

**Please Enroll
Your Eligible
Patients!**

For Patients with Advanced Biliary Tract Cancer

EA2251 Available Through ECOG-ACRIN Cancer Research Group

A Phase II/III Randomized Study of Ivonescimab with Gemcitabine and Cisplatin versus Standard of Care Chemoimmunotherapy in Advanced Biliary Tract Cancer

Patient Population

See protocol Section 3 for complete eligibility criteria

- ≥ 18 years of age, ECOG PS 0-1, adequate labs obtained ≤ 7 days prior to randomization
- Histologically/cytologically confirmed adenocarcinoma of the biliary tract including cholangiocarcinoma (intrahepatic or extrahepatic) or gallbladder carcinoma
- Must not have a diagnosis of ampullary cancer
- Must have documented metastatic or locally advanced unresectable disease on CT/MRI
- Must have measurable disease (defined per protocol) on CT/MRI within 28 days prior to randomization
- No prior systemic therapy for current metastatic or locally advanced biliary tract cancer
 - ◊ Patients who have previously received adjuvant/neoadjuvant chemotherapy and/or RT for curative intent non-metastatic disease are eligible if they developed recurrent disease > 6 months after completion of adjuvant therapy/RT
- Must not be on systemic immunosuppressant therapy other than inhaled/intranasal/topical steroids, or systemic steroids up to 10 mg prednisone equivalent
- Must not have received a live vaccine within 30 days of randomization, while on treatment/up to 30 days after
- No contraindications to VEGF inhibitor therapy (see criterion 3.1.10 for complete details)
- No Grade > 2 peripheral neuropathy at randomization
- No history of allogeneic organ transplantation
- No prior documented autoimmune or inflammatory disorders, systemic lupus erythematosus, Sarcoidosis/Wegener syndrome (see criterion 3.1.18 for details/exceptions)
- Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety/efficacy assessment of the investigational regimen are eligible for this trial
- Patients with known history/current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should be NYHA class 2 or better

Treatment Plan

See protocol Section 5 for complete treatment details

Cycle = 21 days; Treatment must start within 10 calendar days after randomization

Arm A: Gemcitabine + Cisplatin + Durvalumab or Pembrolizumab:

- Repeat for 8 cycles:
 - ◊ **Gemcitabine** 1000 mg/m² IV on Days 1 and 8
 - ◊ **Cisplatin** 25 mg/m² IV on Days 1 and 8
 - ◊ **Durvalumab** 1500 mg IV on Day 1, or **Pembrolizumab** 200 mg IV on Day 1
- Following 8 cycles, continue maintenance durvalumab or pembrolizumab (+/- gemcitabine, at investigator's discretion) at same dosing and schedule, until progression, unacceptable toxicity, other protocol-specified criteria (per Section 5.5), or a maximum of 2 years

Arm B: Gemcitabine + Cisplatin + Ivonescimab:

- Repeat for 8 cycles:
 - ◊ **Gemcitabine** 1000 mg/m² IV on Days 1 and 8
 - ◊ **Cisplatin** 25 mg/m² IV on Days 1 and 8
 - ◊ **Ivonescimab** 20 mg/kg IV over 60 minutes (+/- 10 minutes) on Day 1
- Following 8 cycles, continue maintenance ivonescimab (+/- gemcitabine, at investigator's discretion) at same dosing and schedule, until progression, unacceptable toxicity, other protocol-specified criteria (per Section 5.5), or a maximum of 2 years

Notes:

- Patients may not switch their ICI agent during study
- Institutional guidelines should be followed for the order in which cisplatin, gemcitabine, and pembrolizumab/durvalumab are administered; ivonescimab must be administered before chemotherapy
- See Section 5 for suggested pre- and post-medications
- See Section 5.3 for complete details on dose mods, treatment interruptions/delays, and toxicity management

Study Chair:

Deirdre J. Cohen, MD

Study Co-Chair:

Dan Feng, MD, PhD

NCTN Study Champions:

- **Alliance:** Midhun Malla, MD
- **SWOG:** Gentry King, MD

Patient Enrollment (Oncology Patient Enrollment Network [OPEN])



<https://open.ctsu.org/open>



1-888-823-5923

Protocol Information (ECOG-ACRIN Operations – Boston)



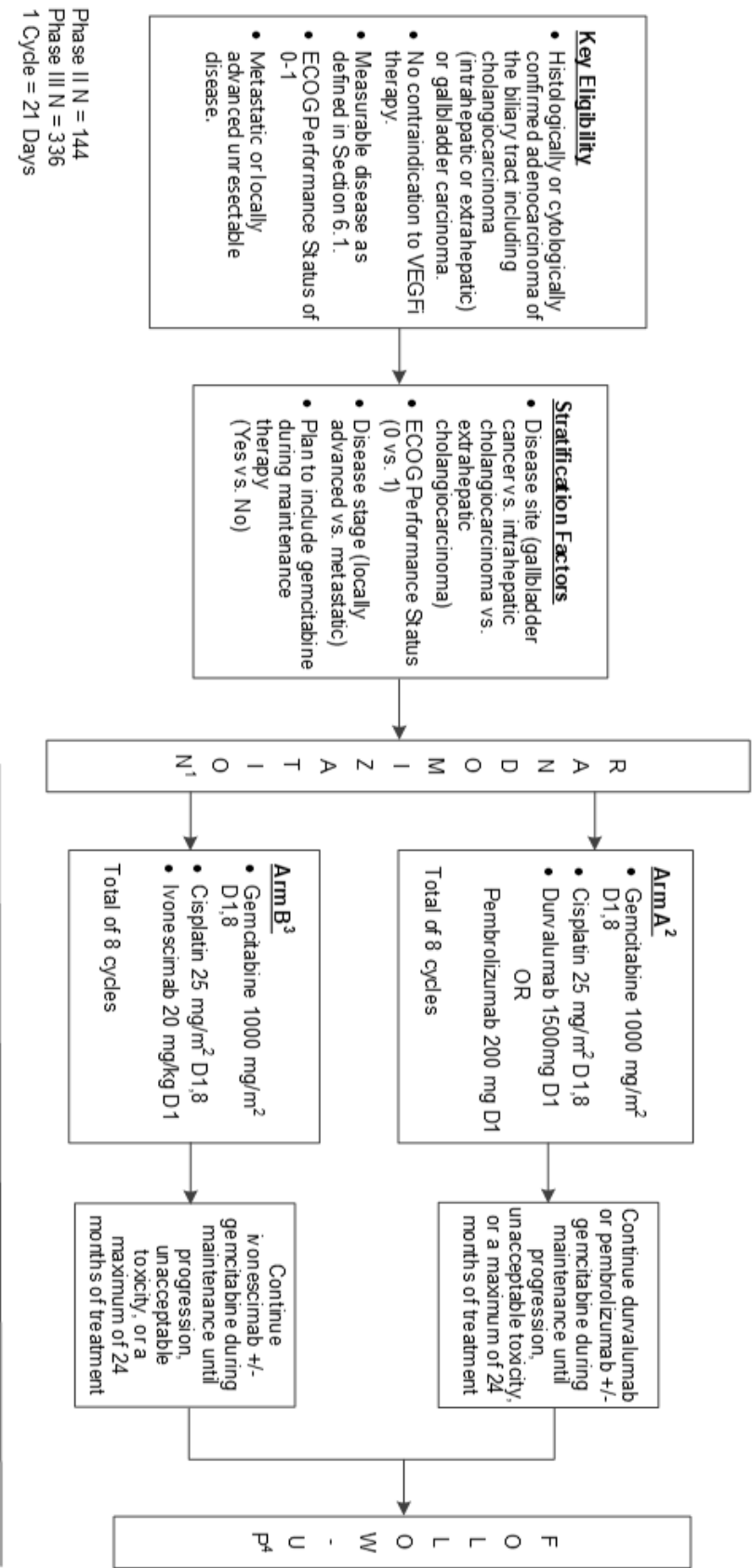
<http://ecog-acrin.org> (Member Login)



1-857-504-2900

EA2251

Schema



1. Randomization is 1:1
2. See Section 5.1.1 for additional treatment details
3. See Section 5.1.2 for additional treatment details.
4. Patients will be followed for 3 years from the date of randomization.