Reviewer's report

Title: Increase in transmitted resistance to non-nucleoside reverse transcriptase inhibitors among newly diagnosed HIV-1 infections in Europe

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Reviewer: Saverio Parisi

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This paper studies the patterns over time for transmitted drug resistance mutations (TDRM) using data from the European Spread program. Clinical, epidemiological and virological data from 4317 patients newly diagnosed with HIV-1 infection between 2002 and 2007 were analysed. Patients were enrolled using a pre-defined sampling strategy based on the geographical and risk group distribution of patients newly diagnosed with HIV in the participating countries.

Data about TDRMs from patients included until 2005 (n=2687) have been reported previously by the same group, in 2008 (AIDS) and 2009 (JID). The current analysis contains 1630 additional patients, included between January 2006 and December 2007.

It is a report with very interesting findings; the population is well studied and the phylogenetic analysis is very precious to better define the origin of the findings.

All findings, limitations and strengths of the paper are well discussed.

Nevertheless a few questions due to be addressed:

Do the enrolling criteria based on risk group distribution reflect a complete risk knowledge by the authors?

For example, in table 1, a known risk is reported from 3940 out of 4317 subjects.

The tab 1 is rather inaccurate. A “not known” section would be added in many items.

In the country section, 2404+919+472+354= 4149 and not 4317. Likewise, all the other columns are wrong.

In the sub-type section, many sub-types are lacking, probably due to a difficult genotype definition; in the total column, 2855+1381= 4236 and not 4317; NNRTI: 94+27=121 and not 125 etc.

Further it is not possible to define the different pictures of TDRMs combinations, because TDRMs from multiple drug classes were found in 49 (22.5%), 39 (31.2%), and 28 (26.2%) patients in the NRTI, NNRTI, and PI drug class, respectively, and are therefore counted in more than one drug resistance column.

It would be interesting to see in a separate picture the already published population in relation to the new one, enrolled from the Jan 2006 - Dec 2007
period.

Pag 6: “For NNRTI and PI, the most prevalent drug resistant mutations were K103N (1.7%)....”

As the authors do about NRTI-TDRMs, more details on the other NN-related TDRMs and their trends over time should be added, being NN-TDRMs trend the main result focused in the work.

In the fig 1 of ref 2, JID-2009, a declining trend for NNRTI related TDRM is showed in the last period, and it differs from the fig.1 sub-a showed in this paper.

Please add more details to the discussion in pag 9, about this item, and add in the figures the population size studied in the different time points.

At least, a final remark: the results are very useful, but the period from which they are derived is somewhat passed; we hope that the SPRAD program will be able to confer more recent data to the scientific community in the future.

In conclusion, after these Major Compulsory Revisions, this valuable paper may be published on BMC-ID.

Level of interest: An article of importance in its field

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