Title: Efficacy of cladribine tablets 3.5 mg/kg added to interferon-beta in patients with secondary progressive multiple sclerosis (SPMS) or relapsing-remitting multiple sclerosis (RRMS): a *post-hoc* analysis from ONWARD

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Background: In the CLARITY study, treatment with cladribine tablets 3.5 mg/kg (CT3.5) significantly improved clinical outcomes vs placebo in patients with RRMS. The ONWARD study showed similar benefits for CT3.5 administered as add-on therapy to interferon-beta (IFN-β) in patients with RMS.

Objective: To assess the effect of CT3.5 in patients with SPMS or RRMS in ONWARD.

Methods: ONWARD was a 2-year, randomized, double-blind study in patients aged 18–65 years, with EDSS scores 1.0–5.5, who experienced ≥ 1 relapse during the 48 weeks prior to the study while receiving IFN-β therapy. At baseline, there were 26 patients with SPMS (placebo+IFN-β, N=9; CT3.5+IFN-β, N=17) and 171 with RRMS. The effect of treatment with CT3.5 on key outcomes during ONWARD was examined in this *post-hoc* analysis of SPMS and RRMS subgroups.

Results: At baseline, there were no clinical differences in relapses in the prior year between the subgroups. Mean EDSS was higher in the SPMS vs the RRMS subgroup. CT3.5 mg/kg demonstrated a nominally significant reduction in ARR vs placebo in both subgroups. In the SPMS subgroup, the relative risk ratio (RRR) for CT3.5 vs. placebo was 0.11 (95% CI, 0.01–0.94) vs 0.50 (95% CI 0.30–0.84) in the RRMS subgroup. Time to 3- and 6-month confirmed EDSS progression was not significantly different in either subgroup, however, treatment with CT3.5 was associated with reductions in mean numbers of T1 Gd+ and T2 lesions vs placebo in both the RRMS and SPMS subgroups.

Conclusions: Despite limitations due to the very low number of SPMS patients, this post-hoc analysis indicates that CT3.5 mg/kg administered with IFN-β was efficacious in patients with SPMS and RRMS in the ONWARD study.

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Author disclosures:

Xavier Montalban: has received speaker honoraria and travel expenses for scientific meetings, steering committee member, and advisory board member of clinical trials for Bayer Schering Pharma, Biogen Idec, EMD Serono, Genentech, Genzyme, Novartis, Roche, Sanofi-Aventis, Teva Pharmaceuticals, and Almirall.

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Fernando Dangond: is an employee of EMD Serono, Inc., a business of Merck KGaA, Darmstadt, Germany.