Estimating long-term effect of siponimod on disability progression versus virtual placebo in SPMS using RPSFT model: EXPAND data up to 7 years

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OBJECTIVE

Present long-term (LT) efficacy of continuous siponimod (LTCS) versus corrected virtual placebo (LTVP) using Rank Preserving Structural Failure Time (RPSFT) and uncorrected IIT analysis (LTPS) in the overall SPMS population and subgroups of active (a) and non-active (na) SPMS patients with up to 7 years of follow-up in EXPAND.

BACKGROUND

In EXPAND, continuous siponimod-treated SPMS patients (siponimod: core+extension) had 22% reduced risk of 6mCDP versus placebo/siponimod-treated patients (placebo: core/siponimod: extension) over up to 5-years (ITT analysis). Placebo to OL siponimod switch after EXPAND-core prevented LT placebo versus siponimod comparison.

DESIGN/METHODS

Analysis included patients who received ≥1 dose of siponimod or placebo in the EXPAND-core and offered a switch to OL siponimod in the ongoing EXPAND-Extension (ITT population: siponimod N=1099, placebo N=546; data cut-off: 10-2020; duration ≤7 years). Time to 6mCDP was assessed for LTCS versus LTVP and LTPS groups.

RESULTS

In the overall population, HR [95% CI] for time to 6mCDP for LTCS was 0.67 [0.52; 0.87] versus LTVP and 0.78 [0.67; 0.92] versus LTPS, resulting in median time to 6mCDP delay by 62% (40.8 vs. 66.1 months) and 29% (51.1 vs. 66.1 months), respectively. In aSPMS patients, HR

[95% CI] for time to 6mCDP for LTCS was 0.58 [0.42-0.81] versus LTVP with 79% delay (38.8 vs. 69.3 months) and 0.69 [0.55-0.87] versus LTPS with 44% delay (48.0 vs. 69.3 months) in median time to 6mCDP. Among naSPMS patients, HR [95% CI] for time to 6mCDP for LTCS was 0.80 ([0.51-1.26]) versus LTVP and 0.89 [0.71-1.12] versus LTPS, corresponding to 44% delay (45.5 vs. 65.4 months) and 19% delay (55.1 vs. 65.4 months) in median time to 6mCDP, respectively.

CONCLUSIONS

This analysis confirms RPSFT virtual placebo arm utility to estimate LT siponimod treatment benefits and supports sustained efficacy up to 7 years in reducing progression risk and prolonging time to 6mCDP in SPMS patients.