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Letters to the editor

Comment on "Camrelizumab combined with transcatheter arterial chemoembolization and sorafenib or lenvatinib for unresectable hepatocellular carcinoma: A multicenter, retrospective study"

Dear Editor,

We read with great interest the recent multicenter, retrospective analysis [1] assessing a three-pronged therapeutic approach for patients with unresectable hepatocellular carcinoma (uHCC), combining camrelizumab, transcatheter arterial chemoembolization (TACE), and either sorafenib or lenvatinib. The results indicated that individuals who underwent the triple combination therapy experienced significantly longer median overall survival (OS) (15.8 vs. 10.3 months; $P = 0.0011$) and median progression-free survival (7.2 vs. 5.2 months; $P = 0.019$) compared to those receiving the dual-agent regimen. Furthermore, 6-, 12-, and 24-month survival rates were markedly higher in the triple therapy group—93.5%, 67.2%, and 17.2%, respectively—versus 66.3%, 36.3%, and 7.6% in the double treatment cohort. Subgroup analyses also revealed extended median OS in patients with hepatitis B virus-related HCC (15.8 vs. 9.6 months; $P = 0.0015$) and in those with tumors ≥5 cm in diameter (15.3 vs. 9.6 months; $P = 0.00055$). Although the findings are compelling, several aspects warrant further clarification and discussion.

Firstly, although tumor diameter (≥5/<5 cm) was reported to be significantly associated with OS in this study [1], the specific time point at which the tumor size was measured was not clearly defined. In patients with uHCC, disease progression can occur rapidly, and tumor dimensions may change substantially over short periods. Therefore, if the assessment of tumor diameter was conducted long before enrollment (e.g., six months), it may not accurately represent the actual tumor burden at the time of inclusion. Likewise, although the study demonstrated significant associations between OS and levels of AFP (≥400/<400 ng/ml) and ALP (≥125/<125 U/L), the exact timing of these laboratory measurements was not specified. Since liver function and tumor biology in HCC patients can fluctuate during the course of treatment, AFP and ALP levels are also prone to dynamic variation. This ambiguity regarding the timing of assessments presents considerable challenges for clinicians attempting to interpret disease progression accurately and apply these biomarkers effectively in clinical decision-making. Thus, it is suggested to clearly specify the timing of such key evaluations to enhance the interpretability and clinical utility of the findings.

Secondly, this study [1] reported that patients with hepatocellular carcinoma (HCC) and hepatitis B virus (HBV) infection had a longer median OS in the triple therapy group compared to the dual therapy group. However, the study did not provide specific data on HBV viral load [2] in these patients. HBV DNA levels are a critical biomarker for assessing the status of infection and predicting disease progression, as viral load can influence HCC development, tumor behavior, and response to therapy [3,4]. In the absence of such data, it becomes challenging to accurately evaluate the prognostic impact of HBV infection, determine the adequacy of antiviral treatment, or assess the need for therapeutic adjustments. Therefore, it is recommended that the study include HBV DNA level data to enable a more comprehensive understanding of the role of HBV infection in HCC progression and its effect on treatment outcomes, thereby facilitating more informed clinical decision-making.

Thirdly, although the authors [1] conducted subgroup analyses for patients with HBV infection and those with tumor diameter ≥5 cm in this study, other potential prognostic factors—such as the extent of vascular invasion, the presence of portal vein invasion, and patient age and sex—were not thoroughly examined. These variables have been shown to significantly influence both treatment response and prognosis. Additionally, tumor biological characteristics, including tumor mutation burden (TMB) and the immune microenvironment [5], may also play a critical role in shaping therapeutic outcomes. However, the study did not address the evaluation or adjustment of these important factors. Future research should incorporate detailed assessments of these variables and perform appropriate adjustment analyses to more comprehensively identify subgroups of patients most likely to benefit from specific treatment strategies.

Declaration of competing interest

None.

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