

Responses to reviewer's comments

Reviewer 02527645 : we thanks the reviewer for his fruitful corrections.

To date, the enhancement models (EASL guidelines and mRECIST) were widely used in practice and were proved in preference to the conventional WHO and RECIST criteria. So, this section requires review. It could be shortened. Indeed, the major clinical unmet need with sorafenib is how to evaluate the effect of the treatment, and when to stop treatment. I think the authors should provide more analysis and comprehensive discussion on this topic based on the current literature.

Response: as required we have shortened this chapter; but, if I agree on the fact that contrast enhanced criteria are widely used, the first demonstration of their interest has been presented in previous ILCA by Lencioni et al, paper to be published.

As author described that knowing the parameters of survival will be of major importance. We think this topic should be discussed with two sub-titles (such as, absolute contraindications and relative contraindications for continuing Sorafenib) based on the current literature. This will be simple and clear instructions to the reader.

Response: We have tried to do so but that looks a little bit too “artificial” and we have reshaped this subchapter.

The authors claim that the role of alfa-fetoprotein serum levels remains unclear. However, several studies (Chan et al, J Clin Oncol. 2009, Shao et al, Cancer. 2010, Personeni et al, J Hepatol.2012) have proposed the significance of alfa-fetoprotein serum levels in patients with HCC undergoing systemic treatment. So it is recommended to introduce these previous studies and interpret the data accordingly.

Response: We fully agree and corrected our paper accordingly.

Biomolecules predictors also play an important role to predict the prognosis.

Response: We fully agree but consider that this is another difficult problem and prefer not to deal with this vast problem.

We also deleted the last sentence of our conclusion.

Reviewer 00182901

In the last sentence “In contrast, if patients do not have worsening PS or Child-Pugh classification or if macrovascular invasion occurs, then sorafenib can be pursued, but we must take into account the important prognostic value of the progression pattern.”, please check whether macrovascular invasion “occurs” is correct. Isn’t it “does not occur”?

Response: many thanks ! correction done.

In the Table 1, it would be good to describe “pattern of progression” in more detail

Response: we tried to do so but this Table was then difficult to read, we then preferred to keep the same presentation.

The title of Ref 31 is missing

Response: correction done, sorry, a copy-and-paste error ...

Reviewer 00182864

Dear Author, I think that your paper needs more data. Sincerely

We have tried to improve our paper ... hoping that this new version will be better...