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LETTER TO THE EDITORS

Time to resize the role of everolimus as treatment of hepatocellular carcinoma recurrence after liver transplant

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We read with interest the recently published systematic review on mammalian target of rapamycin inhibitors (m-TORi), which favors the use of m-TORi instead of calcineurin inhibitors (CNIs) to control hepatocellular carcinoma (HCC) recurrence after liver transplantation (LT) [1]. Two recent meta-analyses have shown that sirolimus is associated with significantly lower HCC recurrence rates, compared with CNIs [2,3].

Because of the results of these data showing a better survival after LT for HCC when m-TOR inhibitors were used as immunosuppressive regimen, the concept of the anticancer role of these drugs as treatment of HCC recurrence after LT has made its way. In particular, some groups used to switch to m-TORi in association with sorafenib as treatment of HCC recurrence after LT.

We believe that the recently published randomized controlled trial (EVOLVE-1) on everolimus for HCC after failure of sorafenib establishes the futility of m-TORi as treatment of HCC [4]. In fact, while the results of this study simply move the issue of HCC treatment forward, the consequences on the role of m-TORi for HCC after LT are even deeper. However, different cases of fatal bleeding in patients treated with m-TORi and sorafenib for HCC recurrence after LT were reported [5–7], while no case has been described during treatment with sorafenib of HCC recurrence after LT when the immunosuppressive regimen did not contain m-TORi, suggesting the concern of a risk of severe bleeding of the association of m-TORi and sorafenib.

In conclusion, we believe that as m-TORi have no proven anticancer attitude for HCC treatment, the role of m-TORi in the context of LT for HCC should be resized. Finally, because of the risk of fatal bleeding, the association of m-TORi with sorafenib should be discouraged as treatment of HCC recurrence after LT.

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Conflicts of interest

None.

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