

To: David.J.Carpenter@gsk.com, ryan, wagner,emslie, strober,
perera, lipschitz, strober, me
From: Marty Keller <Martin_Keller@Brown.edu>
Subject: Re: Confidential Draft Paroxetine Pediatric MDD
Manuscript For Your Review
Cc:
Bcc:
X-Attachments:

To All:

We especially need responses from Neal and Mike and team from GSK, since we worked together on this in response to Jetter and from Karen and Graham since they were part of 329 altho- not engaged in response to Jetter.

I am extremely concerned about certain major pieces of this draft, which I believe very strongly need to be revised before it is submitted. This has to do with 329 and differences reported here from that in 329 paper and response we worked on so hard together to Ms. Jetter , which I will also send in separate memos. What makes this crucial is that 329 is in print as is our response to Jetter, whereas the other 2 studies are not and the comparisons may be done easily and lead to extensive questions which it is better to deal with here and highly reduce the likelihood of those comparisons and questions. As written this paper ignores any attempt to reconcile what we wrote before.

1). Table 10 stands out as being very different from what was reported in 329 and in responses to Jetter. We need to understand and explain these differences in this paper, otherwise they are both confusing, possibly misleading and seem very contradictory to what we wrote before.*****No where before (329 paper or responses to Jetter) did we report any of the 3 significant p values reported here.

What accounts for these differences and how to explain this so that we clarify potential confusing, misleading and contradictory statements.*****

2). On page 10 paper should state when the computerized post hoc search and the unblinded manual review of AE's were done, and point out when they were done in relation to publication date of 329 and in relation to response to Ms. Jetter (I am not sure how to word this-- but this problem is the theme of my other concerns). How much might this account for differences in 3 documents should be discussed.

Also the reporting of 30 days post study events was not done by us. We need a good explanation as to why. I do not recall having that data when 329 and Jetter responses were written.

3). Para-4-Rates of emotional lability and the sub-categories within are different then in 329 andsd jetter response. I assume this is due to recent analyses and possibly extension data. This needs to be explained.

4).page 16-last para- when was supplementary search done in relation to 329 and Jetter response? This should be stated , as well as how this influenced the differences ?

5). page 17- para-1-Similar to comment #2 re: why 30 day post treatment were not part of 329 and jetter response needs to be stated.

Staments to Jetter will be coming.

Thanks,marty

6). page 18-llast para- statement that search criteria may have been overinclusive needs to more prominently refer back to 329 and Jetter response*****as an additional mitigation of different rported rates of " potential cases".

Drs. Wagner, Emslie, Ryan and Keller:

As you know, GSK has conducted three placebo-controlled trials evaluating paroxetine in depressed pediatric patients (329, 377, 701). To date, complete results from only one of these studies (329) have been published in manuscript form (Keller et al, JAACAP 2002). While we still plan to fully publish the 701 and 377 studies via separate manuscripts, there is a corporate need/obligation to communicate the key safety and efficacy data from all of these studies to the medical community in a manner which is consistent with the newly revised labeling ASAP. Consequently, we have drafted a "review" manuscript which we hope to submit for publication very soon (attached below for your review). This paper presents the key efficacy and safety data for each of the three studies individually, and it also presents the results of analyses on the pooled dataset (all three studies combined).

A corporate decision was made to include only GSK authors on this particular paper.

However, because you are expert clinicians who were intimately involved in one or more of these studies, we felt it was important to give you the opportunity to comment on the document. Any thoughts or comments you may have are welcome and will be taken into consideration before the paper is submitted for publication.

Best Regards,

David

Attachment converted: Hard Drive:ParoxPedMDDManuscript April 27, (WDBN/MSWD) (000250BC)