

Indirect Comparison of Lenadogene Nolpharovec Gene Therapy versus Natural History in Leber Hereditary Optic Neuropathy Patients Carrying the m.11778G>A *MT-ND4* Mutation

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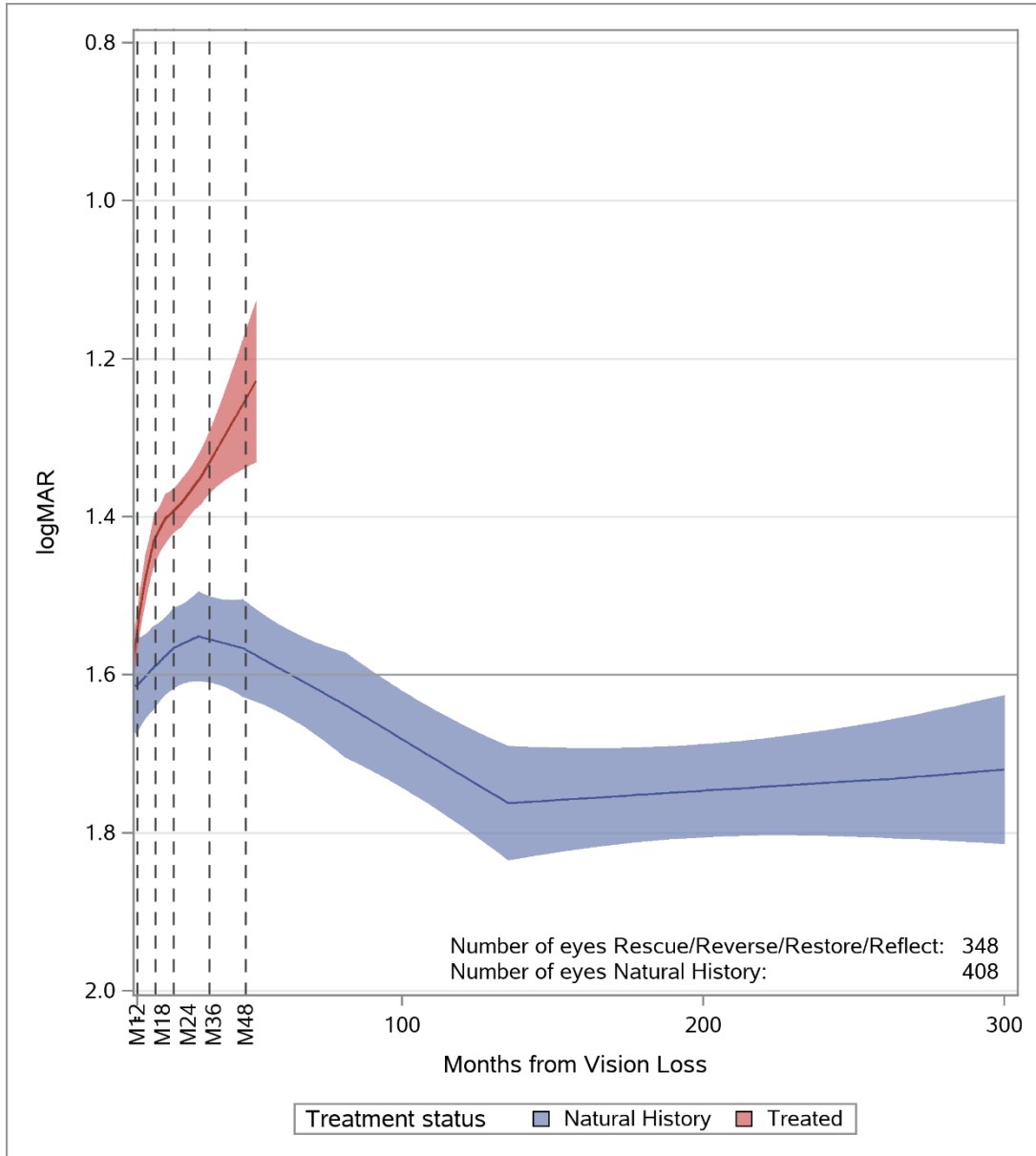
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Supplementary Figure 1: Evolution of Visual Acuity of Treated Eyes versus Natural History Eyes up to 300 Months

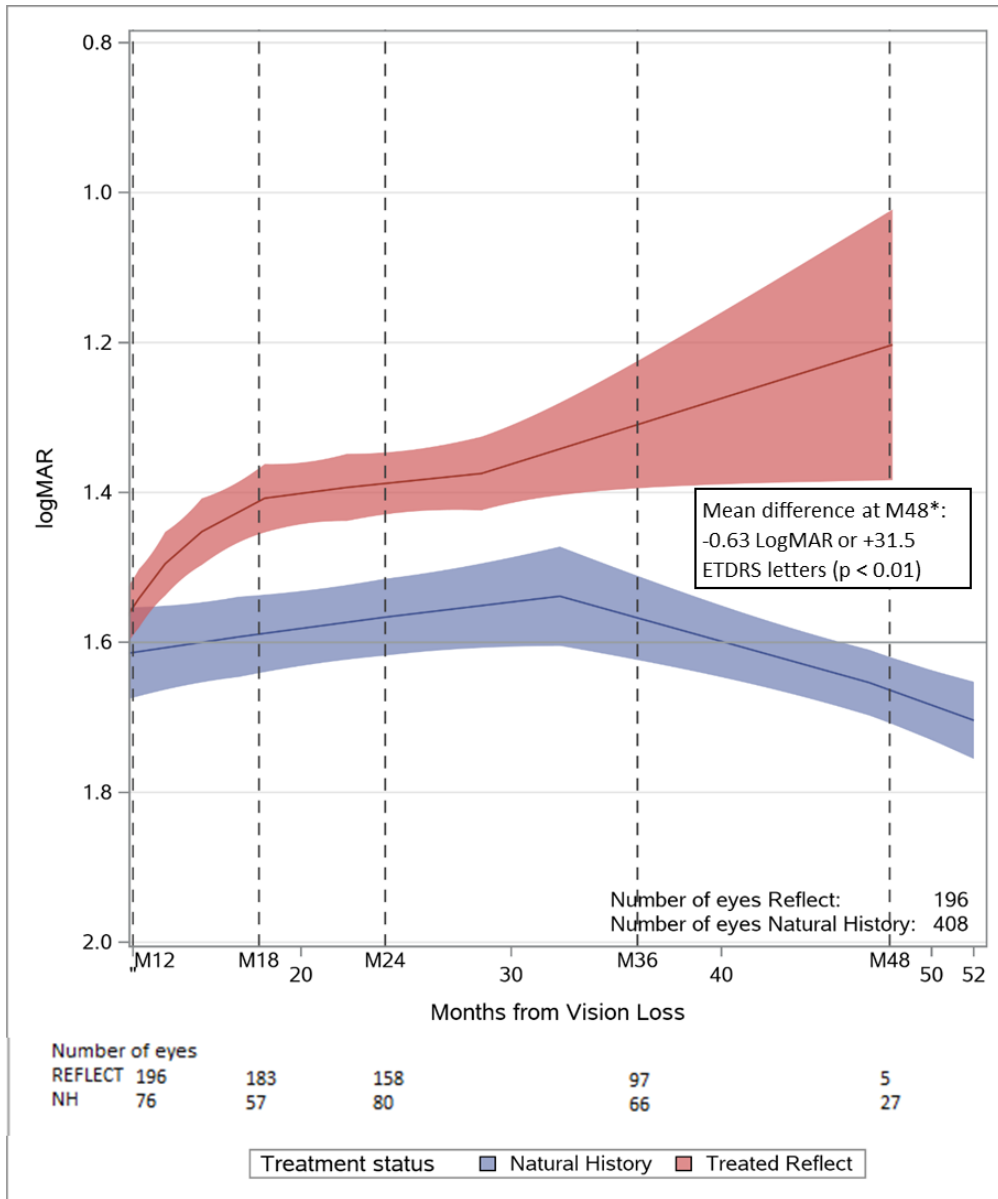


The evolution of visual acuities over time for treated eyes (n=348) and natural history eyes (n=408) was estimated by LOESS regression (solid line) with 95% CI around the fitted curve (shaded area). Visual acuity values > 300 months were assigned to the 300-month timepoint using the next observation carried backward method.

Smoothing parameter: 0.315 for treated eyes and 0.407 for natural history eyes.

The statistically significant difference between treated and natural history eyes is illustrated by the non-overlapping CIs of LOESS curves.

Supplementary Figure 2: Evolution of Visual Acuity of REFLECT Treated Eyes versus Natural History Eyes



The evolution of visual acuities over time for REFLECT eyes (n=196) and natural history eyes (n=408) was estimated by LOESS regression (solid line) with 95% CI around the fitted curve (shaded area). Visual acuity values > 52 months were assigned to the 52-month timepoint using the next observation carried backward method.

Smoothing parameter: 0.315 for treated eyes and 0.408 for natural history eyes.

The statistically significant difference between treated and natural history eyes is illustrated by the non-overlapping CIs of LOESS curves.

Number of eyes with the closest value to the nominal timepoint is indicated for each group based on the prespecified time windows defined in the Methods.

*Mean difference (95% CI) at Month 48 [42, 54] was estimated by a mixed-model analysis of covariance with repeated measures.

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