World Journal of Gastroenterology

Manuscript 40269: Biomarkers for HCC – what's new on the horizon?

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Dear editor,

Thank you for the valuable reviewers' comments. Please find a specific point-to-point reply to each comment.

Looking forward to your positive evaluation, I remain with best regards,

Yours,

Matthias Ocker

Reviewer 1

I thank the reviewer for the positive evaluation of the manuscript.

Reviewer 2

I thank the reviewer for the valuable comments:

1. the abstract is quite vague
   The abstract was rewritten and is now more specific.
2. the immune checkpoint inhibitors need clarification (should be at the key words)
   Immune checkpoint inhibitors were added as a key word.
3. you spend more place to describe the newer treatments than the newer biomarkers
   As currently no predictive biomarkers are available for established therapies, the outlook on upcoming new treatments seems important as these products usually have a biomarker based patient selection in place. Yet, the data for HCC is still very limited and also for immune checkpoint inhibitors available studies were not strongly biomarker-based. Therefore, it is important to describe the new treatments and to show that still no clear predictive biomarkers are in sight there.
4. we need better description of the old biomarkers and more detailed info of the new (eg Osteopontin, Canavaninosuccinate, Glypican 3, High Met expression).Esp when we combine some of those (eg. AFP and Osteopontin)
   Currently, no biomarker that is being predictive for treatment outcome is available in HCC. Also the here mentioned biomarkers like Osteopontin or Glypican 3 are only prognostic biomarkers, i.e. they can be used for diagnosis, surveillance and survival monitoring of patients but were not shown to correlate to e.g. sorafenib response. Thus, these biomarkers are not extensively discussed in this editorial. A brief summary of those biomarkers is added into the Introduction section of the manuscript:

Here, newer biomarkers like osteopontin, glypican-3 or high c-met expression have shown additional value, esp. when combining these parameters as was shown for osteopontin and AFP [11-13].

Additional references 11-13:

11 Duarte-Salles T et al. Circulating Osteopontin and Prediction of Hepatocellular Carcinoma Development in a Large European Population. Cancer Prev Res (Phila) 2016; 9(9): 758-765

12 Xiao WK et al. Prognostic significance of glypican-3 in hepatocellular carcinoma: a meta-analysis. BMC Cancer 2014; 14: 104

13 Kondo S et al. Clinical impact of c-Met expression and its gene amplification in hepatocellular carcinoma. Int J Clin Oncol 2013; 18(2): 207-213

Editorial comments

1. Formatting suggestions were included. All changes are marked in track change mode.
2. Audio core tip is provided.