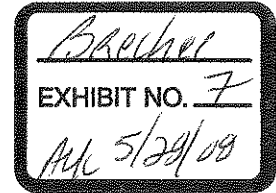


Brecher, Martin

From: Jones Martin AM - PHMS
Sent: Thursday, March 02, 2000 11:07 AM
To: Westhead Emma EK
Subject: RE: Short Report on Weight Gain



Emma

I agree. I have just sent this note to Debbie, Steve, Shawn and Martin B.

Martin



RE: weight claim

From: Westhead Emma EK
Sent: 02 March 2000 10:42
To: Jones Martin AM - PHMS
Subject: FW: Short Report on Weight Gain
Importance: High

Martin,

I don't know if you've had chance to review this report yet but just thought I'd check to see what your opinion of the use of the term weight 'neutral' is? It appears commercial want to cut the OLE IIIb data at 52 weeks as we can then make this claim. I'm concerned about this for a few reasons:

- we're ignoring the full data out to 3 years - is this defensible?
- A publication has gone into CINP on OLE safety which quotes data to 3 years. Although they are different conferences, someone with a sharp eye may query why the publications have different cut-offs.
- When we report the full data from OLE at conferences next year (following database lock in approx June this year). I imagine we will not then be able to defend weight neutral. The graph we supplied for the interim look was on the majority of patients so I imagine the conclusions aren't going to change dramatically. Commercially, could that not be damaging to have to change our position back to 'minimal' weight gain?

I will probably put these comments in my review of the report (not had chance to do this yet) but was interested in your opinion.

Regards,
Emma

From: Rak Ihor IW
Sent: 25 February 2000 19:30
To: Owens Judith J; Wilkie Alison AM
Cc: Holdsworth Debbie D; O'Brien Shawn SP; Gavin Jim JP; Litherland Steve S; Murray Michael MF; Jones Martin AM - PHMS; Denerley Paul PM; Westhead Emma EK; Tumas John JA; Tugend Georgia GL; Czupryna Michael MJ; Gorman Andrew AP; Brecher Martin M
Subject: RE: Short Report on Weight Gain

Judith

Thank you for the opportunity to comment on this very important paper.

1. I think we are giving away too much of our competitive advantage saying repeatedly that atypical antipsychotics (as a class) have a much reduced tendency to cause EPS. Our competitors have been able to undifferentiate themselves from Seroquel, despite our having the only true no dose related advantage. I would tone down the linkage between less EPS with atypicals leading to greater attention on weight changes.

2. We need to emphasize much more that Seroquel treatment is NOT associated with a mean weight gain in patients where it is used alone (without other antipsychotics). That should be the key message; not that there is a small weight gain in a group of patients who were treated with Seroquel (with and without other antipsychotics). The abstract and paper can mention these data, but then stress that finer analyses and more relevant data tell a far better, and more clinically relevant to Seroquel, story.
3. The last key point in the first section after the abstract: only minimal effects on weight is not strong enough. We showed a mean weight loss in patients treated with Seroquel alone long term!
4. Introduction: 5th paragraph: the weight gains in the Allison paper were NOT estimates. (Only the quetiapine weight gain at 10 weeks in the poster not the paper was an estimate.) Later in that paragraph: "psychotic symptoms other than schizophrenia" is incorrect; should be "disorders" replacing "symptoms".
5. The mean dose (446 mg) for the first study (and 475 mg for the second cohort) and the no dose related effect finding are also important messages and should be included in the abstract.
6. The one patient who withdrew from each study: are we certain that this is not the same patient? If it is, we should say it is the same patient and not count the patient twice in two %. Since the second cohort came from the first, it is possible this is one and the same patient.
7. Discussion: The first sentence "... quetiapine treatment was associated with only a modest mean increase in weight" is not the key message of this work, since that analysis did not separate out patients treated with other antipsychotic medications. The net loss on quetiapine alone is the key message. Stressing the importance of this distinction is key.
8. Last paragraph: Sentence "In conclusion, ..." should read more emphatically favorably for quetiapine: "Weight changes in patients treated long term with quetiapine (alone or in combination with other antipsychotics) do not appear to raise potential medical concerns relating to significant weight increases as seen with other atypical antipsychotic agents."
9. Lastly, I respectfully request that my name be added to the authors, in view of my contribution to understanding this issue, data and poster generation since August 99.

Kind regards

Ihor

From: Wilkie Alison AM
Sent: Wednesday, February 23, 2000 7:32 AM
To: Owens Judith J
Cc: Holdsworth Debbie D; O'Brien Shawn SP; Gavin Jim JP; Litherland Steve S; Murray Michael MF; Rak Ihor IW; Jones Martin AM - PHMS; Denerley Paul PM; Westhead Emma EK; Tumas John JA; Tugend Georgla GL; Czupryna Michael MJ; Gorman Andrew AP; Brecher Martin M
Subject: FW: Short Report on Weight Gain
Importance: High

Judith

Thanks for the opportunity to comment - I think this is very good. I've suggested amends to the abstract section, attached.

ALSO: the paper refers to data out to 52 weeks only - therefore table 2 and figure 3 should reflect this - ie be cut at 52 weeks. On this basis, is it possible for us to claim a neutral effect on weight with Seroquel rather than 'minimal'??

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