From: gilmore o'neill/cambridge/biogen;nsf;gilmore.oneill@biogenidec.com;smtp
Sent: Thu Jun 29 2006 03:52:34 EDT
To: [redacted]
CC: cara lansden/cambridge/biogen@biogenidec;[redacted];minhua yang/cambridge/biogen@biogenidec;
Subject: Re: REVIEW REQUEST BG12 PROTOCOLS- 1 question

[redacted]

Since this will be an intention to treat analysis, we should allow patients to reduce dose if they cannot tolerate the drug. I would write it as we wrote it for C1900.

Best regards

Gilmore

Gilmore N. O'Neill, M.B., M.R.C.P.I., M. Med. Sci.
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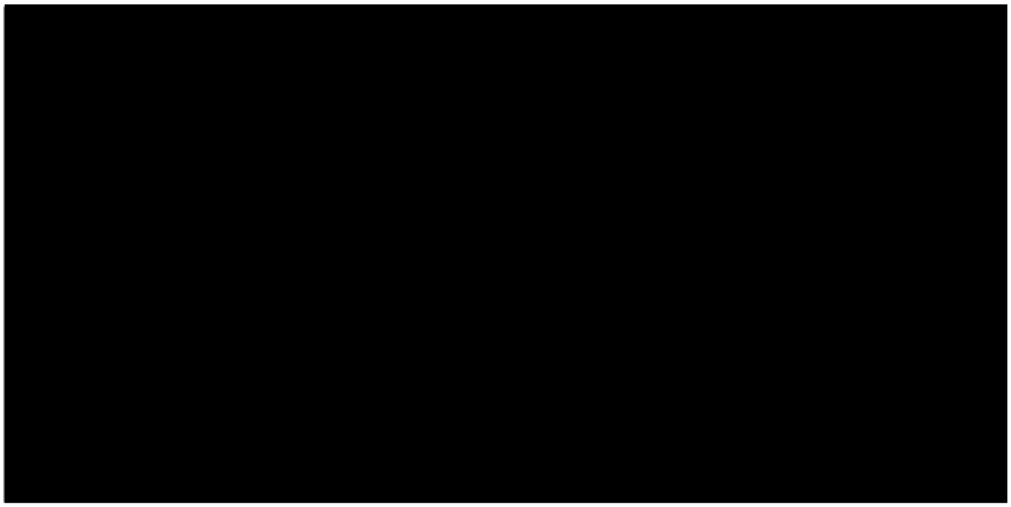
[redacted]

Hi Minhua,
We touched on this a couple of times. For these studies it was my impression, that if subjects did not tolerate BG12 at the higher dose, they would be prematurely discontinued from the study for "intolerance to study drug". From what I understood, it was okay in the C-1900 study because there was a dose ranging study (or dose finding) and for all intent and purposes these phase 3 studies are "fixed" at one dose level.

I realize this is not in the protocol - but we could certainly add it, or clarify based on Gilmore's opinion.
[redacted]



Hi [redacted]/Gilmore:

While I was reviewing the protocols I had a question about dosing. This is a Gilmore question. In C-1900 we allow subjects to take reduced dose i.e. 1 pill each time 3 pills total a day due to study drug intolerance, do we allow that in our phase 3 protocols?

-minhua

[redacted]
26-Jun-2006 05:38 PM
Message Size: 5189.5 KB

To
[redacted] Gilmore O'Neill/Cambridge/Biogen@BiogenIdec,
Minhua Yang/Cambridge/Biogen@BiogenIdec, [redacted]
Ratna Lingamaneni/Cambridge/Biogen@BiogenIdec, [redacted]
[redacted] Tammy Sarnelli/Cambridge/Biogen@BiogenIdec, [redacted]
[redacted] Cara Lansden/Cambridge/Biogen@BiogenIdec
[redacted] Kate Dawson/Cambridge/Biogen@BiogenIdec,
[redacted]
Subject
REVIEW REQUEST BG12 PROTOCOLS

Hello All,
Attached you will find the 2nd DRAFTs of the two BG12 phase 3 protocols: 109MS301(monotherapy) and 109MS302 (3-Arm reference comparator). For your review and comment. Comments are to be sent to [redacted] (cc me) by EOB on Thursday, 29June06.

As per my notice last week, remember our goal is to complete these protocols (approved, but not signed by Carmen Bozic) for the EOP2 submission package due 13July06 - which means our timeline for protocol production has been very condensed. So, please be as timely as possible with your review and comments.

Note:
Section 14.3: Test and Assessments: is not complete and will not be completed until the Study Activity Flowcharts are "final".
Section 15 - Safety: [redacted] made changes to this section, which have been highlighted and strikenthrough, to make it easy to review for those of you in DSRM.

Thank you for your time and attention.
Regards,
[redacted]

[redacted]