Full title: Effects of cladribine tablets on B and T lymphocytes and natural killer cells in patients with early and relapsing MS.

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Background: Efficacy of cladribine tablets 3.5mg/kg (cumulative dose given in short courses annually for 2 years) has been demonstrated in patients with early MS (ORACLE-MS) or RMS (CLARITY/CLARITY Extension).

Objective: Evaluate B and T lymphocyte and natural killer (NK) cell profiles after the first administration of cladribine tablets in ORACLE-MS, CLARITY/CLARITY Extension.

Methods: Longitudinal evaluation of peripheral blood lymphocytes was conducted for patients receiving the first course of cladribine tablets either as part of the 3.5mg/kg treatment groups (ORACLE-MS and CLARITY) or the placebo/cladribine tablets crossover groups (CLARITY Extension). Lymphocytes were immunophenotyped and evaluated at baseline, and Weeks 5, 13, 24 and 48.

Results: Baseline absolute lymphocyte counts (ALC) were similar across studies, as were temporal profiles of CD19+ B lymphocytes and CD4+ and CD8+ T lymphocytes. CD19+ B cells were the most rapidly reduced subtype (~75% at Week 5). Nadir for CD19+ B cells was reached at Week 13: 81–84% median reduction with cladribine tablets in all studies. Reconstitution of CD19+ B cells towards baseline occurred from Week 24 to 48. CD4+ and CD8+ T cells were also markedly reduced, but less so than CD19+ B cells (≤55% at Week 13 for CD4+ cells and 48% at Week 48 for CD8+ cells with cladribine tablets in ORACLE-MS). Reductions in T cells were discontinuous but had not fully recovered by week 48. CD16+/CD56+ NK cells were transiently reduced with cladribine tablets; nadir occurred at Week 13 in ORACLE-MS (44% reduction), with recovery evident at Weeks 24 (29% reduction) and 48 (23% reduction).

Conclusions: Cladribine tablets achieved an early reduction of peripheral blood B cells with a rapid reconstitution to baseline, and a moderate and discontinuous reduction in T cell counts. Treatment with cladribine tablets is associated with early decreases in NK cells followed by rapid recovery.

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