Patient Population

- Age ≥ 18 years, ECOG PS 0-1, and adequate lab values
- Must have histologically-confirmed T2 or T3 gallbladder cancer discovered incidentally at the time of, or following routine cholecystectomy for presumed benign disease
- Must have undergone initial cholecystectomy within 12 weeks prior to randomization
- Must not have any evidence of metastatic disease or inoperable loco-regional disease based on high-quality, pre-operative, cross-sectional imaging (CT or MRI) of the chest, abdomen, and pelvis (C/A/P) obtained within 6 weeks prior to randomization, defined per protocol:
  - No radiographic evidence of distant disease, tumor invasion into multiple extrahepatic organs, or distant lymph node involvement
  - No evidence of new-onset ascites
  - Soft tissue thickening within or in direct communication with the gallbladder fossa, periportal lymph node involvement, involvement of 1 extrahepatic organ, and other disease within the confines of what constitutes “localized resectable” disease are allowable
- Women must not be pregnant or breast-feeding
- HIV, HBV, and HCV patients are eligible per protocol
- Patients with a prior or concurrent malignancy whose natural history or treatment dose not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible
- Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should be NYHA 2B or better

Treatment Plan

1 cycle = 21 days

**Arm A:**
- Surgery: to be performed within 4 weeks of randomization
  - Staging laparoscopy prior to laparotomy; if eligible for re-resection: undergo a partial hepatectomy of segments IVb/V, portal lymphadenectomy, and any other indicated procedure in order to achieve a grossly negative resection status
  - The decision regarding eligibility for re-resection will be left to the operating surgeon
- Adjuvant chemotherapy for patients who undergo successful re-resection. Gemcitabine 1000 mg/m² IV and cisplatin 25 mg/m² days 1 and 8 of each cycle for 8 cycles

**Arm B:**
- Neoadjuvant chemotherapy: Gemcitabine 1000 mg/m² IV and cisplatin 25 mg/m² days 1 and 8 of each cycle for 4 cycles
- Surgery: to be performed within 8 weeks of completion of neoadjuvant chemotherapy
  - Restaging with cross-sectional imaging of the C/A/P; all patients eligible for reoperation will undergo a staging laparoscopy prior to laparotomy
  - If eligible for re-resection: undergo a partial hepatectomy of segments IVb/V, portal lymphadenectomy, and any other indicated procedure in order to achieve a grossly negative resection status
- Adjuvant chemotherapy for patients who undergo successful re-resection. Gemcitabine 1000 mg/m² IV and cisplatin 25 mg/m² days 1 and 8 of each cycle for 4 cycles

Patient Enrollment

All Sites: Oncology Patient Enrollment Network (OPEN), [https://open.ctsu.org](https://open.ctsu.org)

Protocol Information

ECOG-ACRIN Operations-Boston: 857-504-2900, [http://ecog-acrin.org](http://ecog-acrin.org) (Member Login)

Please Enroll Your Eligible Patients!
1. Determination of resectability will be based on review of high-quality cross-sectional imaging (either CT or MRI) of the chest, abdomen, and pelvis.

2. All patients will be restaged with cross-sectional imaging (CT or MRI) of the chest, abdomen, and pelvis at the completion of chemotherapy, prior to resection.

3. Surgery should be performed within 4 weeks of randomization (Arm A) or within 5 weeks of completion of neoadjuvant and chemoradiation (Arm B).

Randomization will be performed in a 2:1 fashion.

1 cycle = 21 days

AmA = AmA

Cycles on days 1 and 8 for 4 cycles
- Carboplatin 250 mg/m² IV + Gemcitabine 1000 mg/m² IV
- AmA

Adjuvant Therapy

NEO Adjuvant Therapy

Schema

ECOG-ACRIN Cancer Research Group

Version 03/03/22 (Add. #1)