

REVIEWER #1

1. You should avoid paragraphs with only one sentence, except for paragraphs that state the purpose of the introduction.
2. You should avoid using the same relative pronoun in a sentence such as “which is a M1 phenotype marker which is associated with macrophage-dependent T-cells activation and favorable prognosis in several cancers[50].”
3. P16 English expression “in which PD-L1 is involved limits is usefulness” is strange.

1. We have modified the text in order to avoid paragraphs with only one sentence.

2 and 3. According to the Reviewer comments, we have modified the text in order to improve the fluency and clarify the meaning (page 8 lines 19-21, page 16 lines 24-29).

REVIEWER #2

1. Authors cited the reference 94 and discussed the reason why the underlying liver diseases affect the tumor response to immunotherapy. What do you think about relationship between the treatment method (ICI monotherapy, combination with ICI and anti-VEGF agents, and ICI + ICI therapy) and etiology of liver diseases? Please authors discuss it more details.

Thanks to the Reviewer for giving us the opportunity to underline this concept. In the chapter “Conclusions and future perspectives” we further summarized data on the efficacy of ICIs and antiangiogenic agents, and we also proposed a differential approach to therapy according to the current evidences (page 18 lines 14-27). We have discussed in detail the relationship between the underlying liver diseases and the response to ICIs and anti-angiogenic drugs in the section “Effectiveness of immunotherapy in NAFLD-related HCC” and “Benefits of antiangiogenic drugs in NAFLD-related HCC”.

2. Please authors cited following real-world data concerning the sorafenib (PMID: 34693661) and lenvatinib (PMID: 34515171), and discuss it. In addition, according to the reference 94 (PMID: 34847382), there are significant differences in patient characteristics at baseline between the NASH correlate- and no NASH correlate-patients, leading to possibly significant bias. I believed that citing reference 94 is not suitable for your manuscript.

We thank the Reviewer for giving us the opportunity to discuss these studies. We have read them with great interest and carefully analyzed them. We added data about sorafenib (PMID: 34693661) and lenvatinib (PMID: 34515171) in the paragraph “Benefits of antiangiogenic drugs in NAFLD-related HCC” and discussed the main findings (page 14 lines 26-29 and page 15 lines 2-6). Moreover we eliminated reference 94 from the text.