Reviewer's report

Title: Adjunctive long-acting risperidone in patients with bipolar disorder who relapse frequently and have active mood symptoms

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Reviewer: Emmanuel Stip

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This was a post-hoc analysis of an open-label study of 162 bipolar patients with persistent mania and/or depression that were treated for 16 weeks with risperidone long-acting injection (RLAI) as adjunctive therapy. Significant improvements in CGI-BP-S, MADRS and YMRS were noted for the population as a whole. Moreover, subjects with predominantly manic/mixed symptoms at baseline showed significant improvements on the CGI-BP-S and YMRS scales and subjects with predominantly depressive symptoms showed significant improvements on the CGI-BP-S and MADRS scales. This article deserves to be published, however we have some suggestions.

We have a few comments in order to improve the manuscript:

1) The persistent symptoms in this population could have been due to noncompliance, which may explain some of the benefits of RLAI. Did the authors measure medication compliance/plasma levels in the patients at baseline? If so, these data would be interesting to report.

2) The authors state that “subjects were receiving therapeutic plasma levels of RLAT by the week 4” (pg.14). Were plasma levels of risperidone obtained to confirm this statement?

3) The purpose of this study was, in part, to compare the effectiveness of RLAI for bipolar patients with predominantly manic symptoms, relative to those with predominantly depressive symptoms. Interestingly, it seems that at week 4, patients with depressive symptoms were showing more remission than patients with manic symptoms, whereas this was the opposite at LOCF endpoint. However, no statistical analyses were performed on these data. Were the differences statistically significant? Could the differences be related to rising plasma levels of risperidone? If these questions are uneasy to answer, the authors might modify the limitations section.