

## Appendix Detailed Response to Reviewer's Comments

**Reviewer #1:** *The authors have addressed an important clinical topic in the management of patients with AAC. As they point out in the introduction and discussion, there is often difficulty accurately classifying the subtype into intestinal or pancreatobiliary which will have implications for both treatment and prognosis. The study is limited by it's small sample size, however, the science is sound and the techniques can (and should) be validated in a larger cohort.*

1. *There are several syntax/s spelling errors throughout the manuscript that need to be corrected and some assistance by scientific editing to improve the overall writing style would make this paper much easier to read and ultimately more impactful.*

RESPONSE: Done. We improved the English language by scientific language editing made by Prof. Sir Alfred Cuschieri.

2. *The authors need a paragraph in the discussion detailing what the limitations/weaknesses of their study are: retrospective, very small cohort, no data regarding type of adjuvant therapy and if there was an observed interaction between type of chemotherapy and histomolecular subtype.*

RESPONSE: Thank you for the helpful suggestion. We added the following paragraph in the discussion detailing the limitations of the study.

"The main limitations of the study are its retrospective nature, the small cohort of patients and the lack of data on type of adjuvant therapy and possible interaction between type of chemotherapy response and histo-molecular subtype. Further prospective randomized or observational studies are needed to validate these results in a larger cohort to address this controversial issue."

3. *I would recommend changing the title to something like: TISSUE MICRO ARRAY-CHIP FEATURING COMPUTERIZED IMMUNOPHENOTYPICAL CHARACTERIZATION MORE ACCURATELY SUBTYPES AMPULLARY ADENOCARCINOMA THAN ROUTINE HISTOLOGY*

RESPONSE: Done

### **Science Editor:**

*1 Scientific quality: The manuscript describes a basic study of the type classification of ampullary adenocarcinoma patients. The topic is within the scope of the WJG. (1) Classification: Grade B; (2) Summary of the Peer-Review Report: The authors have addressed an important clinical topic in the management of patients with AAC. The study is limited by its' small sample size, however, the science is sound and the techniques can (and should) be validated in a larger cohort. There are several syntax/spelling errors throughout the manuscript that need to be corrected. The authors need a paragraph in the discussion to clarify the limitations/weaknesses of this study.*

*a) The questions raised by the reviewers should be answered;*

RESPONSE: We answered all the questions raised by the reviewers.

*and (3) Format: There are 4 tables and 5 figures. A total of 51 references are cited, including 22 references published in the last 3 years. There are no self-citations.*

*2 Language evaluation: Classification: Grade C.*

RESPONSE: We improved the English language by scientific language editing made by Prof. Sir Alfred Cuschieri.

*3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, and the signed Conflict-of-Interest Disclosure Form and Copyright License Agreement.*

*b) The authors need to provide original Institutional Review Board Approval Form.*

RESPONSE: We provided the original Institutional Review Board Approval Form.

*The study was not involved in animals. No academic misconduct was found in the Bing search. The highest single-source similarity index in the CrossCheck report showed to be 9%. According to our policy, the overall similarity index should be less than 30%, and the single-source similarity should be less than 5%.*

*c) Please rephrase these repeated sentences.*

RESPONSE: Done

*4 Supplementary comments: This is an invited manuscript. The study was supported by ARPA Foundation. The topic has not previously been published in the WJG. The corresponding author has published 1 article in the BPG.*

*5 Issues raised: (1) I found the language classification was grade C. Please visit the following website for the professional English language editing companies we recommend: <https://www.wjgnet.com/bpg/gerinfo/240>;*

RESPONSE: Thank for the suggestion. We improved the English language by scientific language editing made by Prof. Sir Alfred Cuschieri.

*(2) I found the authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);*

RESPONSE: Done

*(3) I found the authors did not provide the original figures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor;*

We provided the original figure documents arranging them using Power Point according the author's guidelines.

*(4) I found the authors did not add the PMID and DOI in the reference list. Please provide the PubMed numbers and DOI citation numbers to the reference list and list all authors of the references. Please revise throughout;*

We revised the reference list adding the missing PMID and DOI.

*(5) I found the authors did not write the "article highlight" section. Please write the "article highlights" section at the end of the main text.*

Done

*6 Re-Review: Required.*

Done

*7 Recommendation: Conditionally accepted.*