



# Excellent clinical outcomes can be achieved with neoadjuvant chemoradiation and orthotopic liver transplantation for unresectable cholangiocarcinoma: support for the need of an international transplant protocol

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We thank Dr. He *et al.* for their comments regarding our retrospective study evaluating treatment strategies in the management of hilar and extrahepatic cholangiocarcinoma, published in *Journal of Gastrointestinal Oncology* (1). The combination of neoadjuvant chemoradiation followed by orthotopic liver transplantation via an institutional-based strict protocol/selection process provides the best outcomes for these patients. This has been well validated (2-5). Ultimately, eligibility for this protocol is rigorous: patients may not have metastatic disease, tumor size >3 cm, or medical conditions that would preclude transplant (2,3). Patients with a malignant stricture in the setting of primary sclerosing cholangitis are also eligible (2,3). For several different reasons, approximately 25% of patients who initiate protocol-based therapy become ineligible to proceed with liver transplantation (6). It is important to note that patients with unresectable disease who undergo this protocol may have superior outcomes compared to patients with resectable disease who undergo surgical resection followed by adjuvant therapy (1,6).

He *et al.* presents an excellent discussion regarding current prospective clinical trials incorporating orthotopic liver transplantation for unresectable hilar cholangiocarcinoma. Collecting prospective clinical data

at a national or international scale is the next step to help validate the current protocol of neoadjuvant chemoradiation and liver transplantation for hilar cholangiocarcinoma. While this approach has been well studied in the setting of hilar cholangiocarcinoma, intrahepatic cholangiocarcinoma has previously been a contraindication for liver transplant given its aggressive behavior and poor outcomes (7). We certainly agree with He *et al.* that this approach warrants further investigation. As He *et al.* also noted, the prognosis of intrahepatic, hilar, and extrahepatic cholangiocarcinoma could be enhanced further with new targeted agents and immunotherapy, as well as combinations of these novel systemic options with modern radiotherapeutic approaches. These represent active research areas, all to try and improve the currently poor outcomes for this group of patients.

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