Reviewer's report

Title: A phase II open label trial evaluating safety and efficacy of a telomerase peptide vaccination in patients with advanced hepatocellular carcinoma

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Reviewer: Fabio Grizzi

Reviewer's report:

The Authors investigate the effects of a low dose cyclophosphamide treatment in combination with a telomerase peptide (GV1001) vaccination in a series of patients with advanced hepatocellular carcinoma (HCC). They did not show antitumor efficacy as per tumour response and time to progression.

Although the Authors evaluate a restricted number of patients (total 40 from three different European Centres), the manuscript is well written, well done and of interest.

The Authors conclude that further studies are needed to analyze the effect of a combined chemo-immunotherapy strategy to treat patients with HCC.

Discretionary Revisions:

• Many acronyms have been found throughout the manuscript such as GM-CSF, TTP, TTSP, PFS, OS. For a general reader it should be better to explain in extenso before the use of an acronym.

• The Authors described in the Results sections the patients characteristics. However all of the data presented might be introduced in the Materials and Methods section, more specifically into the Characteristics of patients.

• The criteria adopted by the Authors to define the state of “progressive disease” and that of “Stable disease” should be indicated.

• Because the Authors include patients with HCC and underlying a viral (HBV and HCV) and non viral cause (alcohol) of disease it should be interesting to known whether differences in the frequency of CD4+CD25+Foxp3+ regulatory T cells.

• The Authors stated that all of the patients were evaluable for safety analysis and efficacy evaluation. However, they report that efficacy was not assessed in three patients due to clinical progression or death before treatment was initiated.
• Additionally, the Authors stated that patients were not eligible if they had received any type of anti-tumour treatment or corticosteroids within the 4 weeks of pre-treatment with cyclophosphamide. However, in Table 1 it is not clear whether 65% of patients had prior received therapy and what kind of therapy or not. This point should better clarified

• References should be formatted on the basis of the Journal Instruction for Authors.

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

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interest’s below