

## Comments

This paper presents recent advances in the management of cholangiocarcinoma with particular focus on the expanding role for liver transplantation, updated guidelines in the use of chemotherapy, novel applications of individualized therapy targeting the specific mutation profile of tumors, and management of malignant biliary obstruction. It is a topic of interest to the researchers in the related areas but the paper needs improvement before acceptance for publication. My detailed comments are as follows.

1. The topic is novel but the application proposed is not so novel.
2. "Tumor Directed Therapies", in this part, do the author make sure majority of the therapies had been summarized?
3. The targeted therapy and immunotherapy for cholangiocarcinoma was not comprehensive summarized. Please supply more information, including the results of correlated clinical researches in recent years.
4. Could the author offer fully spelling out the abbreviations to help the readers get more information and understand the review more correctly?
5. Make sure all the references in the right place and really support the author's point.

## Response:

1. We recognize that our approach is not particularly novel but agree that an up to date review is timely and important given recent changes in the literature.
2. We agree, discussion of TACE and thermal ablation was added to this section.
3. We agree that this is not a comprehensive summary. Unfortunately because multiple interventions including surgery, transplant, systemic, and locoregional therapies had to be covered the level of detail able to be presented within the constraints of the format was limited. Table 1 provides a summary of agents and targets which was updated with FDA approval since initial submission. A statement acknowledging the limitations of this discussion was added. The authors also acknowledge that this is a rapidly changing field where going forward the central point for the reader is that molecular profiling of tumors will have an increasing role in the management of cholangiocarcinoma and consultation with a center with expertise in this field is therefore of value. A reference was added of a recent in-depth review of systemic therapies for CCA which includes ongoing clinical trials.
4. The manuscript was reviewed to ensure all abbreviations are appropriately listed. An abbreviation section with a list of all abbreviations was also added.
5. References were reviewed. When appropriate, new references were added and inappropriate references removed.