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Disability status and cognitive functioning in patients with advancing multiple sclerosis switching to siponimod: interim results of the exchange study

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Introduction: Siponimod, a sphingosine-1-phosphate ($S1P_{1,5}$) receptor modulator, is approved in adults for treatment of relapsing multiple sclerosis (RMS) and active secondary progressive MS. Conversion to siponimod from other disease-modifying therapies (DMTs) in patients with advancing RMS is being assessed in EXCHANGE (NCT03623243), a prospective, 6-month, multicentre, open-label, single-arm phase 3b study. Exploratory outcomes included patient-reported disability and cognitive function.

Objective: Explore the effect of siponimod on short-term disease evolution and cognition in patients with advancing RMS

Methods: The study includes patients aged 18-65 years with advancing RMS and an Expanded Disability Status Scale (EDSS) score of 2.0-6.5 who received continuous treatment with DMTs for ≥3 months. Short-term disease evolution and cognition were evaluated using Patient Determined Disease Steps (PDDS) and the Processing Speed Test (PST), respectively. The PDDS is a validated questionnaire measuring patient-reported disability on a scale from 'normal' to 'bedridden'. Patients were classified as normal (no disability) or having mild (gait impairment without device), moderate (assistive device) or severe (non-ambulatory) disability. The PST is a validated, self-administered, iPad-based tool used to measure MS-related deficits in processing speed, scoring the number of correct digits recorded over 120 sec.

Results: 163 patients (74.2% female; mean age 46.6 years; mean baseline (BL) EDSS score of 3.9) were eligible for analysis. For PDDS at BL, 20.3% (27/133) of patients were classified as normal, and 54.1% (72/133), 23.3% (31/133) and 2.3% (3/133) of patients had mild, moderate and severe disability, respectively. The percentage of patients in each category pointed to improvement at Day 84 (normal, 23.8% [24/101]; mild, 50.5% [51/101]; moderate, 23.8% [24/101]; severe, 2.0% [2/101]) and Day 168 (normal, 23.0% [29/126]; mild, 50.0% [63/126]; moderate, 25.4% [32/126]; severe, 1.6% [2/126]). For cognitive processing speed, patients achieved numerical improvement in mean [SD] PST scores on Day 84 (43.1 [18.4]) and Day 168 (46.0 [16.3]) vs BL (40.0 [17.8]).

Conclusions: Findings of this analysis suggest that patients with advancing RMS switching to siponimod reported relative stability in disease progression over the study period, including numerical improvements in self-reported physical disability and cognitive functioning.

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