Author’s response to reviews

Title: Immune control of HIV-1 infection after therapy interruption: immediate versus deferred antiretroviral therapy

Authors:

Paola Paci (p.paci@iac.cnr.it)
Rossella Carello (rossellacarello@tiscali.it)
Massimo Bernaschi (m.bernaschi@iac.cnr.it)
Gianpiero D’Offizi (gdoffizi@inmi.it)
Filippo Castiglione (f.castiglione@iac.cnr.it)

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Response to Reviewers

Article’s title: Immune control of HIV-1 infection after therapy interruption: immediate versus deferred antiretroviral therapy

P. Paci, R. Carello, M. Bernaschi, G. D’Offizi and F. Castiglione

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Reviewer: Radjin Steingrover: in reply to the revisions

Question: (regarding question 6, major)
From the response of the authors it’s clear that there’s a contrast between observations in primary HIV infection (PHI) so far and the results from the model. The authors resolve this by defining different phases of PHI and classifying studies with different results as observations in a different phase of PHI. Therefore, staging PHI now becomes important to this paper. Even though staging PHI is difficult, the authors will need to discuss these cohort and phases along a more accepted staging system like Fiebig stadia (Fiebig/Busch, AIDS) and present some data on which the staging is based. The time from diagnosis as is presented in the table is insufficient for this goal although it adds relevant information.

Answer: We understand the reviewer’s need to have a better specification of our patients’ PHI staging and indeed we have reported in a new table (table 2) the results to assays for each patient that allow to classify the patients in one of the six stages described in Fiebig et al. 2003. From this table we read that, on a total of 18 patients for which we were able to recover the assay result:
0 patients are in class I;
1 patients are in class II;
1 patients are in class III;
4 patients are in class IV;
9 patients are in class V;
4 patients are in class VI;
i.e., almost all of our patients are in class IV, V or VI. With respect to the conclusions of our article, this means that our analysis can be consider valid for patients that are in stage IV or above, that is, about after 25 days from HIV exposure. As a consequence there is no conflict with the results found in Steinrover et al. (2008).
To accommodate for such analysis we have partially rewritten the conclusions according to the data reported in table 2 (available in the material and methods section) that show the staging of all our patients. These modifications are colored in green in the revised version of the article.
Question: (regarding question 7, major)
The authors conclude that early treatment regardless of the phase of infection is unwarranted even though they state that they have only compared (their own) phase 2 and 3. The authors may still need to limit the scope of their conclusion.

Answer: As stated above, the conclusions have been rewritten considering that our patients fall in stages IV and beyond and therefore the results reflect that constraint.

Question: Conclusions regarding the efficacy of HAART during PHI can only be drawn from trials like SPARTAC and Primo-SHM. This model currently lacks the external validation required to make a claim like that. The reply that more discussion follows in a forthcoming paper is insufficient.

Answer: We agree with the reviewer and in fact the conclusion of our simulation study, at this stage, should be taken as it is. Indeed we have partially rewritten few sentences in the conclusions to limit their scope.