

LUCE-1: A First-in-Human Phase I/II Trial of AAVB-081 Gene Therapy Using Dual AAV Platform in Participants with Usher Syndrome Type 1B Retinitis Pigmentosa

Poster #
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Background

Usher Syndrome type 1B (USH1B) is caused by mutations in the *MYO7A* gene¹. Patients experience congenital hearing loss, vestibular dysfunction, and early onset Retinitis Pigmentosa². The large size of *MYO7A* poses a significant challenge for targeted gene therapies³.

AAVB-081, developed using a novel DNA recombination and splicing (dual hybrid) platform, efficiently delivers the *MYO7A* gene as two segments via separate vectors that are reassembled inside target cells⁴ (Fig 1).

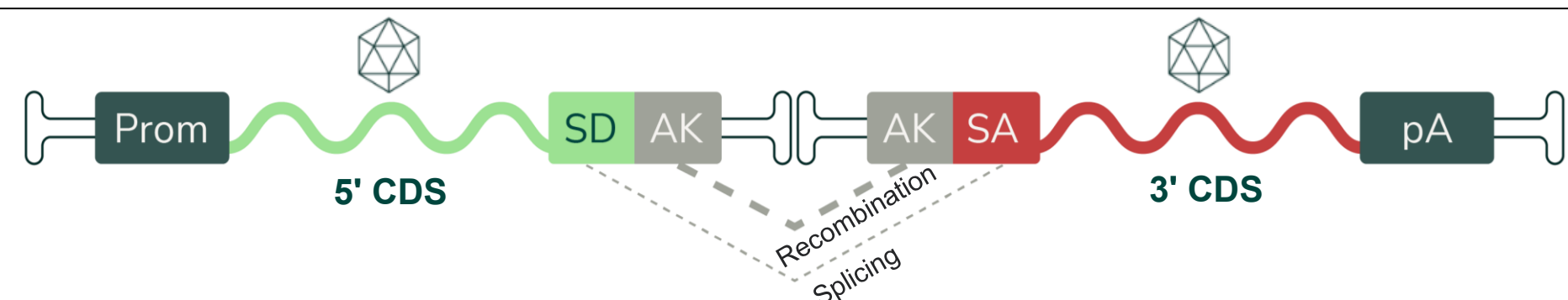
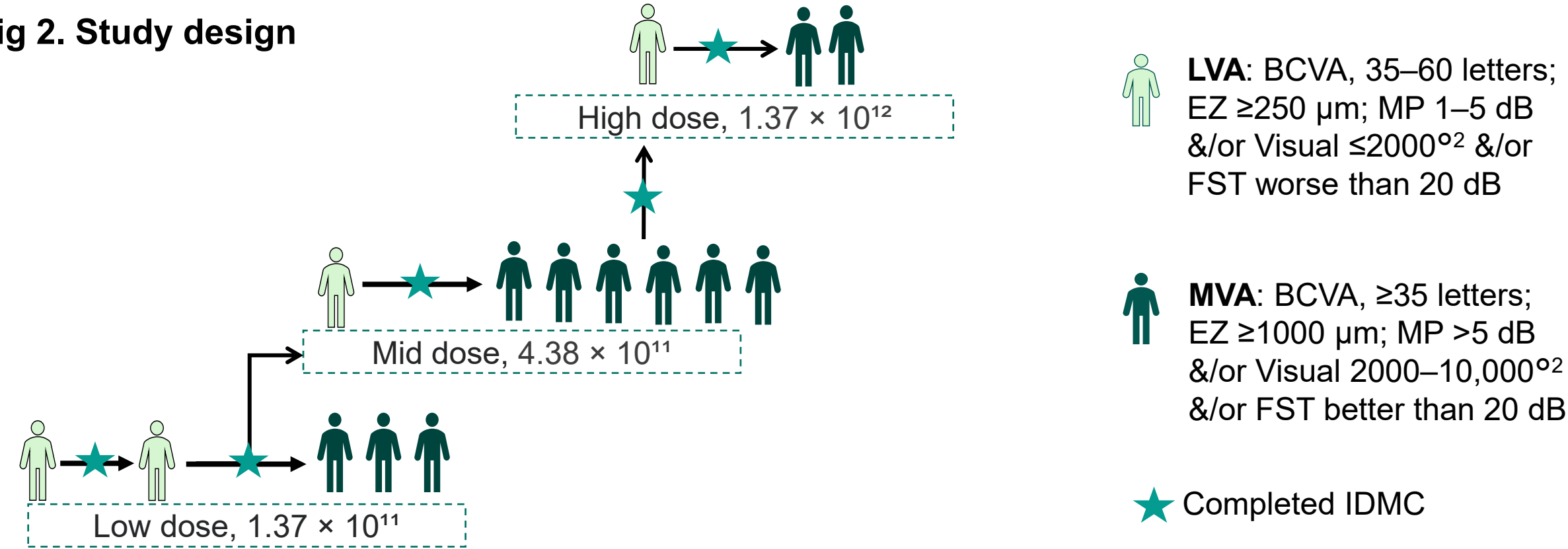


Fig 1. Schematic representation of AAV-based hybrid strategy for large gene transduction
Dotted lines show the splicing occurring between SD and SA; pointed lines show overlapping regions available for homologous recombination; empty horizontal bars represent the ITR sequences

Methods

- LUCE (NCT06591793) is a phase 1/2 open-label study designed to evaluate the safety and efficacy of AAVB-081 in participants with USH1B (Fig 2).
- Primary endpoint:** Incidence of AEs and SAEs over 52 weeks
- Secondary endpoints:** BCVA, LLVA, VF, FST, MP
- Adult (18–60 years) male/female participants with biallelic mutations in *MYO7A* were enrolled into two cohorts (N=15). Enrolment is completed.

Fig 2. Study design



Baseline demographics

Table 1. Baseline demographics

Characteristic	Low Dose (n=5)	Mid Dose (n=7)	High Dose (n=3)
LVA / MVA	2 / 3	1 / 6	1 / 2
Male / Female	3 / 2	1 / 6	2 / 1
Age, years ^a	40 (7.3)	32.3 (7.9)	40.3 (8.4)
Cochlear implant, %	80.0%	57.0%	67.0%
BCVA, letters ^a	59.4 (3.9)	71.4 (7.7)	69.6 (14.3)
LLVA, letters ^a	37.4 (24.3)	61.0 (11.4)	54.6 (23.3)
MP, dB ^a	1.5 (2.4)	7.0 (8.8)	3.4 (2.1)
Kinetic perimetry V4e, °2 ^a	5699.9 (7315.5)	809.0 (837.3)	736.4 (661.0)
EZ, microns ^a	665.0 (287.8)	2852.0 (2644.0)	1474.0 (931.0)
FST (White) ^a	-23.7 (6.7)	-46.28 (13.5)	-29.6 (19.6)
FST (Blue) ^a	-27.20 (6.65)	-50.56 (16.63)	-35.5 (20.34)
FST (Red) ^a	-26.35 (6.20)	-37.82 (7.46)	-26.07 (9.54)

^aValues are reported as mean (SD); the baseline is the median value of the triplicate pre-dose assessments for each test

Safety

- A total of 87 TEAEs were reported (24 systemic and 63 ocular)
- No SAEs** reported
- BCVA** has returned to pre-treatment level in most subjects
- No dose-limiting toxicities**
- No participant** has discontinued from the study

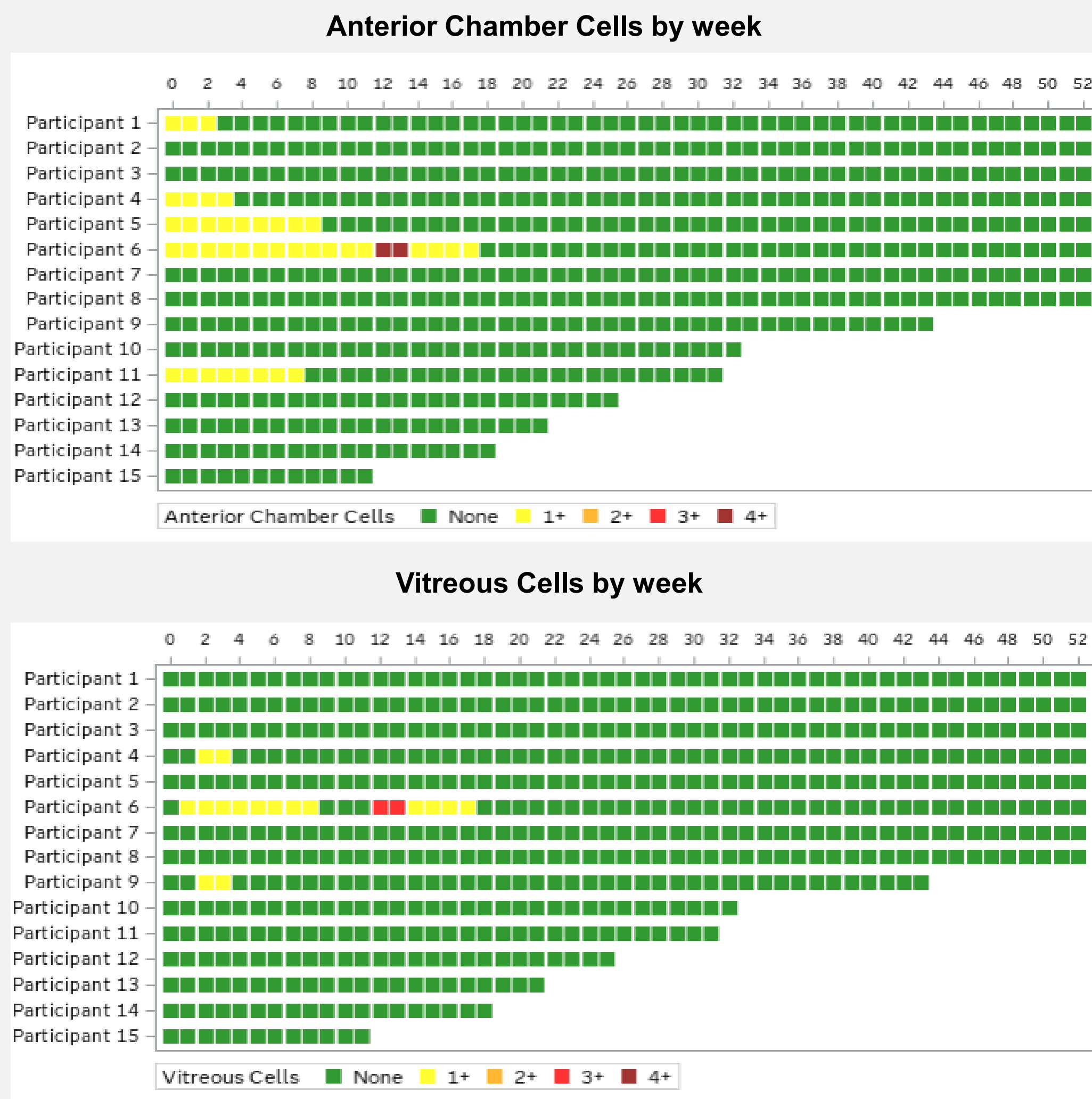


Fig 3. Number of anterior chamber and vitreous cells by week (DCO 25th March 2026)

Steroid Regimen: Day 0: 1 g of IV methylprednisolone + 1 mL sub-tenons steroid injection (40 mg); Oral steroids: Day -3 at 1 mg/ kg body weight and tapered over 16 weeks post-dosing; topical dexamethasone QID tapered over 1 month

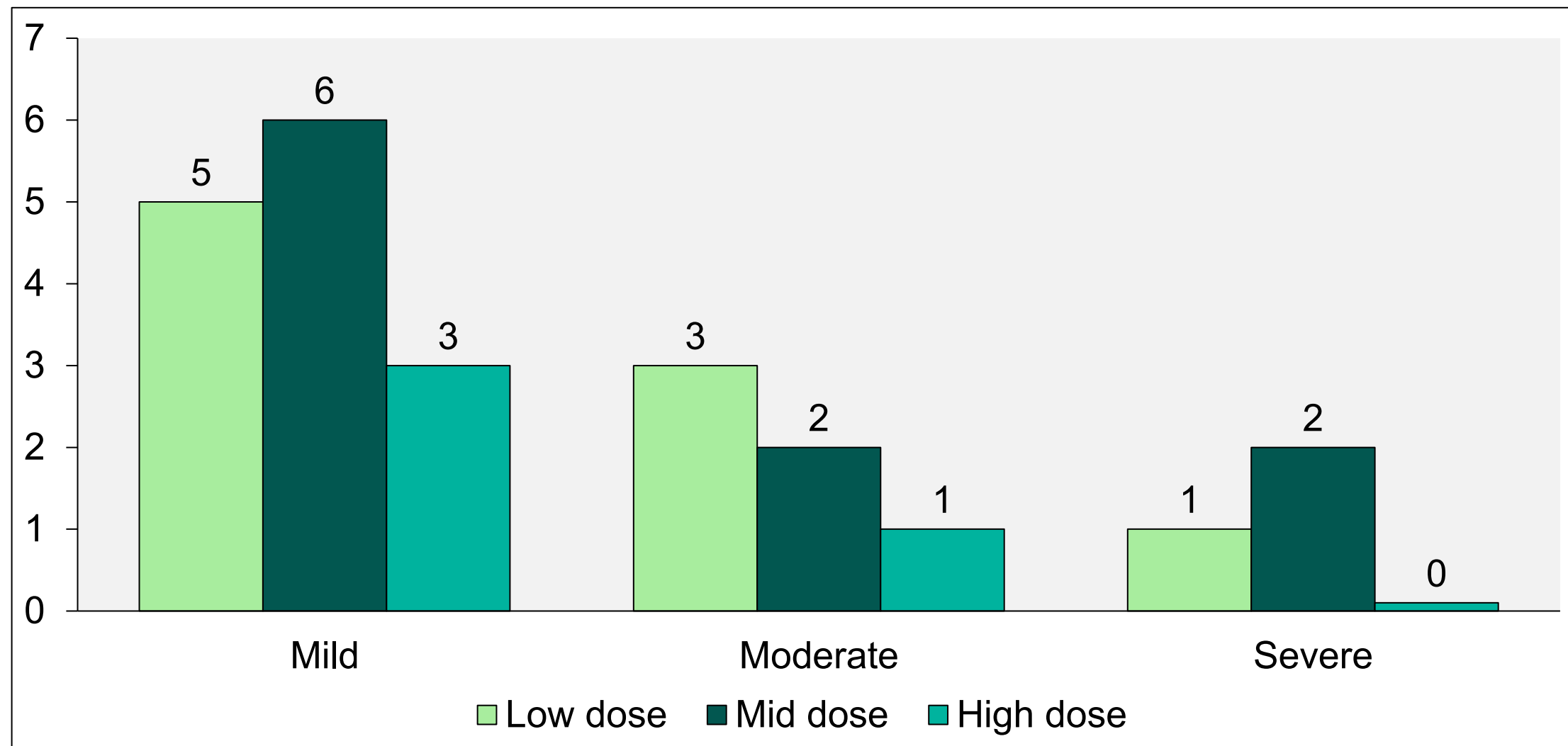


Fig 4. Number of participants experiencing ocular TEAEs in the Study Eye

Results

Efficacy (participants with ≥6 months follow-up)

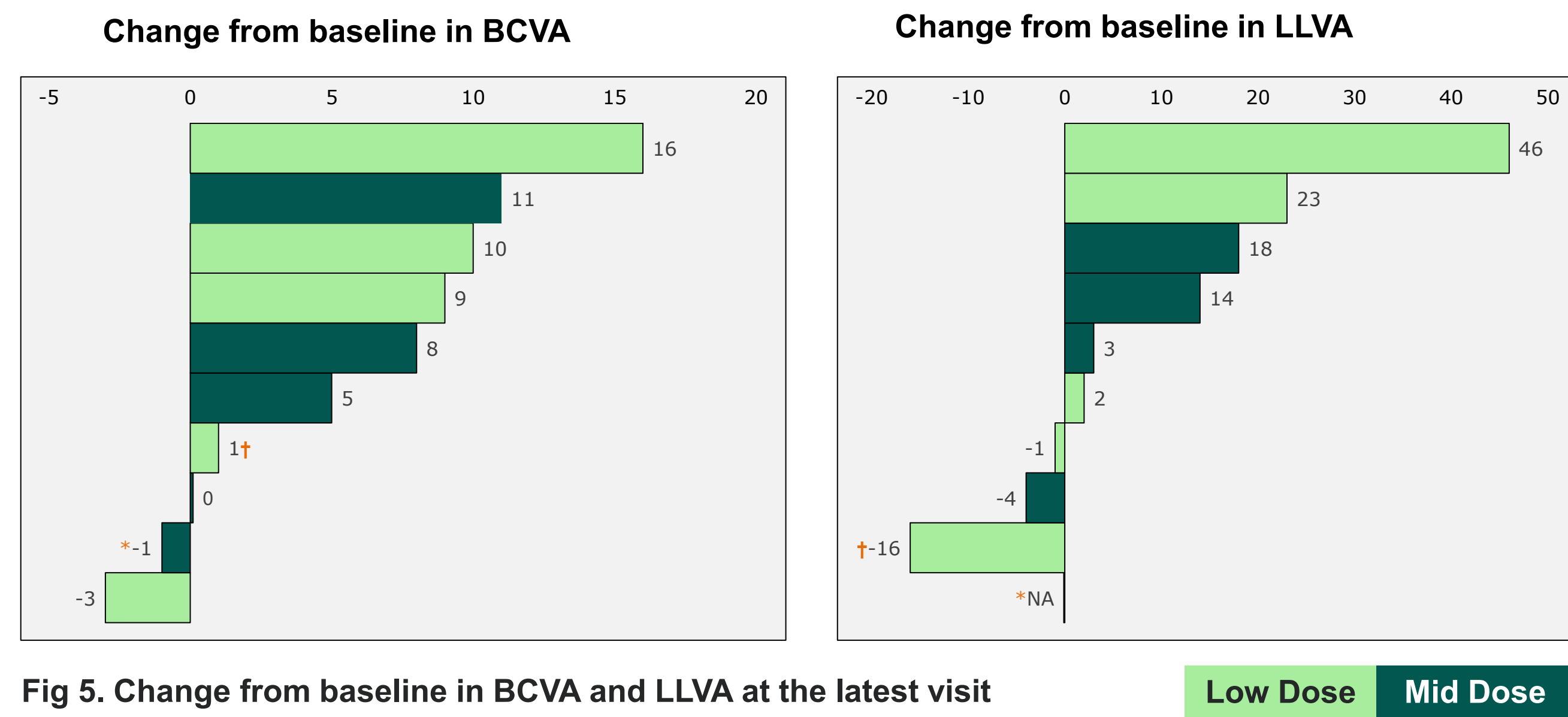


Fig 5. Change from baseline in BCVA and LLVA at the latest visit

† Participant with intraocular inflammation leading to ERM; * Participant with cataract; BCVA post-cataract; LLVA not measured post-cataract

Example of responding eye (improvement in BCEA95%)

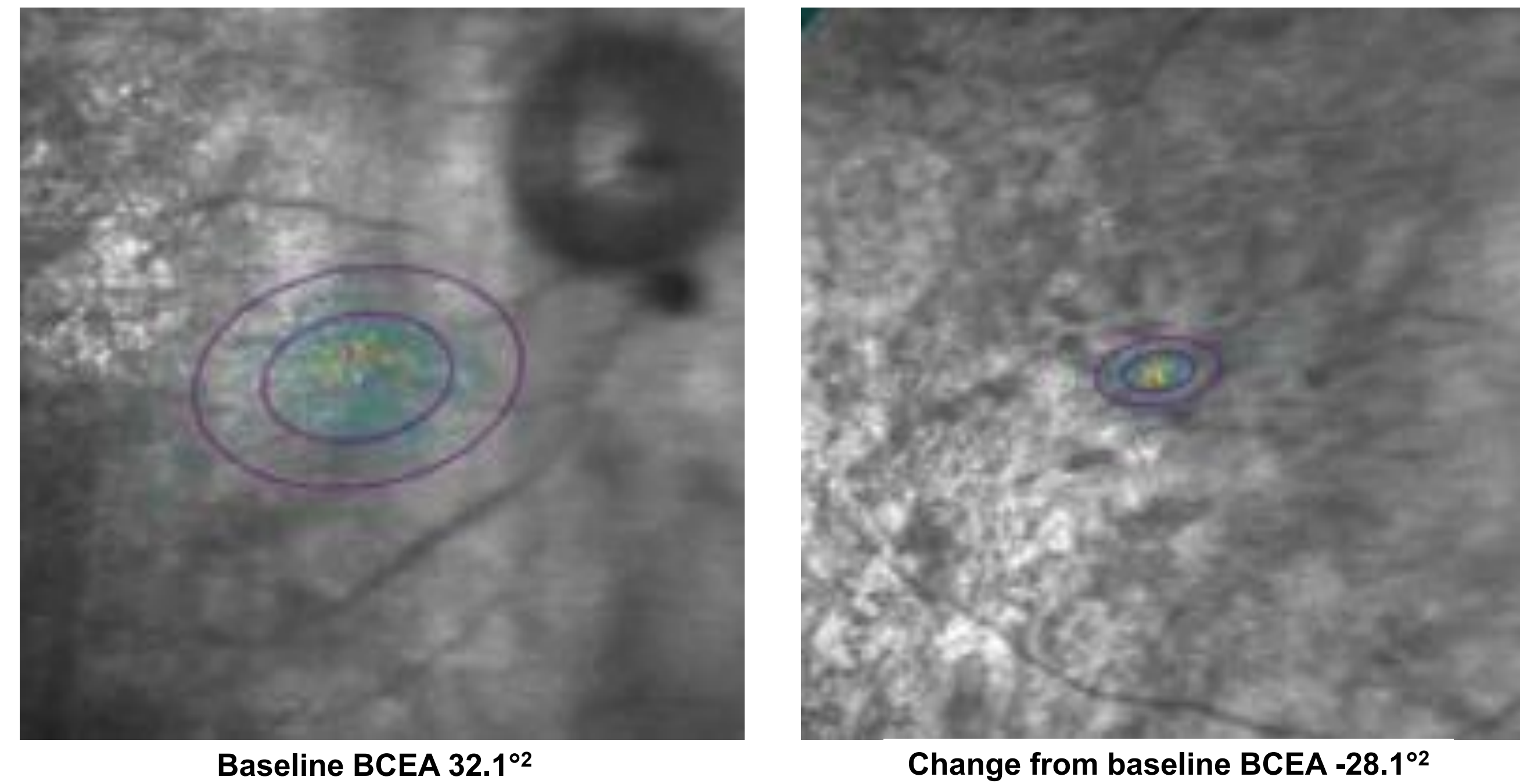


Fig 6. Example of improvement in BCEA95%(Participant #2)

Change from baseline at ≥6 months follow-up

Table 2. Change from baseline at key endpoints ≥6 months follow-up

Assessment	Low Dose (n=5)	Mid Dose (n=5)
BCVA, letters	6.6 (7.57)	4.6 (5.13)
LLVA, letters	10.8 (24.10)	2.0 (15.54)
MP, dB	-0.66 (0.684)	0.20 (0.628)
BCEA area 95%, °2	-1.88 (17.881)	20.08 (47.652)
Kinetic perimetry V4e, °2	104 (3107.3)	-507 (922.3)
FST (White)	2.4 (4.45)	0.4 (2.28)
FST (Blue)	3.14 (5.16)	-0.96 (2.64)
FST (Red)	2.49 (4.87)	0.60 (2.10)

Values are reported as mean (SD); the baseline is the median value of the triplicate pre-dose assessments for each test

Summary

- Encouraging efficacy signals in participants with ≥6 months follow-up in low & mid doses:
- ≥1 line **BCVA improvement** observed in 6 participants;
 - 3 had ≥ 2 lines of improvement
- ≥ 1 line **LLVA improvement** observed in 4 participants;
 - 3 had ≥ 3 lines of improvement
- Improvement in **MP BCEA 95% fixation stability** in 7 participants

Conclusion

AAVB-081 shows a consistent safety profile with encouraging visual function improvements supporting continued clinical development in USH1B

Disclosures

FS (C,R), MMi (C,R), PES (C,R), FT (C,R), VDI (C,R), KX (C,R), CT (R), RH (C,R), JS (E), IM (E), NM (E), MMu (E), EK (E), MDC (C,R), PM (N), SR (N), AA (O,P)

Abbreviations

AAV, adeno-associated virus; AC, anterior cell; AE, adverse event; AK, F1 phage recombinogenic region; BCEA, bivariate contour ellipse area; BCVA, best-corrected visual acuity; CDS, MYO7A gene coding DNA sequence; CRA, chorioretinal atrophy; dB, decibel; DCO, data cut-off; DNA, deoxyribose nucleic acid; ERM, epiretinal membrane; EZ, ellipsoid zone; FST, full field stimulus; IDMC, Independent Data Monitoring Committee; IV, intravenous; LLVA, low luminance visual acuity; LVA, low visual ability; MP, microperimetry; MVA, medium visual ability; MYO7A, myosin 7A gene; NA, not applicable; pA, bovine growth hormone polyadenylation signal; Prom, chimeric promoter, including cytomegalovirus enhancer and chicken beta actin minimal promoter; QID, four times a day; SA, splicing acceptor signal; SAE, serious adverse event; SD (in Fig 1), splicing donor signal; SD, standard deviation; TEAE, treatment-emergent adverse event; USH1B, Usher syndrome type 1B

References

- D'Esposito F, et al. *Genes* 2025; 16:332; 2. Toms M, et al. *Ther Adv Ophthalmol.* 2020;12; 3. Sanie-Jahromi F, et al. *Exp Eye Res.* 2022;217:108961; 4. Ferla R, et al. *Mol Ther Methods Clin Dev.* 2023;28:396-411

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