Reviewer’s report

Title: Trends in CD4 counts in HIV-infected patients with HIV viral load monitoring while on combination antiretroviral treatment: results from The TREAT Asia HIV Observational Database

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Reviewer: Marguerite Guiguet

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The study investigated the slope in CD4 counts after initiation of cART, and the relationship between trends in CD4 and HIV viral load. The study was based on an observational cohort with data collected over 18 sites in the Asia-Pacific region. The present analyses included naïve patients who initiated treatment with triple or more combination antiretroviral treatment, and had at least 3 concurrent CD4 and VL measurements after cART initiation. Factors associated with CD4 slopes measured more than 6 months after cART initiation were studied by random-effect linear regression models. Based on parameter estimates, the authors presented calculation of CD4 slope according to patient characteristics. They concluded that, during the first two years of treatment, a positive CD4 slope would occurred even in patients with uncontrolled viral load, as virological failure has to be of major magnitude to prevent CD4 increase.

Major comments

1. My main concern is about the model. Baseline CD4 and baseline HIV VL were not tested for their effect on CD4 slope. HIV viral load was only considered by a linear increase but no distinction was performed between undetectable viral load (VL<=500) or higher viral load. Did you test any interaction with time, such as HIV viral load and time. Last, compared to patients with CDC stage A, patients with TB and/or ADI, and patients with non-TB ADI, presented a greater gain of CD4. However this striking result was not discussed.

2. The description of the patients included could be completed. Years of inclusion should be given, as well as additional information on initial treatment prescribed, treatment switch, and treatment interruption. After 6 months on cART, how many patients achieved virological success, how many ultimately presented virological failure, how many patients died, or were lost to follow-up.

3. Table 1. All patients included were naïve but 11% had HIV viral load <500 copies/ml at cART initiation. This number seems large.

4. Table 2. Disease stage has been categorized as: no AIDS-defining infection; tuberculosis and/or other ADI; non-TB ADI. I do not understand the distinction between the two last categories. It is also not clear if disease stage represented clinical event at cART initiation or at the time of concurrent measurement of CD4 and viral load.
5. Table 4. Sensitivity analysis was performed restricting the observations to those measured during initial treatment, before any class change or stop for more than 30 days. I am surprised that the number of patients (n=1353) in this sensitivity analysis was also diminished compared to the initial analysis (n=1676).

6. Discussion page 9. You stated that "(your) data showed a two-phase CD4 count response with a high CD4 count slope in the first six months after treatment initiation followed by a lower slope", but these results have not been displayed since "CD4 slopes were calculated from CD4 counts measured 6 months after cART initiation".

**Level of interest:** An article whose findings are important to those with closely related research interests

**Quality of written English:** Acceptable

**Statistical review:** Yes, and I have assessed the statistics in my report.

**Declaration of competing interests:**

I declare that i have no competing interests