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Lumevoq gene therapy in leber hereditary optic neuropathy

Abstract:

Leber hereditary optic neuropathy (LHON) is a rare, maternally inherited mitochondrial genetic disease with a high unmet medical need. Three primary point mutations in the mtDNA are responsible for LHON in 90% of subjects: G3460A, G11778A and T14484C, located respectively in the ND1, ND4 and ND6 genes. The m.11778G>A ND4 mutation causes the most severe clinical form of LHON, and is also the most frequent mutation (75% of LHON). Lenadogene nolparvovec (Lumevoq) is a recombinant adeno-associated viral vector, serotype 2 (rAAV2/2), containing a cDNA coding the human wild-type mitochondrial NADH dehydrogenase 4 protein (ND4), which has been specifically developed to treat ND4 LHON subjects, and is targeting the root cause of the disease. Restoring the expression of the ND4 protein could correct the deficiency due to the m.11778G>A ND4 mutation, leading to the improved activity and assembly of Complex I of the mitochondrial respiratory chain, helping to protect retinal ganglion cells, eventually halting and reversing the disease. The three Phase-3 multi-center clinical trials RESCUE, REVERSE and REFLECT showed sustained bilateral improvement of best-corrected visual acuity (BCVA) following unilateral or bilateral intravitreal injection of lenadogene nolparvovec gene therapy for the treatment of LHON caused by the m.11778G>A mitochondrial DNA mutation in the MT-ND4 gene. Overall, 189 ND4 patients were treated with lenadogene nolparvovec in clinical trials. Early expanded access programs have been granted in the US and Europe. Lenadogene nolparvovec brings a novel and efficacious treatment option, fulfilling an ongoing unmet medical need whilst restoring visual function in ND4 LHON patients.

Biography

Taiel completed her doctorate in Medicine with board certified in Ophthalmology from Lariboisiere Saint Louis University, Paris, France, and her Associate Professor degree. Dr Taiel has been engaged in the Pharma Industry for 25 years. She hold international and management positions in various therapeutic areas at Servier, Pfizer and Eli Lilly. Then, she led the development of antisense oligonucleotides in Inherited Retinal diseases at ProQR Therapeutics. Since 2018, she leads Gene Therapy programs in Inherited Retinal diseases, as the CMO of GenSight Biologics. Dr. Taiel brings extensive years of experience from both academic medicine and pharma industry.