



## Letters to the editor

### Re-evaluating the survival benefit of adding camrelizumab to TACE plus tyrosine-kinase inhibitors in unresectable hepatocellular carcinoma: the undervalued influence of TACE frequency



Dear Editor,

Jiang et al. report that adding camrelizumab to TACE plus sorafenib/lenvatinib prolonged median overall survival (OS) from 10.3 to 15.8 months [1]. We applaud the multicenter effort, yet the uneven distribution of TACE sessions raises concern. The triple-therapy group received  $\geq 2$  TACE procedures in 52.3 % of patients versus 38.6 % in the double-therapy group. More frequent TACE independently improves OS [2]; therefore, the survival gain may partly reflect intensified locoregional therapy rather than PD-1 blockade.

Another discrepancy lies in the multivariable model: TACE count was not included as a covariate. Omitting this variable risks overestimating camrelizumab's effect. Moreover, the study lacks data on post-progression systemic therapies, which could dilute any true immunotherapy benefit [3]. Recent real-world analyses show that cumulative TACE sessions correlate strongly with OS even after immune checkpoint inhibitor initiation [4], and the absence of this parameter weakens causal inference.

To clarify the added value of camrelizumab, we propose three actions. First, repeat the multivariable analysis incorporating the number of TACE sessions, selective TACE intervals, and post-progression treatments. Second, match patients by TACE frequency using propensity-score methods to isolate camrelizumab's contribution. Third, design a prospective trial with a fixed TACE protocol and pre-defined rescue-therapy rules; such rigor is now standard in contemporary combination-therapy trials [5].

In conclusion, the observed survival advantage may be driven, at least in part, by differential TACE intensity. Addressing this confounder will sharpen the evidence for integrating PD-1 inhibitors into TACE-based sequences.

### Author contributions

L.W. and J.Z. drafted the manuscript; J.L. critically revised it.

### Conflicts of Interest

None

### References

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