E-mail from Anna Thornton to Ken Kwong, Jamie Danenberg, Charles Beasley
Dec 6, 1999

Subject: Re: Updating hyperglycemia

Jamie and Ken,

Attached below please find the glucose report that Charles is referring to below. Per the e-mail below, we are in the process of updating this report through September 1999 (first 3 years of olanzapine marketing). The WORD document is the main document and the Excel attachment is the line-listing that is inserted into the WORD document (the page #'s show the order).   If you have problems printing this, please let me know. Also, I will send a copy of the article that Charles is referring to below through inter-office mail to both of you today.

Thanks,

Anna
(x77076)

Final Hyper_report_05_Aug_1999_2.

HPB Glucose_2.xls

E-mail from Jamie Dananberg to Anna Thornton, cc: Charles Beasley

Anna,

Please see to it that I also receive a copy of the EXCEL spreadsheet with all of the reports. This will be extremely important for me to answer questions that have come up in the implementation of protocols. Also, please get the manuscript article to me at your earliest convenience (I'm in 28/1 room 105; my AA is Jenette Condon @ 7-9444).

E-mail from Charles, cc'd numerous persons (including K. Kwong, J. Danenberg)

Anna:

I'm asking you to make this #1 priority and will define a set of serial tasks below. I realize that there are several safety related tasks on your plate at presnet, including the jaundice in Australia task which I have just sent, and overdose which I will hopefully soon send (after this). If you need help, please don't be shy about asking Jeff.

Here's what needs to happen:

1) Using the same search algorithm we used for the HPB report, identify all new cases in ClinTrace through the cutoff for the latest PSUR. Get copies of these to Mary Joe and have

her review and update both the detail and summary spresd sheet. I'm particularly interested in the spread sheet / table labeled Table 4.1 in the HPB submission.

2) Make sure Ken has an electronic copy of the spread sheet labeled "Review of Commercially Marketed (Spontaneous) Olanzapine Hyperglycemic Adverse Event Reports" in a format (EXCEL) that will allow him to search and perform analyses. It is *IMPERATIVE* that we all work from the same database and what comes back from Mary Joe is a double-validated version of ClinTrace.

3) As I believe you are doing, obtain a complete lit search for olanzapine and hyperglycemia, etc. and obtain all articles.

4) Same as #3 for clozapine.

5) Same as #3 for risperidone.

6) Same as #3 for quitiapine.

7) Incorporate into the clozapine section in the notebook (summary and article inclusion) and articles not already summarized/included. The most important is the Melkerson et al. This should be described as the most sophisticated study of the issue to date. Get Jamie Dannenberg to review the article and see if he concurs that the appropriate interpretation of the results is that clozapine appears to impair insulin-insulin receptor function and thereby secondarily leads to an increase in insulin release. Incorporate whatever summary Jamie believes appropriate. Also in this clozapine section incorporate one piece of non archival literature -- Poster P1-377 from the Endocrine Society Meeting (the FDA poster).

8) Incorporate all new olanzapine articles in the olanzapine section. One's I'm aware of include: letter by Gatta in DIABETES CARE; letter by Lindenmayer in AM J PSYCHIATRY; article by Goldstein in PSYCHOSOMATICS; article by Hayek in NERVENARZT (in German, but affiliate has provided translation).

9) Create new notebook section for risperidone if articles are found.

10) Create new notebook section for quitiapine if articles are found.

11) Create new notebook section for olanzapine spontaneous data. For the time being we will need to include the HPB report. We will update this once MJB has completed her update.

12) We will also incorporate some updated comparisons from DrugSafety.com into this section. I'd like Paul Berg to run these. Will discuss soon.

13) Once updated spreadsheet that is analyyzable is available from MJB, will work with Ken on some additional analyses -- especially some more refined analyses of time to onset of the severe cases.

Thanks to all,
Charles