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Efficacy and safety of oral fumarate in patients with relapsing-remitting multiple sclerosis: a multicentre, randomised, double-blind, placebo-controlled phase IIb study.

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Abstract

BACKGROUND:

Oral fumarate (BG00012) might have dual anti-inflammatory and neuroprotective effects. Our aim was to assess the efficacy and safety of BG00012 in patients with relapsing-remitting multiple sclerosis.

METHODS:

257 patients, aged 18-55 years, with relapsing-remitting multiple sclerosis were randomly assigned to receive 120 mg once daily (n=64), 120 mg three times daily (n=64), or 240 mg three times daily (n=64) BG00012, or placebo (n=65) for 24 weeks. During an extension period of 24 weeks for safety assessment, patients treated with placebo received BG00012 240 mg three times daily. The primary endpoint was total number of new gadolinium enhancing (GdE) lesions on brain MRI scans at weeks 12, 16, 20, and 24. Additional endpoints included cumulative number of new GdE lesions (weeks 4-24), new or enlarging T2-hyperintense lesions, new T1-hypointense lesions at week 24, and annualised relapse rate. Analysis was done on the efficacy-evaluable population. Safety and tolerability were also assessed. This study is registered with ClinicalTrials.gov, number [NCT00168701](#).

FINDINGS:

Treatment with BG00012 240 mg three times daily reduced by 69% the mean total number of new GdE lesions from week 12 to 24 compared with placebo (1.4 vs 4.5, $p<0.0001$). It also reduced number of new or enlarging T2-hyperintense ($p=0.0006$) and new T1-hypointense ($p=0.014$) lesions compared with placebo. BG00012 reduced annualised relapse rate by 32% (0.44 vs 0.65 for placebo; $p=0.272$). Adverse events more common in patients given BG00012 than in those given placebo included abdominal pain, flushing, and hot flush. Dose-related adverse events in patients on BG00012 were headache, fatigue, and feeling hot.

INTERPRETATION:

The anti-inflammatory effects and favourable safety profile of BG00012 warrant further long-term phase III studies in large patient groups.

Comment in

- [Oral fumarate for relapsing-remitting multiple sclerosis](#). [Lancet. 2008]

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