

ANSWERING REVIEWERS

Dear Editor,

We would like to thank the reviewers for careful and thorough reading of this manuscript and for the thoughtful comments and constructive suggestions, which help to improve the quality of this manuscript. Our replies are as follows:

Reviewer 1:

No comments.

Reviewer 2:

Q: The Authors should include a short discussion on biliary drainage in this setting.

A: Done. We added in the "Evolution of treatments" section the following: "Preoperative endoscopic biliary drainage is not widely acceptable among pancreatic surgeons in view of the increased morbidity and delays of definite treatment (21). However, the only study involving AC exclusively showed that preoperative biliary drainage reduces postoperative wound infection without influencing mortality (22)."

Reviewer 3:

Q1: The title and introduction are not in concordance with the main body text.

A1: Done. The title, the short title and the introduction have been modified accordingly.

Q2: Clearly state what is already known about chemotherapy in Advanced ampullary carcinoma.

A2: Our manuscript clearly states the actual state of knowledge in advanced ampullary carcinoma in the section "Concurrent chemotherapy treatments in advanced ampullary carcinoma"

Q3: The conclusions overreaches beyond the scope of the study.

A3: Done. The conclusion has been adjusted to the scope of the paper.

Reviewer 4:

Q1: The genetic characters of ampullary carcinoma should be added.

A1: Done. A section of the genetic particularities of ampullary carcinoma was added in the "Novel therapies" section

Q2: Some advanced clinical trials, such as NCT02333188 and NCT02757859, ... etc., should also be included.

A2: Done. The suggested studies have been added to the "Novel therapies" section.

We look to hear positively from you.

Kind regards.