INTRODUCTION

The ORACLE-MS study demonstrated the efficacy of cladribine tablets 3.5 mg/kg in patients with relapsing-remitting multiple sclerosis. It was the first study to report a highly significant reduction in the annualized relapse rate (ARR) in patients with multiple sclerosis. The study also demonstrated a significant reduction in the risk of disability progression and a significant reduction in the rate of new or enlarging T2 lesions. The study results support the use of cladribine tablets 3.5 mg/kg as a treatment option for patients with relapsing-remitting multiple sclerosis.

OBJECTIVES

To examine the effects of cladribine tablets on CD4+ T cell subsets, and naturally occurring regulatory CD4+ T cells, and to evaluate the impact of these changes on disease activity and progression.

METHODS

A prospective, randomized, controlled, double-blind, placebo-controlled, phase III study (CT, Cladribine tablets) was conducted in patients with relapsing-remitting multiple sclerosis. The study included a 24-week treatment period followed by a 48-week follow-up period. Blood samples were collected at baseline and at Weeks 13, 24, and 48. CD4+ T cell subsets were evaluated by flow cytometry using monoclonal antibodies. The proportion of central memory, effector memory, and Th1-type T cells was determined by analyzing the expression of CD45RO and CCR7.

RESULTS

Central Memory Cells, Effector Memory Cells, and Th1-Type T Cells

- The greatest median reductions from baseline in absolute cell numbers occurred at Week 24 for total CD4+ cells (median -33% reduction from baseline), followed by Week 13 for memory CD4+ cells (median -43% reduction from baseline) and Week 48 for Th1-type cells (median -51% reduction from baseline).
- The proportion of central memory cells in total CD4+ cells was reduced at Week 24 for Th1-type cells (median -54% reduction from baseline) and at Week 48 for effector memory cells (median -51% reduction from baseline).
- The proportion of Th1-type cells in total CD4+ cells was reduced at Week 24 for Th1-type cells (median -51% reduction from baseline) and at Week 48 for effector memory cells (median -54% reduction from baseline).
- Naturally Occurring Regulatory CD4+ T Cells
- Absolute numbers of nTreg cells, naïve-like nTreg cells and memory-like nTreg cells in patients treated with cladribine tablets 3.5 mg/kg were decreased at Week 48 by 46%, 41%, and 42%, respectively (Figure 3).

CONCLUSIONS

- Maximal reductions from baseline were similar between T cell subsets containing pathological memory cells (central and effector subsets) and proinflammatory Th1-type cells in patients receiving cladribine tablets.
- Pathological memory cells and Th1-type cells had not recovered to baseline by Week 48, and the proportions of central memory cells were slightly decreased at Weeks 24 and 48.
- Treg cells were also decreased, but the proportion of memory-like nTreg showed a slight increase at Weeks 24 and 48.
- Taken together, the prolonged decrease in pathological T cells and Th1-type cells, combined with the recovery of regulatory T cell function, may contribute to the durable clinical effect of cladribine tablets.

REFERENCES


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DISCLOSURES

No disclosures are required.