

Baerhoe
EXHIBIT NO. 2
MUC 5/28/08

Unknown

From: De Vriese Geert
Sent: Tuesday, December 15, 1998 1:10 PM
To: Hough Nick NW; Davies Diane DE - MMCC
Cc: Lawrence Richard RA; Venables Peter P; Hunt James JG; Price Anna AC; Walker Caroline C; Owens Judith J; Engleman Kurt KH; Raniwalla Joher J; Jones Martin AM - PHMS; Parsons Noreen NE; 'Jonathan Hellewell'; McKinley Marti M
Subject: RE: study 15 abstract for APA

Dear all,

I've seen the correspondence re this abstract and cannot refrain from giving you some thoughts:

1. I haven't seen neither the cognition or the weight abstract, but would think that the value of these abstracts or/and the implications of withdrawing these, outweighs the risk of being asked questions about study 15. We should however be prepared to answer any questions, or make sure the pharmas can answer such questions.
2. it might have been better to combine the Canadian and the study 15 cognition data (if that is possible at all) but now that the work on study 15 has been done, and anticipating a positive outcome, I feel we should go ahead with the abstract and make the best use of it. Similarly for the weight abstract.
3. whatever abstract is issued, we must be confident that the approach taken is scientifically and ethically reasonably sound and acceptable. There may be different levels of "soundness and acceptability", particularly when it comes to analysing subsets of patients, but I would see it as a major role for the DIG team to ensure a certain level of confidence. Once that is done, let's not recycle every DIG decision.
4. these DIG outputs/data need to go through the same QA process as any other external publication, but am I wrong in seeing that as a functional process and responsibility, e.g. Martin has indeed to be reassured that the data in these abstracts are compatible with what we have on file, that the stats analyses are documented, etc. This should be part of the standard operating procedures and be done before abstracts/etc. go through the review process.

Procedural reflections but I hope they provide a way forward on this issue? regards.

From: Davies Diane DE - MMCC
Sent: 14 December 1998 17:33
To: Hough Nick NW
Cc: Lawrence Richard RA; De Vriese Geert; Venables Peter P, Hunt James JG; Price Anna AC; Walker Caroline C; Owens Judith J; Engleman Kurt KH; Raniwalla Joher J; Jones Martin AM - PHMS; Parsons Noreen NE; 'Jonathan Hellewell'; McKinley Marti M
Subject: study 15 abstract for APA

Dear Nick

Please would you advice on the company view regarding continuing the abstract for APA on study 15 (ie should we ditch it or not). I am not sure how strongly you feel about your comment below.

Please note that from my perspective, the DIG team and the commercial planning team decided to pursue study 15 as an abstract (initially for AEP and then for APA). Also, I am not sure how the author would react to having the abstract pulled, as she has presumably spent considerable time working on it (at Zeneca's request). Admittedly this was at a time before the results for the Canadian data were around (but the DIG team and the commercial planning team were aware that the Canadian data were imminent).

Please note: that a precedence has already been set with this study (as a recent paper has been published on the attentional performance aspects of study 15 by Sax et al).

I would welcome your response as soon as possible.

Kind regards

Diane

From: Raniwalla Joher J
Sent: 12 December 1998 17:31
To: Hunt James JG; Davies Diane DE - MMCC; Price Anna AC; Walker Caroline C; Owens Judith J; Engleman Kurt KH; Jones

PERIOD 000-611-6108
DEPOSITION
EXHIBIT
Ruhl-15
11/7/07 MR

Cc: Martin AM - PHMS; Parsons Noreen NE, 'Jonathan Hellewell', Hough Nick NW
Lawrence Richard RA; De Vriese Geert, Venables Peter P
Subject: RE: weight gain abstract- ver 1

Nick
I agree with your comments, both for the weight and study 15 data. Now that we have better data from the Canadian cognitive function study, what is the use of publishing data from study 15.
Joher

From: Hough Nick NW
Sent: 11 December 1998 17:06
To: Hunt James JG; Davies Diane DE - MMCC; Price Anna AC; Walker Caroline C; Owens Judith J; Engleman Kurt KH; Jones Martin AM - PHMS; Parsons Noreen NE, 'Jonathan Hellewell'
Cc: Lawrence Richard RA; De Vriese Geert; Venables Peter P, Raniwalla Joher J
Subject: RE: weight gain abstract- ver 1

Hi,

although we can't yet read Jonathan's abstract from this e-mail message, I'd like to respond to some of the comments that are raised in connection with the discussion Jonathan and I had a couple of days ago.

The point about the poster having more detailed information is based on the principle that this is usually the case anyway, but with this particular topic we may risk alerting the reader to the fact that we have done quite a lot of analysis and know even more than we are showing. For every % figure that we quote in terms of positive messages, there is the opposite (100 - this%) message which can be deduced from the data. If we try to be too clever/selective, it may become obvious that we have extra data; this is a risk we must assess at some point and take also a collective view on how to manage it, if further questions are directed at the pharma's.

We looked at the MR document for comparison with the recent data from studies 13 and 15. It appears that the 'line' for weight gain over time looks worse for the controlled data alone (which presumably is mainly/wholly from study 15?). Therefore, the addition of further data from OLE patients (uncontrolled) when this is available will likely improve the outlook? This was our reasoning anyway. The point is that, if we generate some messages now on the basis of just 2 studies (13 and 15), the least we can hope for is that the message will improve when we add more data to the mix; it shouldn't get any worse if our understanding is correct. This is obviously important for those of us required to sign-off any promotional material etc. I would not be prepared to sign-off something which may change for the worse as this would be misleading and necessitate a climb down in the market place. If the message eventually 'improves', that's all well and good and we can beef up the message - something that will not be so bad for the market place (except that people may wonder why we didn't have it all in place first time around).

I would also add to Martin's concern about the use of data from study 15, especially since it forms such a major part of this analysis (it wouldn't be such an issue if it was only a fraction), and because it will also crop up again in the cognitive function debate. Since this study has been previously described as a 'failed' study, with data that is not so supportive of Seroquel, we need to again consider the risk of questions arising about the main study results. Whilst few people out there know about it, no-one asks about it. Whilst PRIZE now gives us some more positive data against haloperidol to add to the existing evidence from studies 13 and 14, study 15 is something we have handled very carefully in the past. We have argued that it is a failed study, and have not wanted to communicate the results in any format. I raise this for your consideration at this stage; perhaps it will not be a risk, but we should think it.

Sorry to add to the list of 'things to be considered',

best regards

Nick

From: Jonathan Hellewell[SMTP:jonathan@innervision.demon.co.uk]
Sent: 10 December 1998 23:53
To: Hough Nick NW, Hunt James JG; Davies Diane DE - MMCC; Price Anna AC; Walker Caroline C; Owens Judith J; Engleman Kurt KH; Jones Martin AM - PHMS; Parsons Noreen NE
Subject: weight gain abstract- ver 1

Dear all

Please find attached my first draft of the weight gain APA poster. I am grateful to James, Martin and Kurt for bringing together the analyses. Having had the opportunity to discuss the data with a number of you, my opinion is that the abstract is about as strong as it can be, given the data. I appreciate that there are a number of statistics that we have chosen not to use- this is because to do so would have perhaps made it impossible not to include some less attractive statistics.

A further consideration is that the APA abstracts tend to be quite short. As it stands, the abstract may require a bit of pruning. If so, the most obvious place to cut is the first paragraph, in which the reference to appetite and satiety could be removed.

There are two pieces of data we still need before we can finalise the abstract:

- 1) we need to insert the proportion of patients in the short-term trials who experienced weight gain as an AE. I have seen this figure quoted, perhaps in the Promo Guide, but I do not have the document to hand.
- 2) There is a sentence in the abstract to the effect that AEs of weight gain were uncommon in these studies. Can we confirm this? If we could say that no patient complained of weight gain, or that in no case did the investigator think it necessary to classify something as an AE, then that would be great. Obviously, if we aren't able to access this info, or the info doesn't support us, then the line will have to be removed from the abstract.

Finally, we shouldn't forget that while the abstract can be quite terse, the poster will need a lot of info/graphics/data shows, if we are not to look silly. Therefore, we need to start thinking about the poster fairly soon after submission of the abstract.

In a sense, I have a similar view to Nick on this, that we can submit a terse abstract, but that we must be prepared to put a fuller presentation in the poster, perhaps involving innovative data displays. Also, there is a real possibility that people will ask questions on the poster that we wouldn't like to discuss. Finally, we shouldn't forget that this abstract is based on about 30% of the available data- therefore there is the possibility that with further analyses the data will change somewhat. However, on looking through the data with Nick, it seemed to us both that the addition of more uncontrolled data would be likely to reduce the estimates for weight gain, rather than the opposite.

I am aware that a number of you have seen earlier drafts of this info. I would be very interested to see what everyone thinks.

Jonathan

[Section: 1/1 File: Weight gain abstract ver1 short.doc UUencoded by: Turnpike Version 3.05]

begin 644 Weight gain abstract ver1 short.doc

MT\1X*&Q&N\$...../ @ # / L " 0 ' &

M " " # " " " \$ " " # 0 " " \$ " " # ^ " " " " L " " #

M _____

M _____

M _____

M _____

M _____

M _____