Long-term Effect of Fingolimod in Reducing Blood Neurofilament Light Levels in Patients with Relapsing-remitting Multiple Sclerosis

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Objective:
To assess the effect of long-term treatment with fingolimod on blood neurofilament light chain (NFL) levels in patients with relapsing-remitting multiple sclerosis (RRMS).

Background:
NFL, a cytoskeleton protein, is elevated in blood upon neuroaxonal damage. Blood NFL is a promising biomarker for monitoring disease activity, treatment response, and prognosis in MS.

Design/Methods:
This post hoc analysis was based on data from patients who received fingolimod 0.5 mg once daily or placebo/interferon β-1a (IFN) 30 μg once weekly in pivotal studies (24-month FREEDOMS/12-month TRANSFORMS), and then fingolimod in the open-label LONGTERMS extension study for up to 10 years. The analysis included a subset of patients who had blood NFL assessments at baseline, end of core (EoC) in pivotal studies, and end of study (EoS) in LONGTERMS. Patients were categorized into two groups: a continuous group (n=37) who received fingolimod throughout the studies and a switched group (n=42) who transitioned from placebo/IFN group to fingolimod in the LONGTERMS. NFL was measured using Single Molecule Array (SIMOA™) immunoassay. The geometric mean change in NFL levels from baseline to EoS was analyzed using Wilcoxon signed-rank test.

Results:
The mean exposure to fingolimod was 3483 days in the continuous group and 2822 days in the switched group. In the continuous group, baseline NFL levels of 33 pg/mL were significantly reduced by approximately 40% at both EoC and EoS (20 pg/mL; P<0.0001 and P=0.0002, respectively). In the switched group, baseline NFL levels of 29 pg/mL were reduced by 15% at EoC (25 pg/mL, P>0.44) and 41% at EoS (17 pg/mL, P<0.0001).

Conclusions: Fingolimod 0.5 mg significantly reduced blood NFL, maintaining its low levels with continuous treatment for up to 10 years. NFL levels were reduced to a lesser extent during treatment with IFN but decreased further with switch to fingolimod, demonstrating the greater impact of highly effective therapy in RRMS.