decision should obviously take into account, case by case, the initial response to immunotherapy.

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Reply to: 'Management of portal hypertension in patients treated with atezolizumab and bevacizumab for hepatocellular carcinoma'

To the Editor:
We read with interest the comments of Drs. Ollivier-Hourmand, Alaire and Cervoni, who wrote a letter on behalf of the 'Club Francophone pour l'Etude de l'Hypertension Portale' commenting on the management of portal hypertension in the specific group of patients with hepatocellular carcinoma (HCC) treated with atezolizumab and bevacizumab (Ate/Beva).[1]

Underlying cirrhosis is present in over 90% of patients with HCC[2] and thus, the issue of management of portal hypertension (PH) in patients with cirrhosis and HCC is very relevant. To date, there are no studies evaluating whether patients with cirrhosis and HCC require different clinical strategies for screening, treatment, and follow-up of PH-related complications compared to those without HCC. Therefore, we strongly suggest following Baveno VII recommendations[3] in patients with cirrhosis and HCC. Importantly, it has been shown that, in patients with HCC who experienced variceal bleeding, survival was improved in those who undergo secondary prophylaxis

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with non-selective beta-blockers (NSBBs) and endoscopic variceal ligation (EVL).[4]

Dr. Ollivier-Hourmand *et al.* raise concerns about a potentially increased variceal bleeding rate related to Beva treatment. However, several experimental studies suggest that portal pressure and portosystemic collateralization is reduced by inhibition of vascular endothelial growth factor (VEGF) signaling.[5–7] In a small clinical trial including patients with cirrhosis and HCC, hepatic venous pressure gradient was decreased by sorafenib, a tyrosine kinase inhibitor that targets VEGF receptors.[8] These data suggest that anti-VEGF therapy, such as Beva may also have beneficial effects on PH.

Therefore, we consider that Baveno VII recommendations also apply to the specific group of patients with cirrhosis and HCC who are candidates for systemic treatment with Ate/Beva and who have not bled from varices. That is, screening for PH should be performed, and in the presence of clinically significant portal hypertension (CSPH), treatment with NSBBs is recommended,[3] since this not only prevents variceal bleeding but also non-bleeding decompensation.[9]

The authors rightly discuss that non-invasive criteria may not be applicable in patients with HCC, which applies mostly to uncertain effects of the tumor on liver stiffness. In addition, patients with HCC may also develop (malignant) portal vein thrombosis with pre-hepatic PH, and such patients should undergo screening with endoscopy.[3] In patients without portal vein thrombosis, the clinician may have to decide (based on HCC characteristics) whether non-invasive methods can provide helpful information or if an endoscopy is necessary. Since patients with HCC typically undergo cross-sectional imaging, awareness should be raised for the evaluation of signs of CSPH such as presence of portosystemic collaterals or splenomegaly.

Regarding the management of varices and prevention of variceal rebleeding in patients with HCC receiving Ate/Beva, we agree with the authors that special attention should be paid to adequate PH treatment, however, there is little data regarding the optimal strategy for secondary bleeding prophylaxis in this particular setting. We look forward to providing more answers to this clinically relevant question and other issues in Baveno VIII.

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Authors' contributions

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Supplementary data

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