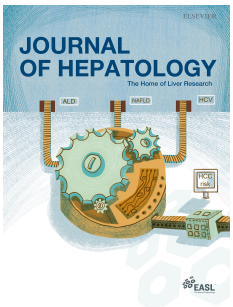

Response to 'Letter to the Editor' written by Dr. Isabelle Ollivier-Hourmand

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Response to ‘Letter to the Editor’ written by Dr. Isabelle Ollivier-Hourmand

Re: (JHEPAT-D-21-02347R1)

BAVENO VII - RENEWING CONSENSUS IN PORTAL HYPERTENSION

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All of the Authors contributed equally to the writing of this letter

Response to 'Letter to the Editor' written by Dr. Isabelle Ollivier-Hourmand

Dear Editors,

We read with interest the comments of Drs. Ollivier-Hourmand, Alaire, Cervoni, who wrote a letter on behalf of the 'Club Francophone pour l'Etude de l'Hypertension Portale' to comment 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 hepatocellular carcinoma[2] and thus, the issue of management of portal hypertension (PH) in patients with cirrhosis and HCC is very relevant. Up 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, those who undergo secondary prophylaxis with non-selective betablocker (NSBB) and endoscopic variceal ligation (EVL) had a better survival than those who did not[4].

Dr. Ollivier-Hourmand *et al.* raise concerns about a potentially increased variceal bleeding rate related to Beva treatment. However, several experimental studies suggests 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 (HVPG) 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 cirrhotic patients with 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 NSBB 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, HCC patients may also develop (malignant) portal vein thrombosis with pre-hepatic PH, and such HCC 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 HCC patients 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 HCC patients 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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