Tecentriq with Avastin in HCC Patients with Pre-existing Gastroesophageal Varices

This article responds to your request for information on the combination of Tecentriq® (atezolizumab) and Avastin® (bevacizumab) in hepatocellular carcinoma (HCC) patients with pre-existing gastroesophageal varices.

In brief

- Bleeding from gastroesophageal varices is a common and life threatening complication in patients with HCC.
- Bleeding is a known adverse event of Avastin.
- To assess varices activity and manage bleeding risks, IMbrave150 enrolment requirements included
  - screening of gastroesophageal varices with upper endoscopy within 6 months prior the treatment with Tecentriq and Avastin,
  - no varices bleeding events during the 6 months prior to enrolment, and
  - varices showing signs of activity had to be treated as per local standard of care before entering the study.

Background

Bleeding from gastroesophageal varices is a known complication in advanced HCC patients. Bleeding, including fatal events, is a known adverse event of Avastin.[1]

Recommendations regarding bleeding and varices for Avastin and Tecentriq

Please refer to your local Avastin and Tecentriq labels for information on Avastin-related bleeding events and screening of patients with oesophageal varices.

There is lack of clinical data to support the safety of Avastin in patients with variceal bleeding within 6 months prior to treatment, untreated or incompletely treated varices with bleeding, or with a high risk of bleeding as these patients were excluded from Avastin clinical trials in HCC.

Recommendations for HCC patients are available in Tecentriq and Avastin product labels in some countries, for example:

- Tecentriq European Medicines Agency Summary of Product Characteristics — Screening for and subsequent treatment of oesophageal varices should be performed as per clinical practice prior to starting treatment with the combination of Tecentriq and Avastin.[2]
- Avastin Food and Drug Administration label — An evaluation for the presence of varices is recommended within 6 months of initiation of Avastin.[3]

Any decision to use Tecentriq in combination with Avastin in patients with pre-existing varices would be a clinical decision, at the discretion of the clinician after an analysis of the benefit-risk ratio. All Roche can recommend is appropriate clinical caution and monitoring.

Phase III IMbrave150 trial in patients with unresectable or advanced HCC

IMbrave150 was a Phase III, open-label study investigating Tecentriq in combination with Avastin compared with sorafenib in patients with unresectable or advanced HCC who had not received prior systemic therapy.[4]

To mitigate the risk of variceal bleeding associated with Tecentriq in combination with Avastin, the IMbrave150 trial design defined strict patient selection and enrolment requirements.[4]

Eligibility criteria regarding gastroesophageal varices

Patients with untreated or incompletely treated varices with bleeding or high-risk for bleeding were excluded from IMbrave150.[4] The requirements for enrolment in the trial were

- esophagogastroduodenoscopy (EGD) not older than 6 months for all patients
- varices showing signs of activity had to be treated as per local standard of care before entering the study, and
- no varices bleeding events during the 6 months prior to enrolment.

Baseline characteristics

The number of patients in the IMbrave150 trial who had varices present at baseline, and treated at baseline are outlined in Table 1. There is no information on the treatment modalities or grade of initial varices in these patients.

Table 1. Patients with varices at baseline in IMbrave150[4]

	Tecentriq and Avastin (n=336)	Sorafenib (n=165)
Present at baseline, n (%)	88 (26%)	43 (26%)
Treated at baseline, n (%)	36 (11%)	23 (14%)

Incidence of varices haemorrhage

Table 2 defines the incidence of haemorrhage in the IMbrave150 trial.[5] Two patients in the Tecentriq and Avastin arm experienced "oesophageal varices haemorrhage" leading to death (grade 5).[6] The investigator considered both events as unrelated to the treatment with Tecentriq and Avastin.[7]

Table 2. Incidence of varices haemorrhage

MedDRA preferred term	Tecentriq and Avastin (n=329)	Sorafenib (n=156)
Oesophageal varices haemorrhage, n (%)	10 (3%)	1 (0.6%)
Gastric varices haemorrhage, n (%)	4 (1.2%)	1 (0.6%)

Published guidelines on monitoring and management of gastroesophageal varices

Several publications describe guidelines for monitoring and management strategies of gastroesophageal varices in patients treated with Tecentriq and Avastin.[8,9] The interested reader is referred to the publications for more information.

References

1. Roche Internal Regulatory Document, accessed on 21-Jul-2023.

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3. FDA Avastin Highlights of Prescribing Information. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2022/125085s340lbl.pdf.. Accessed on July 5, 2023.

4. Finn R, Qin S, Ikeda M, et al. Atezolizumab plus Bevacizumab in Unresectable Hepatocellular Carcinoma. N Engl J Med 2020;382:1894-1905. https://www.ncbi.nlm.nih.gov/pubmed/32402160

5. Roche Internal Clinical Study Report, accessed on 25-Aug-2023.

6. Cheng A, Qin S, Ikeda M, et al. Updated efficacy and safety data from IMbrave150: Atezolizumab plus bevacizumab vs. sorafenib for unresectable hepatocellular carcinoma. J Hepatol 2022;76:862-873. https://www.ncbi.nlm.nih.gov/pubmed/34902530

7. Roche Internal Regulatory Document, accessed on 07-Jul-2023.

8. Hsu C, Rimassa L, Sun H, et al. Immunotherapy in hepatocellular carcinoma: evaluation and management of adverse events associated with atezolizumab plus bevacizumab. Ther Adv Med Oncol 2021;13:17588359211031141. https://www.ncbi.nlm.nih.gov/pubmed/34377156

9. Gordan J, Kennedy E, Abou-Alfa G, et al. Systemic Therapy for Advanced Hepatocellular Carcinoma: ASCO Guideline. J Clin Oncol 2020;38:4317-4345. https://www.ncbi.nlm.nih.gov/pubmed/33197225