(S123) EFFECTS OF CLADRIBINE TABLETS ON LYMPHOCYTE SUBTYPES IN RELAPSING-REMITTING MULTIPLE SCLEROSIS PATIENTS

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Objectives: Cladribine tablets are in advanced-stage development for multiple sclerosis (MS) treatment. Cladribine is a prodrug, and activation in specific cells provides targeted and sustained immunomodulation, allowing the investigation of an oral short-course annual treatment. Here we assess the hematological profiles over time in the CLARITY (CLAdRiBine tablets Treating multiple sclerosis orallyY) study. Methods: Relapsing-remitting MS (RRMS) patients were randomized (1:1:1) to one of two cladribine regimens (cumulative dose 5.25 or 3.5 mg/kg) or matching placebo. Cladribine tablets were given as short courses (once daily for 4–5 days) in weeks 1, 5, 9, and 13 (5.25 mg/kg arm) or weeks 1 and 5 (3.5 mg/kg arm), and in weeks 48 and 52 (both arms). Blood was sampled at intervals from day 1 to week 96 for complete blood cell counts and differential analysis, with analysis of lymphocyte surface markers (CD3, CD19, CD4, CD8, CD16, and CD56) in a patient subset. Data were previously presented at the Annual Meeting of the European Neurological Society in 2009. Results: The intention-to-treat population included 456, 433, and 437 patients randomized to 5.25 mg/kg, 3.5 mg/kg, or placebo; 80, 81, and 79 provided samples for lymphocyte surface marker analyses, respectively. Cladribine 5.25 or 3.5 mg/kg resulted in a rapid decrease in leukocyte counts from baseline (median, 6.6/nL for both) after the first treatment course, reaching nadir values at week 16 and week 13 (4.4 and 5.3/nL, respectively), and at week 55 (median, 4.2 and 4.35/nL, respectively), separated by a period of recovery until redosing at week 48, vs. placebo (median values of 6.6–6.9/nL) at each time point. This was accompanied by a decrease in B cells (CD19) at week 4, reaching their nadir at weeks 13 to 16, with a period of more substantial recovery toward baseline until week 48. CD3, CD4, and CD8 cell counts showed a linear decrease to week 16 (5.25 mg/kg group) or 13 (3.5 mg/kg group) relative to baseline or placebo, remaining at relatively constant levels thereafter, even after redosing at weeks 48 and 52. Conclusions: Cladribine tablets resulted in rapid and sustained effects on cellular subtypes implicated in MS pathogenesis. The results help clarify the mechanism of targeted and sustained efficacy of cladribine tablets therapy.

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