Author's response to reviews

Title: Clinical outcomes and immune benefits of anti-epileptic drug therapy in HIV/AIDS

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May 31, 2010

Dr. Sabina Alam
Senior Scientific Editor
BMC Neurology

Dear Dr. Alam:

RE: M/S# 1675548424334557/Clinical outcomes and immune benefits of anti-epileptic drug therapy in HIV/AIDS

Thank you for your email of May 28, 2010 indicating the revised manuscript had addressed all of the Reviewer’s comments. We have addressed the concerns raised by Editors in a point-by-point manner in attached pages and revised the manuscript in response to Editors’ comments. We hope that the newly revised manuscript is now acceptable for publication in BMC Neurology.

Thank you for your continued interest in our manuscript.

Sincerely,

Christopher Power
Professor
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The comparison is between viremic and aviremic patients but the reason for this comparison is not justified?

• We thank the Editors for raising this issue and have clarified the rationale in the
We used the aviremic status as an indicator of patients who were adequately treated with cART, i.e. the objective of cART is to achieve undetectable viral load in plasma and thus, viremia per se suggests inadequate or no antiretroviral therapy.

Whereas a better comparison would have been with patients on AEDs and those not on AEDs?

- We agree with the Editors that the comparison between patients on AEDs and those not receiving AEDs could be another approach requiring a case-control design, which we intend to pursue in the future. However, our criteria for analyzing immune and virologic status as well as liver toxicity were based on the duration or the initiation of AED therapy; these parameters were not available in patients who were not on AEDs, thus precluding the suggested comparison.

Matching for hepatitis C status and other important variables.

- We agree with the Editors that hepatitis C virus infection might affect immunologic status of individuals; however, on reviewing our findings we realized that there was no significant difference in the HCV prevalence between the viremic and aviremic group. We apologize for this statistical oversight/mistake and have corrected it in the manuscript and table; moreover, we would be pleased to share the raw data with the Editors with they wish to see them.

- As mentioned above, this study was not intended as case-control analysis; although the baseline CD4+ T cell levels differed between viremic and aviremic groups, this variable is not like to influence with respect to AED use. Additionally, the remaining demographic and clinical variables for aviremic and viremic patients were otherwise similar.

They conclude there was an increase in immune markers in aviremic patients on AEDs compared with viremic patients (although the abstract does not actually describe what the comparison is with).

- We thank the Editors for highlighting this pointing. The mean CD4+ T cell levels rose over the 12 month period after the initiation of AED therapy. We have corrected the terminology in the abstract.

Could this not be due to control of HIV viremia?

- The Referee raises an excellent point and as we stated in the second cover letter in response to question 4 of Referee 3, the rise in CD4+ T cell counts might be due to cART. However, all patients in our cohort received similar cART regimens but only patients who received sodium or calcium channel blockers demonstrated the elevation of CD4+ T cell levels while no immune benefit was observed in patients receiving valproate. These data indicate the potential benefits of sodium or calcium channel blocker AEDs in which further verification in a larger cohort is required.

Similarly, it is difficult to know if there is any difference in liver enzymes, etc if there is no comparison group that did not get AEDs.

- As mentioned above, the liver toxicity was analyzed during the duration of AED therapy and it was not possible to determine the duration in patients who were not on AEDs. In addition, about half of patients did not have additional liver
function test (LFT) abnormality and only one-third of patients had one more LFT abnormality after the initiation of AEDs, indicating that the concomitant use of AEDs and ART did not lead to severe hepatotoxicity. This analysis has been added in the results and in Supp. Fig. 1D.