Five-year update for the Phase III voretigene neparvovec study in biallelic RPE65 mutation–associated inherited retinal disease

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INTRODUCTION

Voretigene neparvovec (VN) is the first ocular gene therapy approved in multiple countries including the USA and Europe for treating patients (pts) with visual impairment due to confirmed biallelic *RPE65* mutation-associated inherited retinal dystrophy having sufficient viable retinal cells. Presented here is a five year update from the open label, randomized, controlled Phase III trial performed at 2 sites in the United States

PURPOSE

To determine whether ambulatory navigation, light sensitivity, and visual field (VF) improvements 1 year after voretigene neparvovec (VN) administration in patients with biallelic *RPE65* mutation-associated inherited retinal dystrophy (IRD) are maintained at 5 years and review safety outcomes over the entire period

METHODS

This was an open label, randomized, controlled Phase III trial performed at 2 sites in the United States (Figure 1)

Trial Design

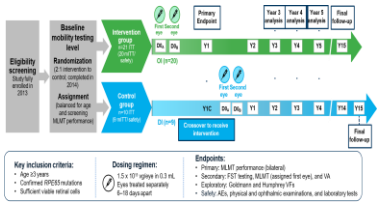

Figure 1: Trial design

RESULTS

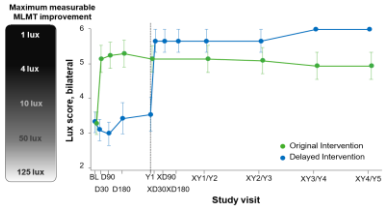

Figure 2: Mean bilateral MLMT change scores over five years

Primary endpoint (Figure 2)

Mean (SD) bilateral MLMT change score

- 1.6 (1.1) levels at Year 5 for OI subjects (n=18)
- 2.4 (1.5) levels at Year 4 for DI subjects (n=8)

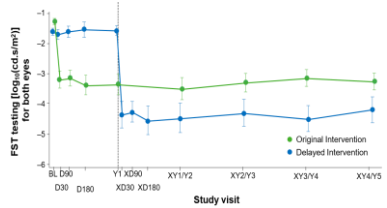

Figure 3: Mean (SD) change in white light FST in $\log_{10}$(cd.s/m^2) averaged over both eyes

Secondary endpoint (Figure 3)

Mean (SD) change in white light FST in $\log_{10}$(cd.s/m^2) averaged over both eyes:

- −2.02 (1.45) at Year 5 for OI subjects (n=17)
- −2.58 (1.04) at Year 4 for DI subjects (n=8)

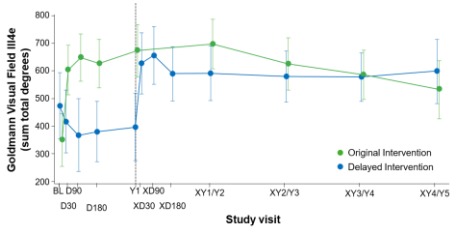

Figure 4: Mean (SD) change in Goldmann VF III4e sum total degrees averaged over both eyes:

Exploratory endpoint (Figure 4)

Mean (SD) change in Goldmann VF III4e sum total degrees averaged over both eyes:

- 166.6 (208.7) at Year 5 for OI patients (n=15)
- 178.8 (241.9) at Year 4 for DI patients (n=8)

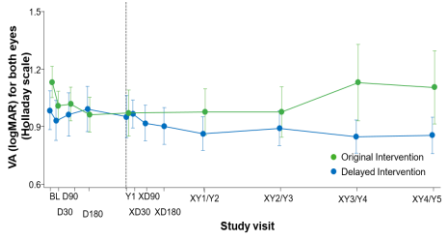

Figure 5: Mean (SD) change from BL in VA averaged over both eyes:

Secondary endpoint

Mean (SD) change from BL in VA averaged over both eyes:

- −0.00 (0.64) at Year 5 for OI patients (n=18)
- −0.06 (0.26) at Year 4 for DI patients (n=8)

Safety

New ocular AEs from Year 4 to Year 5:

- 1 cataract, 1 retinal detachment; both non-serious, probably related to procedure

Cumulative ocular SAEs included through Year 5 follow-up:

- Loss of foveal function related to the administration procedure in one patient (DI group)

Retinal detachment was observed 4 years after treatment administration in one patient (OI group).

Common non serious ocular AEs assessed as related to voretigene neparvovec subretinal injection procedure by Primary Investigator

Reported in ≥3 patients

- Cataract, 11 events in 6 (21%) patients
- IOP increase, 6 events in 4 (14%) patients
- Retinal tear, 3 events in 3 (10%) patients

Nonserious ocular AEs assessed as related to voretigene neparvovec by the Primary Investigators:

- Retinal deposit, 3 events in 3 (10%) patients

CONCLUSIONS

- Improvements in ambulatory navigation, light sensitivity, & VF are generally maintained for at least 5 years after voretigene neparvovec administration in most OI patients
- Improvements in DI patients were consistent with those observed in OI Patients
- Safety profile of voretigene neparvovec is consistent with the administration procedure and no deleterious immune responses were reported

References:

1. Russell S, et al. *Lancet*. 2017;390:849-860
2. Russell S, et al. 53rd Annual Scientific Meeting Retina Society 2020 VR; September 21–22, 2020.

Financial Disclosures

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