Reviewer's report

Title: A novel biomarker TERTmRNA is applicable for an early detection of hepatoma

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Reviewer: Patrizia Pontisso

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The authors describe the diagnostic performance of serum human telomerase reverse transcriptase mRNA for hepatocellular carcinoma. The results indicate that this approach is highly sensitive and specific, allowing the conclusion that hTERT mRNA is superior to conventional tumor markers in the diagnosis and recurrence of HCC.

The availability of useful diagnostic markers for primary liver tumors is still an unmet clinical need and the study has addressed such an important issue. To better define the clinical relevance of the study, the following points should be addressed:

1. HCC occurs in the majority of the cases on a cirrhotic liver, and cirrhosis is the population at risk, where other tumor markers, such as AFP, are frequently positive, lowering the specificity of the biomarker, when compared to this population. On the basis of these considerations, it would be interesting to calculate the diagnostic performances of hTERT mRNA, including ROC curve analysis, using cirrhotic patients and not healthy subjects as controls.

2. The clinical significance of monitoring the effect of therapies using hTERT mRNA has been reported only in two representative cases. It is unclear whether the concordance with clinical outcome is a common behavior in all patients or whether this has not been evaluated in all treated patients. At list 12 months follow-up after treatment should be required to draw any conclusion on the prognostic value of the behavior of this marker.

3. The authors describe that the level of hTERT mRNA correlates with tumor differentiation. However, in Fig. 6 (panel D) the higher levels were shown in poorly differentiated cases, while in the discussion (pag.16) they report that “…hTERT mRNA expression was closely associated with well to moderate differentiation degree..” This point should be clarified.

Minor comments:

- In the Patients and Methods section the list of all the clinical parameters, also reported in Fig 2 (and not in Figure 1) is redundant.

- The authors should specify how the diagnosis of HCC was achieved in tumors of size <10mm.
- English should be substantially improved

**Level of interest:** An article of importance in its field

**Quality of written English:** Not suitable for publication unless extensively edited

**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' below.