

Re: manuscript 67333 - TIPS AND TRICKS FOR THE DIAGNOSIS AND MANAGEMENT OF BILIARY STENOSIS. STATE OF THE ART REVIEW

by Giovanna Del Vecchio Blanco et al.

Point-by-point letter to the Reviewer

We would like to thank the Reviewers for the constructive and helpful comments. We have revised the manuscript considering all the issues raised. All changes in the manuscript have been highlighted in bold.

Reviewer #1: Excellent review Would recommend: creating a flow chart to summarize the article and show the work up. Article need more spyglass pictures like benign and malignant stricture as well as pathology and FNA.

A flow chart has been included among the Figures and a link to the flow chart has been inserted in the manuscript (paragraph “Second step”, page 7, line 15). Spyglass pictures and histology of tissue specimen collected by EUS-FNA has been added in the manuscript as requested

Reviewer #2: The authors reviewed biliary stenosis. This manuscript provided current status of the disease in view of diagnosis and treatment. The manuscript was informative and useful. The contents were rationale. Liquid biopsy of bile is a new technology.

Are the biomarkers protein, nucleic acid? What biomarkers are examined?

In the major part of the study liquid biopsy based on the assessment of mutation or differentially methylated region in the cell free DNA released by tumor cells in plasma or in bile. Other biomarkers have been described including proteins, metabolites and microRNAs. A short addition has been inserted (page 6, line 18).

Is there any concern that protein or nucleic acid degrades in bile?

There is no evidence of acid nucleic degradation in the bile

No texts were found in “Conclusion”. Figure legends. Abbreviations should be spelled out when they first appeared in each legend. Photos of Figure 1 seems to be those of legend of Figure 2. Photos of Figure 2 seems to be those of legend of Figure 1.

A Conclusion paragraph has been added in the manuscript.

Figure legends have been added. Figures position has been corrected

Abbreviations have been spelled out.

SCIENCE EDITOR: all the requested changes were made in accordance with the issues raised