Reviewer's report

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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Reviewer: Giuseppe Montalto

Reviewer's report:

The paper by Tran HA and coll. entitled: “Thyroid disease is a favourable prognostic factor in achieving …”, although improved in this second submission, still presents some criticisms which deserve consideration.

This referee remains the same opinion as before and has serious doubts about the real usefulness of a thyroid hormone overdose in achieving better SVR rates. Currently patients who develop hyperthyroidism during IFN treatment, are corrected with appropriate anti-thyroid drugs. Now, this study doesn’t prove that higher levels of T3 or T4 result in a better response. That is there are no data, hormone dosages (which timing?), that confirm this result. It is also possible that thyroid hormones are not involved, in the sense that it is possible that a more vigorous response to IFN therapy (for individual reasons) could lead to the development of a TD and at the same time a more effective antiviral response, but the two things are parallel and not at all interfering.

The idea pursued by the AA does not convince this reviewer, on the other hand the same authors have previous publications on the subject and this reviewer, whilst not being convinced, believes that they should move to a larger study, to have such strength and numbers to support their idea. It is not with a study on 19 patients (cases) that new evidence may be added to those already expressed by the AA in the literature.

Introduction section

Line 8th: “favourable” is redundant. Please delete the first

Methods section

First paragraph 3rd line: “as previously described”. Previously in this paper or it lacks a reference?

Second paragraph: in the first 4 lines the word “All” is repeated 5 times. Please, try to delete someone

Therapy subsection: the first line is a repetition of the last line of the previous paragraph.

The dose of Ribavirin is set at 800 mg/day for pts with non-1 genotype. OK, but if you look at the table 1, no one patient is mentioned with this dose; ie, all 95 pts
are scheduled at 1.0gm or 1.2gm.

Thyroid disease subsection: it is nor clear from the text when the thyroid balance has been done and, in the case of TD, if further controls have been done, when and if the supraphysiological levels of these thyroid hormones persisted and at what levels. In other terms, this point needs to be stressed because is fundamental for the understanding of the relationship thyroid hormones/response to therapy.

Yet, is there in this study or from the study from where the pts have been extrapolated, any patient who, because of TD, discontinued the antiviral treatment or anti-thyroid treatment was added? In other words, until which levels of thyroid hormones have we to observe?

At what time of the antiviral treatment TD was evident? At this time the HCV-RNA was already negative or the negativity was reached after the development of TD?

Discussion section
Page 8, line 22nd: the reference 8 is wrong, may be the 9 is the correct one.
Page 9, lines 3 and 4: “the patient responded well to thyroxine supplement”. At physiological or supraphysiological dose?

Table 1
The means of age, weight, AST, ALT and viral load are not convincing; i.e. I’m wondering how is possible that the overall mean age was 47 ± 8 years, while the mean age of both the two subgroups is less.

There are some typing and punctuation mistakes along the text

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

Quality of written English: Needs some language corrections before being published

Statistical review: Yes, but I do not feel adequately qualified to assess the statistics.

Declaration of competing interests:
I declare that I have no competing interests