Reviewer 1

The aim of the study was to find prognostic indices in BCLC stage C of HCC. The authors note that HCC patients categorized to BCLC class C are in fact a heterogeneous group of patients and some of them could be permanently cured. It is shown that BCLC stage B patients may benefit of surgery with acceptable long term results (Kamiyama WJS Oncol 2017) but patients belonging to stage C reguires sub-classification according to prognosis such as Jeong-Ju Yoo et al state in their paper in Cancer Res Treatment 2017 https://doi.org/10.4143/crt.2017.126 The present paper does not disclose significantly new aspects compared to the Korean publication with 612 stage C patients. In the present study dynamic changes of AFP and disease control were regarded as findings not reported before. However, it is not surprising that high AFP level at the early stage and disease control long-term were significantly associated with mortality. Some minor remarks:
- Discussion should be started with major findings of the study Actually, the present structure of the discussioni starts with the major findings and follows a logical sequence
- Exact numeric values with confidence levels are not needed in Discussion. Amended in the text
- The finding that high AFP level is associated with poor outcome is a well known fact.
- Table 4. Was the tumor of patient PT3 verified with histology? The size of the tumor could not be measured? Long-term survival with sorafenib only seems a bit suspicious. All the other long-term survivors were treated with intention of curative treatment. The original tumor of patient 3 was a dishomogenous infiltrating area near a portal vein branch with neoplastic thrombosis, liver biopsy confirmed the diagnosis of HCC.

Reviewer 2

The manuscript 'Reverse Time-Dependent Effect of Alphafetoprotein and Disease Control on Survival of Patients with BCLC Stage C Hepatocellular Carcinoma ' by Francesca Romana Ponziani et al. investigated the predictors of survival in HCC patients with BCLC stage C and found that AFP and DC have a reverse and dynamic influence on survival period in a time dependent manner. The authors illustrated this conclusion via statistical analyzing effects of multiple variables on Primary Endpoint: Patients' Survival and Secondary Endpoint: Disease Control. Overall this manuscript is clearly presented, However, this study is merely a retrospective study, in addition, due to the limited sample size, complexity of other factors and strong heterogeneity, the conclusions drawn by the author may exist some bias. Furthermore, with the update of diagnosis and treatment technology, the clinical significance derived from previous samples maybe play a minor role. Some writing and formatting mistakes should be amended, for example, "insitutional" should be "institutional", "anonimous" should be "anonymous", whether "Hepatocatt" should be "Hepatocyte".We have corrected all writing mistakes, however the word Hepatocatt is correct as it is the name of our intitutional board.