Full title: Effects of cladribine tablets on CD4+ T cell subsets in the ORACLE-MS study: An analysis of lymphocyte surface markers.

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Background: ORACLE-MS demonstrated the efficacy of cladribine tablets 3.5mg/kg (cumulative dose over 2 years) for early multiple sclerosis (MS). Evaluation of lymphocyte subtypes in patients receiving cladribine tablets 3.5 mg/kg revealed a transient ~82% median reduction in CD19+ B cells by week 13, reconstituting from weeks 24–48. CD4+ and CD8+ cells were also reduced. Given the durable efficacy of cladribine tablets, the long-term effect on immune cells is of interest.

Objective: Examine effects of first administration of cladribine tablets in ORACLE-MS on central/effector memory CD4+ T cells and naturally-occurring regulatory CD4+ T cells (nTregs).

Methods: Peripheral T lymphocytes were immunophenotyped at baseline, and weeks 5, 13, 24 and 48 in patients treated with cladribine tablets at weeks 1 and 5 (3.5 mg/kg group; n=41). Absolute numbers and proportions of central memory (CD4+RO+CCR7+), effector memory (CD4+RO+CCR7-), Th1-type (CD4+CXCR3+) and nTregs (CD4+CD25+CD127-), including naïve-like (CD4+CD25+CD127-RA[HI]+) and memory-like (CD4+CD25+CD127-RA-), were measured.

Results: Nadir occurred at week 13 for effector memory cells (-54%) and week 24 for central memory (-63%) and Th1-type cells (-51%) with similar or slightly increased levels of these CD4+ cell subtypes at week 48. There was a reduction (~5%) in the proportion of central memory cells in total CD4+ cells, but no change for effector memory and Th1-type cells. Absolute numbers of nTregs (-48%), naïve-like nTregs (-67%) and memory-like nTregs (-42%) were decreased at week 48. Memory-like nTregs proportion in total CD4+ cells slightly increased up to 48 weeks (median increase 11%) but nTregs and naïve-like nTregs proportions were unchanged.

Conclusions: The first administration of cladribine tablets results in no dramatic shifts in the proportions of T cell subpopulations. Further investigation is ongoing to explore the mechanism of action of cladribine tablets in MS and the effects of treatment in the second year.

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Author disclosures:

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