



Multiple  
Sclerosis  
Society of  
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## Medical Update Memo

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### Reporting from the AAN: Promising MS Clinical Trial Results

Multiple sclerosis researchers - including several funded by the Multiple Sclerosis Society of Canada - reported promising clinical trial results during two sessions April 4 at The American Academy of Neurology's 58th Annual Meeting in San Diego. Here are some highlights:

•Dr. Paul O'Connor (St. Michaels Hospital, Toronto) and colleagues reported results from a Phase 2 controlled clinical trial of oral FTY720, or Fingolimod, (Novartis Pharmaceuticals Corp) in active relapsing MS. FTY720 binds to a docking site (sphingosine-1-phosphate receptor) on immune cells, including T cells and B cells that have been implicated in causing nervous system damage in MS, and induces them to remain in lymph nodes, where they can do little harm. The investigators conducted an international, double-blind, placebo-controlled study involving 281 participants with active relapsing MS. The authors had previously reported that after six months, active inflammation on MRI scans was significantly reduced in two groups receiving 1.25 mg and 5 mg of FTY720, versus those on placebo, and more people in the treatment group versus placebo group stayed relapse-free. Now, they report on a six-month, dose-blinded extension of the original study, in which participants in the treatment groups continued on the same dose, and those in the placebo group received either 1.25 mg or 5 mg of FTY720. In all, 227 people completed the extension study. The relapse rate in placebo group participants now taking 1.25 mg was reduced by 70%, and in those who switched to 5 mg, it was reduced by 86%.

On MRI, significant reductions in active inflammation were seen in both groups formerly on placebo. In groups continuing on FTY720, relapse rates and active inflammation on MRI remained low. The incidence of adverse events during the six months' extension was higher in the 5-mg groups (infections, increase in blood pressure, first dose heart rate

reduction, alterations in liver function tests). Further study is needed to confirm this agent's benefits in MS. A large-scale, Phase 3 study is underway in North America and Europe; please see the FTY720 study Web site for details.

- Dr. Mark Freedman (University of Ottawa) presented results of the "BENEFIT" study, which examined the ability of Betaseron® (interferon beta-1b, Berlex Inc.) to delay the onset of MS in people who experience a clinically isolated syndrome (CIS, a single demyelinating event, putting them at high risk to develop MS). A total of 487 participants received either Betaseron 250 mcg or placebo for up to 24 months or until MS was diagnosed. Those on treatment experienced a 50% reduction in risk for developing definite MS, and the development of MS was delayed by 363 days in the Betaseron group compared to the placebo group. There were also significant benefits as seen in MRI scans.

In a separate report on the study, Dr. Chris H. Polman (Vrije Universiteit Medical Centre, Amsterdam) and colleagues also reported that an analysis of various subgroups showed that the treatment benefit was more pronounced in patients whose MRI scans showed less disseminated disease activity and no active inflammation. The risk for developing clinically definite MS was significantly lower in both treatment groups among patients age 30 or under. An extension study in which all participants are eligible to receive active treatment is currently underway. It will assess the impact of early vs. delayed Betaseron treatment on the long-term course of MS, and should be completed in 2008.

- Researchers reported on an early-phase study of BHT-3009 (Bayhill Therapeutics) and Lipitor® (atorvastatin, Pfizer, Inc.) in relapsing-remitting or secondary-progressive MS. BHT-3009 is a construct of DNA containing genetic material that instructs cells to produce myelin basic protein (MBP), a component of myelin, which is an immune target in MS. Lipitor is a cholesterol-lowering drug under study for its effects on immune function in MS. Dr. Timothy Vollmer (Barrow Neurological Institute, Phoenix) and colleagues randomly assigned 30 people with relapsing-remitting MS to receive BHT-3009 (intramuscular injections in weeks 1, 3, 5, 9) or placebo; and Lipitor (80 mg per day, oral capsules) or placebo for 13 weeks. The experimental treatment appeared to be safe in this study and showed some evidence that it decreased immune responses against MBP.

In a separate presentation, Dr. Amit Bar-Or (Montreal Neurological Institute) reported that data on a subgroup of patients where immune assay results are available suggest that BHT-3009 may decrease the production of immune messenger proteins associated with tissue damage in MS. Further study is needed to confirm the benefits of this regimen. The group

is now enrolling participants for a Phase 2 trial.

•Dr. Ingrid Catz (University of Alberta) and colleagues reported on an early-phase clinical trial testing MBP8298 (BioMS Medical Corporation) as a possible treatment for progressive MS. MBP8298 is a synthetic fragment of myelin basic protein (MBP), a component of nerve fiber-insulating myelin. This regimen reduces the production of spinal fluid antibodies that react against MBP. The group administered 500 mg of either MBP8298 or inactive placebo intravenously every six months to 32 people with secondary- or primary-progressive MS.

Results showed no significant difference between MBP8298 and placebo treatments. However, a statistically significant delay in clinical progression was noted in patients with certain genetically determined "HLA" types; HLA is a molecule located on body cells that helps the immune system attack both foreign invaders and, in the case of autoimmune diseases, the body's own tissues. Some HLA types have been linked to increased susceptibility to MS. In the subgroup of patients with HLA types DR2 and DR4, those on placebo experienced clinical progression of MS at an average of 18 months, while those on active treatment experienced progression at an average of 78 months. Further study is needed to confirm the potential benefits of MBP8298; a larger study is underway in secondary-progressive MS. Please see the more information about the study in the Clinical Trials section of the MS Society website ([www.msociety.ca](http://www.msociety.ca))

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

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