Effect of Ibudilast on Neurofilament-light Chain in Progressive MS: Analysis from a Phase II Trial

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Objective: To report the effect of ibudilast on serum and CSF neurofilament-light (NFL) from the phase II trial of ibudilast in progressive MS.

Background: Serum NFL is a candidate biomarker of treatment response in multiple sclerosis (MS) clinical trials. Ibudilast 100 mg/d was found to slow the progression of brain atrophy in SPRINT-MS, a 255-patient randomized, placebo-controlled 96-week phase II trial of progressive MS. We evaluated the effect of ibudilast on serum and CSF NFL in SPRINT-MS.

Design/Methods: Serum samples were collected at screening, 8, 48, and 96 weeks. In an optional sub-study, 75 patients consented to CSF sampling, which was collected at screening, 48, and 96 weeks. NFL was assayed using the SIMOA immunoassay. Analysis utilized a mixed model for repeated measurements with log(NFL) as the response variable and adjusted for treatment, age and log(baseline NFL). The model further included visit-by-treatment and visit-by-log (baseline NFL) interactions, using an AR(1) covariance matrix. Analysis was according to intent-to-treat (ITT) and included all available values in the statistical analysis.

Results: Mean baseline serum NFL was 33.5±22.4 and 40.3±54.1 pg/ml in ibudilast and placebo groups, respectively. Mean baseline CSF NFL was 1616.7±1474.4 and 1301.2±822.2 pg/ml in ibudilast and placebo groups, respectively. Over the course of the study, there was no between-group difference in NFL in either serum (P=0.35) or CSF (P=0.62). In some subjects, changes in NFL were observed concomitantly with new/enlarging T2 lesions, which suggests confounding by active inflammation.

Conclusions: Ibudilast treatment was not associated with a decline in either serum or CSF NFL. Inflammatory activity may have confounded the intended use of NFL to measure neurodegeneration.