Author's response to reviews

Title: Thyroid disease is a favorable prognostic factor in achieving sustained virologic response in chronic hepatitis C undergoing combination therapy: A nested case control study

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Author's response to reviews: see over
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ADRIAN ALDCROFT
EXECUTIVE EDITOR
BMC SERIES JOURNALS
BIOMED CENTRAL

Dear Adrian,

MS: 1307502268439239
Thyroid disease is a favorable prognostic factor in achieving sustained virologic response in chronic hepatitis C undergoing combination therapy: A nested case control study Huy A Tran, Tracey L Jones, Robert Gibson and Glenn E M Reeves

Thank you for your email dated April 14th, 2011 with valuable comments from the editor and reviewers. Please find attached the revised version. The detailed responses to the comments are as follow:

**Editorial requests:**

#1: The abstract has been revised to adhere to guidelines.

#2: The revised manuscript has been reformatted to conform with the journal style as required.

#3: The manuscript has been read by all authors who all contributed to improve the style of written English.

#4: The clinical implications and its speculation have been considerably toned down as requested.

#5: The corrections and changes have been highlighted in yellow (without track changes turned on) to ease the Editors’ decision making.

**Reviewer 1 (Professor Alessio Aghemo):**

The authors appreciate the reviewer’s encouraging remarks.

**Minor revisions:**

Page 4, the first sentence in the Therapy section has been removed as this sentence had been included in the last sentence of the Method section.
The clinical implication of thyroxine is purely speculative as mentioned. Therefore its use has been suggested to be reserved for high risk cases with a poor chance of success. This section has been toned down considerably.

**Reviewer 2 (Professor Guiseppe Montalto):**

We take notice and agree with the reviewer’s sceptical opinion, especially the alternative explanation for the significant improvement in response to treatment. In fact, this was speculated in our previous publications (Tran et al, 2005 and 2009). It is worthwhile however to pursue and explore this hypothesis in a positive fashion as thyroxine is a relatively simple adjunctive treatment with few adverse effects. A multi-centre observational trial is currently set up to prospectively study this issue. Clearly, the confirmatory data for this will have to be very strong before any ethics will allow clinical trials to proceed.

**Minor concerns:**

Introduction, line 8th: “favourable” has been deleted as this is redundant.

Methods section: First paragraph 3rd line: “as previously described”. This should have been referenced and now done so as suggested.

Second paragraph: the word “All” has been reduced to be less frequent.

Therapy subsection: This has been revised as per reviewer 1.

Thyroid disease subsection:
The exposure to supraphysiological levels of thyroid hormones had been studied previously, reference 10, and generally occurs within the first half of treatment duration. Thyroid diseases in all cases were managed *independent* of HCV treatment regimen. That is HCV treatment was not altered in the presence of thyroid disease.

The question of HCV RNA viral load at the time of the TD is an interesting topic and this has been included in the discussion. The final end-point however in this study is related to the achievement of SVR.

Discussion section:
Page 8, line 22nd: reference 8 has been checked and is correct.

Page 9, lines 3 and 4: “the patient responded well to thyroxine supplement”. This is routine and physiological replacement of thyroxine for hypothyroid patients and has been revised. The authors apologise for this confusion.

The suggestion of adjunctive thyroxine supplement is purely speculative. Such treatment, despite our enthusiasm, remains out of bound and unethical until more supportive data is available.

Table 1: These are administrative clerical errors, The results in age, weight, ALT, AST and viral load have been reviewed and revised including patients treated with 0.8gm of Ribavirin. The authors apologise for this oversight and appreciate the reviewer’s astuteness for pointing this out.
Additional comments: The authors relish the opportunity to present these data and are very much encouraged and heartened to be able to engage in such rigorous and constructive discussion.

With kind regards and please let us know of any more requirements.

Yours Sincerely

HuyATran

HUY TRAN