Author's response to reviews

Title: Early onset of treatment effects with oral risperidone

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Author's response to reviews: see over
Dear Emma,

Attached please find my revised manuscript ‘Early onset of treatment-effects with oral risperidone’, which we are resubmitting for publication.

First of all I want to thank Dr. Leucht and Dr. Chiu for their thorough review of our manuscript. In addition to addressing the reviewers’ concerns (see below), I also made some changes in the formatting (e.g. I changed Introduction to Background and changed the formatting of the tables).

I addressed the reviewers’ concerns as follows:

Dr. Leucht’s review:

1. I added some patient characteristics to the manuscript (see Table 1). I also mentioned in the discussion that the subjects in this study were severely ill
2. I included the data of day 3 in the text of the manuscript, including a more detailed statistical analysis
3. In addition to benzodiazepines, oral anticholinergics were also allowed as clinically indicated. I also included the dose-range for benzodiazepines and anticholinergics
4. It seems possible that negative symptoms were masked through the very prominent positive symptoms at the time of admission. Still, the rating for negative symptoms also improved during treatment
5. I mentioned the lack of a placebo-group in the discussion

Dr. Chiu’s comments:
Dr. Chiu’s assessment of our manuscript was not quite as positive as Dr. Leucht’s. Given all the short-comings of a smaller-scale observational study, I still see importance in reporting the results.
I included the reasons for discontinuation in the manuscript (see Table 2). Some of the subjects who discontinued, are clearly non-responders (e.g. the subjects who required im-medication). However, some of the other subjects who discontinued the treatment with risperidone, are not necessarily non-responders (e.g. the subjects who requested an early discharge). After all, this is a difficult to treat population and a high drop-out rate is a part of clinical reality.
A last observation carried forward approach to analysis resulted in comparable results with lower improvement in the clinical ratings.

We are looking forward to your comments. Please do not hesitate to contact me if you have any further questions.

Sincerely

Thomas J Raedler, MD