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**Tecentriq (atezolizumab) and Avastin (bevacizumab):
Atezolizumab in combination with bevacizumab is NOT approved as adjuvant therapy in patients with hepatocellular carcinoma at high risk of recurrence after surgical resection or ablation and the benefit-risk profile does not support the use of atezolizumab plus bevacizumab in this setting**

Dear Healthcare Professional,

F.Hoffmann-La Roche Ltd. in accordance with the “Centre of Drug and Medical Technologies Expertise” SNCO would like to inform you of the following:

Summary

- As of a clinical cut-off date of 3 May 2024, updated analysis data from IMbrave050, a study evaluating atezolizumab in combination with bevacizumab in the adjuvant setting of hepatocellular carcinoma (HCC), show that the recurrence-free survival (RFS) benefit seen at the first interim analysis is not sustained with longer follow-up. Of note, overall survival (OS) data is still immature at the time of this updated analysis. The overall safety profile remains consistent with the first interim analysis. **Based on these data, the benefit-risk profile does not support the use of atezolizumab plus bevacizumab as an adjuvant therapy for HCC.**
- Whilst the combination of atezolizumab and bevacizumab is not approved anywhere for this indication, given the high unmet need, some clinical guidelines list this combination as a potential adjuvant therapy option for HCC patients following curative intent resection or ablation. However, the most recent IMbrave050 study results do not support the use of this combination for the adjuvant treatment of HCC patients; therefore, this Direct Healthcare Professional Communication (DHPC) is being sent to advise against the potential off-label use of atezolizumab in combination with bevacizumab for the adjuvant treatment of HCC.
- There is no impact on the approved indication of unresectable HCC, where the combination of atezolizumab and bevacizumab 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 atezolizumab + bevacizumab vs active surveillance as adjuvant therapy in patients with hepatocellular carcinoma (HCC) at high risk of recurrence after surgical resection or ablation.

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

Although the primary endpoint of RFS was met at the first interim analysis in early 2023, the recently updated RFS data from IMbrave050 show that the initial RFS benefit is not sustained with longer follow-up. The 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 atezolizumab plus bevacizumab as an adjuvant therapy for HCC.

Whilst the combination of atezolizumab and bevacizumab is not approved in this indication, some clinical guidelines currently recommend the use of this combination based on the first interim analysis data.

This DHPC is therefore being distributed to communicate the emerging results of IMbrave050 and advise against the potential off-label use of atezolizumab in combination with bevacizumab for the adjuvant treatment of HCC, as the IMbrave050 study results do not support using the combination of atezolizumab and bevacizumab as adjuvant therapy to treat patients with resected or ablated hepatocellular carcinoma at high risk for recurrence.

There is no impact on the approved indication of unresectable HCC, where the combination of atezolizumab and bevacizumab remains a standard of care treatment option.

Call for reporting

Healthcare professionals should report any adverse events, which are suspected to be associated with the use of Atezolizumab (Tecentriq) and Bevacizumab (Avastin). It is important to inform any Suspicious Adverse Event Report of products. It will help continuously assess the risk/benefits.

Healthcare professionals should report any suspicious adverse event reports online to the “Centre of Drug and Medical Technology Expertise” SNCO via website²: www.pharm.am , emailing:

