Reviewer's report

Title: Mirroring everyday clinical practice in clinical trial design: a new concept to improve the external validity of randomized double-blind placebo-controlled trials in the pharmacological treatment of major depression

Version: 2 Date: 19 May 2012

Reviewer: Bruno Falissard

Reviewer's report:

The paper is better now.

It raises good questions about the relevance of randomised controlled trials versus placebo. It proposes some improvements.

These improvements are going in the good direction, but on my opinion they will not be sufficient. RCTs, in the field of depression in particular, are useful for the approval but quite useless for reimbursement and pricing. And more and more it is reimbursement and pricing which become the critical phases for market access, and thus for treating patients. A consequence is that randomised phase 3 trials will possibly have to be replaced by other designs, like large non randomised pharmacoepidemiological studies which will make possible to deal with the questions of real life effectiveness and personalised medicine.

In this situation, the proposal suggested by the authors will have a limited impact, for instance limited to phase 2 trials.

Quality of written English: Acceptable

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

Declaration of competing interests:

I declare that I have no competing interests