Reviewer's report

Title: Predictors of First-Line Antiretroviral Therapy Discontinuation Due to Drug-Related Adverse Events in HIV-Infected Patients: a Retrospective Cohort Study.

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Reviewer: Giordano Madeddu

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The work by Prosperi et. al. was carried out to evaluate the predictors of first-line antiretroviral therapy discontinuation due to adverse events in HIV-infected patients. The manuscript is well-written and addresses the interesting and still controversial topic of tailoring cART on patient’s demographic, clinical and immuno-virologic characteristics. The research question is well posed and the methodology used is appropriate.

In particular only few data are available in literature about the role of predictors of drug-related adverse events which represent the major cause of therapy discontinuation even in late cART period. Recent international guidelines recommend early initiation of cART but no indication about what regimen to choose depending on patient profile are suggested. The attempt to identify a “patient-based profile” is of interest and could be of great support for clinicians in the strategic decision of first line cART.

As expected, older antiretroviral compounds are associated with high risk of therapy discontinuations. However, efavirenz which is a first line drug was also associated with increase risk but only when co-administered with NRTIs different from fixed dose emtricitabine/tenofovir. Among more recent PIs, lopinavir and atazanavir seem to have no increased risk of discontinuations when compared with efavirenz+ emtricitabine/tenofovir. This “real life” result is of great interest particularly in those patients with baseline resistance and/or in those with psychiatric co-morbidities which do not indicate efavirenz prescription. The attempt to identify virus related predictors of toxicity apart from viral load, which has shown non association with therapy discontinuation, is also of interest and deserves further investigations in larger observational cohort which collect data regarding HIV subtypes.

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.