

Article information: <https://dx.doi.org/10.21037/tgh-23-22>

Reviewer A

In this study, the authors conducted a retrospective exploratory study, which evaluated the role of several SNPs in advanced HCC patients treated with sorafenib or TACE. They find immunomodulatory SNPs with potentially prognostic implications, to be validated in further studies.

Specific Comments/Suggestions:

Introduction

- In the introduction the authors should explicit the acronym VEGF, Ang2, PDGF.

Reply: manuscript updated

Changes in text: page 1 of manuscript

- Insert the reference of the clinical trial IMbrave 150 in line 99 (DOI: 10.1056/NEJMoa1915745)

Reply: manuscript updated

Changes in text: page 3

Objective

- the extended wording of “SNP” must be used the first time it is cited (line 123). Check it.

Reply: manuscript updated

Changes in text: page 4

Methods:

Blood specimen analysis

- Do not describe how you extracted and quantified germline DNA. Complete this.

Reply: DNA extraction/quantification and genotyping process updated in text

Changes in text: page 10

- Were the analyzed SNPs in Hardy Weinberg equilibrium? Add it.

Reply: Descriptions of HWE of SNPS is in results on page 14

Results

-In this section the results obtained from your studies should be reported. The description of the other studies (Studies of SNPs as biomarkers in advanced HCC treated with Sorafenib) should be moved into discussion and shortened.

Reply: This section was moved to the discussion and shortened

Changes in text: starting page 21

-Table 1 can be removed or placed in the supplementary, they are not your results.

Reply: this table was removed, and exists in the supplementary

- This paragraph “Selection of Polymorphisms for Exploratory Analysis” is repeated above. Make more clarity.

Reply: Removed this section from the results to avoid duplication from the section in the Methods

Changes in text: starting page 6

Chapter 8: Conclusion: “Chater 8” probably it is a typo. Correct it.

Reply: fixed

Others comments:

- Next to the rs numbers write the name of the gene, to improve understanding.

Reply: updated throughout body of manuscript

- Text too long and with repetitions. Summarize where possible.

Reply: repetitions removed

- There are no references to the Tables and Figures and Supplementary Tables and Figures within the text. Insert these references in the right place along the text.

Reply: Refernces added to tables/figures and supplementary document

- Improve the English language of the text.

Reply: Edited for grammar/spelling

Reviewer B

This is a very interesting study which the authors have performed a systematic review with genotypic evaluation on patients diagnosed with HCC. However, some modifications should be made to improve the quality of the text.

First, the introduction is well written. But, currently, a study was published on the evaluation on genetic polymorphisms and HCC by a systematic review with Bayesian evaluations (<https://doi.org/10.1016/j.gene.2023.147392>). This study should be cited and discussed in the introduction or discussion section.

Reply: Introduction updated to include this reference

Changes in text:page 3

Second, the authors should include the ethic aspects for the collection of participants.

Reply: ethnicity of patient population specified in table 2, page 12

Third, the authors should detail the genotypic methods (with the complete description of reagents and methods).

Reply: methods updated to elaborate on genotypic methods

Changest in text: page 11