LIGHT - Observational study on the use of voretigene neparvovec (VN) in patients with inherited retinal dystrophy (IRD) at CHNO des Quinze-Vingts: a 1-year follow-up safety and efficacy results (250 characters)

Authors

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General information – Purpose (100 words)

RPE65-related IRD is a rare condition caused by biallelic mutations in the *RPE65* gene. Loss of RPE65 function causes photoreceptor dysfunction and degeneration, leading to blindness. VN was the first gene therapy indicated for treatment of IRD patients with sufficient viable retinal cells and confirmed biallelic *RPE65* mutations. The Centre Hospitalier National d'Ophtalmologie (CHNO des Quinze-Vingts in Paris was the first European center to use VN and has so far one of the largest cohorts and longest follow-up in Europe. The purpose of the LIGHT study was to report the one-year safety and efficacy outcomes of patients treated with VN.

Setting / Venue (50 words)

The LIGHT study is a descriptive, non-interventional study with secondary use of data of patients with RPE65-related IRD, treated with VN at CHNO des Quinze-Vingts between December 2018 and November 2019 and with at least a 1-year follow-up period. Data were collected from patients' medical records.

Methods (200 words)

VN was administered at a dose of 1.5 x 10^{11} vector genomes, delivered in a total subretinal volume of 0.3 ml. The administration to each eye was performed on separate days, no fewer than 6 days apart. Baseline visit was defined as the last visit before the surgery and patients were followed according to routine visits at 1, 3, 6 and 12 months after the surgery of the second eye. The data collected aimed to evaluate efficacy, safety and to describe exploratorily the patients' experience after surgery.

Efficacy was assessed by (1) visual function, using visual acuity (VA), full-field stimulus threshold (FST) and visual field (VF);

(2) functional vision, using a maze platform called Streetlab® that represents a daily life street and include elements of varying contrast and volume. Patients were instructed to follow the path under four lighting conditions (2, 7.5, 50 and 500 lux), while avoiding obstacles and walls. Mobility was assessed by parameters such as the PPWS (Percentage of Preferred Walking Speed) and the course completion time.

Patient's experiences were described with verbatims collected by the medical team just after surgery and at different timepoints. They were classified into the categories defined by Kay *et al.*.

Results (200 words)

Data from 12 patients aged 4-35y (6 adults and 6 children) were collected. Eleven had a diagnosis of Leber Congenital Amaurosis and one of Retinitis Pigmentosa. All of them underwent surgeries in both eyes.

At 1-month, FST presented a median (IQR) decrease of -33.2 (-33.7; -19.8) dB, and this improvement remained stable until the last assessment. No significant change was observed in VA and VF assessments. Functional vision assessment evidenced at 2 lux and at high speed, 1 month after surgery, an increase of PPWS in median(IQR) of 63.9% (47.8%; 88.5%) and the course completion time decreased of 47.23 % (-58.50 %; -41.16 %). The improvement remained overtime. The patient's verbatims classification highlighted three categories mentioned by more than 50% of the patients "Visual function symptoms", "Impact on vision dependent activities of daily living" and "Coping mechanisms and visual aids".

All patients experienced at least one adverse effect (AE) related to surgery and all except one (retinal detachment) were non-serious. 7 patients experienced at least one VN-related AE. All were non serious, reported in both eyes and none required corrective treatment. Chorioretinal atrophy was observed in both eyes of 5 patients and evaluated as possibly related to surgery and VN.

Conclusion (200 words)

This study is the first study to generate real-world data using such a large cohort of patients with a one-year period follow-up in Europe.

This experience with voretigene neparvovec demonstrates significant posttreatment improvements in FST from the 1st month.

The addition by the CHNO of a mobility test to assess the evolution of functional vision in their routine follow-up protocol in addition to the FST allows this study to give further insights on the efficacy of voretigene neparvovec treatment during the first-year post-surgery. The patients' mobility also improved from the first month after surgery for all patients.

In eyes who have experienced chorioretinal atrophy (5/12 patients) following VN treatment, an improvement in the FST measurement was observed compare to baseline values and remained stable until last assessment.

In the absence of patient reported outcome questionnaires to evaluate disease severity of patients with IRDs, LIGHT Study has also been used to collect and analyse patient's verbatim (or parent's verbatim for young children) relative to their experience at different time points after surgery.