History of Changes for Study: NCT00168701

Effacacy and Safety of BG00012 in MS

Latest version (November 14, 2007) on ClinicalTrials.gov

- A study version is represented by a row in the table.
- Select two study versions to compare. One each from columns A and B.
- Choose either the "Merged" or "Side-by-Side" comparison format to specify how the two study versions are to be displayed. The Side-by-Side format only applies to the Protocol section of the study.
- Click "Compare" to do the comparison and show the differences.
- Select a version's date link to see a rendering of the study for that version.
- Edits or deletions will be displayed in ~~red~~.
- Additions will be displayed in *green*.
- The yellow choices in the table indicate the study versions currently compared below. A yellow row indicates the study version being viewed.
- Hover over the "Recruitment Status" to see how the study's recruitment status changed.

Study Record Versions

Version	A	B	Date	Changes
1	◉	◉	September 9, 2005	Nothing (earliest Version on record)
2	○	○	October 13, 2005	Outcome Measures, Study Description, Study Status and Eligibility
3	○	○	October 24, 2005	Study Identification and Study Status
4	○	○	June 7, 2006	Contacts/Locations and Study Status
5	○	○	November 14, 2007	Recruitment Status and Study Status

Compare

Comparison Format: ◉ Merged ○ Side-by-Side

Scroll up to access the controls

Study NCT00168701
on Date: September 9, 2005 (v1)

Study Identification

Unique Protocol ID:	C-1900
Brief Title:	Effacacy and Safety of BG00012 in MS
Official Title:	Double-Blind, Placebo-Controlled, Dose-Ranging Study to Determine the Effacacy and Safety of BG00012 in Subjects with Relapsing-Remitting Multiple Sclerosis
Secondary IDs:	

Study Status

Record Verification:	September 2005
Overall Status:	Unknown status [Previously: Active, not recruiting]
Study Start:	October 2004
Primary Completion:	
Study Completion:	
First Submitted:	September 9, 2005
First Submitted that Met QC Criteria:	September 9, 2005
First Posted:	September 15, 2005 [Estimate]
Last Update Submitted that Met QC Criteria:	September 9, 2005
Last Update Posted:	September 15, 2005 [Estimate]

Sponsor/Collaborators

Sponsor:	Biogen
Responsible Party:	
Collaborators:	

Oversight

U.S. FDA-regulated Drug:	
U.S. FDA-regulated Device:	
Data Monitoring:	

Study Description

Brief Summary:	DMF, the active ingredient in BG00012, is an immunomodulator

demonstrating definite therapeutic efficacy in psoriasis (Carboni et al, 2004; Altmeyer et al, 1994; Mrowietz et al, 1999) and possible therapeutic efficacy in MS (Schimrigk et al, 2001). However, the target site of action and the exact mechanism of action of DMF are unknown.

Like psoriasis, MS has been postulated to be driven by a Th1 cytokine reaction and to therapeutically respond to either immunosuppression or Th2 suppression (Weiner and Selkoe, 2002). Putative effects of BG00012 include suppression of circulating T cell population, down regulation of adhesion molecule expression, modulation of the Th1/Th2 cytokine expression profile, inhibition of neutrophil burst, and TNF-induced CD62E expression through suppression of NF-kB nuclear translocation.

Methyl fumaric acid esters (FUMADERMÒ) have been shown to reduce peripherally in vivo circulating CD4+, CD8+ and CD52+ mononuclear cells (Hoxtermann et al, 1998). This circulatory reduction has been associated with a decrease in intradermal mononuclear cell infiltration in psoriasis patients (another T cell-mediated disease) (Vandermeeren et al, 1997). DMF was recently shown to induce substantial plasma membrane alterations potentially linked to the deactivation via apoptosis of lymphocytes (Sebök et al, 2000).

Methylfumarates have been shown to modulate in vitro T cell cytokine profile from Th1 to Th2 (Ockenfels et al, 1998). DMF and MMF inhibit the proliferation of keratinocytes, possibly due to a temporary rise in the intracellular calcium concentration (Nibbering et al, 1993). Methylfumarates have been shown to prevent acute and chronic rejection in rat kidney transplantation models (Risch et al, 2001). It is difficult to assess the validity of some in vitro data that have been derived using doses that exceed serum levels found in human trials (Mrowietz et al, 1999).

In summary, the putative immunomodulatory effects, the psoriasis efficacy of FUMADERM®, and the efficacy data in the pilot MS study of BG00012 support a proof of concept study in MS

Detailed Description: The study will be divided into two parts: Part 1 will be a 24□week, blinded, placebo-controlled treatment phase followed by Part 2, a 24-week blinded, safety extension phase in which all subjects will receive BG00012.

All investigational drug (BG00012 or placebo) will be given orally.

In Part 1, subjects will be randomized in equal numbers to one of the following treatment groups:

Treatment Group BG00012 Dosing Regimen BG00012 Total Daily Dose

a. 120 mg once a day (qd) 120 mg
b. 120 mg three times a day (tid) 360 mg
c. 240 mg tid 720 mg
d. Placebo Placebo

All subjects will be evaluated for tolerance to investigational drug after the first week of dosing. In addition, subjects in the highest dose group (Group 3) will dose at 120 mg tid for the first week. After 1 week, Group 3 subjects who tolerate 120 mg tid (as determined by the subject's tolerance of flushing episodes and gastrointestinal [GI] disturbances) will have their dose increased to 240 mg tid.

In Part 2, subjects who received BG00012 in Part 1 of the study will remain on the same BG00012 dose throughout the Part 2 extension phase. Subjects who received placebo in Part 1 of the study will receive BG00012 120 mg tid for one week in Part 2 and then, if well-tolerated, the BG00012 dose will be increased to 240 mg tid.

Dose reduction will be allowed for subjects who are unable to tolerate investigational drug. Dosing interruptions (or investigational drug discontinuation) will be required for significantly elevated liver or renal function tests or decreased white blood cell count (WBC). Any subject who prematurely discontinues BG00012 dosing should remain in the study for the time period specified in the protocol and continue protocol-scheduled evaluations.

Subject treatment assignments will remain blinded throughout the study. Safety will be monitored during the study by the Advisory Committee and the Clinical Safety Committee.

Conditions

Conditions:	Multiple Sclerosis
Keywords:	Multiple Sclerosis MRI

Study Design

Study Type:	Interventional
Primary Purpose:	Treatment

Study Phase:	Phase 2
Interventional Study Model:	Parallel Assignment
Number of Arms:	
Masking:	Double
Allocation:	Randomized
Enrollment:	260

Arms and Interventions

Intervention Details:

Drug: BG00012

Outcome Measures

Primary Outcome Measures:

1. The primary endpoint for the primary objective is the total number of Gd-enhancing lesions over four scans at Weeks 12, 16, 20, and 24 (calculated as the sum of these four MRI scans).

Secondary Outcome Measures:

2. Secondary MRI endpoints include:
3. · the cumulative number of new Gd-enhancing lesions from baseline to Week 24, and
4. · the number of new or newly-enlarging T2 hyperintense lesions at Week 24 compared to baseline.
5. Additional endpoints include:
6. · the number of new T1 hypointense lesions at Week 24 compared to baseline
7. · the incidence and severity of adverse events
8. · EDSS scores and change from baseline in EDSS scores at Weeks 12, 24, 36, and 48, and
9. · annualized relapse rate from Week 0 to Weeks 24 and 48, and the proportion of relapse-free subjects at Weeks 24 and 48.

Eligibility

Minimum Age:	18 Years
Maximum Age:	55 Years
Sex:	All
Gender Based:	
Accepts Healthy Volunteers:	No
Criteria:	Inclusion Criteria:

1. Must give written informed consent and authorize the release and use of protected health information (PHI), as required by local law

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