UNIVERSITY OF CINCINNATI CHOLANGIOCARCINOMA TRANSPLANT PROTOCOL

Inclusion criteria:
- unresectable hilar (perihilar) cholangiocarcinoma after review at University of Cincinnati Medical Center Hepato-Biliary conference
- hilar (perihilar) cholangiocarcinoma in the setting of primary sclerosing cholangitis (PSC)

Diagnosis of cholangiocarcinoma[1-3]: at least 1 of the following:
- intraluminal brush cytology or biopsy positive for adenocarcinoma
- radiographic malignant stricture and serum CA 19.9 > 100 ng/ml
- radiographic malignant stricture in setting of PSC
- biliary aneuploidy in fluorescent in situ hybridization (FISH)

Staging:
- CT chest, abdomen
- Endoscopic ultrasound (EUS) with fine needle aspiration of suspicious lymph nodes
- Laparoscopy for staging if suspicion of extrahepatic disease

Exclusion criteria:
- mass > 3cm [4,5]
- extrahepatic disease (including regional lymph node involvement)
- previous operation or attempted resection of the tumor
- uncontrolled infection

Neoadjuvant Therapy
- Fractionated chemoradiation will be provided to the primary tumor and regional lymphatics to a dose of 45 Gy at 1.8 Gy per fraction with a concurrent flouropyrimidine based sensitizer.
- This will be followed by a conformal, hypofractionated 20 Gy boost to the primary tumor (4Gy x 5 fractions)

Staging operation
- performed 4 weeks after completion of neoadjuvant therapy.
- laparoscopy or laparotomy
- biopsy of lymph nodes overlying common hepatic artery and common bile duct (GDA and BD node)
- biopsy of any abnormal lymph nodes/mass
- Patients with negative staging will be listed for transplant.
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Maintenance Chemotherapy
- Patients will receive 3 cycles Cisplatin/gemcitabine based chemotherapy .
- Patients will go on to receive additional maintenance Capecitabine until the time of transplant.

Imaging Surveillance:

- Contrast CT scans of the chest, abdomen, and pelvis will be obtained every 3 months after the time of restaging operation until transplant or the development of metastatic disease.

Transplant

- hilar structures are divided as low as possible close to the duodenum
- frozen section of the bile duct margin
- pancreatoduodenectomy in case of bile duct involvement
- caval-sparing hepatectomy and piggy-back implantation unless caudate involvement is suspected (caval interposition with bicaval anastomosis in case of caudate involvement)
- Aorto-hepatic jump graft with conduit
- Roux-en-Y hepatico-jejunostomy

Schedule

Start time	
0	Staging: CT or MRI abdomen/pelvis, CT chest, EUS, DSE, Social worker
0	Neoadjuvant chemoradiation
11th week	Staging laparoscopy or laparotomy, MultiD clinic and listing for liver transplant
13th week	Initiate 3 cycles of Gemcitabine/cisplatin
19th week	Maintenance capecitabine chemotherapy

Post-transplant follow-up

- CT chest non-contrast, CT biphasic abdomen, Ca 19.9 every 6 months for years 1 and 2
- CT chest non-contrast, CT biphasic abdomen, Ca 19.9 annually for years 3, 4, and 5

Reported Outcomes

- survival rate after liver transplantation: 91% at 1 year, 82% at 5 years[2]
- recurrence-free survival after transplantation: 78% at 2 years, 65% at 5 years[4]
- recurrence rate: 12% at 5 years[2]
- mean time to recurrence : 40 months[2]
- drop-out rate (from enrollment to transplantation): 25%[4]

References

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