

AAV5-RPGR (Botaretigene Sparoparvovec) Gene Therapy for X-Linked Retinitis Pigmentosa Demonstrates Localized Improvements in Static Perimetry

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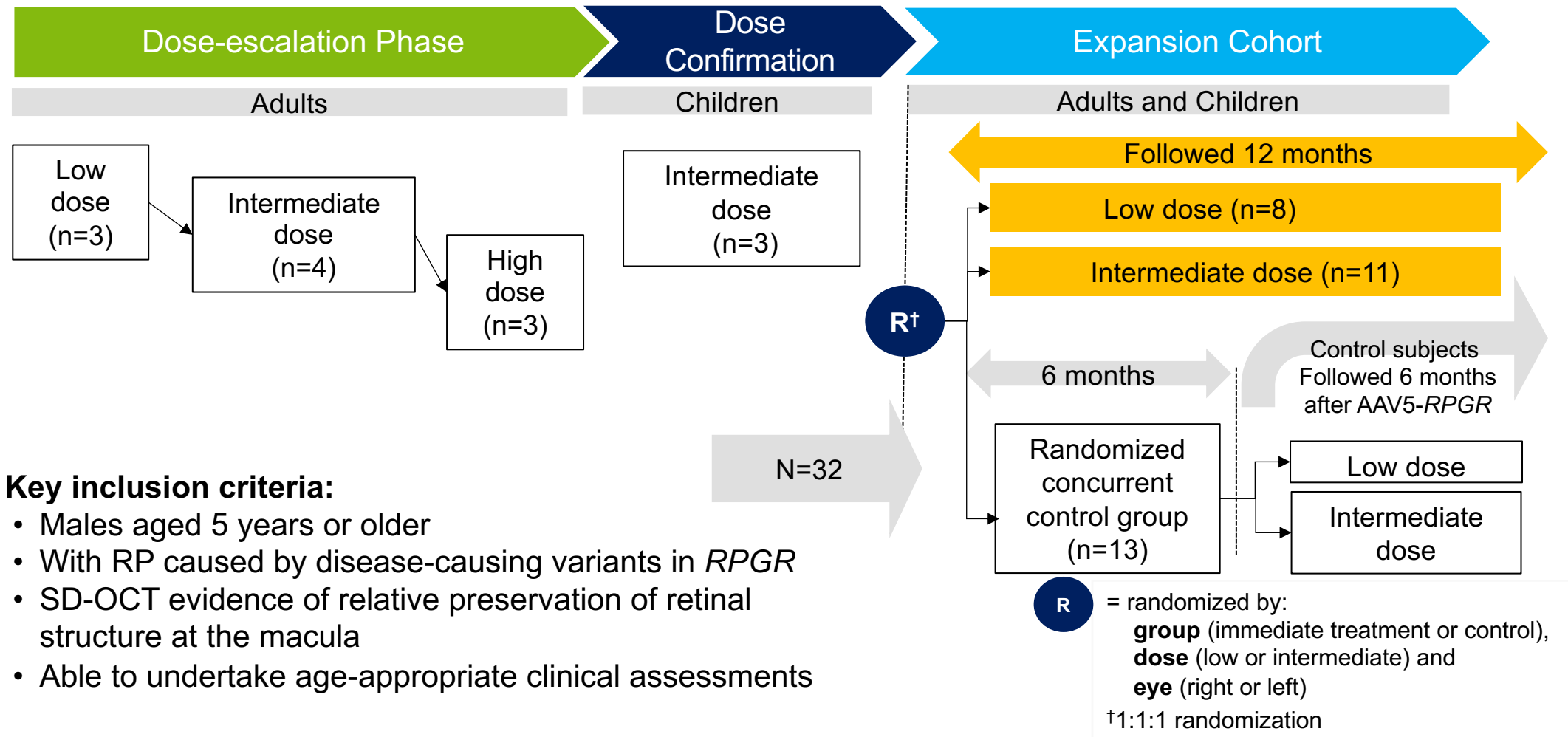
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MGT009: Phase 1/2 Trial of AAV5-RPGR

Open-label study of an AAV5-RPGR gene therapy (NCT03252847) conducted at 5 sites in the **US and UK**



Improvement in Mean Retinal Sensitivity and V30 in Low- and Intermediate-dose Cohorts¹

Dose-escalation Phase

Parameter	Treated-Untreated Eye Difference @ 12 months (90% CI adjusted for baseline)
Mean Retinal Sensitivity (dB)	
Low (n=2) [†]	0.76 (−0.14, 1.66)
Intermediate (n=4)	1.05 (0.81, 1.29)*
High (n=3)	−1.05 (−1.77, 0.06)
Central 30° Hill-of-Vision (V30, dB-sr)	
Low (n=2) [†]	1.10 (0.10, 2.10)*
Intermediate (n=4)	1.26 (0.65, 1.86)*
High (n=3)	−0.89 (−1.70, −0.01)

Response was treated-untreated eye adjusted for baseline (double-delta).

*Statistically significant effects at a one-sided 5% level (nominal p-values).

[†]Excludes one patient with panuveitis in the low-dose cohort.

1. Michaelides, M et al. Presentation at the American Academy of Ophthalmology (AAO) 2020 Virtual Annual Meeting, Nov 13–15.

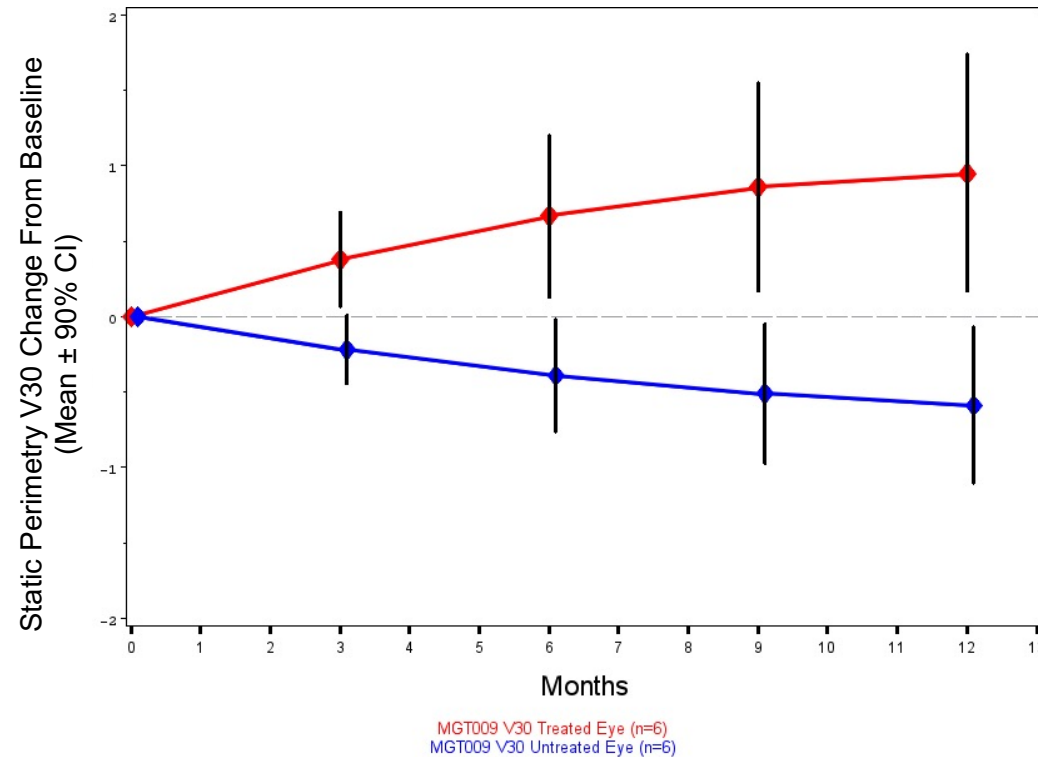
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Improvement in Retinal Sensitivity in Low- and Intermediate-dose Cohorts (n=6)¹

Dose-escalation Phase



Eye	M3	M6	M9	M12
Treated	0.38 (0.07, 0.69)	0.67 (0.13, 1.20)	0.86 (0.17, 1.55)	0.95 (0.17, 1.74)
Untreated	-0.22 (-0.44, 0.01)	-0.39 (-0.76, -0.02)	-0.51 (-0.97, -0.05)	-0.59 (-1.10, -0.07)

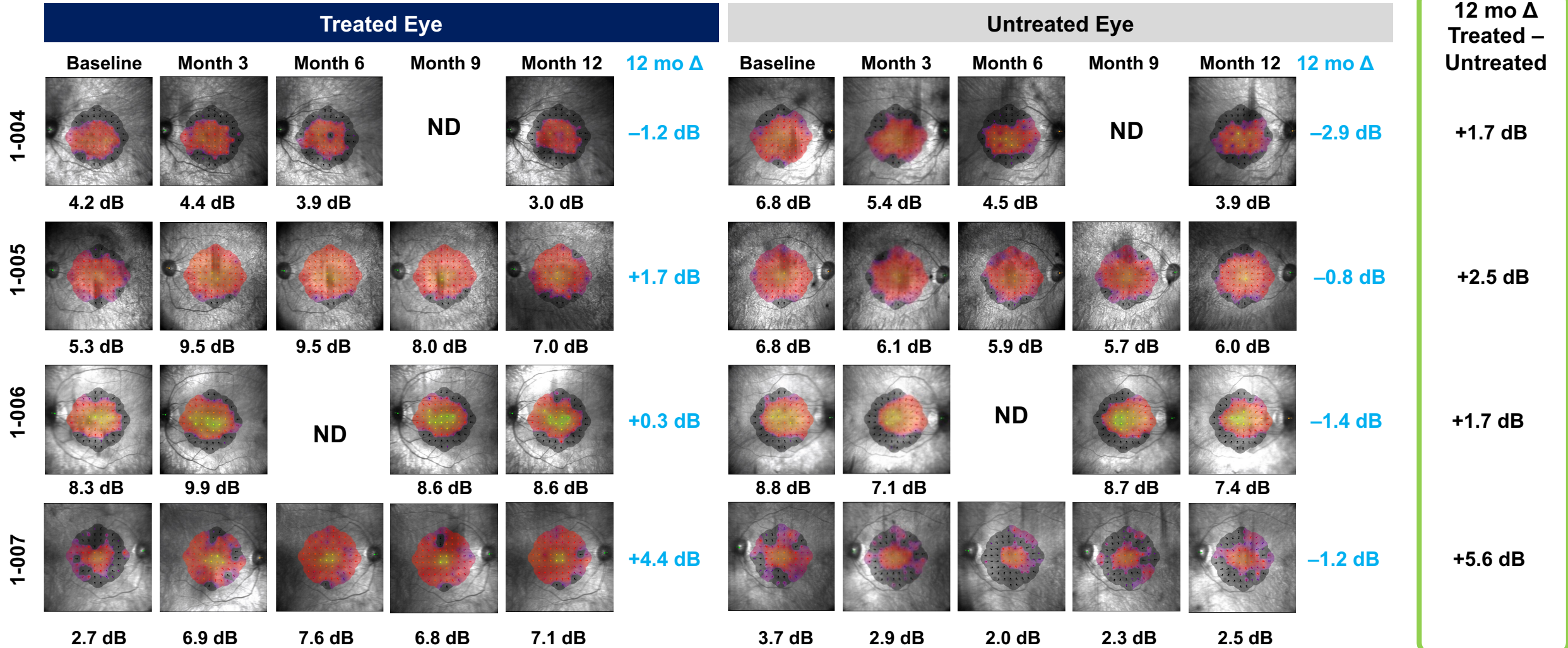
Excludes one patient with panuveitis in the low-dose cohort.

1. Michaelides, M et al. Presentation at the American Academy of Ophthalmology (AAO) 2020 Virtual Annual Meeting, Nov 13–15.



Retinal Sensitivity Improvements on Mesopic Microperimetry: Intermediate-dose Cohort at Month 12¹

Dose-escalation Phase



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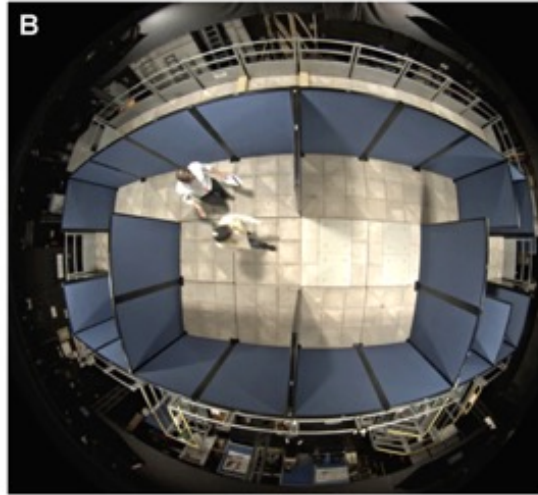
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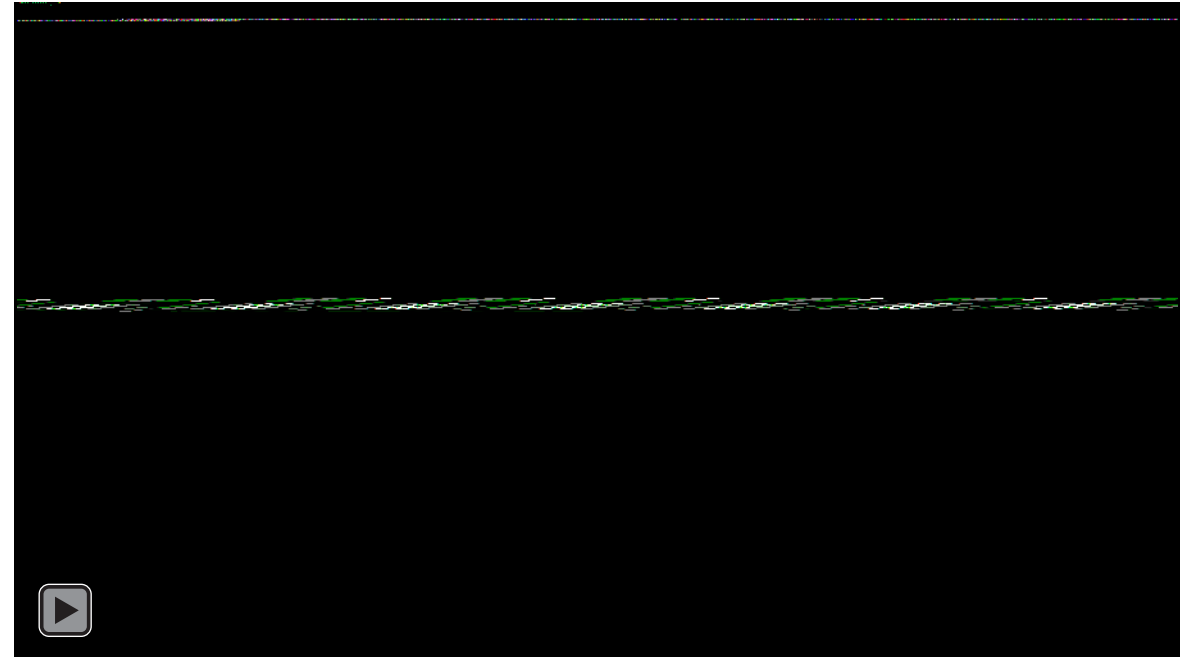
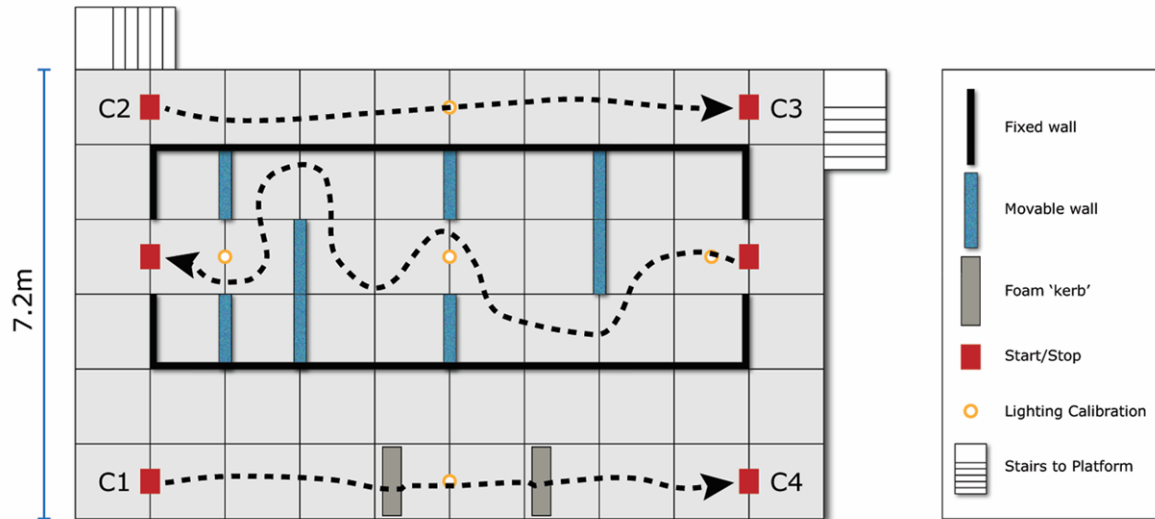


Functional Vision Assessment: Mobility Maze¹

Dose-escalation Phase



10.8m



Patient 01-007

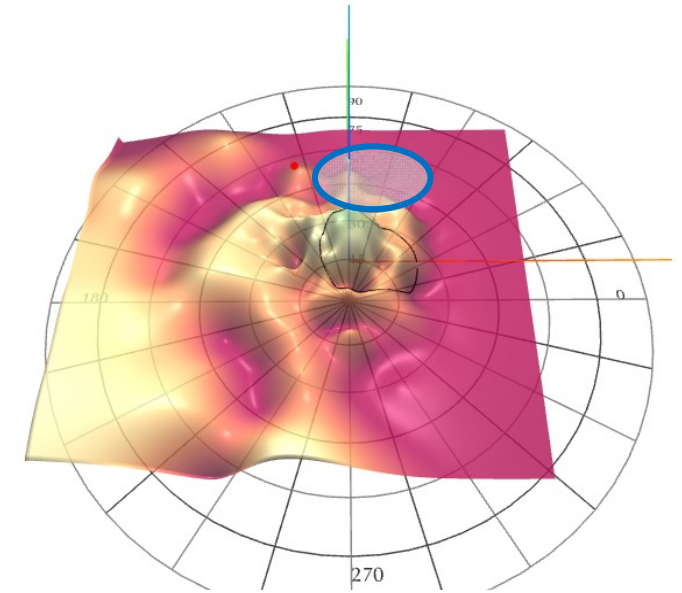
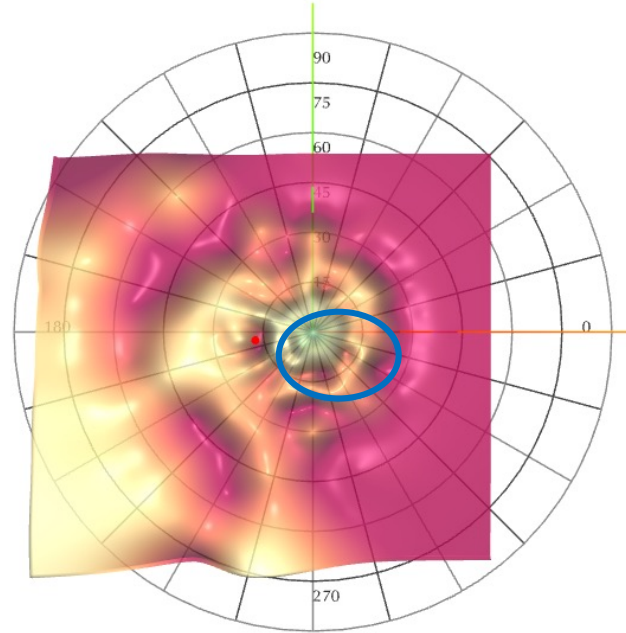
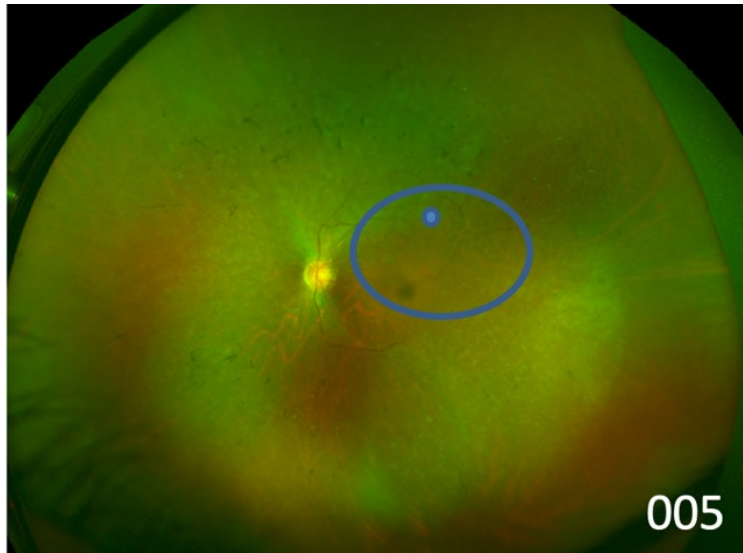
Maze assessment shown at 9-month timepoint.

- Light level: 1 lux
- Baseline performance: 61.7 seconds with 2 errors
- 9-month performance: 16.4 seconds with no errors

1. Michaelides, M et al. Presentation at the American Academy of Ophthalmology (AAO) 2020 Virtual Annual Meeting, Nov 13–15.



Bleb Overlay Subanalysis Methods



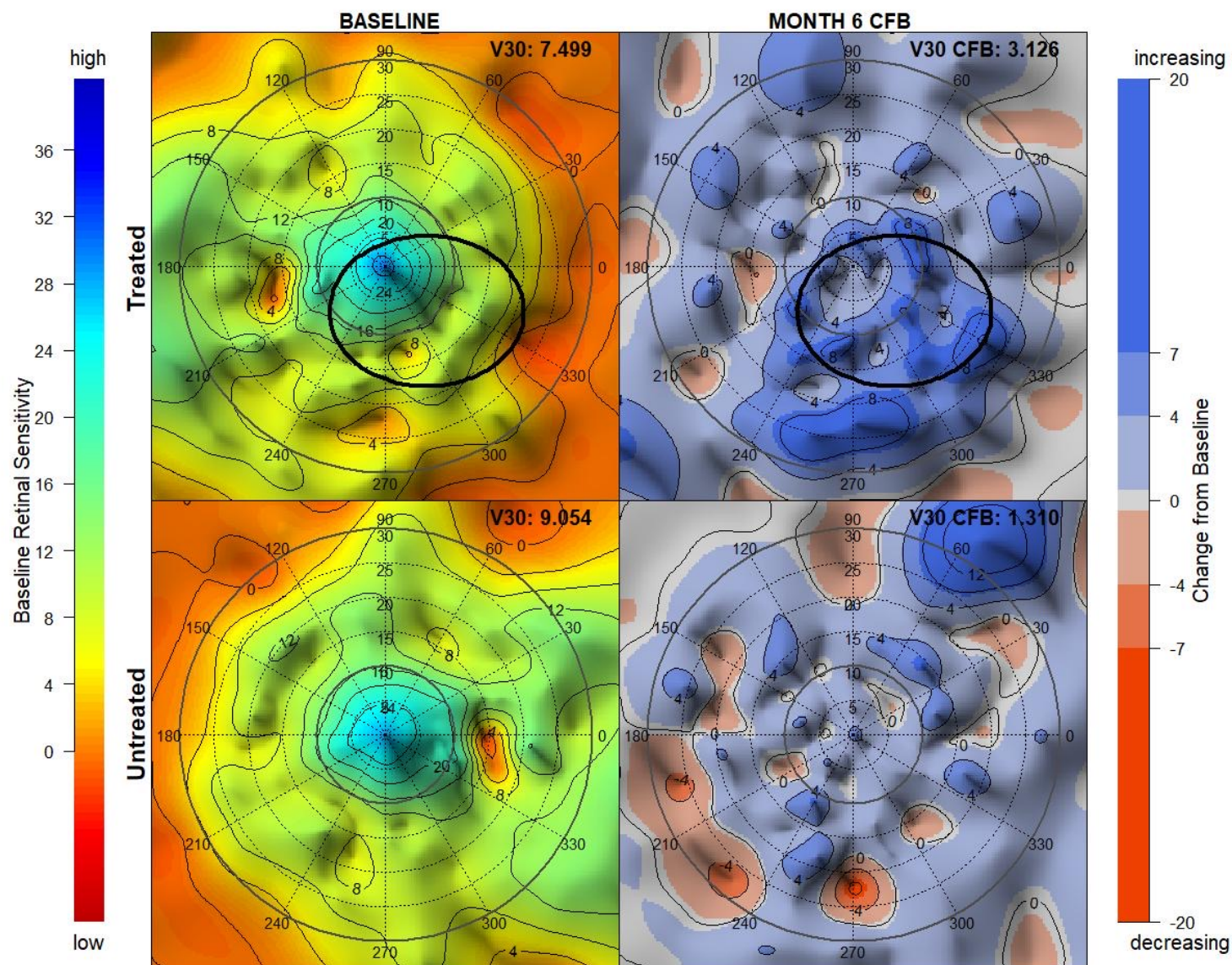
- Location/extent of bleb(s) was (were) documented with intraoperative video and delineated by the surgeon
- Hill of vision (HOV) surface was flipped 90 degrees vertically along the horizontal axis (for proper alignment) and superimposed onto the color fundus image
- Visual field center grid point in HOV map was aligned with the fovea location, and the 15-degree temporal point was aligned with the center of the optic nerve
- The HOV volumes were calculated within/outside the bleb(s) within 30-degree hill-of-vision (V30) at baseline through 6 and 12 months with fully automated custom software



Example of V30 Bleb Overlay: 6 months

Patient 01-005

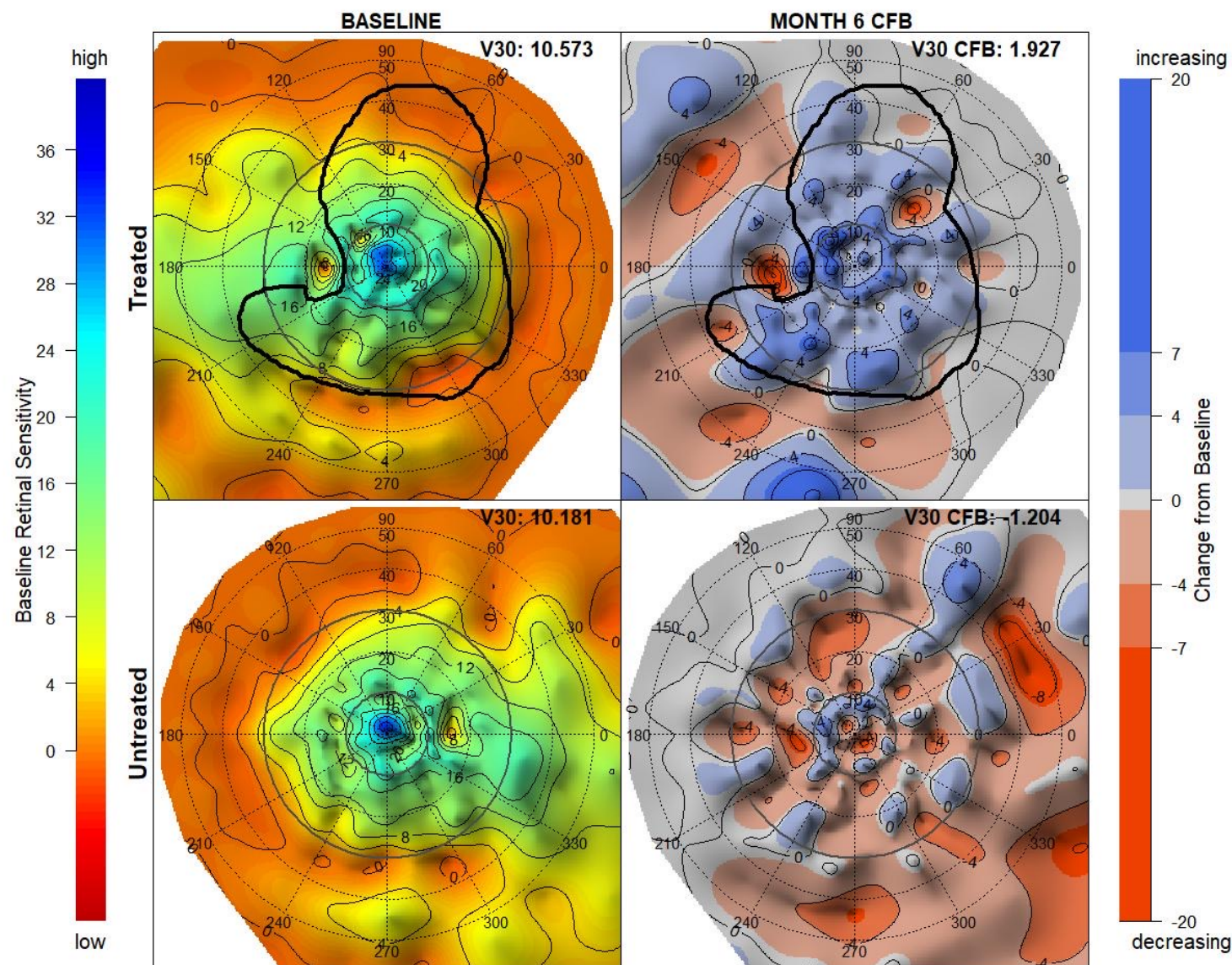
Escalation Cohort



Example of V30 Bleb Overlay: 6 months

Patient 02-022

Expansion Cohort



V30, 30-degree hill-of-vision.

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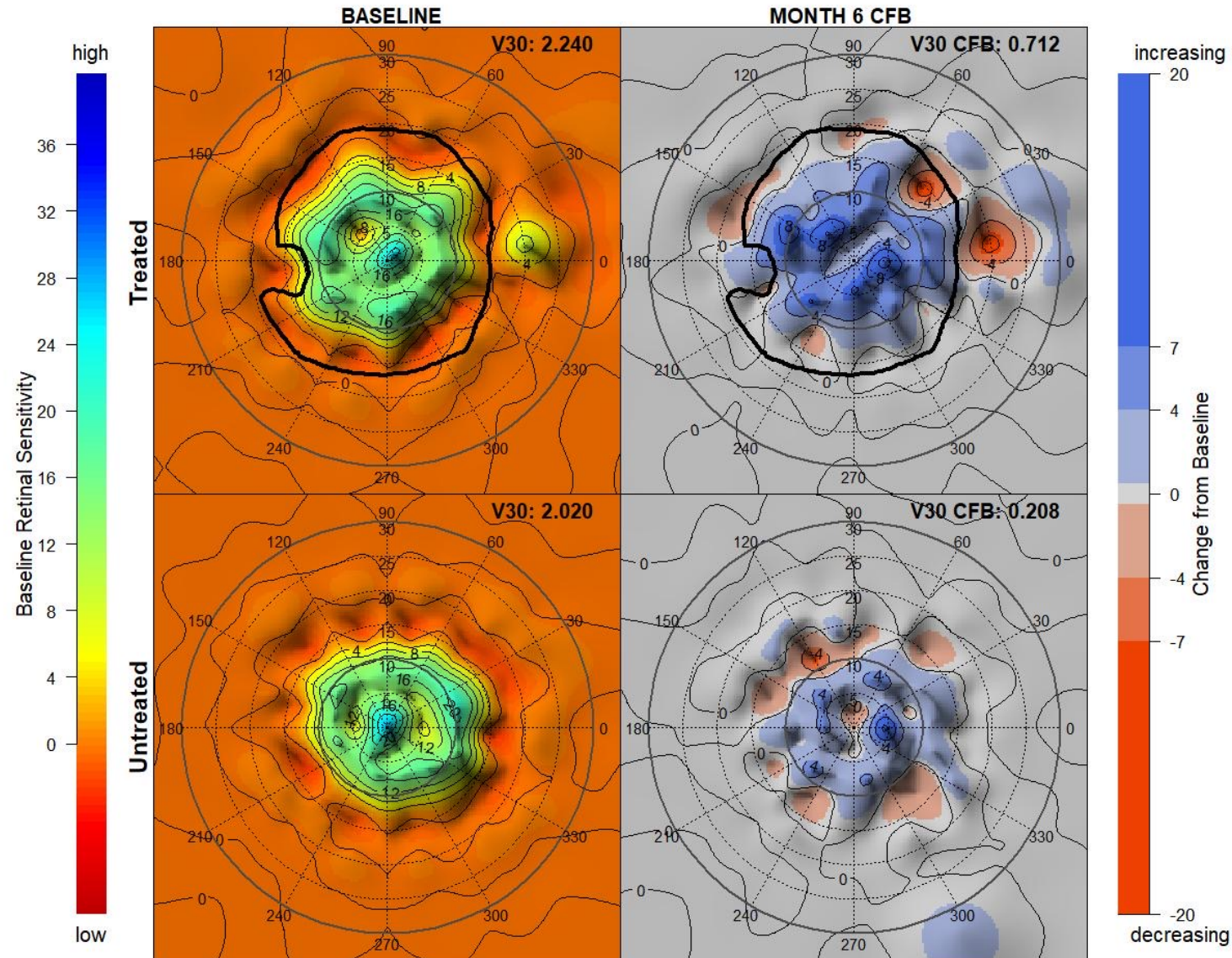
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Example of V30 Bleb Overlay: 6 months

Patient 02-028

Expansion Cohort



V30, 30-degree hill-of-vision.

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Conclusions

- Patients treated with the low- and intermediate-dose of AAV5-*RPGR* (botaretigene sparoparvovec) in MGT-009 achieved improvements in retinal sensitivity
- Individual patients demonstrated improved visual mobility at low light levels
- Exploration of the association between the location of AAV5-*RPGR* delivery and changes in retinal sensitivity was undertaken by overlaying bleb topography onto sensitivity heat maps
- Increases in baseline-subtracted retinal sensitivity after treatment indicate improvements in photoreceptor function, suggesting efficacy local to the treated area
- The treatment effect may extend beyond the margins of the bleb following surgery owing to subretinal extension before retinal reattachment
- Further development of this therapy is warranted
 - A phase 3 study of AAV5-*RPGR* is underway (NCT04671433)



Acknowledgments

- Participants and families
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- Trial funding: MeiraGTx and Janssen



OHSU, Oregon Health and Science University; MCW, Medical College of Wisconsin.

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