Author’s response to reviews

Title: Older age does not influence CD4 cell recovery in HIV-1 infected patients receiving Highly Active Anti Retroviral Therapy.

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PDF covering letter
Dear Dr. Borthwick,

This communication will serve as our response to the critical comments regarding the manuscript entitled “Older age does not influence CD4 cell recovery in HIV-1 infected patients receiving Highly Active Antiretroviral Therapy” (Manuscript 1288593109290465), submitted to *BMC Infectious Diseases*. We have carefully read the helpful comments of reviewers 1 and 2 and have either modified the text accordingly or addressed the concerns of the reviewers in the text of this letter, as detailed below. Each revised sentence has been indicated according to page and line, as it appears in the text.

As requested we have modified the manuscript according to the specific formatting checklist.

We want to stress that the manuscript submitted to *BMC Infectious Diseases* contains the complete results and the extended follow up of a study previously published in AIDS (as a research letter). This previous paper, published in January 2003 and reporting data up to June 2001 must be considered only a preliminary report that differs from the present manuscript in few parts, obviously also in consideration of the limited extension of the paper previously published as a letter on AIDS.

In addition, we have decided to further update the present manuscript adding the data of 32 new older patients included up to June 2003 and extending the follow up to December 2003 (page 7 lines 9-12 and page 8 lines 2-6).
Reviewer’s 1 comments

General

The study has been revised by an English mother tongue person.

Major compulsory revisions

"the selection criteria….."
Older and younger patients who were given HAART regularly and with a follow-up of at least six months, were included as cases and controls, respectively (ratio 1:2). The control group was matched by sex, year of HIV diagnosis, presence of AIDS defining conditions and type of HAART (i.e. NNRTI containing regimens or PI containing regimens). A patient (either case or control) was considered as regularly HAART-treated if he/she was under antiretroviral therapy with a combination of two nucleoside reverse transcriptase inhibitors (NRTI) plus either a non nucleoside reverse transcriptase inhibitor (NNRTI) or a protease inhibitor (PI), as single drug or with the addiction of a low dose of ritonavir (i.e. 100 mg bid), for at least three months (page 4 lines 20-21 and page 5 lines 1-8).

“the analysis is not complete…”
We have included in the present version the requested data on the effect on % of CD4 cells and on CD8 cells at baseline (page 8 lines 13-15).

“The criteria used…..”
It is not possible to include in the definition of immunological success the delta CD4 at this point of the work because of the difficulty to retrospectively calculate the delta CD4 value.

“The immunologic effect…..”
We apologise for the omission, the cases and controls were also matched for type of HAART (i.e. NNRTI containing regimens or PI containing regimens). This is now specified in the method section (page 5 lines 2-3).

“HIV viral load....”

We apologise for the mistake, we have corrected the figure 3.

Minor essential revisions

No patients received immunomodulants.

Reviewer’s 2 comments

General
As above indicated, we want to stress that the manuscript submitted to BMC Infectious Diseases contains the complete results and the extended follow up of the study previously published in AIDS (as a research letter). This previous paper, published in January 2003 and reporting data up to June 2001 must be considered only a preliminary report that differs from the present manuscript in few parts, obviously also in consideration of the limited extension of the paper previously published as a letter on AIDS.

In addition, we have decided to further update the present manuscript adding the data of 32 new older patients included up to June 2003 and extending the follow up to December 2003 (page 7 lines 9-12 and page 8 lines 2-6).

Major compulsory revisions

We have included the number of valid cases computed at each time point and the standard deviation around the mean (Figures 1, and 3). We don’t think it is useful to add the number of valid cases and the standard deviation around the mean for Figure 2 representing T CD4+ cell count/mmcl six month increment.
In closing, on behalf of my colleagues and myself, I would like to express our appreciation for the reviewers' critical comments and suggestions for this manuscript and very much hope that, in the present format, our scientific effort fulfils the criteria for publication in *BMC Infectious Diseases*.

Sincerely Yours

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