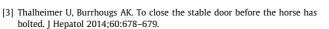
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- [4] Bucsics T, Schwabl P, Soucek K, Mandorfer M, Ferlitsch A, Peck-Radosavljevic M, et al. Is acute kidney injury stage 1 (AKI 1) according to modified AKIN criteria associated with higher mortality in cirrhotic patients with ascites? Hepatology 2013;58:864A, [abstract].
- [5] Tsien CD, Rabie R, Wong F. Acute kidney injury in decompensated cirrhosis. Gut 2013;62:131–137.



Sorafenib efficacy for treatment of HCC recurrence after liver transplantation is an open issue

To the Editor:

We read with interest the case-control study on sorafenib treatment for hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT) recently published in the Journal of Hepatology [1]. The study reports the consecutive experience on 15 patients with no otherwise treatable HCC recurrence after LT, who underwent treatment with Sorafenib. Outcome was compared with those of 24 historical consecutive controls. Overall, an outcome benefit statistically attributed to sorafenib was reported for the former group. Despite some strong bias, namely the case-control design of the study and the different immunosuppressive regimes between the two groups, possibly affecting HCC outcome, the take home message of both the study and the accompanying Editorial seems to be that since sorafenib is already of proven efficacy for HCC recurrence treatment after LT, its indication should be added to the next guidelines [1,2]. However, overall evidence of sorafenib efficacy for HCC recurrence after LT is actually weak.

Previous studies reported non homogeneous outcome after treatment of HCC recurrence after LT using sorafenib. In fact, despite the optimist results of some studies, more than one centre reported negative experiences [3–9].

In disagreement with the findings of the present study, we and others previously reported significant toxicity of sorafenib in the post-transplant setting [6,7]. In particular, one group reported grade 3–4 adverse events in 92% of 13 patients, resulting in sorafenib discontinuation in 77% [6]. Our experience on 15 consecutive patients, as partially reported on 11, describes a high rate of intolerance or side-effects, causing drug discontinuation in 36% of 11 patients [7]. Moreover, one patient died because of massive gastrointestinal bleeding, as previously fully described [10], suggesting the concern that everolimus and sorafenib interaction could facilitate gastrointestinal bleeding [3].

In conclusion, we believe that there is not yet enough evidence to draw any definite conclusion on indication of sorafenib for HCC recurrence treatment after LT. Albeit difficult to perform, a multicenter prospective sorafenib *vs.* placebo controlled trial should be advocated.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding or conflict of interest with respect to this manuscript.

References

- [1] Sposito C, Mariani L, Germini A, Reyes MF, Bongini M, Grossi G, et al. Comparative efficacy of sorafenib vs. best supportive care in recurrent hepatocellular carcinoma after liver transplantation: a case-control study. J Hepatol 2013;59:59–66.
- [2] Toso C, Mentha G, Majno P. Integrating sorafenib into an algorithm for the management of post-transplant hepatocellular carcinoma recurrence. J Hepatol 2013:59:3–5.
- [3] Bhoori S, Toffanin S, Sposito C, Germini A, Pellegrinelli A, Lampis A, et al. Personalized molecular targeted therapy in advanced, recurrent hepatocellular carcinoma after liver transplantation: a proof of principle. J Hepatol 2010;52:771–775.
- [4] Newell P, Toffanin S, Villanueva A, Chiang DY, Minguez B, Cabellos L, et al. Ras pathway activation in hepatocellular carcinoma and anti-tumoral effect of combined sorafenib and rapamycin in vivo. J Hepatol 2009;51:725–733.
- [5] Gangadhar TC, Cohen EE, Wu K, Janisch L, Geary D, Kocherginsky M, et al. Two drug interaction studies of sirolimus in combination with sorafenib or sunitinib in patients with advanced malignancies. Clin Cancer Res 2011;17:1956–1963.
- [6] Zavaglia C, Airoldi A, Mancuso A, Vangeli M, Vigano R, Cordone G, et al. Adverse events affect sorafenib efficacy in patients with recurrent hepatocellular carcinoma after liver transplantation: experience at a single center and review of the literature. Eur J Gastroenterol Hepatol 2013;25:180–186.
- [7] Staufer K, Fischer L, Seegers B, Vettorazzi E, Nashan B, Sterneck M. High toxicity of sorafenib for recurrent hepatocellular carcinoma after liver transplantation. Transpl Int 2012;25:1158–1164.
- [8] Weinmann A, Niederle IM, Koch S, Hoppe-Lotichius M, Heise M, Duber C, et al. Sorafenib for recurrence of hepatocellular carcinoma after liver transplantation. Dig Liver Dis 2012;44:432–437.
- [9] Piguet AC, Saar B, Hlushchuk R, St-Pierre MV, McSheehy PM, Radojevic V, et al. Everolimus augments the effects of sorafenib in a syngeneic orthotopic model of hepatocellular carcinoma. Mol Cancer Ther 2011;10:1007–1017.
- [10] Mancuso A, Airoldi A, Vigano R, Pinzello G. Fatal gastric bleeding during sorafenib treatment for hepatocellular carcinoma recurrence after liver transplantation. Dig Liver Dis 2011;43:754.

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