Reviewer's report

Title: Subjective Response to Antipsychotic Treatment and Compliance in Schizophrenia. A Naturalistic Study Comparing Olanzapine, Risperidone and Haloperidol (EFESO Study).

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Reviewer: Prof Peter Buckley

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Accept after revision, which I do not need to see

This report examines the relative subjective tolerability and compliance between olanzapine, risperidone, and haloperidol during a 6 month naturalistic study. Subjective response and compliance are reported as superior for olanzapine over both risperidone and haloperidol, with risperidone also superior to haloperidol in patient tolerability. The report is well written and the literature review is comprehensive and current-although the authors should also discuss their findings in relation to the recent paper by Voruganti et al (Schizophrenia research 2000) which also compares subjective tolerability across new and older antipsychotics.

The authors note that the DAI is a well validated scale for assessing subjective tolerability to antipsychotic medications. However, it was developed with respect to-and reflects accordingly-the subjective impact of extrapyramidal side effects. Given this focus, it is unlikely to capture the spectrum of side effects with atypicals and is weighted toward comparisons of EPS consequences. This point needs to be emphasized. Also, since the doses of olanzapine and risperidone here are not dissimilar from those of the pivotal trials (Tollefson et al, Marder and meibach) for each agent, it would be helpful to include some discussion of EPS findings from these studies and also the impact of dosing on EPS.

The evaluation of compliance, categorized into several groups, is based on physician rating during this naturalistic trial. The authors note that validity of this measurement is untested. However, compliance is notoriously difficult to evaluate. Accordingly, the robustness of the paper's message would be enhanced by greatly minimizing these findings in the text and by removing tables 4 and 6.

Tables 2 and 3 should also be combined.

Competing interests:

Professor is a consultant to and has also received research funding from Eli Lilly and from Janssen Pharmaceutica