

Medical Update Memo

March 17, 2010

Ibutilast in relapsing-remitting multiple sclerosis

Summary

Ibutilast is a new drug which, based on animal and pilot human studies, seems to have some anti-inflammatory properties, and reduce the damage to white matter in the brain, as observed in neurological diseases other than MS. The results of this multicenter, double-blind, phase 2 trial with oral ibutilast for people with relapsing-remitting MS, suggest that although no beneficial effect on the rate of newly active lesions and relapses was observed, ibutilast might act in a neuroprotective way and may have beneficial clinical effects on disability progression. **Neurology. 2010 Mar 3**

Details

Ibutilast is a phosphodiesterase inhibitor influencing inflammation and neurodegeneration in multiple sclerosis (MS). This study evaluated the safety, tolerability, and effects on MRI parameters of 2 different doses of ibutilast in relapsing forms of MS.

In this multicenter, double-blind, phase 2 trial, patients with relapsing MS and gadolinium-enhancing lesions were randomly assigned 1:1:1 to receive 30 or 60 mg ibutilast or placebo every day for 12 months. The primary endpoint was the cumulative number of newly active lesions on bimonthly brain MRI over 12 months. Secondary endpoints included relapse rate, change in Expanded Disability Status Scale (EDSS) score, T2-hyperintense and T1-hypointense lesion volumes, and percent brain volume change (PBVC).

A total of 297 patients were randomized in 19 centers. During the first 12 months, the mean number of active lesions and relapse rate did not differ between treatment arms. A reduction in PBVC ($p = 0.04$) was found in the 60-mg group (0.8%) compared with placebo (1.2%). Post hoc analysis showed a reduction in the proportion active lesions that evolved into persistent black holes for the 60-mg (0.14; $p = 0.004$) and 30-mg (0.17; $p = 0.036$) groups compared with the placebo group (0.24). Over 2 years, there were fewer patients ($p = 0.026$) with confirmed progression on the EDSS. Treatment with ibutilast was generally safe and well tolerated.

Ibutilast showed no beneficial effect on the rate of newly active lesions and relapses. However, preliminary evidence suggests that ibutilast seems to act in a neuroprotective fashion as measured by 2 independent MRI outcomes, with a possible beneficial clinical

effect on disability progression. Classification of evidence: This interventional study provides Class III evidence on the effect of ibudilast on disease activity.

National Research and Programs

Offert 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.