

Reviewer 1:

Au and Chok found that mTOR inhibitor could be a potential prognostic factor for prolonged survival after post-transplant HCC recurrence. This study involved a severe bias of time generation, as they discussed. I cannot entirely agree with their comments about the potential time effect rather than a fundamental time effect. Although all these biases, it might present valuable clinical information. The dose-effect of calcineurin inhibitor should be compared among the mTOR vs. no mTOR. I strongly suspect the dose of CNI at the recurrence in mTOR could be lower than that in no mTOR. CNI should include in the multivariate analysis.

Response to Reviewer 1:

Thank you for your comments and advice. We agree that the time effect is fundamental and have revised the manuscript. The median dose level of CNI has been incorporated into the univariate and multivariate cox regression analysis. Upon univariate analysis lower dose of CNI was associated with improved survival. We agreed that lower dose of CNI in the mTOR inhibitor group did contribute to improved survival. The protective effect of mTOR inhibitor, though weakened, persisted in multivariate analysis.

Reviewer 2:

The authors present a retrospective study to evaluate the effect of mTOR inhibitors in HCC patient's survival after liver transplant. The study has been well conducted and the main limitations have been evaluated and exposed by the authors. I personally feel that the use of mTOR inhibitors in HCC transplanted patients has been already explored (many references available) with similar conclusions and better statistics (likely resulting from larger cohorts). However, although the novelty is relative, the study might be of interest to reinforce the notion of the positive effect and eventual advantages of mTOR inhibitors for the management of these patients.

Response to Reviewer 2:

Thank you for your comments and advice. We have further addressed the limitation of this retrospective study by incorporating tacrolimus trough level into the survival analysis. The results still reinforced the notion of using mTOR inhibitors in this group of patients.

Reviewer 1:

Au and Chok revised the manuscript. However, the presentation of the Tables and Figures is still inappropriate, including discrepancies between the tables and the manuscript. In all tables, the number of patients should be numeral rather than a percent, or it could present both of them. Survival analysis should include tables for presenting numeral of the patients, including centered patients with time course. The number of each group is different from each table. For example, the mTOR inhibitor group consists of 48 sirolimus and 29 everolimus in the text, which ended up 76 patients. However, the mTOR group consists of 79 patients in Table 2. Where did three patients go? The presentation of the Tables and Figures seems to hide the results to prevent us in confirming the accuracy.

Response to Reviewer 1:

Thank you for your advice. The Tables have been revised to include both the patient numbers and percentages. The Kaplan Meier Curves have been revised to include the number at risk at each timepoint.

Thank you for your question concerning number of patients. Among the mTOR inhibitor group, 48 received sirolimus and 29 received everolimus. They added up to 77 patients. The remaining 2 patients were initially started on sirolimus but were subsequently converted to everolimus. As these 2 patients received both drugs, they were not included in the survival comparison between the two drugs. They constituted 79 patients in the mTOR inhibitor group. The

information has been included in the 'Immunosuppression after recurrence' section under 'Results'.