Author's response to reviews

Title: The Management of Bipolar Mania: a national survey of Baseline data from the EMBLEM study in Italy

Authors:
   Cesario Bellantuono (Cesario.bellantuono@univr.it)
   Alessandra Barraco (barraco_alessandra@lilly.com)
   Andrea Rossi (rossi_andrea_a@lilly.com)
   Iris Goetz (goetz_iris@lilly.com)

Version: 3 Date: 24 January 2007

Author's response to reviews: see over
Florence, September 8th 2006

Subject: Revised version of the manuscript by Bellantuono et al

Dear Editor,

Please find enclosed a revised version of the paper about the study entitled “The Management Of Bipolar Mania: A National Survey Of Baseline Data From The Emblem Study In Italy” by Bellantuono et al.

- As requested the paper was revised according with BMC Psychiatry editorial guidelines.

The remaining comments have been addressed as follows:

Reviewer Michael J Ostacher:

Q: Major Compulsory Revisions

The initial study design of the European Mania in Bipolar Longitudinal Evaluation of Medication (EMBLEM) study should be disclosed: two cohorts of patients were recruited, one in which the baseline treatment was changed to olanzapine and another in which the baseline treatment was changed to another drug. It is not surprising that the rate of olanzapine use is so high, as this is an Eli Lilly funded study in which one of the stated purposes of the study was to follow patients started on olanzapine. By not stating so, the authors imply that this high rate of olanzapine prescribing is random, but it is clearly not. To quote from another publication of data from the EMBLEM study "Investigators were asked, but not required, to include 50% of patients into the study who were initiated or changed to olanzapine and 50% of patients initiated or changed to non-olanzapine treatment." (Touloumis C, et. al. Annals of General Psychiatry 2006, 5(Suppl 1):S197) For this reason, data regarding what medications the patients were switched to should be either removed from the manuscript or described in the methods section as part of the study protocol. Because the treating psychiatrists were specifically asked to recruit half the subjects to be prescribed olanzapine and half to be prescribed other compounds, the choice of subjects for participation was not random. Half the sample are patients whose psychiatrists believed would be appropriate for treatment with olanzapine. This should be explicitly stated as a limitation of the study. It is not a limitation of the study that the patients are heterogeneous; bipolar patients are a heterogeneous group. This is also not a "naturalistic observational study". It is an observational study, but not naturalistic, since the treating psychiatrist were asked to include specific proportions of patients. It is not clear that CGI-BP be reliably used to rate the past year's symptoms; the retrospective diagnosis of past year's symptoms should be stated as a limitation of the study.

A: This observation was considered particularly useful to the authors as this let us aware that the description of the Italian sample was not entirely perceived by readers. The Italian sample included in the EMBLEM study was not requested to follow any restriction of prescriptions. This is one of the reasons that gives this sample an intrinsic added value compared with the whole sample included in the EMBLEM study. The paper has been modified to been highlight this aspect in several parts, as the literature reference where the EMBLEM design was described was added Haro JM, van Os J, Vieta E, Reed C, Lorenzo M, Goetz I and the EMBLEM Advisory Board: Evidence for three distinct classes of typical, psychotic and dual mania: results from the EMBLEM study. Acta Psychiatr Scand 2005: 1-9 ). This is the reason why the EMBLEM Italian sample was considered as a naturalistic one in such paper. We hope the modifications included in the text are enough to clarify the difference between the Italian sample and the global one.

Minor Essential Revisions

Q: Data on obesity rates (proportion with BMI > or = to 30) would be interesting to include

A: The incidence of obesity per se, does not seem us to add any particular added value to the description of such sample, as the paper is mainly focused on the description of clinical characteristics of the sample and not on metabolic ones. We think more interesting present these data in a further paper where will be presented the results of the longitudinal follow-up phase..

Reviewer: George Kirov

Minor Essential Revisions
Q: I found the Abstract not informative enough: I feel that giving some details on the medications used prior to inclusion would be more relevant than the scores on YMRS and CGI. These give me no information about the treatment of mania in Italy and they would depend on the setting where patients are recruited, making these statistics of no interest. The types of medications used and combined therapies are the more useful part of this paper and should figure in the abstract.
A: The abstract was modified according with reviewer suggestions.

Q: On p12 there appear to be 2 mistakes: 36 patients with TCA is not 65.8%, perhaps it is 6.58%. Later on the same page reads: "Benzodiazepines were taken prior to baseline by 379 patients (69.3%) and were then prescribed in 379 (59.2%)". Presumably one of these figures is wrong.
A: The figures were modified as requested