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Supplementary data
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Author names in bold designate shared co-first authorship

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Reply to: "Correspondence on the <BCLC strategy for prognosis prediction and treatment recommendation: The 2022 update>"

To the Editor:

We appreciate the interest garnered by the BCLC 2022 model update. The new version has incorporated the evidence-based novelties generated in recent years, while also adding a section devoted to clinical decision making at the time of first evaluation and during a patient's clinical evolution. No clinical practice guideline or recommendation review will ever have enough granularity to firmly recommend the most beneficial approach for an individual patient.

The comments by Hallemeier *et al.*[1] call for the incorporation of radiation therapy into the recommendations based on scientific society guidelines and a series of published studies. Current data are encouraging and indicate that radiation has activity. However, the degree of evidence of survival benefit is not high and the recommendation could just be conditional. This justified the current BCLC model, but at the same time we already stated at the right part of the figure that other alternative sequences of treatment may be considered but that they are not proven. In this setting, SBRT could be considered and in the text we stated that *"Stereotactic body radiation bears antitumoral activity but further prospective studies are needed to define its role"*. This is fully concordant with the strong support of Hallemeier *et al.* for further prospective randomized controlled trials of radiation therapy.

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The letter by Xu *et al.*[2] raises the controversy around the evaluation of performance status (PS) and to what extent PS 0 and 1 should be joined in a single category, while also asking for BCLC model guidance for specific clinical scenarios where the evidence is limited. Clinical evaluation of patients is not easy and clinicians have to spend the required time to assess the symptomatic or asymptomatic status of their patients. Performance status 0 is easy to assess because the patient is asymptomatic. When tumor-related symptoms are present the outcome of patients is impaired whether they are treated at an early, intermediate or advanced stage, or if left untreated. Hence, we strongly disagree with the proposal to merge PS 0 and PS 1 and we stress again that symptoms related to comorbidities do not mean PS 1. Regarding hepatic vein invasion, we have to recall that the BCLC model already includes the term vascular invasion, which also accounts for the hepatic veins. Such a pattern is far less common than portal vein invasion, which is why comments about vascular invasion usually refer to the portal vein. Management of biliary invasion is a complex and heterogeneous clinical event. It implies poor prognosis and interventions are usually palliative with limited impact on survival. Finally, recommendations for ruptured tumors are not included in the BCLC model because this is a complication of HCC and the heterogeneity of the clinical profiles of patients suffering such an event is part of the clinical decision-making section. The lack of prospective studies prevents a robust recommendation about its management.

Finally, the letter by Elhence and Shalimar[3] comments on the evaluation of liver function and the need to provide a well-defined tool for it. We comment in the manuscript that evaluation of liver function will not be fully accomplished by the Child-Pugh system or MELD; clinicians should consider several parameters to provide an optimal assessment of the liver functional reserve for an adequate treatment recommendation for the specific evolutionary stage of the patient. This is why we felt that preserved *vs*. non-preserved were valid terms that require the evaluation by an expert hepatologist who should become a very active member of any multidisciplinary team devoted to liver cancer.

In summary, we are pleased with these debates and interactions, and are confident that the updated BCLC model will be a key tool both for conventional clinical practice and research.

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