FDA Approves Atezolizumab plus Bevacizumab for Unresectable Hepatocellular Carcinoma

The FDA has approved atezolizumab in combination with bevacizumab (Avastin® and Tecentriq®, Genentech), both monoclonal antibodies, for patients with metastatic or unresectable hepatocellular carcinoma that have not received previous systemic treatment.

"Hepatocellular carcinoma is a common cancer worldwide and a leading cause of cancer-related death. Although early-stage disease may be curable by resection, liver transplantation, or ablation, most patients present with unresectable disease and have a poor prognosis" wrote Dr. Richard S. Finn, MD, Professor of Medicine in the Hematology/Oncology Department of the David Geffen School of Medicine at the University of California, Los Angeles, and colleagues, in their publication of the IMBRAVE150 trial (NCT03434379), on which the approval was based. "The combination of atezolizumab and bevacizumab showed encouraging antitumor activity and safety in a clinical trial involving patients with unresectable hepatocellular carcinoma."

In a global, open-label, Phase III trial, a total of 501 patients with unresectable hepatocellular carcinoma who had not received prior systemic therapy were randomly assigned in a 2:1 ratio to receive either 1200 mg of atezolizumab plus 15 mg/kg of bevacizumab intravenously every 3 weeks or a twice-daily dose of 400 mg of sorafenib orally. The primary end points of the study were overall survival and progression-free survival, and the secondary end points included the objective response rate and the duration of response.

Overall survival at 12 months was significantly higher in patients treated with the atezolizumab–bevacizumab combination (67.2%) compared with that of patients treated with sorafenib (54.6%). Median progression-free survival was also significantly longer, with 6.8 months compared to 4.3 months for the respective groups. The objective response rate (27.3% vs. 11.9%) and the duration of response (87.6% vs. 59.1%) figures were also significantly higher in patients receiving the atezolizumab–bevacizumab combination compared to those of the patients receiving sorafenib.

The most common adverse reactions reported with atezolizumab plus bevacizumab, in more than 20% of the patients in the study, were hypertension, fatigue, and proteinuria, while the most common laboratory abnormalities, reported in more than 10% of patients in the study, were increased levels of aspartate aminotransferase, alanine aminotransferase, blood bilirubin, and a decrease in platelet count.

"Treatment with atezolizumab plus bevacizumab was associated with significantly better overall survival and progression-free survival outcomes than sorafenib in patients with advanced unresectable hepatocellular carcinoma not previously treated with systemic therapy," concluded Dr Finn and colleagues in their May 2020 publication of the results in *The New England Journal of Medicine*.

The recommended dose of atezolizumab is 1200 mg, followed by 15 mg/kg of bevacizumab on the same day, administered by intravenous injection every 3 weeks. In the event that bevacizumab is discontinued, atezolizumab should be given according to one of the following dosage regimens: 840 mg every 2 weeks, 1200 mg every 3 weeks, or 1680 mg every 4 weeks.

For More Information

Finn R, Qin S, Ikeda M, et al (2020). Atezolizumab Plus Bevacizumab in Unresectable Hepatocellular Carcinoma. *N Engl J Med,* 382(20):1894-1905. DOI:10.1056/NEJMoa2103485

Clinicaltrials.gov (2021). A Study of Atezolizumab in Combination With Bevacizumab Compared With Sorafenib in Patients With Untreated Locally Advanced or Metastatic Hepatocellular Carcinoma (IMBRAVE150). NLM identifier: NCT03434379.

Tecentriq® (atezolizumab) prescribing information (2020). Genentech. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/761034s025lbl.pdf

Avastin® (bevacizumab) prescribing information (2020). Genentech. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2020/125085s332lbl.pdf

US Food & Drug Administration (2020). FDA approves atezolizumab plus bevacizumab for unresectable hepatocellular carcinoma. Available at: https://www.fda.gov/drugs/resources-information-approved-drugs/fda-approves-atezolizumab-plus-bevacizumab-unresectable-hepatocellular-carcinoma