Medical Xpress

Clinical trial of adjuvant therapy combination shows improved recurrence-free survival in liver cancer patients

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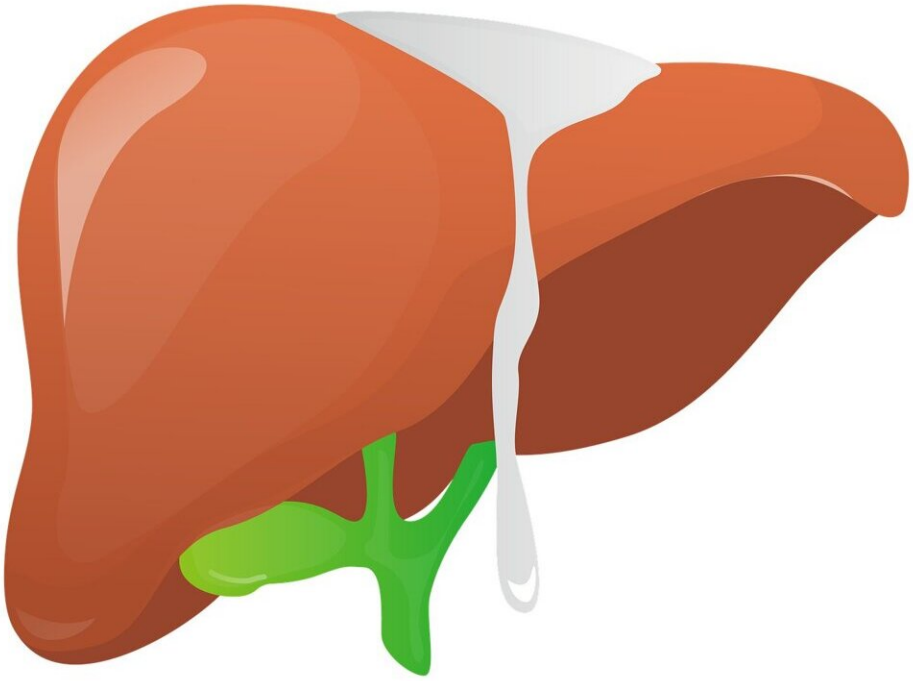

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An international randomized controlled trial, advised by a steering committee co-led by a senior clinician-scientist from the National

Cancer Centre Singapore and Duke-NUS Medical School, Singapore, has reported that the combination therapy of atezolizumab and bevacizumab in the adjuvant setting is safe and effective in reducing cancer recurrence in patients with the primary liver cancer, hepatocellular carcinoma (HCC), at high risk for recurrence after curative intent resection or ablation.

Liver cancer is the sixth most common cancer in the world and fourth most common cause of cancer deaths globally. In Singapore, it is the third most common cause of cancer deaths in males and fifth most common cause in females; as HCC is usually diagnosed at a late stage, when prognosis is poor. Liver resection or ablation, a process that uses heat to destroy tumors, are potentially curative treatment options for HCC.

Still, 70 to 80% of patients experience cancer recurrence within five years of receiving these treatments. Currently, there is no recognized standard of care for adjuvant therapy in patients with HCC after potentially curative treatment. As a result, clinical outcomes after curative intent liver resection and ablation in HCC are poorer than that of other common cancers which have efficacious adjuvant therapy, such as breast and colorectal cancer.

To address this significant unmet clinical need in HCC, IMbrave050, a global, open-label phase III trial was conducted between 2019 and 2022 to evaluate the safety and efficacy of adjuvant atezolizumab and bevacizumab. A total of 668 patients with HCC at high-risk of cancer recurrence after surgical resection or ablation were enrolled from 134 sites in 26 countries.

The age range of participants was between 51 and 68 years, with a median age of 58 years. Most participants were male (83%) and Asian (82%), and the main underlying cause of HCC was Hepatitis B (62%).

Participants were randomly and equally divided into two groups, with one group receiving atezolizumab and bevacizumab and the other group put under active surveillance, which is the current standard-of-care after surgical resection and ablation.

Participants in the treatment arm received intravenous atezolizumab and bevacizumab every 3 weeks for up to 12 months or 17 cycles.

Trial results were positive at the first analysis and show that cancer recurrence was decreased by one-third at the end of the first year. The risk of disease recurrence or death was 28% lower in the group who received adjuvant atezolizumab plus bevacizumab compared to the group who had undergone active surveillance. The safety profile of the adjuvant therapy was consistent with prior studies of atezolizumab and bevacizumab.

"The positive outcomes of IMbrave050 brings new hope to liver cancer patients. It is a landmark study and the first in the world to demonstrate an effective adjuvant therapy for patients with hepatocellular carcinoma. These results have the potential to be practice-changing, and we are encouraged that they may lead to a reassessment of recommendations for surgical resection and the treatment of hepatocellular carcinoma," said study corresponding author and IMbrave050 steering committee co-chair Professor Pierce Chow, Senior Consultant Surgeon, Singapore General Hospital and National Cancer Centre Singapore and Professor, Duke-NUS Medical School.

"The successful completion of a large-scale clinical trial advised by a steering committee co-led by a Singapore clinician scientist validates efforts to establish an integrated network of scientists and clinician-scientists who work with industry to deliver impactful research and position Singapore as a vibrant biomedical research hub," said Professor Tan Say Beng, Group Chief Research Officer, SingHealth and Senior

Associate Dean, Office of Research, and Professor, Duke-NUS Medical School.

Next steps for this combination therapy are further studies in a larger population and in curative settings for HCC. At the time of publication there are three other ongoing trials of adjuvant immunotherapy after surgical resection or ablation of HCC.

The research is published in *The Lancet*.

More information: Shukui Qin et al, Atezolizumab plus bevacizumab versus active surveillance in patients with resected or ablated high-risk hepatocellular carcinoma (IMbrave050): a randomised, open-label, multicentre, phase 3 trial, *The Lancet* (2023). DOI: 10.1016/S0140-6736(23)01796-8

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