Voretigene neparvovec (AAV2-hRPE65v2) gene therapy for inherited retinal dystrophy - 2017

THE LENS

Objective

To assess efficacy and safety of voretigene noriparvovec gene augmentation therapy in patients with *RPE65*-mediated inherited retinal dystrophy

Methods

Design: Randomized, controlled, open-label, phase 3 trial

Sample Size: N = 31

- 3 years and older with best corrected VA of 20/60 or worse, or visual field less <20 degrees, with biallelic *RPE65* mutations

Treatment Groups:

- 21 to bilateral subretinal injection of $1.5x10^{11}$ vg
- 10 to control

Outcome Measures:

- 1-year change in multi-luminance mobility testing (MLMT) performance

Results

Point 1: Voretigene neparvovec intervention led to rapid and significant improvement in ability to navigate in low-medium light conditions

- At 1 year, mean bilateral MLMT change score for intervention group was 1.8 (SD 1.1) and control group was 0.2 (SD 1.0), with a difference of 1.6 (95% CI 0.72 - 2.41, p = 0.0013)
- 13/20 (65%) of intervention subjects demonstrated the maximum MLMT improvement possible at 1 year
- MLMT score improved in the intervention group by day 30 post-injection and remained stable through 1 year

Point 2: Secondary measures of retinal and visual function also demonstrated rapid and substantial improvements

- Light sensitivity (FST) had a >2 log units improvement compared to controls
- Mean sum total degrees of visual field nearly doubled in the intervention group

Point 3: This was the first randomized, controlled, phase 3 study of a gene therapy for a genetic disease, a major advancement in the field

TLDR: Voretigene neparvovec gene replacement improved functional vision in *RPE65*-mediated inherited retinal dystrophy that had been previously medically untreatable.

Russell S, et al. Efficacy and safety of voretigene neparvovec (AAV2-hRPE65v2) in patients with RPE65-mediated inherited retinal dystrophy: a randomised, controlled, open-label, phase 3 trial. Lancet. 2017;390(10097):849-860. doi:10.1016/S0140-6736(17)31868-8.