ld: i.m.1c410850894554945d81f36421b63267

CN: SO1ED00099292

Date: Saturday, February 26, 2000 6:48:00 PM GMT

From: Murray Michael MF

To: Owens Judith J; Rak Ihor IW; Wilkie Alison AM

Cc: Brecher Martin M; Czupryna Michael MJ; Denerley Paul PM; Gavin Jim JP; Gorman Andrew AP; Holdsworth Debbie D; Jones Martin AM - PHMS; Litherland Steve S; OBrien Shawn SP; Tugend Georgia GL; Tumas John JA; Westhead

Emma EK

Subject: RE: Short Report on Weight Gain

Custodians: Jones, Martin

From: Murray Michael MF

Sent: 2/26/2000 10:18:42 AM

To: Owens Judith J; Wilkie Alison AM; Rak Ihor IW

CC: Holdsworth Debbie D; O'Brien Shawn SP; Gavin Jim JP; Litherland Steve S; 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

BCC:

Subject: RE: Short Report on Weight Gain

## lhor,

Thank you for your excellent comments!!! Totally on mark. I agree we should be as aggressive as possible on the weight gain issue. You make a great point about us giving up too much with EPS, lets not concede all atypical are the same, they are not.

Ihor should definitely be one of the authors of this paper.

Thanks again for this input.

Mike Murray

Senior Product Strategist, SEROQUEL

1-800-456-3669 ext. 4328

michael.murray@astrazeneca.com

EXHIBIT 14
WIT: PAK
DATE: 11-24-68
LINDA ROSSI RIOS

>From: Rak Ihor IW

>Sent: Friday, February 25, 2000 2:30 PM >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 MI: Gorman Andrew AP; Brecher Martin M
  - >Subject: RE: Short Report on Weight Gain

>ludith

>

>

>

>

>

>

>

>

- >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 antispychotics) 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 > >lhor > > > -----> 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 Iim IP: Litherland Steve S: Murray Michael MF: Rak Ihor IW; Jones Martin AM - PHMS; Denerley Paul PM; Westhead Emma EK; Tumas John JA; Tugend Georgia GL: Czupryna Michael MI: Gorman Andrew AP: Brecher Martin M > Subject: FW: Short Report on Weight Gain > Importance: High > > ludith > > 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'?? > > << File: Weight brief report.doc>> > >