRegen following subretinal delivery
- **Secondary:** potential activity of OpRegen by assessing changes in visual function and retinal structure

# Subgroup analysis among patients in Cohort 4 (less advanced GA): Functional and anatomic outcomes in eyes with and without delivery of OpRegen to central GA

## Extensive bleb coverage (n=5)

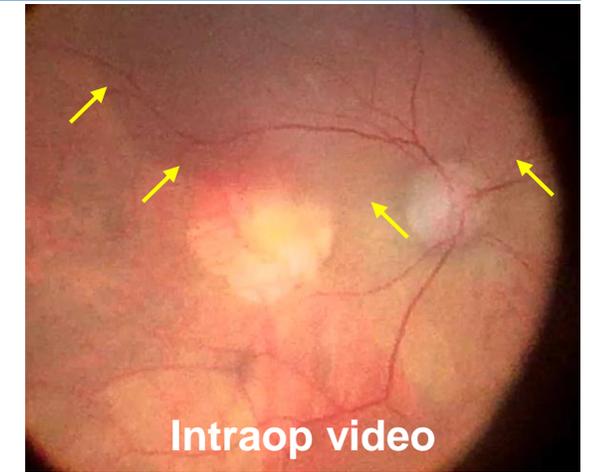
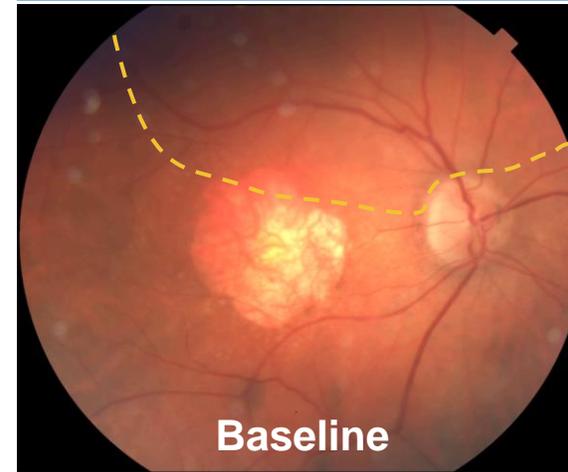
Extensive bleb coverage of GA (including fovea)



Case #14

## Limited bleb coverage (n=7)

Minimal to no bleb coverage of GA

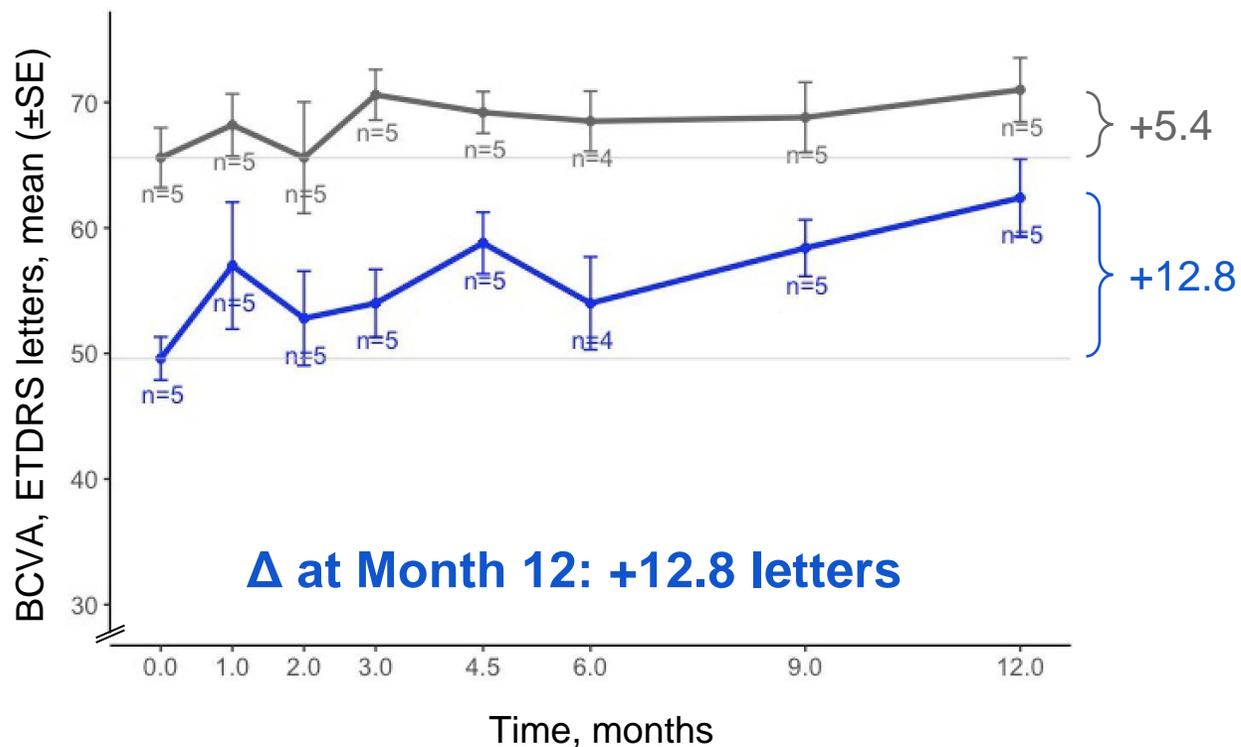


Case #18

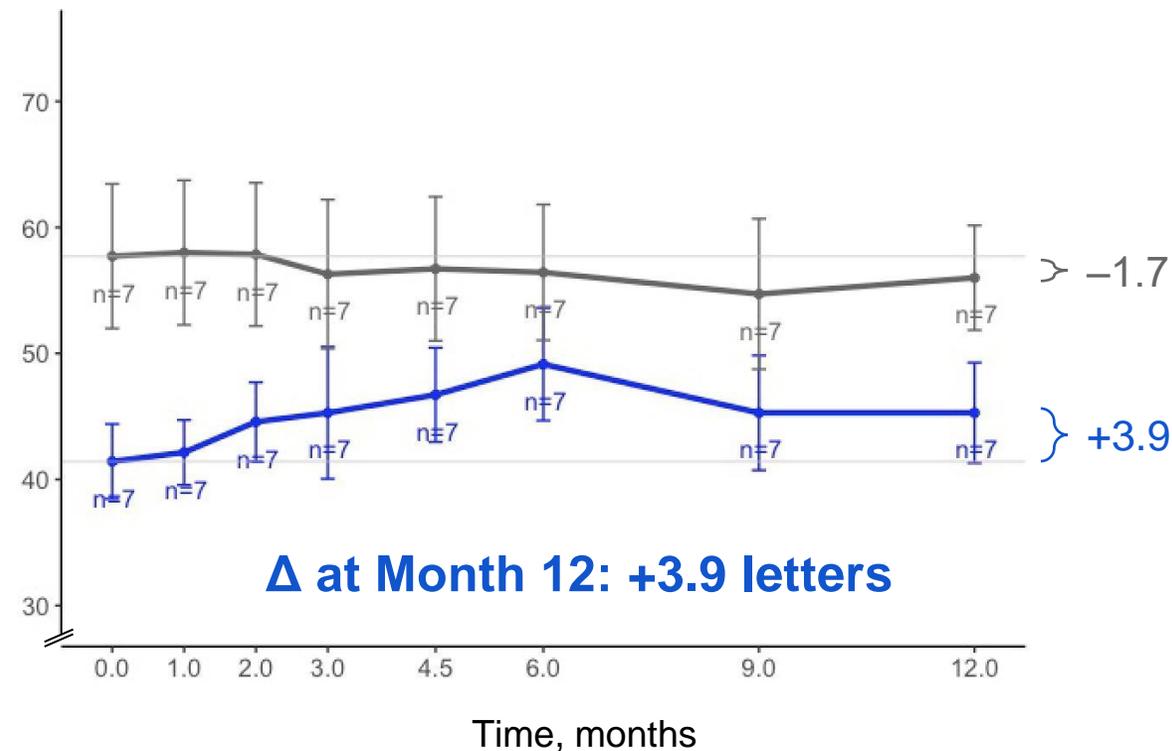
OpRegen bleb coverage of GA determined by surgical video  
for all Cohort 4 cases (n=12)

# Greater BCVA gains with extensive OpRegen bleb coverage of GA in Cohort 4 patients

Eyes with **extensive** bleb coverage (n=5)

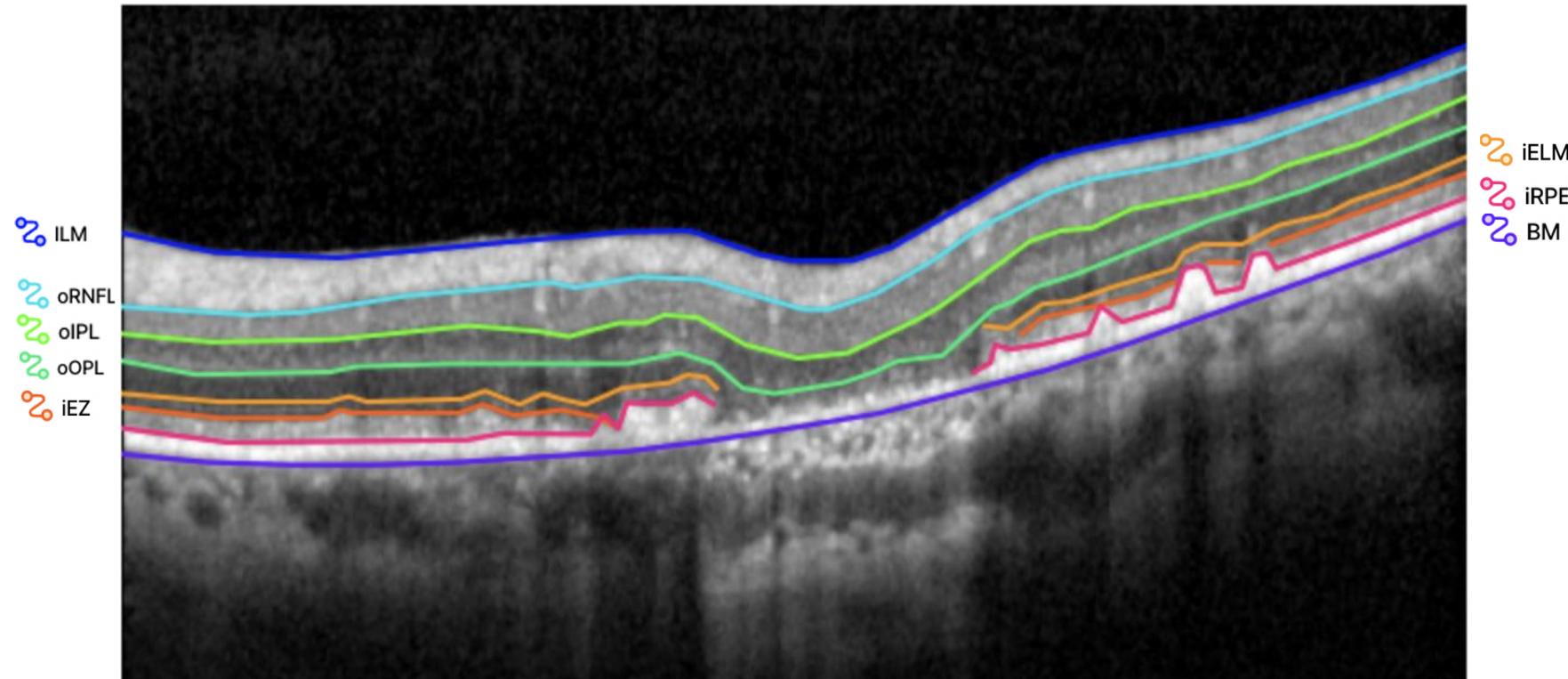


Eyes with **limited** bleb coverage (n=7)



— Study Eye — Fellow Eye

# Outer retinal structure analyzed using EyeNotate OCT segmentation algorithm in Cohort 4 patients



## ELM (external limiting membrane):

Graded as present or absent (orange line).

## RPEDC (retinal pigment epithelium drusen complex):

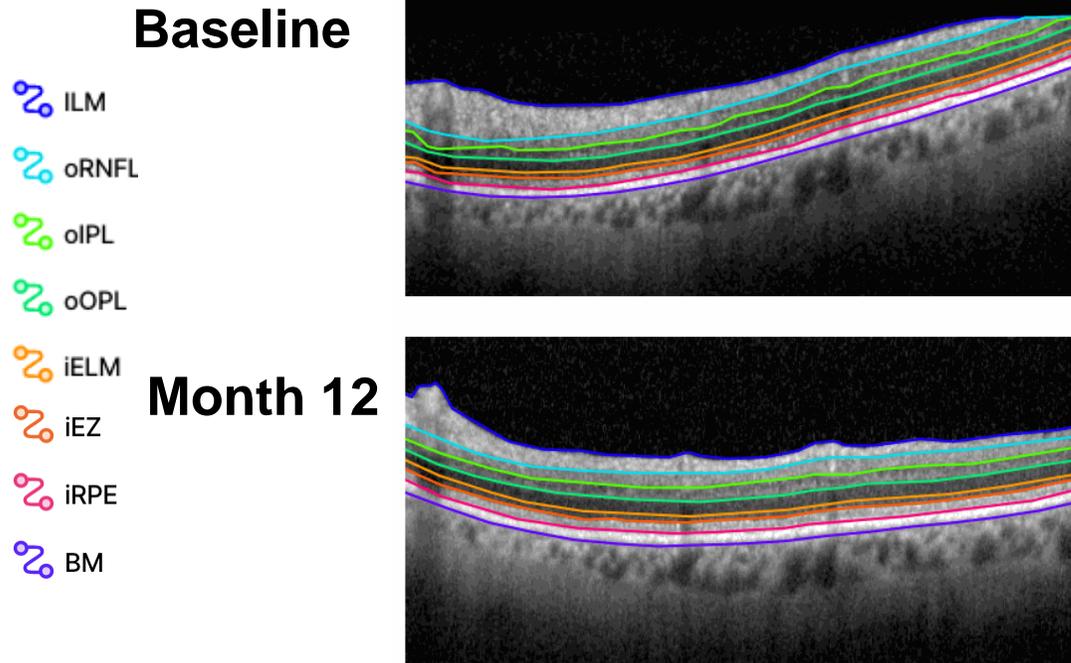
The thickness between the hyper-reflective bands representing inner border of RPE (red line) and **BM (purple line)** when RPE is present.

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

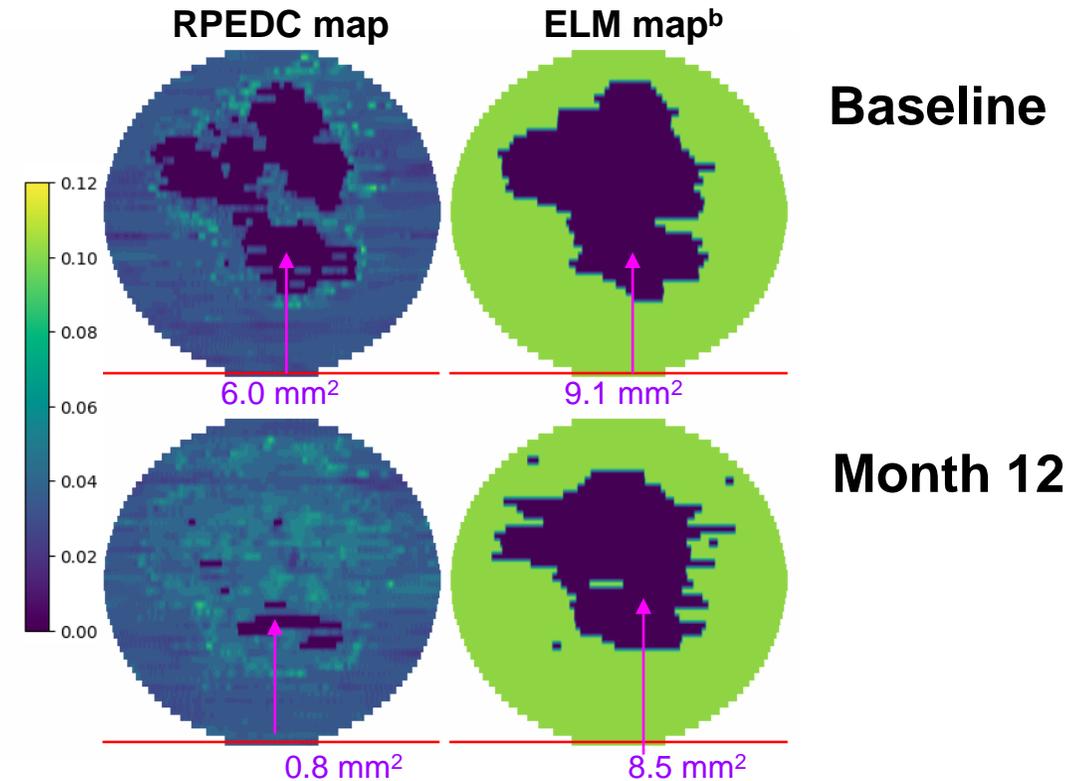
BM, Bruch's membrane; EZ, ellipsoid zone; i-, inner boundary of layer; ILM, internal limiting membrane; IPL, inner plexiform layer; o-, outer boundary of layer; OPL, outer plexiform layer; RNFL, retinal nerve fiber layer.

# Generation of RPEDC and ELM area maps with quantification of change between baseline and 12 months

## SD-OCT segmentation<sup>a</sup>



## Quantification



ELM, external limiting membrane; RPEDC, retinal pigment epithelium drusen complex.

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

<sup>b</sup>ELM map, binary external limiting membrane presence/absence map, green when ELM is present, dark blue when ELM is absent.

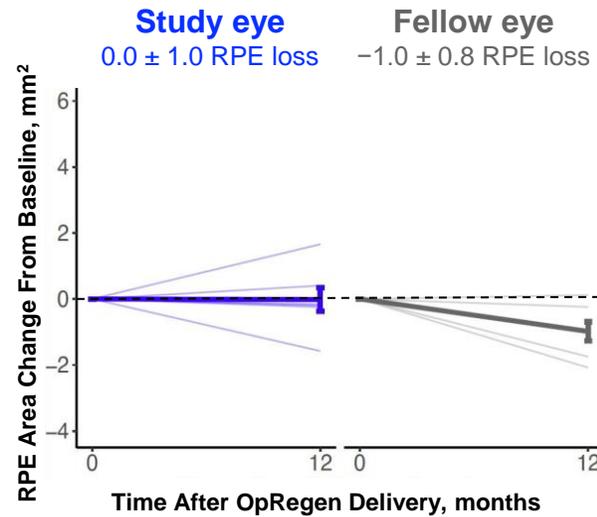
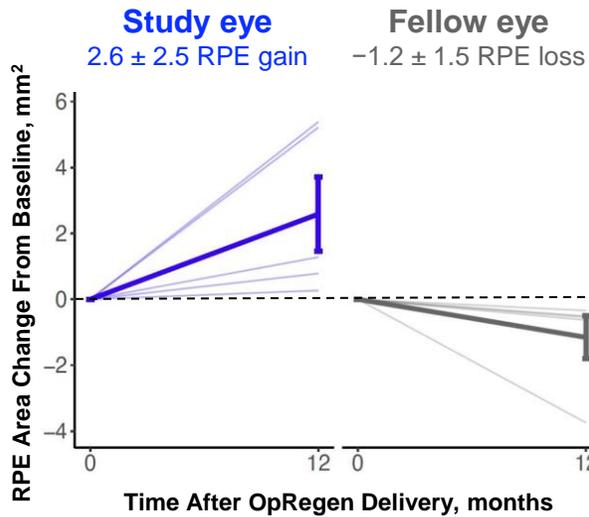
**Case #14**

# Maintenance or improvement of outer retina structure was observed in patients with extensive OpRegen bleb coverage

## Area of RPE change

**Extensive Bleb Coverage**  
(n=5)

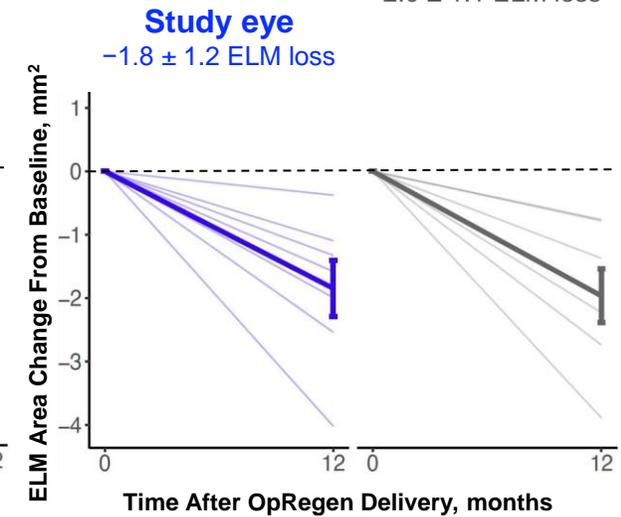
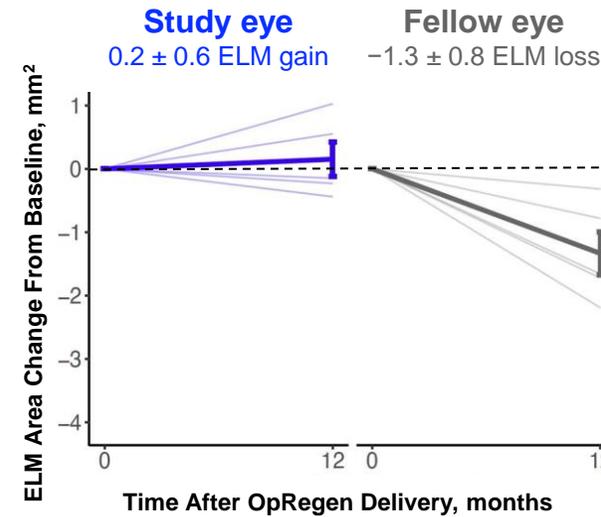
**Limited Bleb Coverage**  
(n=7)



## Area of ELM change

**Extensive Bleb Coverage**  
(n=5)

**Limited Bleb Coverage**  
(n=7) Fellow eye  
-2.0 ± 1.1 ELM loss



Thick lines represent the mean and error bars represent standard error.  
Data cutoff: 18 Jan 2022.

# Maintenance or improvement of outer retina structure was observed in patients with extensive OpRegen bleb coverage

## Area of RPE change

**Extensive Bleb Coverage**  
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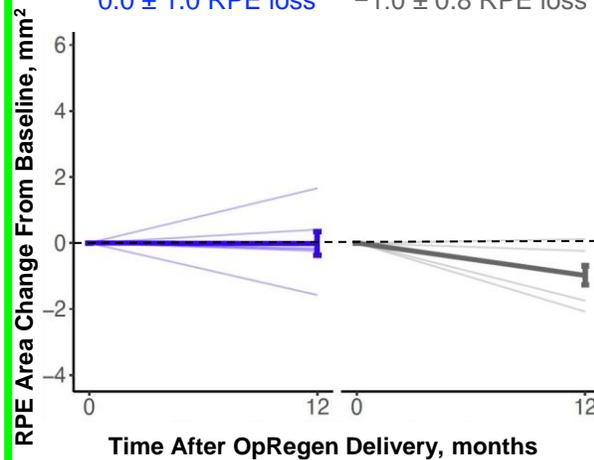
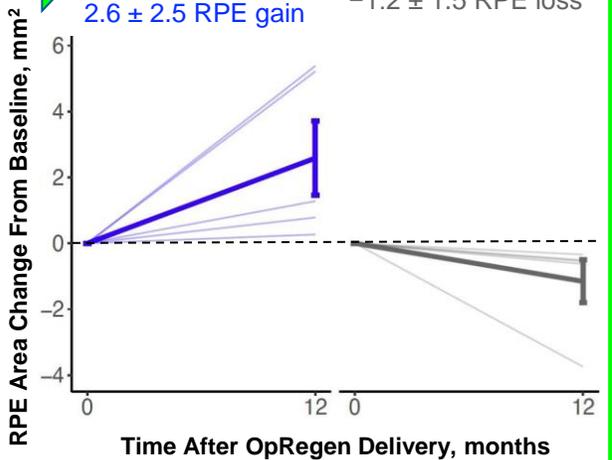
**Limited Bleb Coverage**  
(n=7)

**Study eye**  
 $2.6 \pm 2.5$  RPE gain

**Fellow eye**  
 $-1.2 \pm 1.5$  RPE loss

**Study eye**  
 $0.0 \pm 1.0$  RPE loss

**Fellow eye**  
 $-1.0 \pm 0.8$  RPE loss



## Area of ELM change

**Extensive Bleb Coverage**  
(n=5)

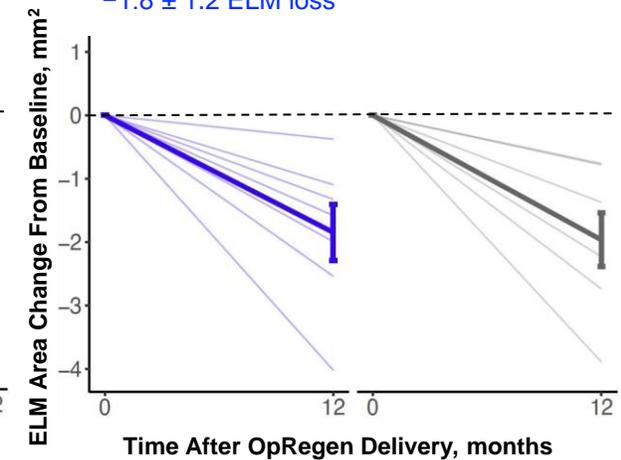
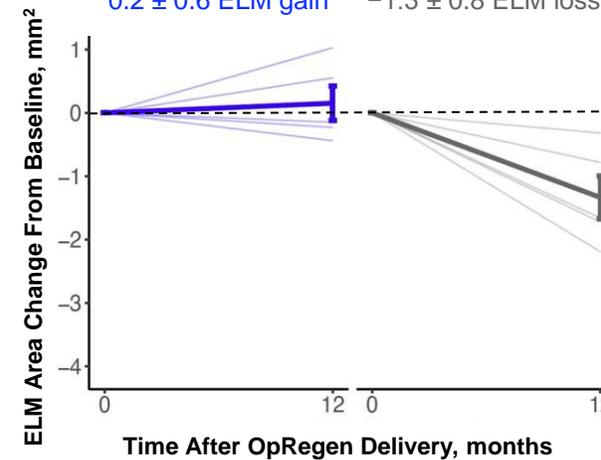
**Limited Bleb Coverage**  
(n=7) Fellow eye

**Study eye**  
 $0.2 \pm 0.6$  ELM gain

**Fellow eye**  
 $-1.3 \pm 0.8$  ELM loss

**Study eye**  
 $-1.8 \pm 1.2$  ELM loss

$-2.0 \pm 1.1$  ELM loss



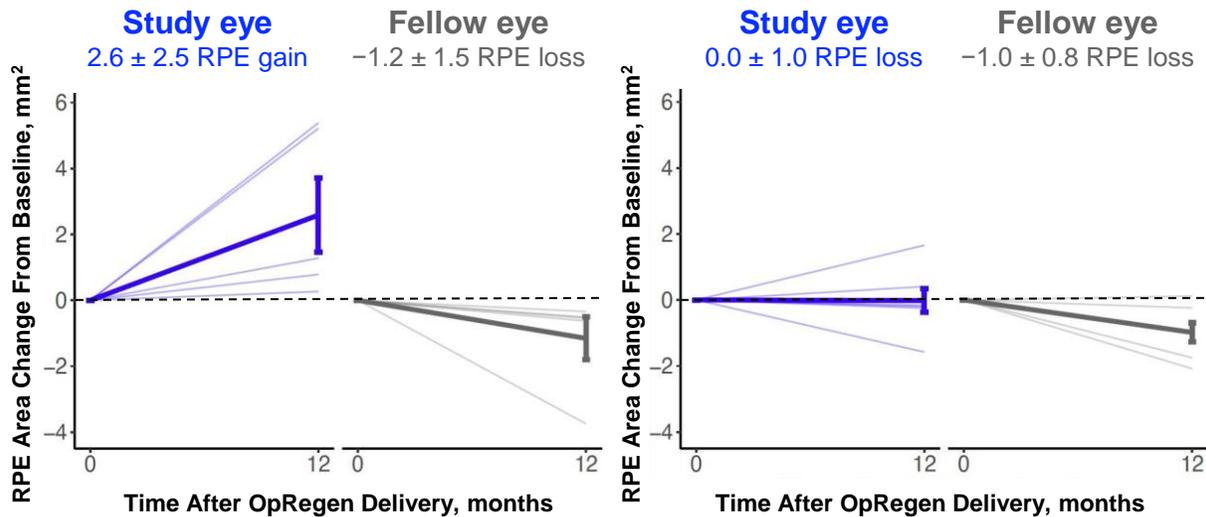
Thick lines represent the mean and error bars represent standard error.  
Data cutoff: 18 Jan 2022.

# Maintenance or improvement of outer retina structure was observed in patients with extensive OpRegen bleb coverage

## Area of RPE change

### Extensive Bleb Coverage (n=5)

### Limited Bleb Coverage (n=7)

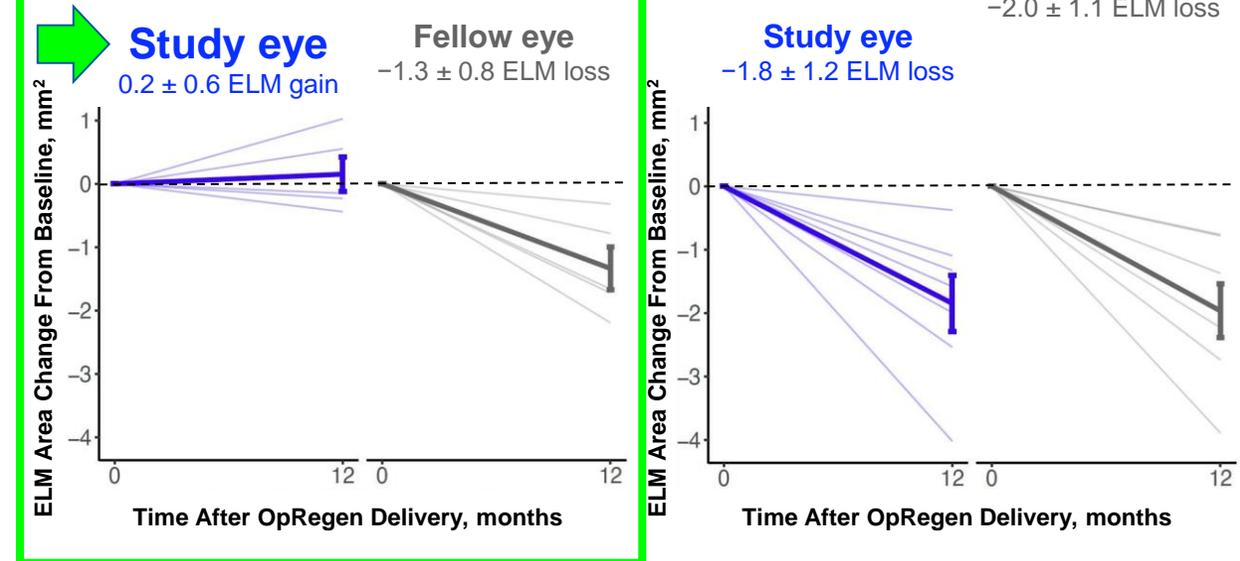


## Area of ELM change

### Extensive Bleb Coverage (n=5)

### Limited Bleb Coverage (n=7) Fellow eye

$-2.0 \pm 1.1$  ELM loss



Thick lines represent the mean and error bars represent standard error.  
Data cutoff: 18 Jan 2022.

# How early is retinal improvement observed?

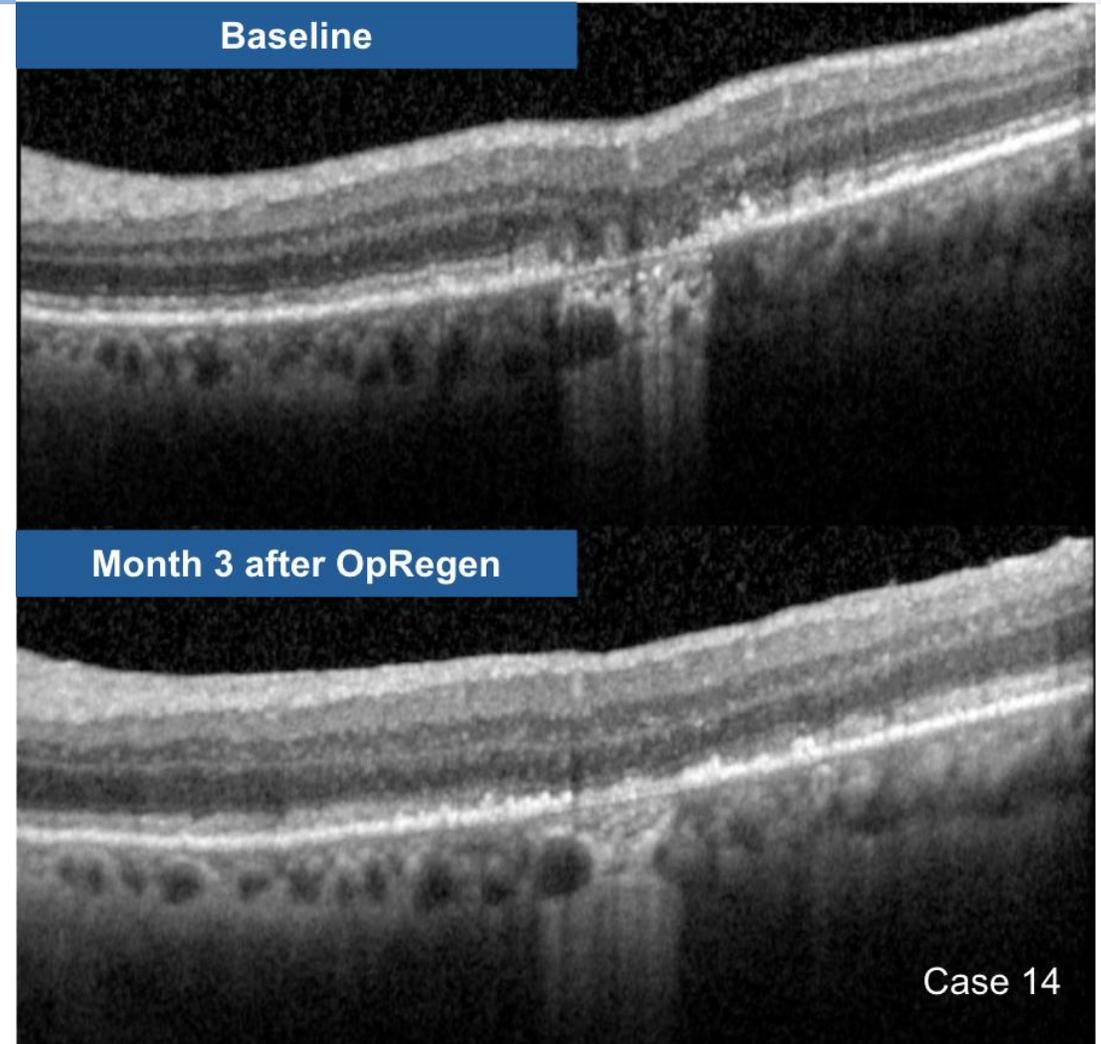
Qualitative assessment of time to retinal structure improvement in patients with extensive OpRegen bleb coverage (n=5)

Structural improvement was assessed by 3 independent expert reviewers and based on meeting all of the following pre-specified criteria<sup>a</sup>:

- a. Reduction in outer plexiform layer and/or inner nuclear layer subsidence
- b. Reappearance of external limiting membrane
- c. Increased hyperreflectivity of RPE and/or Bruch's membrane or reduction of hypertransmission

All 5 cases were assessed to have structural improvement by at least 2 of the 3 reviewers

<sup>a</sup>On at least two non-adjacent B scans; the onset of improvement may be confounded by surgical bleb resolution. Follow-up mode was turned on during acquisition of these OCT scans to enforce longitudinal registration. Registration was verified manually by comparing choroidal patterns. There may be slight offset of inner retina blood vessels due to eye orientation difference during acquisition.



# How early is retinal improvement observed?

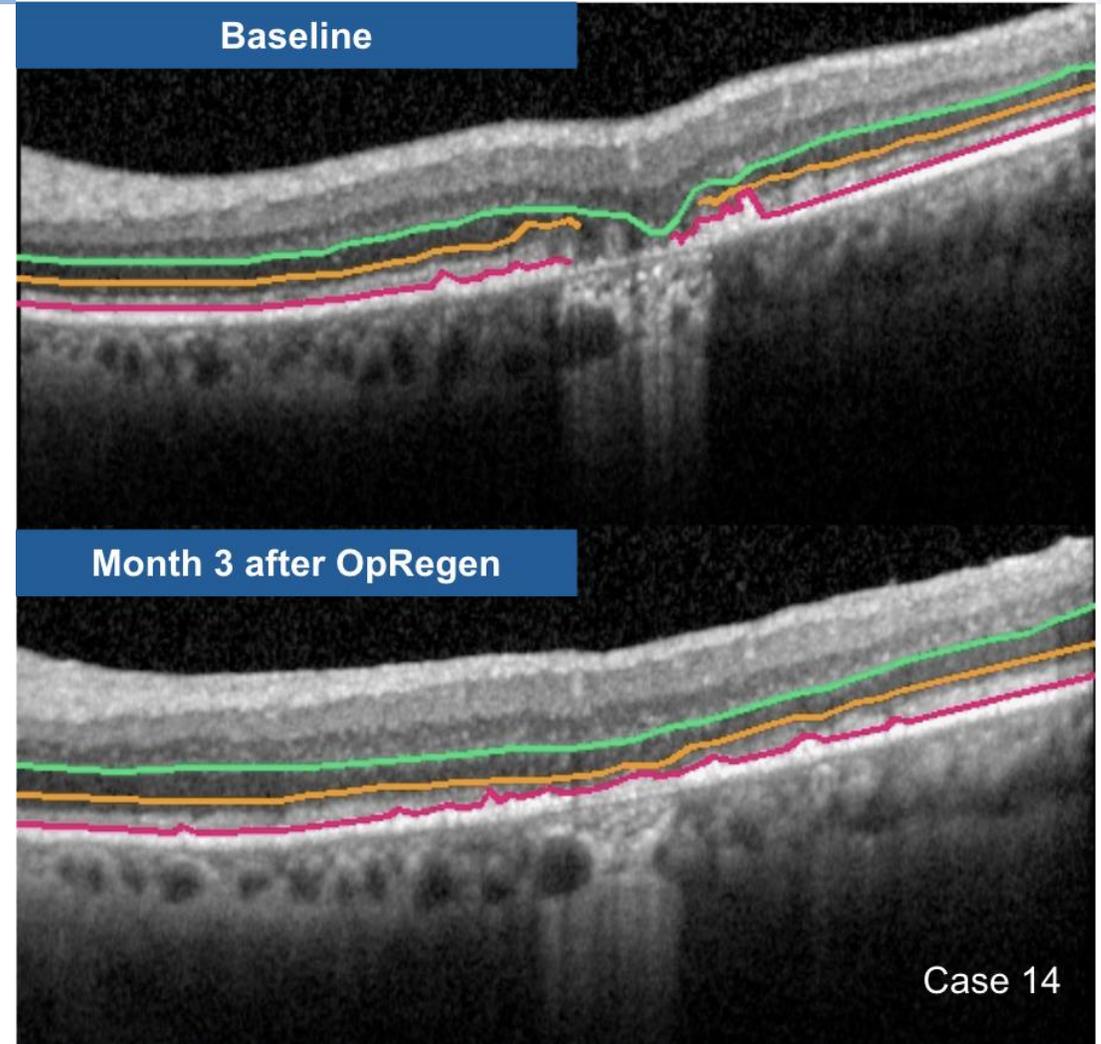
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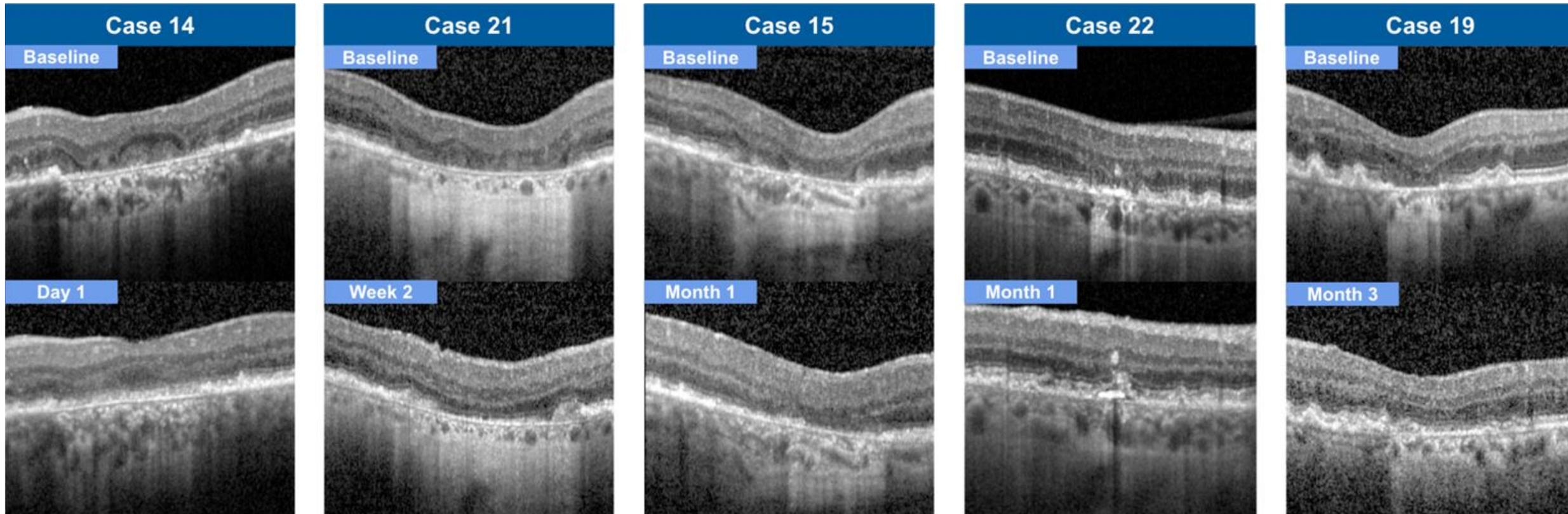
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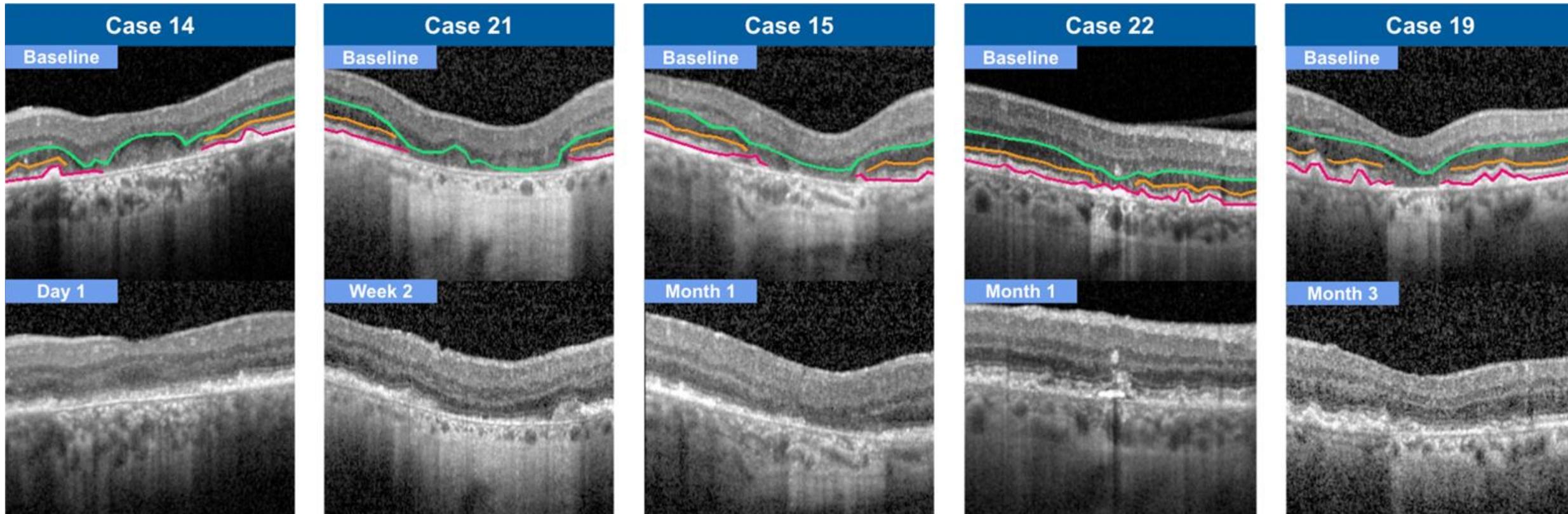


# Onset of structural improvement within 3 months in all 5 patients with extensive OpRegen bleb coverage



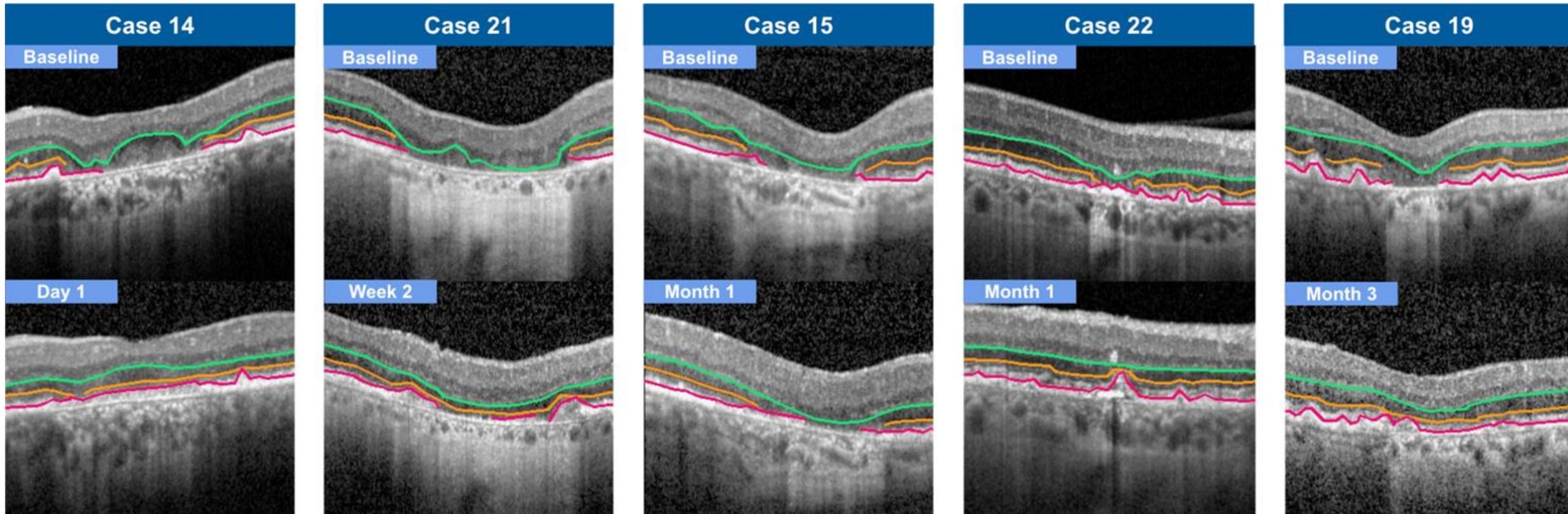
- Structural improvement was only observed within GA lesions covered by surgical bleb
- Maintenance and/or greater structural improvement was observed over time

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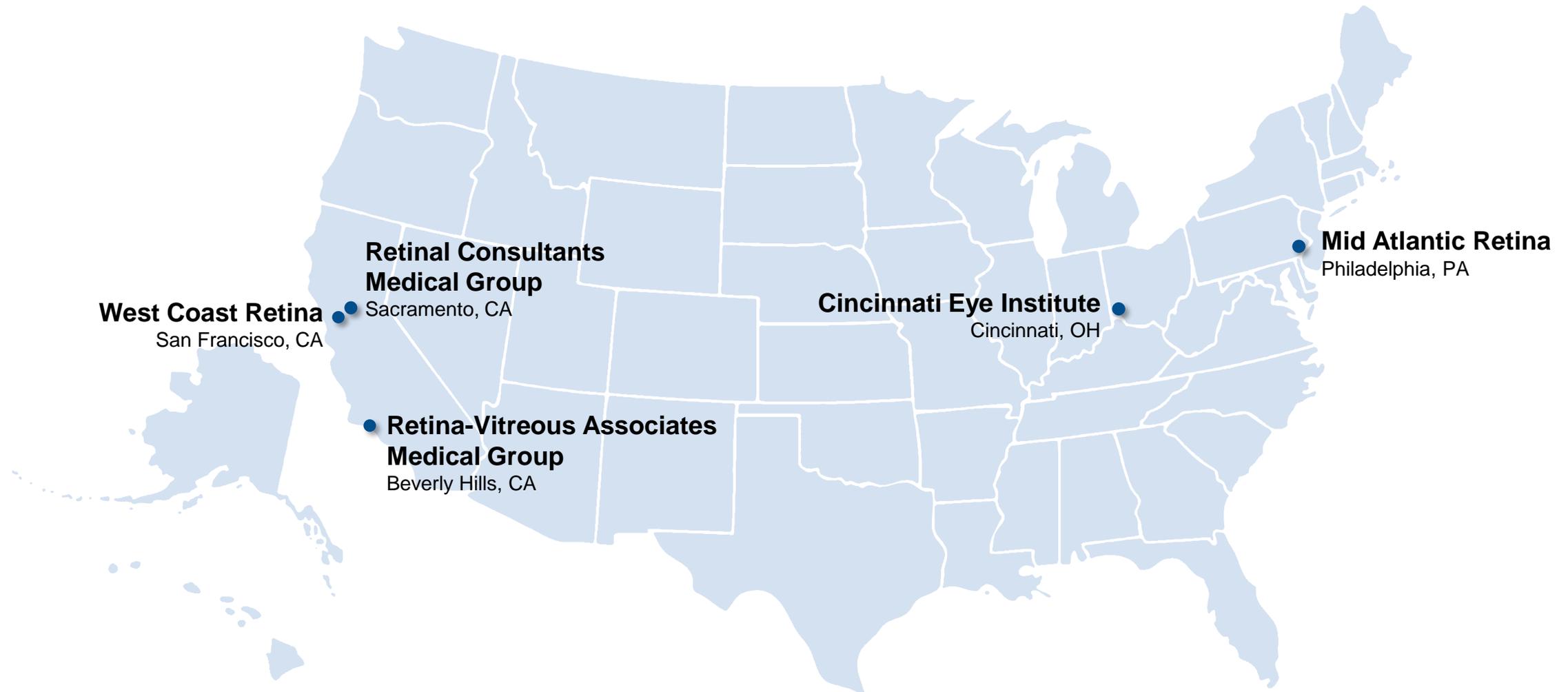


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- Maintenance and/or greater structural improvement was observed over time

# Conclusions

- Following subretinal administration of OpRegen in a Phase I/IIa study, all patients with extensive delivery to GA showed improvement in outer retinal structure on quantitative OCT analysis by a masked grader
- Anatomic improvement correlated with greater gains in BCVA and was detectable within 3 months of administration
  - The extent of OpRegen bleb coverage may be important to optimize patient outcomes
  - Time of onset may be influenced by postoperative changes and interpatient variability
- These data suggest that OpRegen RPE cells may counteract RPE cell dysfunction and loss in GA by providing support to the remaining retinal cells within atrophic areas

# A Phase IIa study evaluating the success of OpRegen delivery to target areas of GA is currently enrolling patients (ClinicalTrials.gov: NCT05626114)



**Thank You to All Patients,  
Participating Study Sites, and Investigators!**