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LETTER TO THE EDITOR

Atezolizumab and bevacizumab: the revolutionary duo as a game changer in advanced hepatocellular carcinoma

To the Editors,

I read with great interest a recent article about treating advanced hepatocellular carcinoma (HCC) with the combination of atezolizumab and bevacizumab,[1] and I am excited to summarise and share the key findings from the study, as well as some future perspectives.

Liver cancer is the sixth most common cancer and the fourth leading cause of cancer-associated deaths worldwide.[2] HCC, the major type of liver cancer, is most prevalent in Asia and Africa, but its incidence is increasing in Western countries.[3] For the past decade, the kinase inhibitor drug sorafenib has been considered the first-line treatment for advanced unresectable HCC.[4] No other drug has exceeded the efficacy of sorafenib, although lenvatinib was found to be non-inferior to sorafenib.[5]

Recently, we have seen some very encouraging results from the global, open-label, randomised phase 3 trial IMbrave150 (NCT03434379). Combination therapy using the anti-programmed cell death-ligand 1 (PD-L1) drug atezolizumab and anti-vascular endothelial growth factor (VEGF) drug bevacizumab showed superior overall survival and progression-free survival compared with sorafenib in patients with unresectable HCC.[1] The atezolizumab—bevacizumab group had 42% lower hazard of death compared with the sorafenib group. Moreover, 18 patients (5.5%) who received atezolizumab—bevacizumab reported a complete response, compared with no patients in the sorafenib group.[1] With the promising data and safety and tolerability profiles, we can expect that the combination of atezolizumab and bevacizumab will revolutionise the treatment landscape for advanced HCC, and soon become the new first-line option.[1,6,7]

With the above inspiring results, the following aspects warrant further investigation.[1,8] Firstly, certain adverse reactions are to be addressed.[1] For instance, haemorrhage is a recognised adverse effect of bevacizumab, especially when patients with HCC are at higher risk of life-threatening upper gastrointestinal haemorrhage.[1,9] A slightly higher incidence of upper gastrointestinal haemorrhage was observed in the atezolizumab—bevacizumab group compared with the sorafenib group (7% versus 4.5%, respectively).[1] In the trial, varices were evaluated and treated if required prior to trial enrolment,[1] and prophylaxis can be considered.[10] Secondly, efficacy and safety are to be assessed for a broader intention-to-treat population. The current trial recruited patients with advanced HCC who demonstrated Child—Pugh Class A liver function and had not received prior systematic treatment.[1] Clinical benefits remain to be evaluated for patients who have received systematic therapy previously, show worsened liver function (Child—Pugh Class B/C) or are in other categories yet to be investigated. Finally, further analysis is needed to assess whether there is an association between biomarker levels, such as PD-L1 and VEGF, and therapeutic benefits of atezolizumab—bevacizumab treatment.[11] As we enter the era of combination cancer immunotherapy, this information will be helpful in personalising treatment regimens to maximise therapeutic potential.

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