



Multiple  
Sclerosis  
Society of  
Canada

Société  
canadienne  
de la sclérose  
en plaques



175 Bloor Street East  
Suite 700, North Tower  
Toronto, Ontario M4W 3R8  
Telephone: 416-922-6065  
Fax: 416-922-7538  
www.mssociety.ca

# Medical Update Memo

Originally posted September 22, 2006

**Updated November 3, 2006 and January 29, 2007**

## **Clinical trial results for oral therapy fingolimod show reduction of disease activity: Larger study now recruiting participants**

### **Summary**

Results of a Phase II controlled clinical trial of oral fingolimod (also known as FTY720) have been published in *The New England Journal of Medicine*. The study found fingolimod significantly reduced MS attack rates and signs of inflammation on MRI scans. Fingolimod binds to a docking site (sphingosine-1-phosphate receptor, or S1P receptor) on immune cells, including T cells and B cells that have been implicated in causing nervous system damage in MS. The once-a-day pill induces them to remain in lymph nodes, preventing these cells from migrating into the brain and spinal cord. A larger Phase III clinical trial is underway at 125 centres worldwide, including 10 in Canada. Results from the Phase III studies are needed before marketing approval of fingolimod can be obtained. Novartis Pharmaceuticals Corp is sponsoring the study.

### **Details**

The results of the Phase II controlled clinical trial of oral fingolimod (also known as FTY720) published recently in *The New England Journal of Medicine* (2006;355(11):1124-1139) by Ludwig Kappos, MD (University Hospital, Basel, Switzerland) and colleagues were previously reported at medical meetings.

The investigators conducted a double-blind, placebo-controlled study involving 255 participants with active, relapsing MS at various study sites around the world, including Canada. After six months, active inflammation on MRI scans was significantly reduced in two groups receiving 1.25 mg or 5 mg of daily fingolimod, versus those on placebo, and more people in the treatment group versus placebo group

stayed relapse-free. MS attacks were reduced by more than 50 percent, as was the number of new active (enhancing) MS lesions as shown on MRI scans. Fingolimod binds to a docking site (sphingosine-1-phosphate receptor, or S1P receptor) on immune cells, including T cells and B cells that have been implicated in causing nervous system damage in MS. The once-a-day pill induces them to remain in lymph nodes, preventing these cells from migrating into the brain and spinal cord.

In a six-month extension of the original study, people in the treatment groups continued on the same dose, and people in the placebo group received either 1.25 mg or 5 mg of fingolimod. In all, 227 people completed the extension study. The relapse rate in placebo group participants switched to 1.25 mg was reduced by seven percent, and in those switched to 5 mg, it was reduced by 86 percent. Significant reductions in active inflammation were seen on MRI scans in both groups formerly on placebo. In groups continuing on fingolimod, relapse rates and signs of active inflammation on MRI remained low.

In the original study, adverse events – mainly inflammation of the nasal passages, breathing difficulties, headache, diarrhea, and nausea – occurred more often in people receiving 5 mg of fingolimod. A brain infection occurred after 10 weeks of treatment in one person taking 5 mg, which improved after treatment was withdrawn, but has resulted in some neurological damage.

Adverse events were less frequent in the extension study, and were mainly nasal inflammation, flu, and headache. Two serious infections occurred, including facial herpes and an infection of the colon. Other adverse events associated with fingolimod were alterations in liver function, reduction in heart rate after the first dose, decreases in blood cell counts, and breathing difficulties.

In an accompanying editorial, Drs. Steffen Massberg and Ulrich H. von Andrian (Harvard Medical School) comment on these adverse events. They note that heart rate and breathing difficulties are not surprising, because S1P is involved in the regulation of heart rate and in the proliferation of cells in the airway. Newer compounds that target specific docking sites of S1P might help to avoid such side effects. “All inhibitors of this pathway would need to be evaluated for their potential to increase the patient’s susceptibility to infections,” the authors caution.

**Disclaimer**

The Multiple Sclerosis Society of Canada is an independent, voluntary health agency and does not approve, endorse or recommend any specific product or therapy, but provides information to assist individuals in making their own decisions.

A large-scale, Phase III study is underway that will eventually involve 100 centres worldwide, although not all sites are recruiting yet. The study is called FREEDOMS (FTY720 Research Evaluating Effects of Daily Oral therapy in MS). This 24-month study is comparing the safety and effectiveness of daily treatment with 1.25 mg fingolimod, 0.5 mg fingolimod, or inactive placebo in more than 2,000 people with relapsing-remitting MS (a course of MS characterized by clearly defined flare-ups followed by partial or complete recovery periods). The primary outcome that will be measured is the reduction of relapse rate, and secondary outcomes will include frequency of relapse, disease activity on MRI scans, and time to progression of disability. Results from such Phase III studies are needed before Novartis could apply for marketing approval of fingolimod.

For more information about the study, please call 1-866-788-3930 or contact one of the participating Canadian clinical trial sites listed below. You can also visit [http://www.msclinicaltrials.ca/participate-MS-study.do?pl\\_id=bmrmsl000000](http://www.msclinicaltrials.ca/participate-MS-study.do?pl_id=bmrmsl000000)

[With information from the National MS Society (USA)]

### **Canadian clinical trial sites**

- Dalhousie University, MS Research Unit, Halifax, Trudy L. Campbell, 902-473-7947
- Maisonneuve-Rosemont Hospital, Neurology Research Clinic, Montreal, Dr. Jacques Lachapelle, 514-252-3400, #3298
- Nepean Medical Centre, Ottawa, Isabelle D. Bedirian, Clinical Trials Coordinator, 613-224-1223
- Kingston General Hospital, MS Clinic, Kingston, Dr. Donald G. Brunet or Vee McBride 613-548-2308
- St. Michael's Hospital, Toronto, Dr. Paul O'Connor, 416-864-5830
- University of Saskatchewan, Regina, Felix Veloso, Principal Investigator 306-525-3586
- University of British Columbia, Vancouver, Wendy Morrison, Study Coordinator, 604-822-1756

**ASK MS Information System Code: 1.4.1.75.b**

National Research Department

National Marketing and Communications Department

\medmmo-fingolimod-jan07

Disponible en français.

#### **Disclaimer**

The Multiple Sclerosis Society of Canada is an independent, voluntary health agency and does not approve, endorse or recommend any specific product or therapy, but provides information to assist individuals in making their own decisions.