Effect of oral ponesimod on clinical disease activity and MRI-based outcomes in patients with relapsing multiple sclerosis: Phase 3 OPTIMUM study

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ABSTRACT (300/300 words)

Background: In the phase-3 OPTIMUM study (NCT02425644), ponesimod (PON), a selective modulator of sphingosine-1-phosphate receptor 1, showed superior efficacy vs teriflunomide (TER) in patients with relapsing multiple sclerosis (RMS). Prespecified MRI-based endpoints and no evidence of disease activity (NEDA) status were evaluated.

Methods: Patients (18-55 years) with RMS (expanded disability status scale scores: 0-5.5) were randomized (1:1) to PON 20-mg or TER 14-mg for 108 weeks. MRI endpoints: percentage change from baseline to week 108 in brain volume (BV), mean number of new gadolinium-enhancing (Gd+) T1-lesions and volume/count of new/enlarging T2-weighted (T2)-lesions. NEDA-3 (absence of confirmed relapse, 12-week confirmed disability accumulation, Gd+T1 and new/enlarging T2-lesions on annual MRIs) and NEDA-4 status (NEDA-3 and no average annual BV decrease ≥0.4%) were evaluated from baseline to week-108.

Results: 985/1133 (86.9%) randomized patients completed the study. MRI findings for PON vs TER, respectively, were: LS mean percent change in BV: −0.91% vs −1.25% (difference:0.34%, 95%-CLs:0.17;0.50, p<0.0001); LS mean difference (PON−TER) for change in total T2-lesion load: −399.2 mm^3 (95% CLs:−651.5;−146.8, p=0.002); mean number of new/enlarging T2-lesions per year: 1.40 vs 3.16 (rate ratio [RR]:0.44, 95%-CLs:0.36;0.54, p<0.0001); PON vs TER odds ratio (OR [95%-CL]) for absence of new/enlarging T2-lesions: 1.71 (1.30;2.25, p=0.0001); mean number of new Gd+T1-lesions per scan: 0.18 vs 0.43 (RR:0.42, 95%-CLs:0.31;0.56, p<0.0001); PON vs TER (OR [95%-CL]) for absence of new Gd+T1-lesions: 2.18 (1.61;2.95, p<0.0001). At week 108, 28.2% (159/564) PON vs 18.3% (102/558) TER patients (OR:1.70, 95%-CL:1.27;2.28, p=0.0004) achieved NEDA-3; 15.0% (79/526) PON vs 8.5% (45/532) TER

patients (OR:1.85, 95%-CL:1.24;2.76, p=0.0026) achieved NEDA-4. The most common reason for not achieving NEDA-3/ NEDA-4 status was presence of new/enlarging T2-lesions.

Conclusions: PON showed benefit vs TER for all MRI outcomes including BV loss and a significantly higher proportion of patients achieved NEDA-3 and NEDA-4 status, supporting the effects observed on clinical endpoints.

Previous presentation: The poster was previously presented at the 8th joint ACTRIMS - ECTRIMS Meeting, (MSVirtual 2020), September 11-13, 2020.