Rapid reduction of lesion accumulation in specific white matter tracts as assessed by lesion mapping in patients with clinically isolated syndrome

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INTRODUCTION AND PURPOSE
• Administration of interferon (IFN) beta-1a in patients with relapsing remitting (RR) MS reduces brain lesion accumulation over time, as assessed by magnetic resonance imaging (MRI). Our study aims to identify treatment-specific spatio-temporal areas using lesion probability mapping (LPM).

METHODS
• We performed a post-hoc analysis of MRI data in RRMS patients from the IMPROVE study, a randomized (2:1) clinical study (ClinicalTrials.gov identifier NCT00441103) comparing patients treated with IFN beta-1a 44 mcg given subcutaneously three times per week (n=120) versus placebo (n=60).

RESULTS

WM lesion distribution analysis
• The treated group presented 50% reduction in CUA lesions compared to the Placebo group, these differences were observed as early as week 4 and were sustained through week 16 (Treated group: 41 cm³ at week 4; 95 cm³ at week 16; mean: 48 cm³/month; Placebo group 62 cm³ at week 4; 196 cm³ at week 16; mean: 48 cm³/month) (Fig. 1).

Fig. 1. Follow-up LPM (week 4-16) of the spatial distribution of cumulative CUA lesions in the Placebo and Treated groups. The intensity corresponds to the probability, for that voxel, that a new lesion occurs.

Fig. 2. Follow-up LPM (week 4-16) of the spatial distribution of cumulative CUA lesions at the level of WM tracts in the Placebo and Treated groups. The intensity corresponds to the probability, for that voxel, that a new lesion occurs.

Fig. 3. LPM showing clusters of significant lower frequency of CUA lesion occurrence in Treated with respect to Placebo at week 16. At each voxel, the color intensity corresponds to the p-value.

WM lesion frequency analysis
• On voxelwise analysis, LPM of the Treated group showed lower frequency of CUA lesions than the Placebo group since week 4. This became particularly pronounced at week 16 in the left CST (p<0.005), ATR (p<0.005) and SLF (p=0.02) (Fig. 3).

DISCLOSURES
A. Giorgio, M. Battaglini, G. Gentile, M. L. Stromillo and A. Visconti have nothing to disclose. N De Stefano has received honoraria from Biogen-Idec, Genzyme, Merck Serono, Novartis, Roche and Teva for consulting services, speaking and travel support. He serves on advisory boards for Merck Serono, Novartis, Biogen-Idec, Roche, and Genzyme, he has received research grant support from the Italian MS Society.

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CONCLUSIONS
• Treatment with IFN beta-1a, in comparison to placebo, rapidly reduces lesion accumulation in RRMS patients in WM tracts, reaching after 16 weeks the highest local differences in clinically eloquent WM areas such as CST, SLF and ATR.