Author's response to reviews

Title: Randomized Pilot Trial of a Synbiotic Dietary Supplement in Chronic HIV-1 Infection

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Author's response to reviews: see over
Carmela S. Quidoles
Journal Editorial Office
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Re: Revised Manuscript 1321383882691136

May 15, 2012

Dear Carmela,

Thank you for the opportunity to submit our revised manuscript entitled *Randomized Pilot Trial of a Synbiotic Dietary Supplement in Chronic HIV-1 Infection*. It has been revised in response to reviewer reports that you provided us on May 7, 2012. All revisions in the manuscript file are shown in underlined text. Below is a point by point response to reviewer queries. As requested, we also checked the format of our Abstract and structure of the manuscript to conform to the journal and article type.

**Reviewer 1.** No points of concern or questions were expressed.

**Reviewer 2.**

1. The question was raised whether our method of measuring microbial translocation justified our conclusion that microbial translocation did not change. It was pointed out “..using only a segment of the DNA sequence to test for the presence of microbial translocation is misleading as numerous bacterial organisms are present in the Gut. However, in (a) subsequent or future study, efforts should be made to use a metagenomic approach.”

**Response.** We agree that translocation can change both quantitatively and qualitatively, and that to identify the actual bacterial species in circulation using sequencing would be valuable information. Our Real Time qPCR was designed to measure total bacteria, quantitatively, since it was based on a bacterial 16S ribosomal sequence that is highly conserved across bacteria. Thus, we feel that our conclusion that translocation was quantitatively unchanged is not misleading. To improve our clarity on this issue, we removed “qualitatively unaffected” from the section heading on page 17 since our indirect approach to measuring qualitative changes (evaluation of Tm profiles) is indirect and rudimentary. We also added text on pages 17 and 23...
stating that the sequence being amplified in the qPCR assay is highly conserved. In addition, at the bottom of page 25 we acknowledge that our method does not yield information on specific types of bacteria being translocated, but this would be useful information to obtain in future studies.

Reviewer 3.

1. It was requested to clarify the \( p \)-values in Table 2, using a footnote.
   **Response.** A descriptive footnote has been added to Table 2.

2. The suggestion was made to express plasma viral load in Table 1 as a geometric mean.
   **Response.** For subjects with detectable plasma viral load (>50 HIV-1 copies/ml), we replaced the arithmetic mean with the geometric mean in Table 1, and we added descriptive text at the top of page 17.

3. The question was raised as to whether our results would have been different had we included subjects with more advanced HIV disease.
   **Response.** This is a very relevant question, but one we do not have the answer to. We did, however, add text addressing this point and speculating on the outcome (see upper half of page 25).

4. The data in Table 2 was recognized as using multiple comparisons that might account for \( p \)-values that are of borderline significance. It was asked that we discuss this point and not overstate the significance of the findings.
   **Response.** We completely agree with the reviewer, and though we had attempted to interpret the data in Table 2 conservatively, we fell short of this. To correct this, we modified the discussion of this data at bottom of page 22 and top of page 23.

We would like to thank the reviewers and BMC staff for their efforts in evaluating our work. If there are any additional changes that would improve our manuscript please let us know.

With appreciation and on behalf of all authors,

Bill

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