**Objective:** Cladribine is activated preferentially in lymphocytes, resulting in targeted and sustained immunomodulation, which provides the rationale for its use as a short-course annual multiple sclerosis (MS) treatment. This was explored further through investigation of hematological outcomes in patients with relapsing-remitting MS (RRMS) in the CLARITY (CLAdRbine tablets TreA TED W ITH CLA DRIBINE TA BLETS) study. **Methods:** Patients with RRMS (McDonald criteria; Expanded Disability Status Scale [EDSS] score 0–5.5) were randomized 1:1:1 to receive cladribine tablets (cumulative dose of 5.25 or 3.5 mg/kg) or matching placebo. Cladribine tablets were given in short courses (once daily for 4–5 days) in 2 or 4 consecutive months (28-day periods) in the first 48 weeks, then two short courses at weeks 48 and 52. Blood was sampled at intervals from day 1 to week 96 for complete blood cell counts and differential analysis. Data were previously presented at the Congress of the European Committee for Treatment and Research in Multiple Sclerosis in 2009. **Results:** The intention-to-treat population consisted of 456, 433, and 437 patients randomized to receive 5.25 mg/kg, 3.5 mg/kg, or placebo, of whom 454, 430, and 435 provided data for this analysis (safety population) and 86.2%, 91.2%, and 86.3% completed full-course treatment, respectively. Cladribine 5.25 and 3.5 mg/kg treatment led to rapid and sustained decreases in leukocyte counts, reaching median nadir values at week 16 and week 13 of 4.4 and 5.3/nL (median change from baseline, −2.3 and −1.4/nL), respectively. A slight recovery was noted until redosing at week 48 led to a second nadir at week 55 (median, 4.2 and 4.4/nL; median change from baseline, −2.6 and −2.2/nL). These results were mainly driven by reductions in lymphocytes (median change from baseline in 5.25 and 3.5 mg/kg groups, −1.2/nL [−64%] and −0.8/nL [−44%] at week 16 and 13; −1.2/nL [−65%] and −1.2/nL [−58%] at week 55; with median lymphocyte counts corresponding to grade 2 or lesser lymphopenia according to CTCAE criteria). Changes in other peripheral blood cell counts, including neutrophils, eosinophils, and erythrocytes, were minimal. Hemoglobin levels were marginally affected. **Conclusions:** Cladribine tablets resulted in a predominant effect on peripheral blood lymphocytes, with relative preservation of other cell types and components.

**Supported by:** EMD Serono, Inc, Rockland, MA

**Disclosure:** P. Soelberg-Sorensen: Merck Serono, Biogen Idec, Teva, Genmab, Novartis (consulting fees); Bayer Schering, Merck Serono, Biogen Idec, Teva (other financial benefits). G. Comi: Merck Serono, Bayer-Schering Pharma (consulting fees); Biogen Idec, Teva-Aventis, Merck Serono, Bayer-Schering Pharma (other financial benefits). S. Cook: Merck Serono, Bayer Health Care, Genmab (consulting fees); EMD Serono, Bayer Health Care (other financial benefits). G. Giovannoni: Merck Serono, Bayer-Schering Pharma (consulting fees); Biogen Idec, Teva-Aventis, Merck Serono, Bayer-Schering Pharma (other financial benefits). K. Rammohan: Bayer Pharmaceuticals, EMD Serono/Pfizer, Teva, Genentech, Biogen, Genzyme, Acorda, UCB Pharma, Novartis (consulting fees); Bayer, EMD Serono/Pfizer, Teva, Biogen, Genzyme, Acorda, UCB Pharma (other financial benefits). P. Rieckmann: Merck Serono, Biogen Idec, Teva, Bayer, Novartis (consulting fees); Merck Serono, Biogen Idec, Teva (other financial benefits). P. Vermersch: Merck Serono, Bayer Schering, Teva-Aventis, Biogen Idec, Novartis (consulting fees); Merck Serono, Biogen Idec, Bayer Schering, Novartis (other financial benefits). P. Chang: EMD Serono (salary). A. Hamlett: EMD Serono (salary). V. Viglietta: EMD Serono (salary). R. Verjee: Merck Serono (salary). B. Musch: EMD Serono (salary). S. Greenberg: EMD Serono (salary).

**Keywords:** disease-modifying treatment in MS, immunology and MS