From: gilmore o'neill/cambridge/biogen;nsf;gilmore.oneill@biogenidec.com;smtp
Sent: Tue Jan 31 2006 17:05:01 EST
To: lkappos@uhbs.ch;
BCC: rachel lebouteiller/london/biogen@biogenidec;
Subject: C1900 ENS abstracts

Dear Ludwig,

it was good to see you and to meet Sofia at the National Faculty Meeting. I am now inspired to start bringing my children with me to meetings when they are older.

Thank you for your help and advise with the presentation of the "top line" C1900 data.

I have attached two draft abstracts on the 24 week C1900 data. Would you be able to review them and make whatever changes or suggested changes that you like. I have left out the specific numbers and data so that they be freshly presented at ENS.

If you send it back to me, I could disseminate it to the other members of the SAC. I will also ask Rachel to pull out the Steering Commitee charter section on authorship that was agreed at the inaugural meeting. I will also ask her to find the names of the highest recruting investigators, per the charter section. Would that be okay with you?

Best regards

Gilmore

PS Hope that your drive along Alligator alley was interesting.


ENS BG00012 safety in MS abs 3.doc


ENS BG00012 efficacy in MS abs 3.doc

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Efficacy of a Novel Oral Single-Agent Fumarate, BG00012, in Patients With Relapsing-Remitting Multiple Sclerosis: Results of a Phase 2 Study

<<Please enter authors and affiliations>>

<<Character limit: 2500; Character count: 2145>>

Objective: To determine the efficacy of three dose levels of BG00012, a novel single-agent oral fumarate, on brain lesion activity as measured by magnetic resonance imaging (MRI) in patients with relapsing-remitting multiple sclerosis (RRMS).
Methods: This was a randomized, double-blind, placebo-controlled clinical trial of BG00012 in patients with RRMS. Men and women 18 to 55 years of age were eligible for the study if they had a diagnosis of RRMS and an Expanded Disability Status Scale (EDSS) score between 0.0 and 5.0. In addition, patients must have had either ≥1 relapse within 12 months prior to randomization or gadolinium-enhancing (Gd+) lesions on cranial MRI at screening. Patients received BG00012 120 mg by mouth (PO) once daily (120 mg/day), 120 mg PO three times daily (360 mg/day), 240 mg PO three times daily (720 mg/day), or placebo for 24 weeks. The treatment period was followed by a 24-week dose-blinded safety-extension period during which all patients received BG00012. The primary end point was the total number of Gd+ lesions over four MRI scans at weeks 12, 16, 20, and 24 (calculated as the sum of the four scans). Secondary end points included the cumulative number of new Gd+ lesions from week 4 to week 24 and the number of new/enlarging T2-hyperintense lesions at week 24. Additional end points included the number of new T1-hypointense lesions at week 24, relapse rate, and disability progression as measured by EDSS.
Results: A total of 257 patients were enrolled in the study; 64 patients each were randomly assigned to receive one of the three BG00012 doses and 65 patients to placebo. Approximately 90% of patients completed the 24-week treatment period. BG00012 (720 mg/day) significantly reduced the mean number of new Gd+ lesions (the primary end point) compared with placebo. In addition, BG00012 reduced the cumulative number of new Gd+ lesions, the number of new/enlarging T2-hyperintense lesions, and the number of new T1-hyperintense lesions, compared with placebo.
Conclusion: BG00012 significantly reduces brain lesion activity as measured by MRI in patients with RRMS over 24 weeks of treatment.

Safety of a Novel Oral Single-Agent Fumarate, BG00012, in Patients With Relapsing-Remitting Multiple Sclerosis: Results of a Phase 2 Study

<<Please enter authors and affiliations>>

<<Character limit: 2500; Character count: 1716 >>

Objective: To determine the safety and tolerability of BG00012, a novel single-agent oral fumarate, in patients with relapsing-remitting multiple sclerosis (RRMS).
Methods: This was a randomized, double-blind, placebo-controlled, phase 2 clinical trial conducted at 45 clinical centers in Europe. Men and women 18 to 55 years of age were eligible for the study if they had a diagnosis of RRMS and an Expanded Disability Status Scale score between 0.0 and 5.0. Patients also must have had either ≥1 relapse within 12 months prior to randomisation with lesions on cranial MRI consistent with MS, or had gadolinium-enhancing (Gd+) lesions on cranial MRI within 6 weeks of randomisation. Patients received BG00012 120 mg by mouth (PO) once daily (120 mg/day), 120 mg PO three times daily (360 mg/day), 240 mg PO three times daily (720 mg/day), or placebo. The study consisted of 2 phases: a 24-week double-blind treatment phase followed by a 24-week, blinded, safety-extension phase in which all patients received BG00012. Patients received physical exams and had haematological assessments and urinalysis during both phases. All adverse events (AEs) were reported, regardless of severity or relationship to study drug. Results of the treatment phase are reported and data are pooled among BG00012 dose groups.
Results: Of 257 patients enrolled, 176 (92%) BG00012 patients and 59 (91%) placebo patients completed the 24-week treatment phase. The most common AEs were flushing headache, nasopharyngitis, and nausea. The overall incidence of infection was similar in patients treated with BG00012 and patients treated with placebo.
Conclusion: BG00012 was safe and well tolerated in RRMS patients over 24 weeks of treatment.

From: "ludwig kappos" <lkappos@uhbs.ch>
Sent: Tue Jan 31 2006 19:05:26 EST
To: <gilmore.oneill@biogenidec.com>;
Subject: Antw: C1900 ENS abstracts

Dear Gilmore
I also enjoyed the meeting and having some time to discuss issues of the BG12 program with you and Al. We had a wonderfull trip by the everglades to Miami.
I have reviewed the abstracts and find them fine; have added some suggestions as attached.
Best regards
Ludwig

>>> Gilmore O'Neill <Gilmore.ONeill@biogenidec.com> 31.01.2006 22:05:01 >>>
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- ENS BG00012 safety in MS abs 3_LK.doc - ENS BG00012 efficacy in MS abs 3_LK.doc

Efficacy of a Novel Oral Single-Agent Fumarate, BG00012, in Patients with Relapsing-Remitting Multiple Sclerosis: Results of a Phase 2 Study

<<Please enter authors and affiliations>>

<<Character limit: 2500; Character count: 2169>>

Objective: To determine the efficacy of three dose levels of BG00012, a novel oral fumarate preparation, on brain lesion activity as measured by magnetic resonance imaging (MRI) in patients with relapsing-remitting multiple sclerosis (RRMS).
Methods: This was a randomized, double-blind, placebo-controlled clinical trial of BG00012 in patients with RRMS. Men and women 18 to 55 years of age were eligible for the study if they had a diagnosis of RRMS and an Expanded Disability Status Scale (EDSS) score between 0.0 and 5.0. In addition, patients must have had either ≥1 relapse within 12 months prior to randomization or gadolinium-enhancing (Gd+) lesions on cranial MRI at screening. Patients received BG00012 120 mg by mouth (PO) once daily (120 mg/day), 120 mg three times daily (360 mg/day), 240 mg three times daily (720 mg/day), or placebo for 24 weeks. The treatment period was followed by a 24-week dose-blinded safety-extension period during which all patients received BG00012. The primary end point was the total number of Gd+ lesions over four MRI scans at weeks 12, 16, 20, and 24 (calculated as the sum of the four scans). Secondary end points included the cumulative number of new Gd+ lesions from week 4 to week 24 and the number of new/enlarging T2-hyperintense lesions at week 24. Additional end points included the number of new T1-hypointense lesions at week 24, relapse rate, and disability progression as measured by EDSS.
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Conclusion: BG00012 significantly reduces brain lesion activity as measured by MRI in patients with RRMS over 24 weeks of treatment.

Safety of a Novel Oral Single-Agent Fumarate, BG00012, in Patients With Relapsing-Remitting Multiple Sclerosis: Results of a Phase 2 Study

<<Please enter authors and affiliations>>

<<Character limit: 2500; Character count: 1716 >>

Objective: To determine the safety and tolerability of BG00012, a novel oral fumarate preparation, in patients with relapsing-remitting multiple sclerosis (RRMS). (Add something about mode of action and long term safety data in psoriasis?)
Methods: This was a randomized, double-blind, placebo-controlled, phase 2 clinical trial conducted at 45 clinical centres in Europe. Men and women 18 to 55 years of age were eligible for the study if they had a diagnosis of RRMS and an Expanded Disability Status Scale score between 0.0 and 5.0. Patients also must have had either ≥1 relapse within 12 months prior to randomisation with lesions on cranial MRI consistent with MS, or had gadolinium-enhancing (Gd+) lesions on cranial MRI within 6 weeks of randomisation. Patients received BG00012 120 mg by mouth (PO) once daily (120 mg/day), 120 mg three times daily (360 mg/day), 240 mg three times daily (720 mg/day), or placebo. The study consisted of 2 phases: a 24-week double-blind placebo controlled treatment phase followed by a 24-week, dose blinded, safety-extension phase in which all patients received BG00012. Patients received physical exams and had haematological assessments and urinalysis during both phases. All adverse events (AEs) were reported, regardless of severity or relationship to study drug. Results of the treatment phase are reported and data are pooled among BG00012 dose groups.
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Conclusion: BG00012 was safe and well tolerated in RRMS patients over 24 weeks of treatment.