

Time to retinal structure improvements following OpRegen subretinal delivery in patients with geographic atrophy (GA)

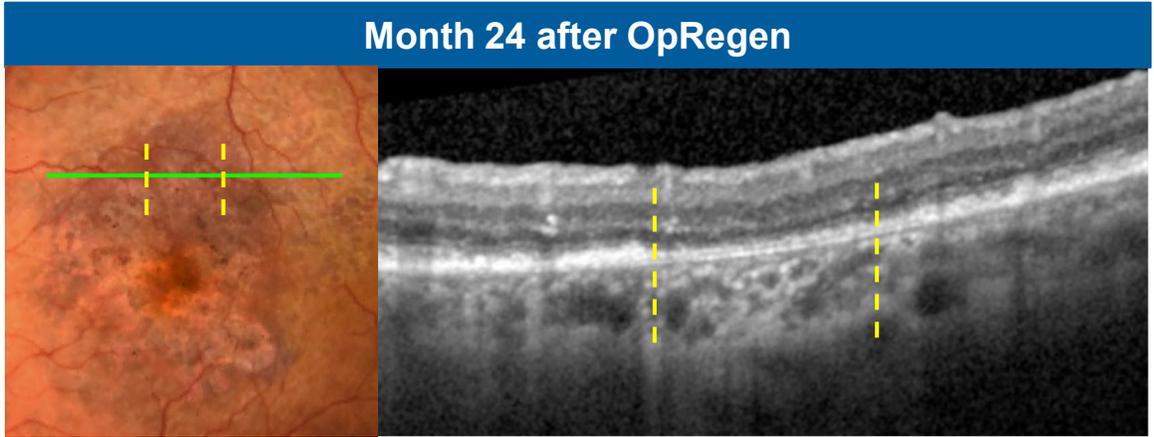
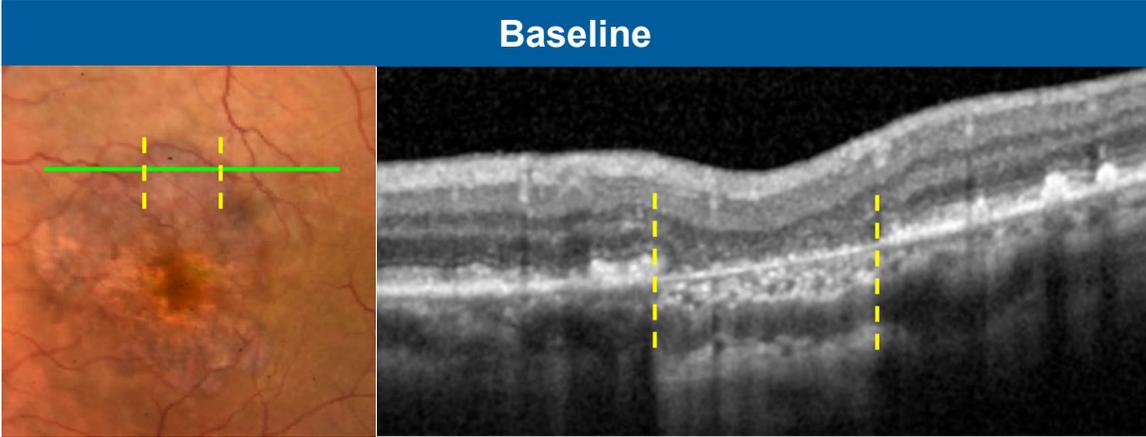
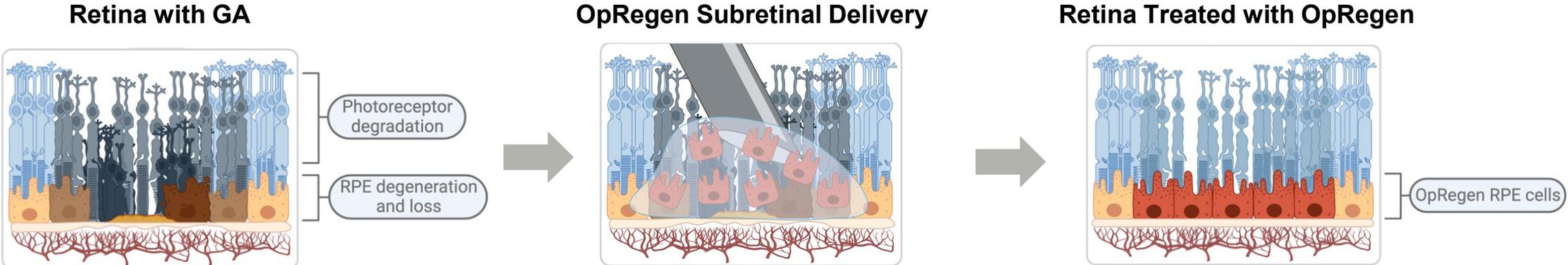
Adiel Barak, MD

Sourasky Medical Center, Tel Aviv, ISR

Banin, Eyal; Boyer, David; Ehrlich, Rita; Ho, Allen C.; Jaouni, Tareq; McDonald, Richard; Riemann, Christopher D.; Telander, David G.; Zhang, Miao; Gao, Simon S.; Litts, Katie M.; Ma, Ling; Chang, Dolly; Ben-Shabat, Avi; Hogge, Gary S.; Reubinoff, Benjamin

Financial Disclosures: AB is a shareholder for Sinai Medical; paid consultant for Byeonics Ltd; and received an institutional grant from Cellcure.

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



RPE, retinal pigment epithelium.

Phase I/IIa Study Design (NCT02286089)

An Open-Label, Single-Arm, Multi-Center, Dose-Escalation Trial

Key Eligibility Criteria

Patients with bilateral GA secondary to AMD

Cohorts 1-3 (n=12):

- Legally blind (BCVA: $\leq 20/200$)
- GA area: 1.25–17 mm²

Cohort 4 (n=12):

- Impaired vision (BCVA: $\geq 20/250$ and $\leq 20/64$)
- GA area: ≥ 4 and ≤ 11 mm²

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

Objectives & Follow-up

Primary and secondary objectives assessed at 12 months following OpRegen subretinal delivery; patients followed for up to 5 years

Primary Objective:

- To evaluate the safety and tolerability of OpRegen following subretinal delivery

Secondary Objective:

- To evaluate the potential activity of OpRegen by assessing changes in visual function and retinal structure



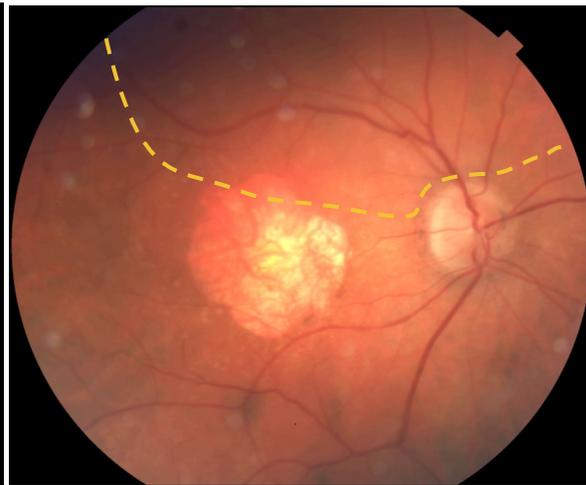
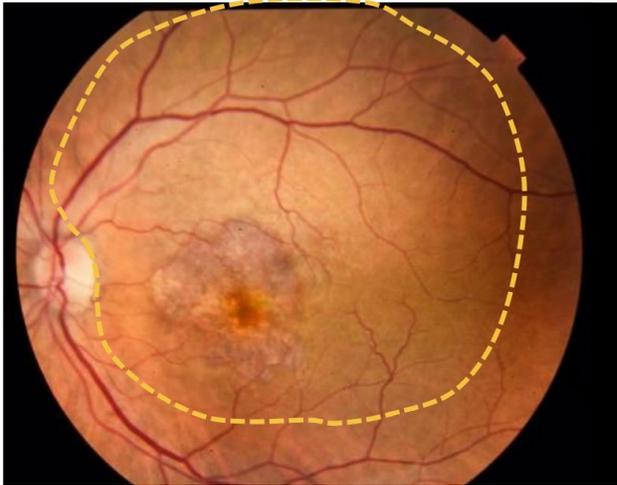
Subretinal Delivery Via:

- Vitrectomy/retinotomy (n=17)
- Suprachoroidal cannula using Orbit SDS™ (Gyroscope Therapeutics) in Cohort 4 only (n=7)

Perioperative Immunosuppressive Regimen:

- Tacrolimus 0.01 mg/kg daily administered until up to 6 weeks after surgery
- Mycophenolate up to 2.0 g daily administered until at least 3 months after surgery

Greater Visual and Structural Improvements in 5 Patients in Cohort 4 with Extensive Bleb Coverage



Extensive

Bleb Coverage

Considerable bleb coverage of GA area (including fovea) (n=5)

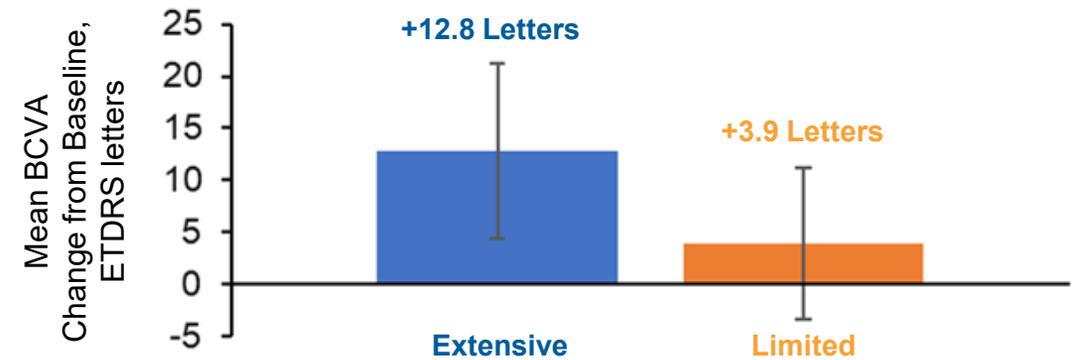
Limited

Bleb Coverage

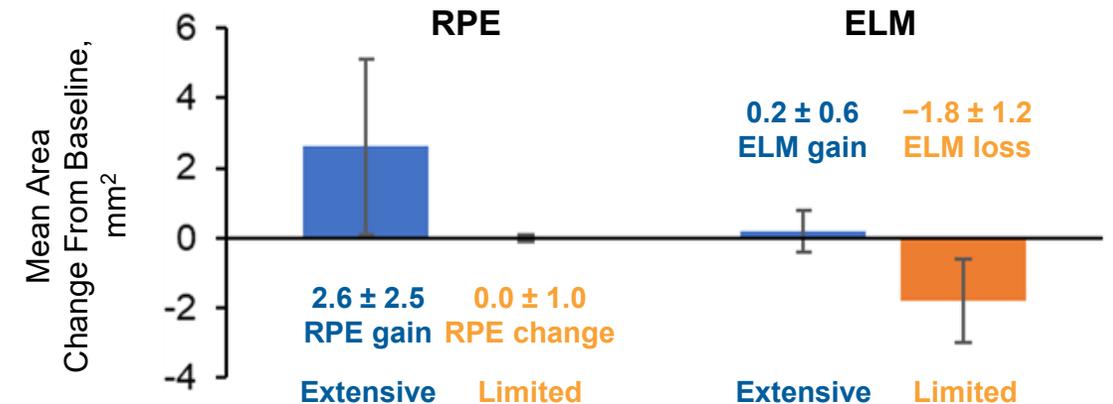
Minimal to no bleb coverage of GA area (n=7)

ELM, external limiting membrane.
Error bars represent standard error.
Data cutoff: 18 Jan 2022.

BCVA Change in Study Eye at Month 12



RPE and ELM Change in Study Eye at Month 12



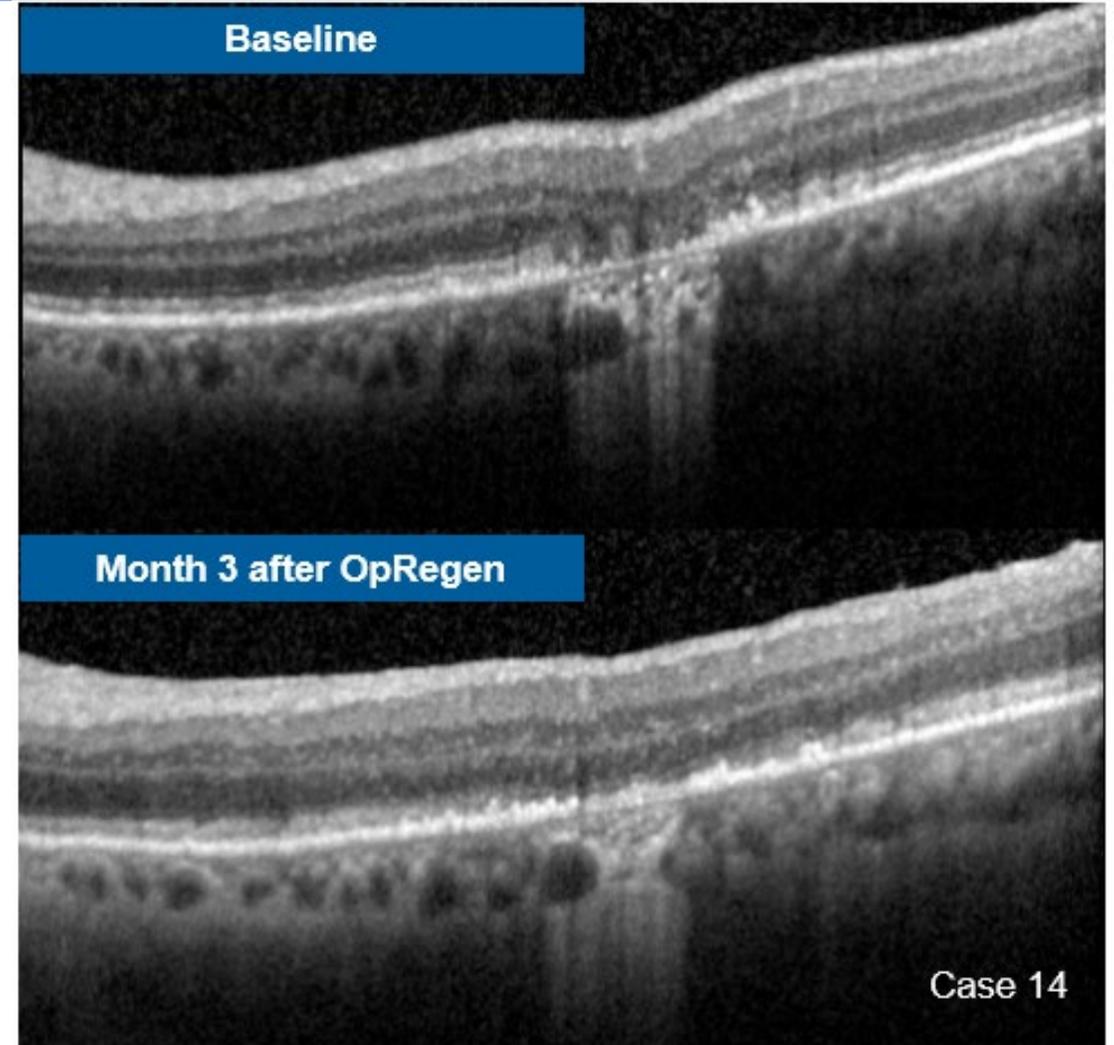
Exploratory Objective: Onset of Structural Improvement In Study Eyes with Extensive OpRegen Bleb Coverage (n=5)

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

- 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

^aOn 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.



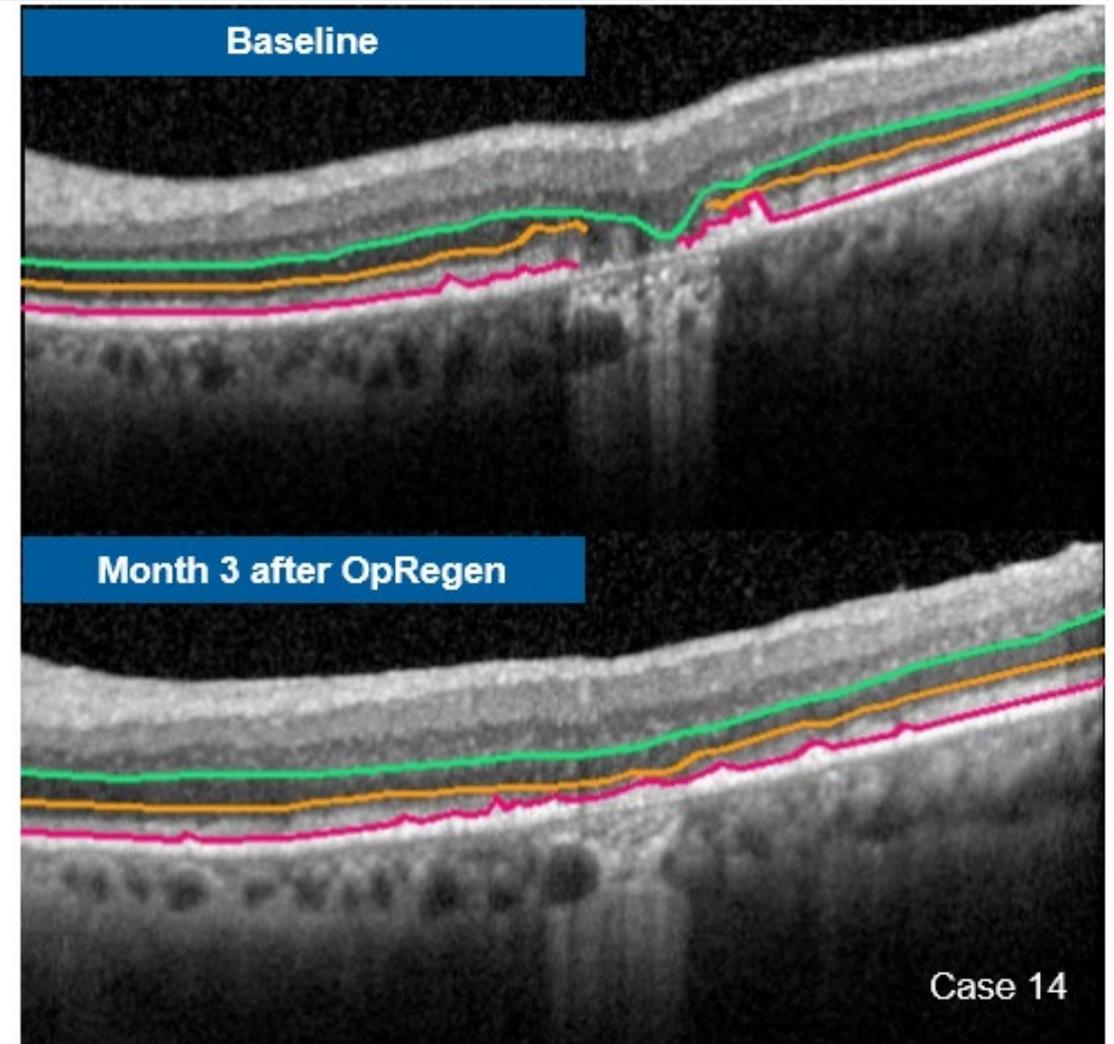
Exploratory Objective: Onset of Structural Improvement In Study Eyes with Extensive OpRegen Bleb Coverage (n=5)

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

- 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

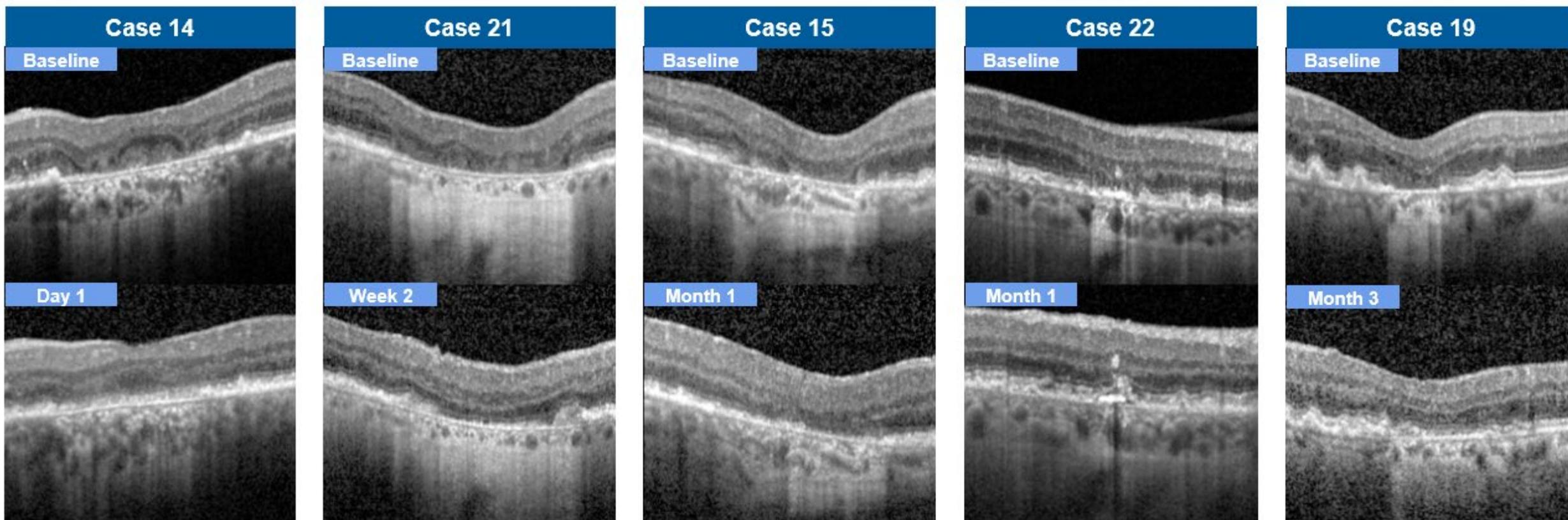
All 5 cases were assessed to have structural improvement by at least 2 of the 3 reviewers

^aOn 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.



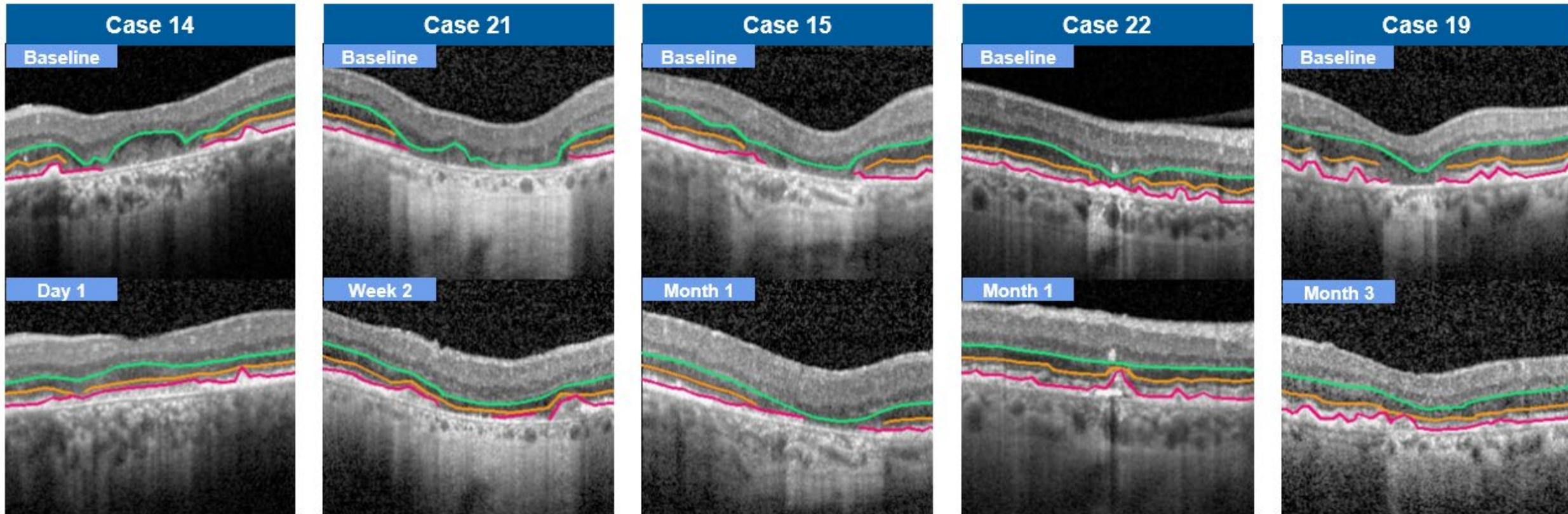
Case 14

Onset of Structural Improvement Within 3 Months in All 5 Patients with Extensive Bleb Coverage



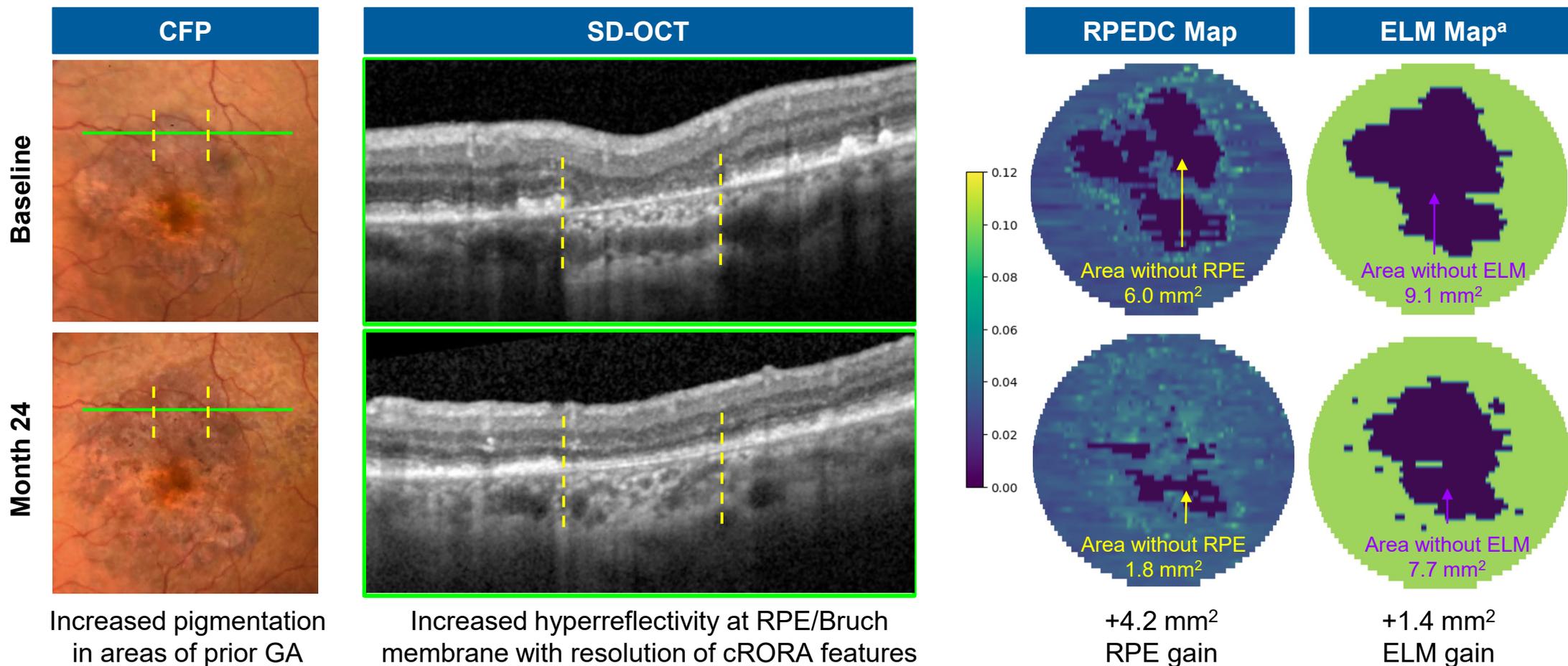
- Structural improvement was only observed within GA lesions covered by surgical bleb
- Maintenance and/or greater structural improvements were observed over time
- These patients also had an average +4.4 letter BCVA gain at Month 3 and +12.8 letter BCVA gain at Month 12

Onset of Structural Improvement Within 3 Months in All 5 Patients with Extensive Bleb Coverage



- Structural improvement was only observed within GA lesions covered by surgical bleb
- Maintenance and/or greater structural improvements were observed over time
- These patients also had an average +4.4 letter BCVA gain at Month 3 and +12.8 letter BCVA gain at Month 12

Preliminary Evidence of Maintenance of Structural Improvement 24 Months Post-Treatment: A Case Study



Increased pigmentation in areas of prior GA

Increased hyperreflectivity at RPE/Bruch membrane with resolution of cRORA features

+4.2 mm²
RPE gain

+1.4 mm²
ELM gain

CFP, color fundus photography; cRORA, complete RPE and outer retinal atrophy; RPEDC, retinal pigment epithelium drusen complex.

^aELM map, binary external limiting membrane presence/absence map, green when ELM is present, dark blue when ELM is absent.

RPEDC and ELM maps are generated by Genentech EyeNotate OCT segmentation algorithm; the segmentation results are reviewed and corrected by a single masked expert grader.

Conclusions

- Following subretinal administration of OpRegen, SD-OCT imaging showed evidence of improvement in outer retinal structure within the first 3 months and as early as within a few days
 - 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 provide support to the remaining retinal cells within atrophic areas by counteracting RPE cell dysfunction and loss
- A Phase IIa study evaluating the success of OpRegen delivery to target areas of GA is currently enrolling patients (ClinicalTrials.gov: NCT05626114)