LETTER

Immune checkpoint inhibitors: use them early, combined and instead of TACE?

We read with interest the recent Gut roundtable paper by Gerbes et al. As highlighted by these authors, treatment of HCC has rapidly changed: currently, four tyrosine kinase inhibitors, ramucirumab and two immune checkpoint inhibitors (ICP) are approved in different lines of treatment. Survival of patients with advanced disease have improved correspondingly, and more progress is expected from the burgeoning of trials of ICP-based combination treatment schemas (figure 1).

Due to the increasing efficacy of pharmacological treatment, many physicians are inclined to initiate systemic therapy, rather than trans-arterial chemoembolisation (TACE), in patients with more advanced intermediate-stage HCC (patients with more numerous or large lesions) or to switch earlier from TACE to systemic treatment. This propensity is accentuated by studies increasingly highlighting some limitations of the current use of locoregional treatment: median overall survival (mOS) under TACE treatment, expected to amount to over 30 months in well-selected patients, doesn’t exceed the real-world and the expected survival (ie, based on the selection of ‘ideal’ candidates for TACE) in BCLC-B patients. The list of trials is not exhaustive and, due to the heterogeneity of patients’ population, not suitable for direct cross-comparison between the trials. Atezo/Bev: combined atezolizumab and bevacizumab; pH, phase of clinical study; TACE, trans-arterial chemoembolisation.

Figure 1 Schematic representation of the development in the treatment of advanced-stage HCC based on median overall survival (mOS) data from some recent trials. The arrows are proportional to the reported (grey) or hypothetical (blue) mOS indicated by the respective numbers. The green overlapping arrows represent respectively the real-world and the expected survival (ie, based on the selection of ‘ideal’ candidates for TACE) in BCLC-B patients. The list of trials is not exhaustive and, due to the heterogeneity of patients’ population, not suitable for direct cross-comparison between the trials. Atezo/Bev: combined atezolizumab and bevacizumab; pH, phase of clinical study; TACE, trans-arterial chemoembolisation.
of TACE. This may not reduce the benefits of the combination but could save liver function, thus translating into a survival benefit and contributing to solve the year-long dilemma of when to start and stop TACE.

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**Figure 2** Schematic representation of the DEMAND study, a randomised, two-arm non-comparative phase II study on the efficacy of atezolizumab and bevacizumab (Atezo/Bev) followed by on-demand selective TACE (sdTACE) on detection of disease progression (PD), or of initial synchronous treatment with TACE and Atezo/Bev on 24 months survival rate in the treatment of unresectable hepatocellular carcinoma patients. The use of local ablation is allowed for lesions which cannot be targeted sufficiently selectively by TACE. TACE, trans-arterial chemoembolisation.