Genentech
A Member of the Roche Group

August 2024

Subject:
Tecentriq (atezolizumab) in combination with Avastin (bevacizumab) is NOT approved as adjuvant therapy in patients with hepatocellular carcinoma at high risk of recurrence after surgical resection or ablation and should not be used in this setting

Dear Healthcare Provider:

The purpose of this letter is to inform you of important new information that impacts the benefit-risk of off-label use of Tecentriq and Avastin in hepatocellular carcinoma (HCC) patients in the adjuvant setting, following curative resection or ablation.

Unfavorable benefit-risk for Tecentriq and Avastin as an adjuvant therapy for HCC patients

- The combination of Tecentriq and Avastin is not approved or marketed in the United States or any other country for the adjuvant treatment of HCC. Based on the positive recurrence-free survival (RFS) results at the first interim analysis of the IMbrave050 study and the high-unmet need in this setting, the NCCN Clinical Practice Guidelines in Oncology for Hepatocellular Carcinoma and the AASLD Practice Guidance on prevention, diagnosis, and treatment of hepatocellular carcinoma currently recommend the use of Tecentriq plus Avastin in the adjuvant setting for patients at high risk of recurrence.
- Based on an updated analysis of IMbrave050, this Direct Healthcare Professional Communication (DHCP) is being sent to advise against the off-label use of Tecentriq in combination with Avastin for the adjuvant treatment of HCC.
- There is no impact on the approved indication of unresectable or metastatic HCC, where the combination of Tecentriq and Avastin remains a standard of care treatment option.

Background on the recent benefit-risk data

IMbrave050 is a Phase 3, multicenter, randomized, open-label study of Tecentriq + Avastin vs active surveillance as adjuvant therapy in patients with HCC at high risk of recurrence after surgical resection or ablation.

The primary endpoint was independent review facility (IRF)-assessed RFS[1]. Select secondary endpoints included overall survival (OS) and safety.

The primary endpoint of RFS was met at the first interim analysis in early 2023. As of a clinical cut-off date of 3 May 2024, updated analysis data shows that the RFS benefit seen at the first interim analysis is not sustained with longer follow-up. Of note, OS data remain immature and continue to not show a benefit. The overall safety profile remains consistent with the first interim analysis. The data from this analysis will be presented at an upcoming medical congress.

Based on this data, the benefit-risk profile does not support the use of Tecentriq plus Avastin as an adjuvant therapy for HCC.

There is no impact on the approved indication of unresectable or metastatic HCC, where the combination of Tecentriq and Avastin remains a standard of care treatment option.

Prescriber Action

Do not prescribe off-label use of Tecentriq in combination with Avastin for the adjuvant treatment of HCC.

Reporting Adverse Events / Product Complaints and Company Contact

Health Care Providers should report any adverse events suspected to be associated with the use of **Tecentriq and Avastin** to Genentech at 1-888-835-2555. Alternatively, this information may be reported to FDA's MedWatch reporting system by phone (1-800-FDA-1088) or online (www.fda.gov/medwatch).

Please report any product complaint suspected to be associated with the use of **Tecentriq and Avastin** to Genentech at (800) 334-0290.

Should you have any questions about the information in this letter or the safe and effective use of **Tecentriq and Avastin,** please feel free to contact us at: Genentech Medical Communications Department at (800) 821-8590.

This letter is not intended as a complete description of the benefits and risks related to the use of **Tecentriq and Avastin**. Please refer to the enclosed full prescribing information for Tecentriq and full prescribing information for Avastin (and medication guide, *if there is a medication guide for this product,* or any other approved patient information).

Annexes

[1]Qin S, Chen M, Cheng AL, 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. Lancet 2023;402:1835-1847. https://pubmed.ncbi.nlm.nih.gov/37871608/

Sincerely,

Toby Patterson, MBBS
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