

EXHIBIT 14

From: Tumas John JA
Sent: 5/11/1999 1:20:48 PM
To: Murray Michael MF; Davies Diane DE - MMCC; Lawrence Richard RA;
Price Anna AC; Hough Nick NW; Jones Martin AM - PHMS; Litherland Steve
S; Rak Ihor IW; Raniwalla Joher J; Tumas John JA
CC: Goldstein Jeffrey JM
Subject: RE: Small Review

Dear All,

Thank you to those who have commented on this review - I will collate the comments and pass them on to Dr. Small. Dr. Small has contacted Jeff and explained that the schedule for this review has been moved up. We will now have to send our comments to her tomorrow (Wednesday). Therefore, if anyone has any further comments, please pass them along.

Best regards,

John

From: Tumas John JA
Sent: Wednesday, May 05, 1999 9:47 AM
To: Murray Michael MF; Davies Diane DE - MMCC; Lawrence Richard RA; Price Anna AC; Hough Nick NW; Jones Martin AM - PHMS; Litherland Steve S; Rak Ihor IW; Raniwalla Joher J
Cc: Goldstein Jeffrey JM
Subject: Small Review
Importance: High

Dear All,

Attached is a draft review of quetiapine by Dr. Joyce Small. You may recall, Dr. Small was the lead investigator for Trial 8, high dose, low dose quetiapine vs placebo.

Dr. Small has asked that we review the document to ensure that the most current information is included. May I ask that comments be limited to this request and any inaccuracies found. She is not looking for editing support and would like to keep Zeneca's influence on this review minimal.

Please return any comments to me by Thursday, May 13.

Best regards,

John

<<File: QUETIAPI.NE.doc>>

From: Hough Nick NW
Sent: 5/10/1999 9:06:26 AM
To: Murray Michael MF; Davies Diane DE - MMCC; Lawrence Richard RA;
Price Anna AC; Jones Martin AM - PHMS; Litherland Steve S; Rak Ihor IW;
Raniwalla Joher J; Tumas John JA
CC: Goldstein Jeffrey JM
BCC:
Subject: RE: Small Review

John,

here are my comments on 'Small', some of which reflect my usual concerns, ie selective use of QUEST, overlooking what happened in study 14 etc; however there are also some obvious positive messages that could be added:

- * elderly data should be based on 52 weeks if possible
- * selective inclusion of QUEST data and not COSTAR means that this paper is unsuitable for 'promotional purposes' - this paper goes even further than the visual aid ('data display' approach?) since the author actually makes a comparative statement - 'with advantages for QTP on depression ratings and the CGI'
- * therefore, not 'approvable' for international promotional purposes
- * selective inclusion of QUEST data is in conflict with our publication policy since we have no plans to do anything with COSTAR
- * study 14, the head to head comparison against haloperidol unfortunately resulted in a 'p-value' in favour of HAL on the positive symptom scale; therefore it is not possible to say that relief of positive symptoms appears comparable to standard neuroleptics
- * 1st para under 'neurological effects' tends to switch back and forth between the HAL and CPZ comparative data and doesn't flow logically therefore
- * could perhaps include the CLOZ to QTP switch data wrt to weight gain 'reversal'/ improved diabetic symptoms ??
- * need medical check on what is said wrt ECG/ QTc intervals
- * under therapeutic potential, 2nd para - 'studies of these applications' ...this is written as though something has been described immediately previously relevant to this statement??

Hope this is helpful,

Cheers,

Nick

>-----

>From: Tumas John JA
>Sent: 05 May 1999 14:47
>To: Murray Michael MF; Davies Diane DE - MMCC; Lawrence Richard RA;
Price Anna AC; Hough Nick NW; Jones Martin AM - PHMS; Litherland Steve
S; Rak Ihor IW; Raniwalla Joher J
>Cc: Goldstein Jeffrey JM
>Subject: Small Review
>Importance: High
>
>Dear All,
>
>Attached is a draft review of quetiapine by Dr. Joyce Small. You may recall, Dr. Small was the lead investigator for Trial 8, high dose, low dose quetiapine vs placebo.

>
>Dr. Small has asked that we review the document to ensure that the most
>current information is included. May I ask that comments be limited to
>this request and any inaccuracies found. She is not looking for editing
>support and would like to keep Zeneca's influence on this review
>minimal.
>
>Please return any comments to me by Thursday, May 13.
>
>Best regards,
>
>John
>
><<File: QUETIAPI.NE.doc>>
>

Unknown

From: Gavin Jim JP
Sent: Wednesday, December 08, 1999 12:32 PM
To: De Vriese Geert
Cc: Holdsworth Debbie D;Tumas John JA;Tugend Georgia GL;Czupryna Michael MJ;Gorman Andrew AP;Wilkie Alison AM;Litherland Steve S;Murray Michael MF;Rak Ihor IW;Owens Judith J;O'Brien Shawn SP;Denerley Paul PM;Goldstein Jeffrey JM
Subject: RE: 2 EPS Abstracts for APA
Attachments: jamapubs.pdf

Thanks for this Geert. If I could add my own thoughts in advance of the GPT tomorrow...Certainly any progress on the (selective) use of data from COSTAR would be particularly appreciated, as I'm currently getting mixed messages on whether we use the EPS data from this trial.

I was interested to hear that we are discussing the recent JAMA article on the reporting of clinical trials (link attached). This article concerns me as it highlights what appears to be an increasing scepticism among journal editors with regards to certain aspects of company-sponsored publications. Janssen have had their fingers burned in the past in this regard, and are consequently cited every time such an editorial appears, something that presumably irritates the hell out of them. Quite apart from any ethical considerations, if they thought we were publishing positive data vs risperidone from QUEST while results from a second trial were being buried, they'd be onto it in a flash. Selectively using (for example) the EPS data from COSTAR is pushing it too far in my opinion, and might prove extremely damaging in the long run (and you can bet Janssen would push it), and would destroy our current high standing in the publishing community.



jamapubs.pdf (112 KB)

Regards
Jim

From: Owens Judith J
Sent: 08 December 1999 09:24
To: Gavin Jim JP
Subject: FW: 2 EPS Abstracts for APA

FYI

From: De Vriese Geert
Sent: 08 December 1999 08:42
To: Baker Kendra; Tumas John JA
Cc: Scanlon Rose Ann RA; Denerley Paul PM; Owens Judith J
Subject: RE: 2 EPS Abstracts for APA

Kendra,
John,

REDACTED

From: Baker Kendra
Sent: 07 December 1999 22:49
To: Owens Judith J; De Vriese Geert
Cc: Tumas John JA; Scanlon Rose Ann RA; Denerley Paul PM
Subject: FW: 2 EPS Abstracts for APA

PRIVILEGED AND CONFIDENTIAL

REDACTED

Best regards,
Kendra Baker
Attorney
Legal Department
AstraZeneca
Tel. (302) 886-4233 Fax: (302) 886-8221
Kendra.Baker@astrazeneca.com

From: Scanlon Rose Ann RA
Sent: Tuesday, December 07, 1999 2:33 PM
To: Baker, Kendra
Subject: FW: 2 EPS Abstracts for APA

REDACTED

Rose Ann Scanlon
Assistant General Counsel
AstraZeneca
Telephone: 302 886 4009
Fax: 302 886 8221

From: Denerley Paul PM
Sent: December 07, 1999 10:24 AM
To: Scanlon Rose Ann RA
Subject: FW: 2 EPS Abstracts for APA

From: Tumas John JA
Sent: Monday, December 06, 1999 11:45 PM
To: Owens Judith J; Jones Martin AM - PHMS; Litherland Steve S; Gavin Jim JP
Cc: Holdsworth Debbie D; Tugend Georgia GL; Czupryna Michael MJ; Gorman Andrew AP; Wilkie Alison AM; Murray Michael MF; Rak Ihor IW; O'Brien Shawn SP; Denerley Paul PM; Goldstein Jeffrey JM; Woods Paul PB; Holdsworth Debbie D; De Vriese Geert; Shadwell Pamela PG
Subject: RE: 2 EPS Abstracts for APA

Please allow me to join the fray.

There has been a precedent set regarding "cherry picking" of data. This would be the recent Velligan presentations of cognitive function data from Trial 15 (one of the buried trials). Thus far, I am not aware of any repercussions regarding interest in the unreported data.

That does not mean that we should continue to advocate this practice. There is growing pressure from outside the industry to provide access to all data resulting from clinical trials conducted by industry. Thus far, we have buried Trials 15, 31, 56, and are now considering COSTAR.

The larger issue is how do we face the outside world when they begin to criticize us for suppressing data. One

could say that our competitors indulge in this practice. However, until now, I believe we have been looked upon by the outside world favorably with regard to ethical behavior. We must decide if we wish to continue to enjoy this distinction.

The reporting of the COSTAR results will not be easy. We must find a way to diminish the negative findings. But, in my opinion, we cannot hide them.

Best regards,

John

From: Gavin Jim JP
Sent: Monday, December 06, 1999 1:59 PM
To: Owens Judith J; Jones Martin AM - PHMS; Litherland Steve S
Cc: Holdsworth Debbie D; Tumas John JA; Tugend Georgia GL; Czupryna Michael MJ; Gorman Andrew AP; Wilkie Alison AM; Murray Michael MF; Rak Ihor IW; O'Brien Shawn SP; Denerley Paul PM; Goldstein Jeffrey JM; Woods Paul PB; Holdsworth Debbie D; De Vriese Geert; Shadwell Pamela PG
Subject: RE: 2 EPS Abstracts for APA

Steve's comments are pertinent, as the EPS abstracts (for the APA) and the Scourge of EPS review both emanate from the ECNP symposium, and as such represent a potential transition of COSTAR data from a "closed" mtg to a public forum. Coming in late to the debate, the only directive I have on QUEST/COSTAR (contained in a document compiled by Ihor & Martin in August) suggested using them "as clinically appropriate", but independently.

I believe the newly-formed Commercial Support Team will be considering looking at potential ways of using COSTAR. With regards to the present outputs however, a short-term solution (given the impending APA deadline) is to avoid reference to COSTAR in the proposed APA abstract. Whether or not we discuss it in either the poster or the review subsequently will need to be decided by the team, with reference to how we would then need to approach the efficacy story.

Regards
Jim

From: Litherland Steve S
Sent: 06 December 1999 11:51
To: Owens Judith J; Jones Martin AM - PHMS
Cc: Holdsworth Debbie D; Tumas John JA; Tugend Georgia GL; Czupryna Michael MJ; Gorman Andrew AP; Wilkie Alison AM; Gavin Jim JP; Murray Michael MF; Rak Ihor IW; O'Brien Shawn SP; Denerley Paul PM; Goldstein Jeffrey JM; Woods Paul PB; Holdsworth Debbie D; De Vriese Geert
Subject: RE: 2 EPS Abstracts for APA

Martin has drawn our attention to an enduring problem which requires resolution as soon as possible.

- should we publish COSTAR? The disadvantages are obvious, not least that we provide the opposition with potentially damaging data when they calculate p values re the primary efficacy endpoint
- if not, can we extract some information and use this to support our messages? The following is scheduled to appear in Clear Vision (proceedings of the ECNP EPS meeting):

A second study comparing flexible dosing of risperidone (6-10 mg daily) and quetiapine (300-600 mg daily) reported that over 10 weeks significantly more risperidone patients (31.4%) than quetiapine patients (14.1%) In my draft 30.4 and 13.1% ; need to check experienced EPS or akathisia (30.4% and 16.6 15.4 in MR doc%, respectively) (p<0.001 for both comparisons) (Data on file).

This was sanctioned for the meeting but when it appears in Clear Vision it will be in the public domain. We can be accused of "cherry picking" and this may fuel demands to see the entire study (Cochrane would be most interested, for example).

- Are we using QUEST promotionally? If so, we could be accused of not telling the complete story

I am concerned that by doing nothing re COSTAR, except to allow details to emerge in dribs and drabs we are not taking control of the situation. An initial step may perhaps be to canvass expert opinion

outside the Company (I know that we have had some feedback but I understand this was conflicting and uncoordinated).

Steve

From: Jones Martin AM - PHMS
Sent: 06 December 1999 10:55
To: Owens Judith J
Cc: Holdsworth Debbie D; Tumas John JA; Tugend Georgia GL; Czupryna Michael MJ; Gorman Andrew AP; Wilkie Alison AM; Gavin Jim JP; Litherland Steve S; Murray Michael MF; Rak Ihor IW; O'Brien Shawn SP; Denerley Paul PM; Goldstein Jeffrey JM
Subject: RE: 2 EPS Abstracts for APA

Judith

I have no real comments on the Juncos abstract, but am concerned about Tandon's.

In Tandon's results section, he refers to a randomised comparative study. This study is COSTAR. I think that we are still not comfortable about communicating the overall results of this study. Whilst this data may have been presented orally in London, I think this abstract would be the first time we have put anything 'down on paper'. Are we sure that this we can present the EPS data in isolation given the nature of the other results? Will we not create a desire for further information about the study? Can we not refer to published (non-comparative) data for risperidone, as we must be doing this for olanzapine? Should we be looking at the ziprasidone data too? They seem to have dose-response effect as well.

Martin

From: Owens Judith J
Sent: 02 December 1999 17:14
To: Wilkie Alison AM; Gavin Jim JP; Litherland Steve S; Murray Michael MF; Rak Ihor IW; Jones Martin AM - PHMS; O'Brien Shawn SP; Denerley Paul PM; Goldstein Jeffrey JM
Cc: Holdsworth Debbie D; Tumas John JA; Tugend Georgia GL; Czupryna Michael MJ; Gorman Andrew AP
Subject: 2 EPS Abstracts for APA
Importance: High

Dear All

Please find attached, for your review, 2 EPS abstracts that are intended for submission to APA. The abstracts are based on presentations at the AstraZeneca symposium 'CLEAR VISION - A fresh look at EPS' held during this year's ECNP.

Please return any comments you may have by midday (UK time) **Monday 6 December**.

Kind regards

Judith

<<File: Juncos abstract.doc>><<File: Tandon abstract.doc>>

Judith Owens

Ext: 24164

11F34 Mereside