Peer Review File

Article information: https://dx.doi.org/10.21037/hbsn-23-646

Reviewer A:

Analysis Based on the Chinese Population.
An interesting paper discussing a timely topic in HCC.
Some changes are required in my opinion:
- the discussion should be expanded and a more personal perspective should be included
- The background of the role of systemic treatments in HCC should be better discussed, and some recent papers regarding this topic should be included (PMID: 35031442 ; PMID: 32772560; PMID: 36579504 ; Atezolizumab in advanced hepatocellular carcinoma: good things come to those who wait.
Rizzo A, Ricci AD, Brandi G.
Immunotherapy. 2021 Jun;13(8):637-644. doi: 10.2217/imt-2021-0026. Epub 2021 Apr 6.
PMID: 33820447), only for a matter of consistency

Reply:
Thanks for your professional comments, and we have further discussed the role of systemic treatments in HCC patients in the Introduction and Discussion section of the revised version.

- A linguistic revision is needed.
Reply:
Language refinements has been done.

Changes in the text:
Add the following content (see Page 4, line 9-11): Radical treatment and locoregional therapies are appropriate for HCC patients in the early to intermediate stages, while the majority of HCC patients receive systemic treatments[4].
Add the following content (see Page 5, line 32-34): The phase III trial of IMbrave150 showed that atezolizumab (a PD-L1 inhibitor) combined with bevacizumab (an antiangiogenic agent) result in encouraging survival benefits compared to sorafenib alone[9,10].

Add the following content (see Page 10, line 179-180):
Additionally, in the realm of liver cancer adjuvant therapy, numerous clinical trials are underway, showing significant potential [24].

Add the following content (see Page 10, line 181-185):

Immunotherapy for liver cancer does not have definitive predictive markers; however, some studies suggest that certain indicators may predict the efficacy of immunotherapy in liver cancer. Gender is also one of the factors affecting the efficacy of immunotherapy, with similar benefits among men and women in immune combination therapy, but more benefits among men in the population treated with immune drug monotherapy [25].

Reviewer B:

This study's topic is interesting. The approach is original and the validation part of the study appreciable. Indeed, the retrospective part of the study is the main issue.

I would stop at the validation steps to build up an article.

I would ask the authors to discuss about the abstract sentence on findings: " The DCA underscored the clinical utility of the nomogram-29 based prognostic model, further substantiated by the Area Under the Curve (AUC). ". Could you please expand the discussion on it ?

English used is appropriate.

Figures' graphical quality has to be improved.

Reply:
1.The language expression and the quality of the pictures have been further improved.
2. The validation of DAC by the AUC curve result, has further strengthened and expanded in the discussion section.
3. Thanks for your valuable suggestion, we have further improved the Figures' graphical quality.

Changes in the text:
Add the following content(see Page 12, line 228-229):
The DCA emphasized the practical value of the prognostic model based on the nomogram, supported by the Area Under the Curve (AUC).

Reviewer C:

The study population consisted of a large number: 485 patients
Immunotherapy is of high interest in HCC and the nomogram approach is a new area.

1. The title should indicate, that it is a single center study
2. The statistics might be cross examined by a statistician

3. I found at least two recent publications dealing with nomograms in HCC patients receiving immunotherapy that should be added into the discussion.

First article: Published online 2023 Jun 16. doi: 10.1186/s12885-023-11064-1
PMCID: PMC10273750
PMID: 37328805
Nomogram for predicting survival in patients with advanced hepatocellular carcinoma treated with PD-1 inhibitors: incorporating pre-treatment and post-treatment clinical parameters

Second article: Development and Assessment of Nomogram Based on AFP Response for Patients with Unresectable Hepatocellular Carcinoma Treated with Immune Checkpoint Inhibitors
Cancers 2023, 15(21), 5131; https://doi.org/10.3390/cancers15215131

Reply:
1 The title has been changed and the content of the single-center study has been included.
2. The statistics of this study has been reviewed with statistical experts again and are correct.
3. Two more recent studies on immunotherapy have been included in the discussion.

Changes in the text:
Change the following content (see Page 1, Title):
A Novel Nomogram for Predicting the Prognosis of Hepatocellular Carcinoma Patients Following Immune Checkpoint Inhibitors Treatment Beyond Progression: A Single Center Study Based on Chinese Population

Add the following content (see Page 10-11, line 185-189):

Peripheral blood biomarkers can predict the prognosis of HCC patients treated with PD-1 antibodies. The development of nomogram models can help screen potential patients who may benefit from immunotherapy. However, the sample size included in this study was limited, and further expansion of the sample is needed to confirm the conclusions of this study [26]. Meanwhile, AFP can also be used as a predictor of the efficacy of immunotherapy in liver cancer [27].