Author's response to reviews

Title: Characteristics and management of HIV-1-infected pregnant women enrolled in a randomised trial: differences between Europe and the USA

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Version: 2 Date: 7 February 2007

Author's response to reviews: see over
Dear Mr Hodgkinson-Barrett,

Re: MS: 2125262063109380 - Characteristics and management of HIV-1-infected pregnant women enrolled in a randomised trial: differences between Europe and the USA

Thank you for your email of 18 January 2007, with the peer-review comments for the above paper. Please find below a point-by-point response to the comments of referee 3 (referee 1 and 2 having no comments to respond to).

Response to Reviewer's Report – Referee 3

Trivial
This date has now been altered in the reference and the figures updated for 2004.

Minor
Regarding a discussion on time-related changes relating to epidemiology, clinical practices, obstetric history etc, we discuss some changes in the therapeutic and obstetric management of HIV-infected women (pg12 3rd paragraph, re. the predominance of HAART today in Europe (text changed slightly); pg14 1st paragraph, re. the use of elective caesarean section in Europe), and we have modified some text on pg 13 relating to mode of delivery in the USA.

Major
In the light of statements made about issues such as lack of an effect of HAART on the risk of premature delivery in American trials and studies not confirming European data we felt it important to use this large data set to show that there are differences between the continents not only in terms of women but also in terms of clinical practice. The aim of this secondary analysis was therefore to provide a comparative analysis of the characteristics of HIV-infected pregnant women in the USA and in Europe and the observations highlight the marked differences between the two continents in the HIV epidemic in pregnant women. The key finding of significant population differences between continents (most likely caused by a variety of underlying biological, cultural and other factors) is of importance in interpretation of results from previous research, for example, the geographic discrepancy regarding the association between prematurity and antenatal HAART use. With the current very low MTCT rates in resource-rich settings, many of the outstanding questions relating to the optimal management of HIV-infected pregnant women, e.g. the effectiveness of elective caesarean section in PMTCT in women with undetectable viral loads, or the optimal duration/type of neonatal prophylaxis for PMTCT among infants born to women on HAART, can only be addressed through cohort collaborations and pooled analyses. The population differences described here should therefore be considered in the design of future studies. We have made some additions to the text in the conclusion.

As an epidemiological study focusing on MTCT, it was never an aim of this analysis to add to the evidence-base with regard to natural history of HIV or its pathogenesis.

There were only 20 vertical transmissions in the trial, which was stopped early because of the unexpectedly low MTCT rates in both experimental and placebo groups. As a result, the PACTG 316 data set is underpowered to investigate MTCT risk factors (as illustrated in an earlier secondary analysis by Cunningham et al (JAIDS 2004). We agree with the reviewer that underlying population differences may have impacted on transmission rates in the two settings in different ways, with an overall “balancing” of the rates. However, for the
statistical reasons outlined above, we were unable to address this issue. We have modified the final paragraph of the results section to make this clearer.

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With regard to the trial reported in this paper, I confirm that it is in a publicly accessible registry, and the trial registration number has now been included in the abstract.

Yours sincerely,

Dr Claire Thorne