Reviewer's report

Title: A comparison of low-dose risperidone to paroxetine in the treatment of panic attacks: a randomized single-blind study.

Version: 2 Date: 7 October 2008

Reviewer: Francisco Moreno

Reviewer's report:

- Discretionary Revisions

The study seeks to assess the effects of low dose risperidone versus "standard of care" paroxetine for panic attacks. There are several design issues, some of which could be better acknowledged or discussed in order to improve the quality of this manuscript.

Because of the design of the study in which patients with panic symptoms and different diagnosis were considered, it is difficult to generalize findings to a specific condition "like panic disorder".

Patients with concomitant use of antidepressants and mood stabilizers were allowed to participate. This is a potential concern for various reasons, but especially since the standard treatment used as active comparator is an antidepressant. This design issue could have favored the inclusion of antidepressant resistant panic patients. It is assumed that concomitant use of neuroleptics was an exclusion criterion.

For studies of this size, small randomization blocks should be considered to minimize group differences in total N (in this study randomization yielded a 3:2 rather than the proposed 1:1 ratio).

Different pathology underlying panic may in turn carry differential treatment responses. It does not appear that assignments to different treatment groups were stratified based on diagnosis or other criteria.

A standardized diagnostic questionnaire does not appear to have been used to rule out other disorders.

It is not clear why the HAM-A of 17 or greater was required.

It is not clear why people ages 18-20 or over 55 were excluded.

The APA practice guidelines, referenced by the authors as standard of care,
actually encourage low dose initiation and gradual titration of paroxetine as tolerated over time (10 mg initially instead of 30 mg). This issue is of potential concern as it could have importantly influenced the drastic 60% drop out rate in the paroxetine group.

Clear criteria for change of dose of either medication are not specifically spelled out. Maximum doses are not described prospectively.

The risks benefit assessment resulting from neuroleptics could be better described.

How were EPS quantified?

CGI was considered a categorical outcome variable rather than continuum scale, however percentage change is reported. This seems inconsistent.

Subject attrition was very large 60% in the paroxetine group versus 40% with risperidone, this is very large for an 8 week trial although the reported statistics do not show a significant difference here.

The writing can be improved; especially the abstract can be more descriptive.

Level of interest: An article of importance in its field

Quality of written English: Needs some language corrections before being published

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

In the last five years I have received funding for consultation from BMS although not related to the use of paroxetine, or the treatment of panic.