

Reply to reviewer :

Reviewer's code: 02544209

SPECIFIC COMMENTS TO AUTHORS

I think the authors missed adding information about the schedule of aflibercept in the treatment protocols section. Their retrospective findings confirms the efficacy of FOLFIRI3 protocol and its feasibility with antiangiogenic agents.

Response: we add information of the aflibercept schedule in the method part

Reviewer's code: 00505440

SPECIFIC COMMENTS TO AUTHORS

This is a very good study and well written manuscript. Recommend publication.

Reviewer's code: 00068723

SPECIFIC COMMENTS TO AUTHORS

The authors compared adverse events and overall survival among patients treated with FOLFIRI3, FOLFIRI3+Bevacizumab, and FOLFIRI3+Aflibercept. They found out that FOLFIRI3+Aflibercept was superior to the other two regimens in survival. The criteria of choice of treatment was not clear. How were the patients determined to the three regimens? The criteria might affect the overall survival.

Response: this study is retrospective and the decision to select a particular regimen was the choice of the oncologist who take in charge the patient. So the retrospective design of the study may induce some biased. However patients are comparable in the main clinical characteristics and multivariate analysis underline that usage of aflibercept is independently associated with outcome.

The authors concluded that FOLFIRI3+Aflibercept was superior to FOLFIRI3 18 and FOLFIRI3+Bevacizumab. Patients numbers were FOLFIRI3 18, FOLFIRI3+Bevacizumab 99, and FOLFIRI3+Aflibercept 36. Number of each group was relatively different. Were there any possibilities that the different numbers of patients might affect the results of overall survival? Were there any reports on

combination of FOLFIRI3 and the other chemotherapeutic agents?The results of this study should be compared with the other similar regimens. Superiority and inferiority of FOLFIRI3+Aflibercept should be compared.

Reponse: All literature on combination of FOLFIRI3 with target therapies are quote in the discussion and our result are compared with these data.