Adjuvant treatment may delay recurrence after surgical resection in patients with liver cancer

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Pierce Chow, FRCS(E), PhD. Credit: American Association for Cancer Research

Adjuvant therapy with atezolizumab (Tecentriq) and bevacizumab (Avastin) increased recurrence-free survival of patients with hepatocellular carcinoma (HCC) following surgical resection or ablation, according to the results from the phase III IMbrave050 clinical trial, which were presented at the AACR Annual Meeting 2023, held April 14–19.

The mainstays of curative therapies for early-stage HCC include surgical resection and thermal ablation, a treatment that destroys the cancer cells with heat or cold. However, the risk of recurrence reaches 70%–80% five years after resection or ablation with curative intent, said presenting author Pierce Chow, FRCS(E), Ph.D., senior consultant surgeon at National Cancer Center Singapore and Singapore General Hospital, and professor and program director at Duke-NUS Medical School, Singapore.

"Due to the lack of proven adjuvant therapy strategies for HCC, patients who are treated with surgical resection or thermal ablation with curative intent tend to have significantly higher recurrence rates and shorter overall survival than patients with other types of cancer, for example, colorectal and breast cancer treated with similar curative intent," said Chow. "The positive results of IMBrave050 address this huge and urgent unmet clinical need in HCC."

The randomized, controlled phase III IMbrave050 trial was designed to investigate the efficacy of an adjuvant treatment combination of the checkpoint inhibitor atezolizumab and the targeted therapy bevacizumab in delaying or preventing recurrence compared with active surveillance, which represents the current standard of care after complete surgical resection or ablation.

The trial enrolled patients with HCC who were at high risk of recurrence following tumor resection or ablation, based on criteria such as size and

number of tumors, presence of cancer cells within the lumen of blood and/or lymphatic vessels, and tumor grade. Study participants were randomly assigned (1:1) to receive atezolizumab plus bevacizumab every three weeks for a period of one year or 17 cycles or undergo active surveillance for one year. Patients in the control arm were eligible to switch to the experimental arm in case of recurrence. The primary endpoint was independent review facility-assessed recurrence-free survival (IRF-RFS).

According to the results of an interim analysis conducted after a median follow-up of 17.4 months, the trial met its primary endpoint, and the combination of atezolizumab and bevacizumab significantly increased IRF-RFS when used as adjuvant therapy following surgical resection or ablation. Patients who received the combination treatment had their risk of recurrence or death reduced by 28% compared with patients in the active surveillance arm. At this timepoint, the median IRF-RFS was not reached for either arm.

Chow noted that the patients stayed on treatment longer than in the previous IMbrave150 trial that evaluated the same combination of drugs for unresectable HCC (median duration of treatment for atezolizumab and bevacizumab, respectively, was 11.07 and 11.02 months in IMbrave050 and 7.4 and 6.9 months in IMbrave150). "Despite the longer duration of treatment, the incidence of serious therapy-related adverse events was comparable to that in the IMbrave150 trial, indicating tolerability of this regimen when used as adjuvant therapy," he said.

"IMbrave050 is a landmark study and the first to demonstrate an efficacious adjuvant therapy for patients with HCC who have undergone surgical resection or ablation," Chow said. "These results have established a benchmark in adjuvant therapy for HCC and have the potential to be practice-changing."

Chow added that better clinical outcomes following treatment with this adjuvant regimen might also have an impact on the clinical indications for surgical resection and ablation in HCC. "Currently, surgery is not offered to many patients with potentially resectable disease if rapid recurrence is expected based on tumor burden or the presence of vascular invasion," said Chow. "The availability of an efficacious adjuvant therapy may lead to a reassessment of which patients may benefit from surgical resection."

According to the author, the limitations of the study include that, since the trial met its primary endpoint earlier than expected, the data were not mature enough to allow the researchers to determine the outcomes of the trial's secondary endpoints, including overall survival. "For these results, we will have to wait for subsequent analyses," Chow said.

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