Reviewer’s report

Title: Long-term outcomes and risk factors of thyroid dysfunction during pegylated interferon and ribavirin treatment in patients with chronic hepatitis C infection in Taiwan

Version: 0 Date: 31 Jul 2018

Reviewer: Akihito Tsubota

Reviewer's report:

Authors reported the long-term impact of pegylated interferon plus ribavirin combination therapy and other factors on the onset of thyroid dysfunction. This nationwide study was analyzed based on data collected from a large number of cases in Taiwan. The results obtained in this study are reasonable and support numerous previous reports of major interferon-induced adverse events.

Major comments:
1. Among patients, 42.9% were diagnosed with hypothyroidism, 31.2% with hyperthyroidism, and 25.9% with thyroiditis. As known well, hyperlipidemia is closely associated with hypothyroidism. Conversely, hypothyroidism generally causes hypolipidemia. All patients with thyroid dysfunction were not always those with hypothyroidism; nevertheless, hyperlipidemia was one of the independent factors associated with thyroid disorders including hyperthyroidism. Did even patients who developed hyperthyroidism have hyperlipidemia at baseline? Would you please elucidate the association clearly?

2. Would you please clarify the definitions of hyper-/hypo-lipidemia and hyper-/hypo-thyroidism in the revised text?

3. Could you refer to the ratios of hypothyroidism, hyperthyroidism, and thyroiditis that were reported in previous studies in the revised Discussion section?

4. Although this is a long-term study, by when was the onset of thyroid dysfunction considered as being induced by interferon-based therapy? For instance, a patient developed thyroid dysfunction five years after the completion of treatment. Is this case related to interferon?

5. Thyroid dysfunction might be caused by HCV infection. If so, did not patients who achieved SVR with interferon-based therapy develop after treatment?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

No

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Acceptable

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