Reviewer's report

Title: Three year naturalistic outcome study of panic disorder patients treated with paroxetine

Version: 1 Date: 5 January 2004

Reviewer: Giampaolo Perna

Reviewer's report:

General
This is an interesting study trying to give an answer to one of the main questions related to the treatment of patients with panic disorder with SSRIs that is the optimal duration of active drug treatment to minimize the relapse risk. As correctly pointed out by the authors, few data are available in literature on this central topic so this study is welcome. The main finding presented suggest that 12 months of treatment with paroxetine seem to be enough to obtain a good prevention of relapse and an additional year of treatment does not improve the situation. The low relapse rate (14%) suggest that medication are able to protect against relapse similarly to cognitive-behavioral therapies. Despite the importance of the issue studied, there however some aspects that the authors should clarified before this study might be acceptable for publication.

Discretionary Revisions (which the author can choose to ignore)

- Minor Essential Revisions (such as missing labels on figures, or the wrong use of a term, which the author can be trusted to correct)
  There are mistakes in the reported rates of relapsed patients 21/127 (17%), 13/72 (18%), 8/55 (15%).

Major Compulsory Revisions (that the author must respond to before a decision on publication can be reached)
This reviewer ask the authors to clarify and/or to comment the following points:
1) Since it has been often shown that comorbid psychiatric disorders might influence treatment course and the rate of comorbid psychiatric disorders are high among patients with panic disorder, the authors should report not only data on drugs and alcohol abuse but also on other psychiatric disorders comorbidities in their sample, then analysing and discussing their influence on the reported findings.
2) Since mean age of patients examined is relatively high, please provide age of onset and duration of illness and include them in the analyses.
3) The rate of patients with a positive family history of anxiety disorders (18%) and with Agoraphobia (41%) seem to be lower than what described in literature. Authors should comment on these specific features of their sample.
4) Define clearly "Full recovery". Does it refer to all kind of panic attacks, also to limited symptoms attacks? only to spontaneous panic attacks or what? Absence of panic attacks during the last week of whatever? This means that some patients might have strong anticipatory anxiety or agoraphobia and be considered having responded with a "full recovery". If so, authors should clarify how many patients of the first group (71 patients) were still symptomatic. Moreover, it is not clear how many patients showed a full recovery. It is clearly state that 72 patients showed a full recovery. Of the other 71, 55 were described as having a "full response", without a clear definition of it (what is the difference from full recovery?) and the last 16 as showing a significant improvement (zero to two
panic attacks per week) definition that overlap with the definition of full recovery (no panic attacks). Authors should clarify this issue.

5) An equal possibility to taper was offered to all the patients or there have been some selection criteria? if authors used selection criteria please clarify what.

6) It seems that the 67 patients who received BDZ in addition to paroxetine, received them only for the first 8-12 week of treatment (as described on page 5). If this is correct the greater tendency to relapse seem to be specifically related to the initial need of BDZ. This might link a higher sensitivity of patients to SSRI s a the risk of subsequent relapse. Please clarify if and how many patients were assuming BDZ during the whole course of treatment with paroxetine. It is not plausible that all 143 patients did not received any BDZ after the first 12 weeks.

7) It seems that being agoraphobia potentiates the sexual side effects induced by paroxetine in patients with panic disorder. This finding should be discussed.

What next?: Unable to decide on acceptance or rejection until the authors have responded to the major compulsory revisions

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No

Declaration of competing interests:

None