Answering reviewers

Reviewer Number ID: 05630791

The manuscript is a retrospective cohort study investigating the outcomes of regorafenib vs cabozantinib as second-line therapy for advanced hepatocellular carcinoma. The study is very well documented and the results are based on a solid statistic analysis. This study adds important evidence about the real life results encountered in clinical practice in terms of effects in controlling the neoplastic disease and the side effects encountered. The discussions are well conducted and includ the most relevant studies. The conclusions have potential clinical value, as the authors found that inflammation-related factors (CRP and NLR ratio) and AST increased over time were associated with a higher risk of TKI failure and propose an online score to assess progression risk based on these variables after two months of treatment. I recommend accept for publication.

Response:

we are very grateful to the reviewer for accepting to revise and evaluate our manuscript. We also thank him for his comments. In line with his judgment, we have made no changes.

Reviewer Number ID: 02936529

This multicenter retrospective trial compares two broad-spectrum tyrosine kinase inhibitors (TKIs), regorafenib (REG) and cabozantinib (CBZ) as a second-line rescue treatment for HCC after first-line systemic treatment failure... with progression-free survival (PFS) as primary endpoint. A 2-month online progression risk calculation is also proposed. The study is impecable regarding the methodology and selection criteria of patients, and the subject of the study is extremely justified. The results are clear and tables very well disposed. The discussion session is concise and invites the reader for future perpectives in the HCC systemic treatment scenario. The only limitation of the research is its retropective nature and the possible selection bias inherent of retropective studies. Congratulations for the authors.

Response:

we once again thank the reviewer for reviewing and evaluating our manuscript. we felt that this study was important; patients with advanced hepatocellular carcinoma from clinical trials do not always fit with patients from routine practice. Moreover, in the present situation, two different molecules are being used for the same population, and we do not currently have a comparative study. We are very grateful for his comments. In accordance with his judgment, we have not made any changes.