

Response to Reviewer reports:

The reviewers raise extremely valid points. Mentioned below are the point by point responses from author and changes made in the revised manuscript.

Reviewer's code: 03647053

COMMENTS TO AUTHORS: Moole et al., aimed to perform a systematic review and meta-analysis on clinical outcomes of photodynamic therapy (PDT) in non-resectable cholangiocarcinoma. The review, that has the same structure of other reviews of the same author, in general is well designed, and although clinical data appear to be limited, they might be applied to clinical practice? the interpretation seems adequate. To improve this review could be useful to add in the discussion more recent data on Photodynamic Therapy vs cholangiocarcinoma.

RESPONSE TO REVIEWER 024554595: This systematic review and meta-analysis included the most recent and peer reviewed data/studies on this topic. A thorough search strategy was mentioned in the methodology section of the manuscript. We have added two new studies to the discussion of this manuscript. References 55 and 56 mention these new studies, The added content in highlighted in the manuscript.

Reviewer's code: 03254227

COMMENTS TO AUTHORS: This is a very good study. Strengths of this meta-analysis is the high quality methodology of statistical analysis. I do believe it needs just a minor revision. At page 17 the authors stated: "This is the first meta-analysis to pool the evidence for the utility of PDT plus biliary stenting in palliation of non resectable cholangiocarcinoma". Nevertheless, the authors should complete the discussion by means of citation of other meta-analysis on this topic (example: Lu Y et al. Efficacy and safety of photodynamic therapy for unresectable cholangiocarcinoma: A meta-analysis. Clin Res Hepatol Gastroenterol. 2015). At page 15 the authors stated: "Chemotherapy and radiotherapy do not add any benefit to patient survival and quality of life". I do believe the authors should consider other article on this topic reporting results of chemotherapy and/or radiotherapy, in particular but not exclusively when associated

to PDT (example: Wentrup R et al. Photodynamic Therapy Plus Chemotherapy Compared with Photodynamic Therapy Alone in Hilar Nonresectable Cholangiocarcinoma. GUT Liver. 2016). Finally, in the discussion the option of liver transplant (with eventual neo-adjuvant therapy) should be mentioned, since this option has been studied even in patients with initially non resectable cholangiocarcinoma.

RESPONSE TO REVIEWER 02460781: As rightly suggested by this reviewer, we have added these two new studies (Lu et al; Wentrup et al) to the discussion of this manuscript. References 55 and 56 mention these new studies, The added content in highlighted in the manuscript. We have also included the verbiage regarding the utility of liver transplantation as suggested by this reviewer.

Reviewer's code: 00069371

COMMENTS TO AUTHORS: The manuscript presents a very excellent research in medical treatment of non-resectable cholangiocarcinoma with photodynamic therapy (PDT) using meta-analysis approach. The authors have chosen a good set of objective criteria, aggregated enough information and performed well data analysis with high statistic. The language is well written. The study results should be benefits to medicinal field.

RESPONSE TO REVIEWER 02451558: Thank you

Reviewer's code: 03505873

COMMENTS TO AUTHORS: This is a good study. The authors aimed to perform a systematic review and meta-analysis on clinical outcomes of photodynamic therapy (PDT) combine with bile duct stent in non-resectable cholangiocarcinoma. The study design and text language is good. In this study, some point need to describe more clear and thorough. Personal opinions: First, as mentioned in introduction cholangiocarcinoma include intra and extra hepatic cholangiocarcinoma, and extra be devied into hilar and distal cholangioarcinoma. So here if it is possible, to compare the subtype in detail. Second, it is better to describe which method these reports used to make insertion of biliary stent, ERCP or PTBD?



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RESPONSE TO REVIEWER 02451558: In regards to the route of stent insertion & type of stent inserted, we have clearly mentioned in the table at the end of the manuscript file (Table 1). However, there was no data included in the individual studies regarding the location of the cholangiocarcinoma. Hence we were unable to comment on location if it was hilar vs distal.

We believe that the revisions suggested by the reviewers have made the manuscript more valid and exceptionally appropriate for the readers.

Thank you for the comments made, and thank you for giving us the opportunity to make the revisions. We truly appreciate it.

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