Reviewer’s report

Title: Hepatic profile analyses of tipranavir in Phase II and III clinical trials

Version: 1 Date: 29 May 2009

Reviewer: Nicola Abrescia

Reviewer’s report:

1. The question posed by the authors is well defined
2. the methods are appropriate and well described
3. the data are sound
4. the manuscript adheres to the relevant standards for reporting and data deposition
5. the writing is acceptable

Minor Essential Revisions.

1. The number of female subjects evaluated in the study is low. It is not according to what we see in clinical practice. Moreover, it is possible that women are more predisposed to ARVs toxicity. Then, with a more representative number of women, there could be more toxic events. This could be reported.

2. Tipranavir is a drug that can cause allergic reactions (see DHHS guidelines). In the paper is not reported whether AES occurred in allergic subjects. In any case it should be remembered that the allergic predisposition is another risk factor for hepatotoxicity.

3. A severe steatosis, with or without HCV and/or HBV coinfection, is an important risk factor for ARVs related hepatotoxicity. In the paper is not reported the impact of a preexisting steatosis on the frequency of hepatotoxicity. Perhaps it should be reported. One steatosis is only reported among 5 patients with SAEs. It should be remembered that a severe steatosis is a risk factor for HAART hepatotoxicity.

4. On page 13 of the paper the authors say: Following the development of Grade 3/4 ALT/AST elevations, 64.6% (93/144) of patients continued TPV/r treatment without interruption, and in 94.6% of these, ALT/AST returned to Grade 2 or less in a median of 32 days (IQR=14-84 days), while remaining on treatment. This is not concordant with DHHS guidelines. These suggest that HAART must be discontinued when grade 3-4 ALT elevation is symptomatic. HAART discontinuation must be carried out also in the case of asymptomatic grade 4 ALT elevation. Perhaps the authors should clarify why the protocols of analyzed trials were not adhering to the guidelines.

5. to which conferences were the abstracts of references no. 5,24,34,36 submitted?
Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:

'I declare that I have no competing interests'