Reviewer's report

Title: Drug resistance in HIV patients with virological failure or slow virological response to antiretroviral therapy in Ethiopia

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Reviewer: Valeria Micheli

Reviewer's report:

Dear authors:

the article is well written but I’d like to suggest the following modifications:

• Major Compulsory Revisions

1. Results: the authors mentioned a total of 318 with 6 dropped out resulting in 312 eligible patients. In addition 7 died and 10 were lost to follow up: the total is seventeen (5.5%) instead of twenty seven (8.6%), as reported. Please modify or better explain the cohort.

2. Virological outcomes and immunological criteria: to better define the three patients with good viral suppression at 6 months but slow response at 3 months, please mention their baseline viral load.

3. Virological outcomes and immunological criteria: “only five of the 14 participants with virological failure 4/14 (28.6%)”; this sentence is not clear, I mean: are the failures 4 or 5? In table 2 there are only four immunological failure.

4. HIVDR mutations at baseline: the authors mentioned 2 patients presenting combination of NNRTIs and PIs mutations (1 patient: T74S associated with a reduction of Nelfinavir susceptibility and 1 patient: A71T). A71T/V are polymorphisms that occur in 2-3% of untreated persons, so it could be better not to include them in a HIV drug resistance analysis at baseline.

5. HIVDR mutations at 6 months: the sentence “nine of 11 participants with virological failure received ART regimens that were not or only partially active” is wrong, as you showed on table 3 (only 5 patients received a partially active regimen due to the resistance to the NNRTI at baseline). The other four became resistant to their regimen during the therapy in spite of a fully active antiretroviral regimen at baseline.

6. HIVDR mutations at 6 months: the sentence “four out of nine participants with resistance mutations at 6 months had a drug concentration below the limit of quantification” is wrong, because only two patients presenting <0.01 microg/mL had drug resistance mutations at 6 months (#213 and #269); #357 is wild-type and #373 misses drug resistance genotyping.

7. Discussion: the authors mentioned 12% of immunological failure in presence of virological suppression; the rate of immunological failures was 8.7% (22/251) as reported in the results. Please explain the discrepancy. In addition it isn’t clear
the percentage 29% of correct identification of patients experiencing immunological failure. Please better specify.

8. Discussion: the patient presenting slow virological response with a high level resistance to all three drugs; it isn’t strange that the viral load is low, due to the impact of the mutation K65R on the viral fitness. Please add this comment.

9. A warning for the conclusion: don’t underestimate the immunological failure; patients with virological suppression but immunological failure are considered “discordant patients” that deserve a strict follow-up in order to avoid the progression of the infection.

• Minor Essential Revisions

1. Abstract/Results: please modify “harboring resistance mutations in 6/265 patients” into “resulting in 2.2% of acquired drug resistance mutations prevalence”

2. Background: please modify “the challenge of potential emergence” into “the risk of potential emergence”

3. Background: where NNRTIs or NRTIs or PIs are mentioned use the plural form NNRTIs, NRTIs and PIs instead of NNRTI, NRTI and PI in whole paper, tables and legends too.

4. Background: please modify “to have full historical knowledge about primary and secondary resistance mutations” into “to define the pattern of both primary and secondary resistance mutations”

5. Study participants: please specify the unit of CD4 count (cells/microL)

6. Specimen collection and processing: please modify “CD4 count and viral loads were done” into “CD4 count and viral loads were measured”

7. Resistance genotyping: please modify “final extension at; 66°C” into “final extension at: 66°C” as previously indicated

8. Baseline characteristics of the study participants: after Table 1 please modify “all participants were prescribed an ART regimen as per” into “according to the 2008 Ethiopian ART guidelines”

9. Baseline characteristics of the study participants: please uniform the unit for viral load using copies/mL instead of copies/ml

10. HIVDR mutations at 6 months: please specify the technical difficulties for 3 participants missing HIVDR both at baseline and at failure (viral load significantly high!)

11. HIVDR mutations at 6 months: Please modify “resistance to all the three ART” into “resistance to all the three antiretroviral drugs”

12. List of abbreviations: please correct some editing errors.

Kind regards

Level of interest: An article whose findings are important to those with closely related research interests
Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:
I declare that I have no competing interests