

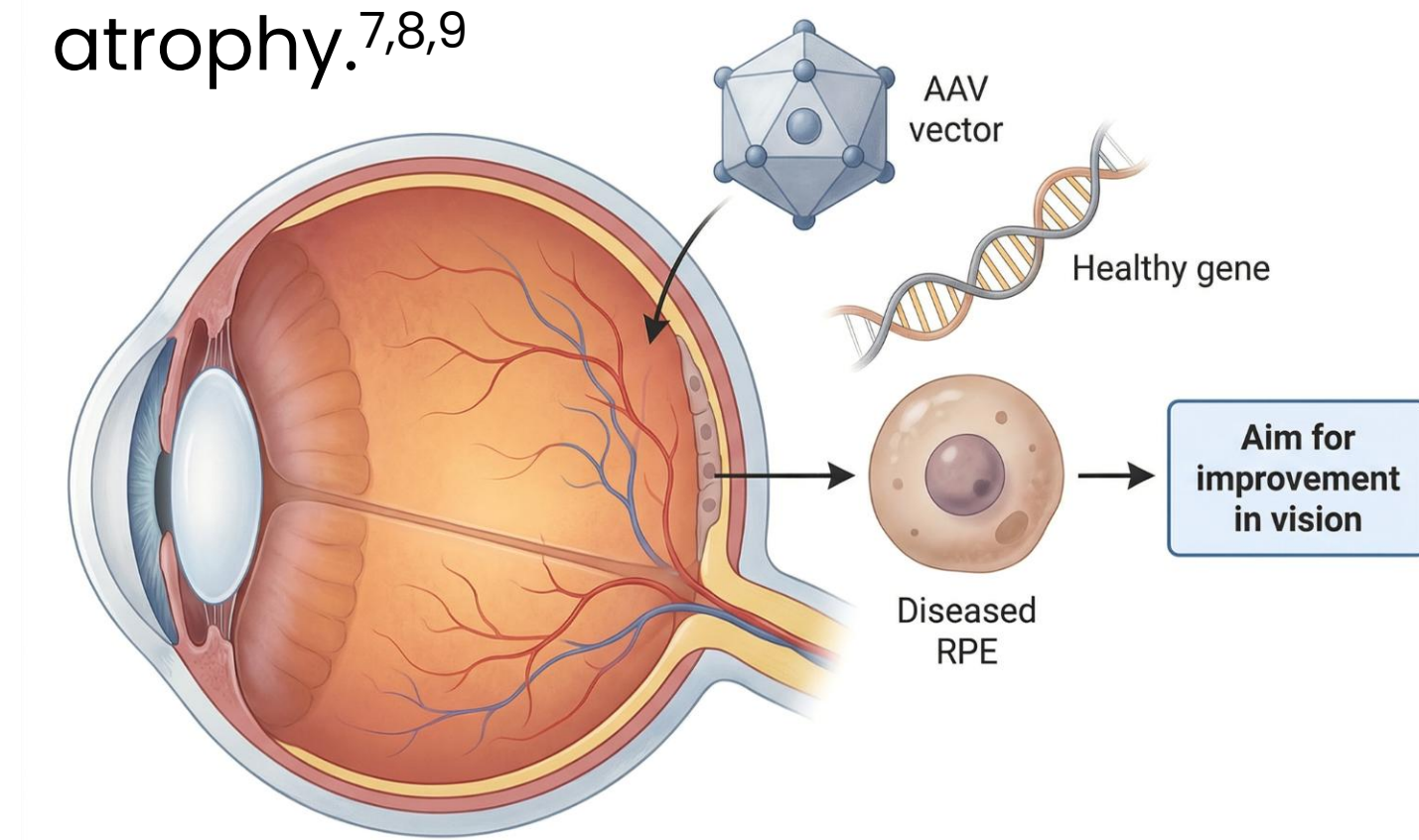
Real-world paediatric outcomes of Voretigene Neparvovec for RPE65 mediated retinal dystrophy: A single-centre case series

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2. No financial interest to declare in the material presented

1 INTRODUCTION

RPE65-mediated retinal dystrophy is an autosomal recessive condition causing nyctalopia and impaired visual development from childhood.^{1,2} Voretigene neparvovec is the first licensed ocular gene therapy for patients with biallelic RPE65 mutations.^{3,4} Children are a distinct treatment group due to visual system neuroplasticity.^{5,6} There have been previously reported complications such as inflammation and progressive chorioretinal atrophy.^{7,8,9}



This study reports real-world paediatric outcomes from a UK tertiary centre, focusing on functional vision, amblyopia-related effects and inflammatory complications

2 METHOD

Retrospective Case Series (2021-2025)

Children aged ≤16, Biallelic RPE65-mediated retinal dystrophy

Treatment:
Subretinal Voretigene Neparvovec

Primary Outcomes

Best-corrected visual acuity (logMAR)
Functional vision (patient/parent report)
Electrodiagnostic testing

Secondary Outcomes

Amblyopia or strabismus
Intraocular inflammation
OCT-defined retinal structural changes

3 RESULTS

Six paediatric patients (11 eyes) were included, with a median age at treatment of 8.5 years (range 4-16). Mean follow up duration was 3.8 years (range 1-5 years). Mean change in best-corrected visual acuity was +0.01 logMAR, with improvement or stability observed in 72% of eyes (Table 1). Despite modest overall mean improvement, at least one eye improved in 4 of 6 patients, and functional visual benefit was reported by most families.

Table 1: Results summary

Patient	Eye	Age at surgery (years)	Baseline BCVA (logMAR)	Post surgery BCVA (logMAR)	Change from baseline (logMAR)
1	Left	8	1.30	0.78	+0.52
2	Right	4	1.20	0.125	+1.08
2	Left	4	1.10	1.78	-0.68
3	Right	16	1.30	1.30	0.00
3	Left	16	1.30	1.30	0.00
4	Right	5	0.56	0.56	0.00
4	Left	5	0.60	0.60	0.00
5	Right	9	0.80	0.80	+0.02
5	Left	9	0.80	0.80	+0.04
6	Right	13	0.30	0.68	-0.38
6	Left	13	0.40	0.90	-0.50

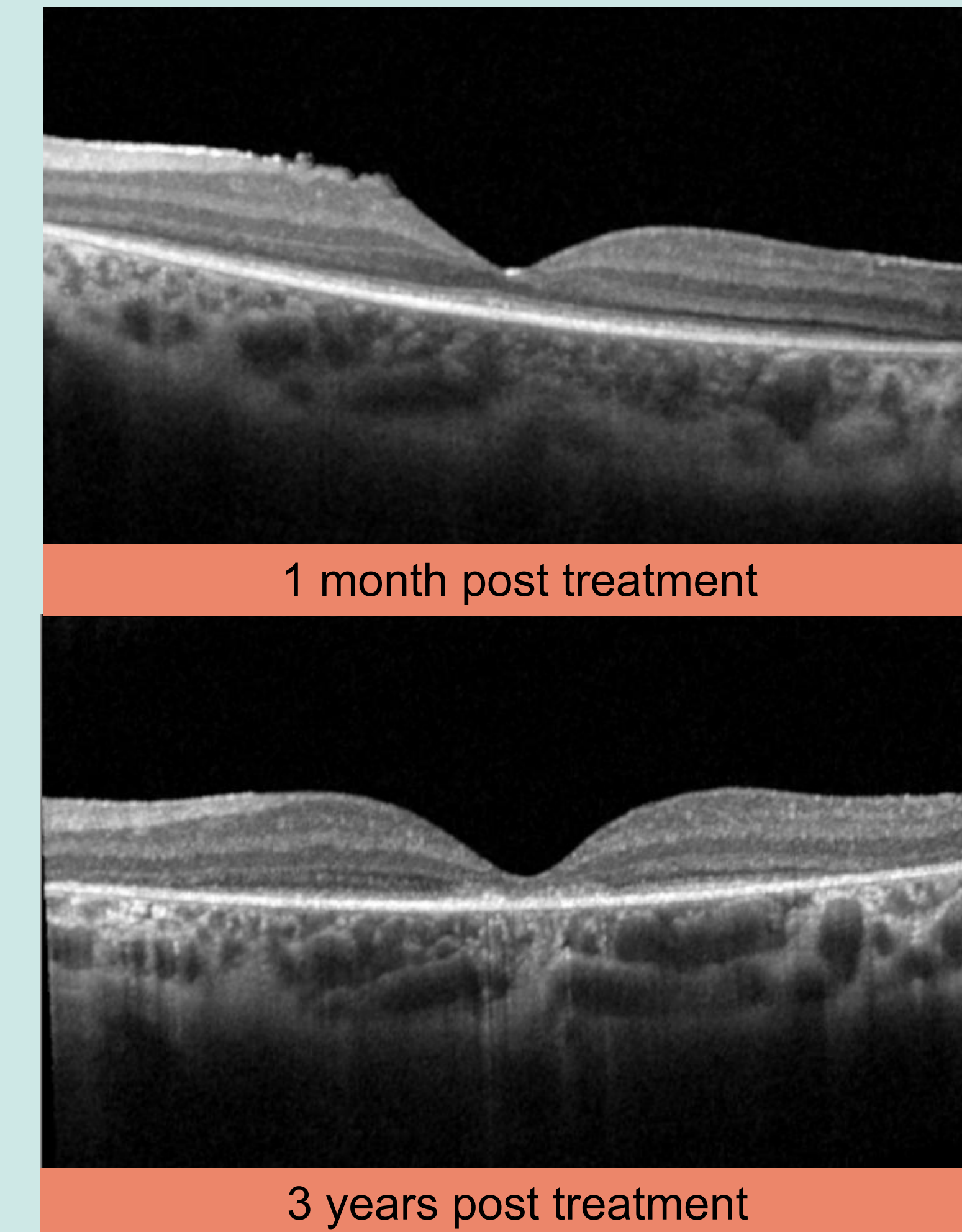
Amblyopia and binocular effects

One child (with eyes treated eight months apart) developed reverse amblyopia with manifest esotropia. There was poor compliance with occlusion therapy, and the reverse amblyopia has persisted at the latest follow up. This may reflect the interaction between gene therapy and visual development in early childhood. Considerations should be given to the timing of treatment for children of an amblyogenic age.

Inflammation and structural changes

Two eyes (18%) developed post-operative intraocular inflammation, which resolved with corticosteroid therapy. One adolescent developed late foveal ellipsoid zone atrophy with visual decline. In this adolescent, baseline and immediate post-operative OCT showed preserved foveal ellipsoid zone integrity, with ellipsoid zone atrophy emerging only on long-term follow-up at least three years after treatment (Figure 1).

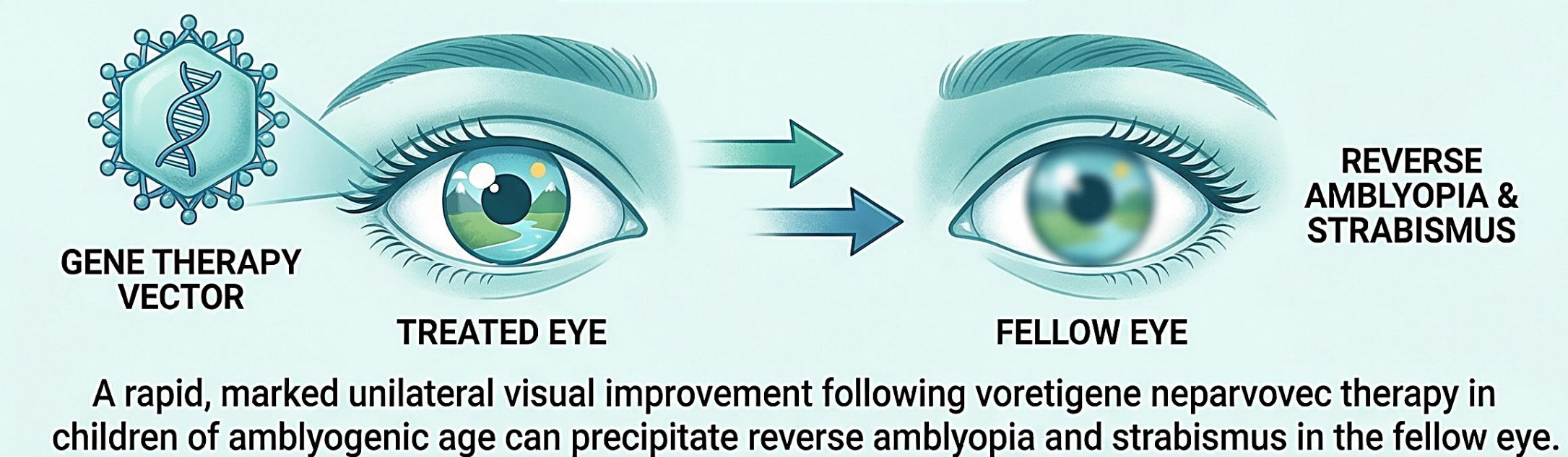
Figure 1: Pre-operative and post-operative OCT
Highlighting the late ellipsoid zone atrophy in one patient three years post surgery.



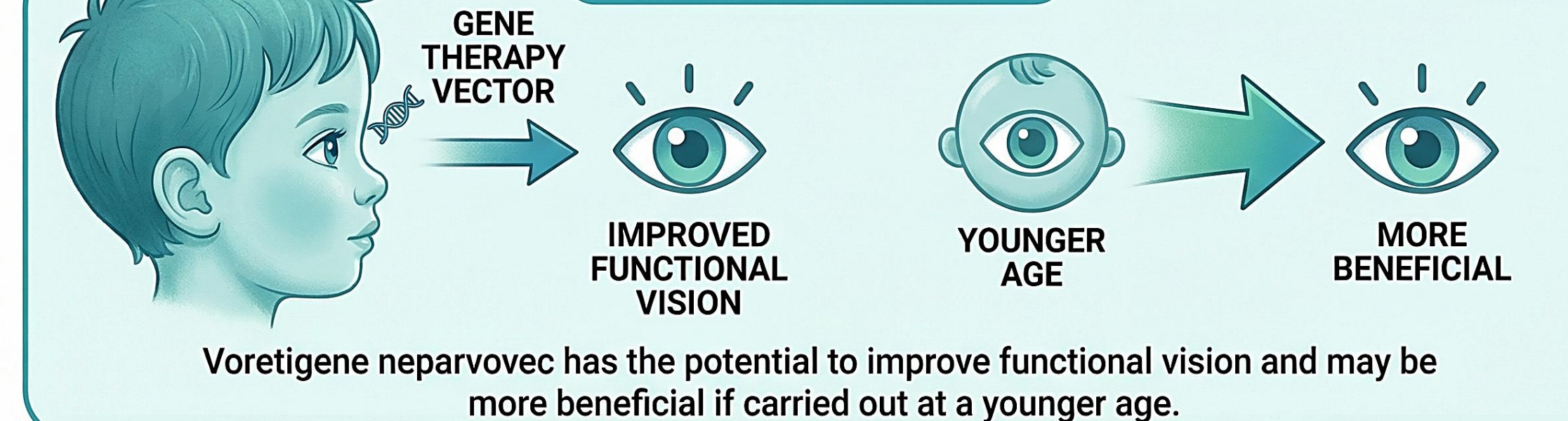
4 DISCUSSION

Reverse amblyopia following asymmetric visual recovery represents a distinctly paediatric complication that has not been reported in clinical trials. In this cohort, one of six children developed reverse amblyopia following sequential bilateral treatment. While amblyopia is recognised as a confounder in inherited retinal disease,^{10,11} the interaction between gene therapy-induced visual improvement and binocular visual development remains poorly understood. These findings emphasise the importance of early orthoptic involvement and close monitoring after treatment in younger children.

KEY LEARNING POINT 1



KEY LEARNING POINT 2



5 CONCLUSION

Voretigene neparvovec provides clinically meaningful functional visual benefit in children with RPE65-mediated retinal dystrophy in a real-world setting. However, paediatric-specific factors such as amblyopia may influence durability.

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