Effect of Fingolimod on the Immune Response to Vaccination

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INTRODUCTION AND PURPOSE

- Fingolimod (FTY720) works as a novel class of immunosuppressant, the sphingosine 1-phosphate receptor (S1P3), and is the first drug developed for relapsing-remitting multiple sclerosis (RRMS). Modulation of S1P receptors on lymphocytes by fingolimod partially inhibits the autophosphorylation of the cell-surface sphingosine kinase, which causes the cell to migrate.
- A selective and reversible inhibition of lymphocytes in secondary lymphoid organs, such as lymph nodes, leading to a reduction in the peripheral blood lymphocyte count, is expected to reduce in vivo immune responses to vaccination.
- This was investigated in healthy volunteers who received FTY720 at 0.5 mg at 1 day to investigate the impact of the drug on the peripheral blood lymphocyte count and its effect on the antibody response to vaccination.

METHODS

- Male and female patients, aged 18 to 50 years, with relapsing RRMS according to the McDonald criteria, who had received previous treatment with fingolimod and were on stable medication for at least 12 weeks, and who were scheduled to receive a booster vaccine, were eligible to participate. Patient recruitment was from August 2001 to December 2002 with a vaccination visit from September 2003 to January 2004.

RESULTS

- The study consisted of a 2-period, crossover design with a 12-week washout period. The primary outcome was the change in peripheral blood lymphocyte count and its effect on the antibody response to vaccination.

EFFICACY

- Patients were randomized to receive either FTY720 at 0.5 mg or placebo at day 1, followed by a booster vaccination at week 12.
- The percent change in the lymphocyte count at the time of the booster vaccination was compared between the two groups.

CONCLUSIONS

- Both novel and recall antigens elicited an immune response in patients treated with fingolimod 0.5 mg, which indicates that effective vaccination can occur despite fingolimod treatment.
- Treatment with fingolimod 0.5 mg resulted in a slower immune response to seasonal influenza vaccine and tetanus toxoid compared with placebo at week 9 (3 wk after vaccination) and week 12 (6 wk after vaccination).

No newly identified safety concerns were noted in patients on fingolimod following vaccination. Treatment with fingolimod allows safe and effective vaccination in patients with MS, but physicians may need to monitor antibody levels following administration of vaccinations in selected cases.