Expanded Disability Status Scale (EDSS) score between 0.0 and 5.0, inclusive

At least 1 relapse within the 12 months immediately prior to study entry with a prior cranial MRI scan demonstrating lesions consistent with MS **OR** evidence of Gd+ lesions of the brain on an MRI performed within the 6 weeks prior to study entry

Willingness to use appropriate contraceptive measures during the study

clusion Criteria

A progressive form of MS

Treatment with IFNβ (3 months), glatiramer acetate (3 months), or intravenous immunoglobulin (6 months), or natalizumab (6 months) within the 6 months prior to randomization

Corticosteroid treatment within 30 days of randomization

An MS relapse within 50 days prior to randomization and/or not stabilized from a previous relapse

A history of malignancy, severe allergic or anaphylactic reaction, or known drug hypersensitivity

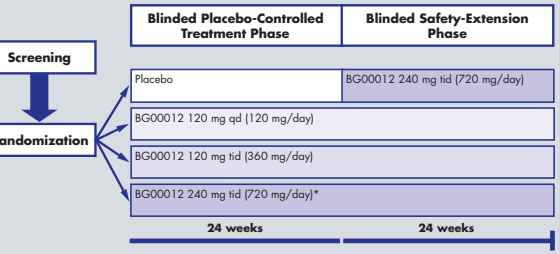
A history of abnormal laboratory results, HIV infection, drug or alcohol abuse

udy Design

Randomized, double-blind, placebo-controlled, parallel-group, dose-ranging study conducted at 42 clinical centers in Europe

The study consisted of a 24-week double-blind, placebo-controlled treatment phase followed by a 24-week, blinded, safety-extension phase (*Figure 2*).

gure 2. Study Design



atients received 120 mg tid during the first week to determine tolerability.

Patients were equally randomized to one of four treatment groups:

- Placebo
- BG00012 120 mg once daily (qd) (120 mg/day)
- BG00012 120 mg three times daily (tid) (360 mg/day)
- BG00012 240 mg tid (720 mg/day)

- Study drug was administered according to the schedule shown in Table 1. Patients in the BG00012 720 mg/day dose group received 120 mg tid for the first week to determine tolerability.

Table 1. Schedule for Study Drug Administration

Treatment Group	Morning	Midday	Evening
Placebo	2P	2P	2P
120 mg of BG00012 (1 capsule)	1A + 1P	2P	2P
360 mg of BG00012 (3 capsules)	1A + 1P	1A + 1P	1A + 1P
720 mg of BG00012 (6 capsules)	2A	2A	2A

P=placebo; A=active (BG00012, 120 mg of fumaric acid ester per capsule).

- In the blinded safety-extension phase, the three BG00012 treatment groups continue at the dosage assigned in the placebo-controlled treatment phase, and the placebo group receives BG00012 720 mg/day (120 mg tid was given the first week).

Study Endpoints

- The primary endpoint is the total number of new Gd+ lesions on MRI scans performed at Weeks 12, 16, 20, and 24 (calculated as the sum of these 4 MRI scans).
- Secondary MRI endpoints include:
  - Cumulative number of new Gd+ lesions from baseline to Week 24
  - Number of new or newly enlarging T2-hyperintense lesions at Week 24 compared to baseline
- Other endpoints include:
  - Number of new T1-hypointense lesions at Week 24
  - Annualized relapse rate
  - Proportion of relapse-free patients
  - Disability progression as measured by EDSS
  - Safety/tolerability

RESULTS

- A total of 257 patients were enrolled in the study.
- The patient population was 63% females and the mean age of patients enrolled was 36 years (*Table 2*).
- The mean (±SD) disease duration of patients was 4.6 (±4.9) years, the mean EDSS score was 2.6 (±1.2), and the mean number of relapses during the 3 years prior to enrollment was 2.5 (±1.3) (*Table 2*).

Table 2. Patient Demographics and Clinical Characteristics

	All Patients (N=257)
Age, mean years (±SD)	36.0 (±9.3)
Women, %	63
Caucasian, %	98
Time since onset of symptoms	
Mean years (±SD)	7.8 (±6.0)
Time since diagnosis	
Mean years (±SD)	4.6 (±4.9)
EDSS score, n (%)	
≤3.5	203 (79)
4.0-5.0	54 (21)
≥5.0	0 (0)
Mean (±SD)	2.63 (±1.2)
Median	2.5
Min, max	0.0, 5.0
Relapses,* n (%)	
0	1 (<1)
1	50 (19)
2	87 (34)
3	78 (30)
≥4	41 (16)
Mean (±SD)	2.5 (±1.3)
Median	2.0
Min, max	0, 10

SD=standard deviation; EDSS=Expanded Disability Status Scale.
*During the 3 years prior to study enrollment.

CONCLUSIONS

- BG00012 represents a potentially important therapeutic option for patients with MS.
- This study will provide the first double-blind, placebo-controlled data to evaluate the efficacy and safety of BG00012 in patients with MS.

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