RETINA australia

Leber Congenital Amaurosis (LCA)

Leber Congenital Amaurosis (LCA) is a rare genetic eye disease that appears at birth or in the first few months of life. The extent of vision loss varies from person to person, but can be quite severe (with little to no light perception).

LCA is an umbrella term given to a group of diseases that are caused by mutations in at least 18 known genes. The gene mutations lead to failure in function of the photoreceptor cells (rod and cones cells that receive light), ultimately causing cell degeneration. Given the severity of the condition, it is one of the most extensively researched inherited retinal disorders, and a number of clinical trials have begun recently.

What are the symptoms of LCA?

There are many different types of LCA, and the disease can present differently in different children. However, there are some basic symptoms that are often associated with LCA. These include nystagmus (involuntary jerky rhythmic eye movement), photophobia (sensitivity to light) and slow pupillary response to light.

Eye-pressing and rubbing the eyes with a knuckle or finger can be common with babies and children who have very little vision. This can cause damage to the cornea (keratoconus) and lens and may result in a loss of fatty tissue around the eyes causing the eyes to look deep-set. The extent of degeneration depends on the type of LCA the child has and for some types of LCA the vision (or lack of vision) remains stable.

What is the cause of LCA and how is it inherited?

LCA is a very rare condition which is estimated to affect around 1 in 80,000 in the population. Forms of LCA are caused by a mutation in one of a number of genes that are important for retinal function and it is usually inherited in an autosomal recessive manner. However, there are rare incidences where the inheritance pattern may be autosomal dominant.

What treatments are available?

At present, there are no proven effective treatments for LCA. However a number of clinical trials have begun or are due to begin for some subtypes of the condition. On the 19th of December 2017, the FDA approved the first ever retinal gene therapy for the treatment of Leber's Congenital Amaurosis caused by mutations in the RPE65 gene. The drug, voretigene neparvovec-rzyl (Luxturna) is manufactured by Spark Therapeutics in Philadelphia, and is a single dose gene therapy administered via an injection into the retina.

In 2017, ProQR Therapeutics in the Netherlands commenced their Phase 1/2 human clinical trial for safety and efficacy of QR-110, a treatment for LCA 10 caused by the p.Cys998X mutation in the CEP290 gene.

The trial is being conducted across three centres: The University of Iowa, the Scheie Eye Institute at the University of Pennsylvania, and the Ghent University Hospital, Belgium. Patients (six adult and six children enrolled) will receive a dose of QR-110 every three months for a total of four doses in one eye.

In July 2014, QLT Inc announced promising results from a human clinical trial investigating an oral drug (QLT091001) for the treatment of LCA from mutations in the RPE65 and LRAT genes. There were positive improvements in visual function for 11 of the 14 patients who received a seven-day oral dose of the drug.

These therapies aim to improve vision by bypassing the biochemical effects of lack of RPE65 or LRAT and thus “reawakening” dormant or sleeping retinal cells in order to allow the patient to see. It is extraordinary that this very uncommon, and severe, inherited retinal degeneration is the subject of two different clinical trials, both of which have shown early evidence of success. This gives justifiable hope that less severe inherited retinal degenerations might also be treatable in the foreseeable future.