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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.

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