

For Patients with Advanced Intrahepatic Cholangiocarcinoma

EA2187 Available Through ECOG-ACRIN Cancer Research Group

A Phase II Study of Pevonedistat in Combination with Carboplatin and Paclitaxel
in Advanced Intrahepatic Cholangiocarcinoma

Patient Population

See Section 3.0 for Complete Eligibility Details

- ≥ 18 years of age, ECOG PS 0-1, life expectancy ≥ 12 weeks, and adequate lab values
- Must have histologically confirmed intrahepatic cholangiocarcinoma or biphasic hepatocellular carcinoma and cholangiocarcinoma that is metastatic or unresectable and who have progressed on or been intolerant of 1 prior line of systemic gemcitabine containing chemotherapy regimen (prior immunotherapy/targeted therapies are allowed and will not be considered a line of therapy unless administered with cytotoxic chemotherapy)
- Must have measurable disease defined per protocol
- No major surgery within 14 days of randomization; patients with planned surgery during the study are ineligible
- HIV/HBV/HVC patients must meet criteria per protocol
- No persistent \geq grade 2 diarrhea lasting more than 3 days within 14 weeks of randomization
- No known CNS involvement
- Patients with known history/current symptoms of cardiac disease/history of treatment with cardiotoxic agents should have a clinical risk assessment of cardiac function using NYHA; to be eligible, patients should be class 2B or better; patients with known cardiopulmonary disease are ineligible (see protocol for details)
- Must not have received chemotherapy/radiotherapy within 2 weeks of randomization; must not have received immunotherapy within 8 weeks of randomization
- No history of allergic reaction attributed to compounds of similar chemical/biologic composition to pevonedistat, carboplatin, or paclitaxel; no prior pevonedistat treatment
- No treatment with clinically significant metabolic enzyme inducers within 14 days of the first dose of study drug
- No uncontrolled intercurrent illness/coagulopathy or bleeding disorder; no active, uncontrolled infection/severe infectious disease
- No known moderate chronic obstructive pulmonary disease/interstitial lung disease/pulmonary fibrosis

Treatment Plan

See Section 5.0 for Complete Treatment Details

1 cycle= 21 days

Arm A- Pevonedistat Monotherapy

- 50 mg/m² IV over 60 mins (+/- 10) on days 1, 3, 5
- Repeat cycles until disease progression, unacceptable toxicity, or patient desire to discontinue

Arm B- Pevonedistat in Combination with Carboplatin and Paclitaxel:

- Pevonedistat 20 mg/m² IV over 60 mins (+/- 10 mins) on days 1, 3, and 5 every cycle x 4, followed by
- Paclitaxel 175 mg/m² IV over 3 hrs (+ 20 mins) or utilizing local standard procedures, on day 1 of every cycle x 4, followed by
- Carboplatin AUC 5 IV over 15-60 mins on day 1 of every cycle x 4
- At any time after 4 cycles of combination therapy, the treating physician is given discretion whether to continue with:
 - ◇ **OPTION A:** Pevonedistat 50 mg/m² days 1, 3, and 5 every cycle OR
 - ◇ **OPTION B:** Pevonedistat 20 mg/m² IV days 1, 3, and 5 every cycle followed by Paclitaxel 175 mg/m² day 1 every cycle followed by Carboplatin AUC 5 IV day 1 every cycle
 - ◇ Both options will continue until disease progression, unacceptable toxicity, or patient desire to discontinue; patient can switch from option A to B

Notes:

- Treatment is administered on an outpatient basis
- Doses are based on actual body weight
- See protocol for premedications
- If the patient required a dose reduction attributable to pevonedistat, then the patient should be maintained at the single agent dose that they were reduced to

Patient Enrollment

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

Protocol Information

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

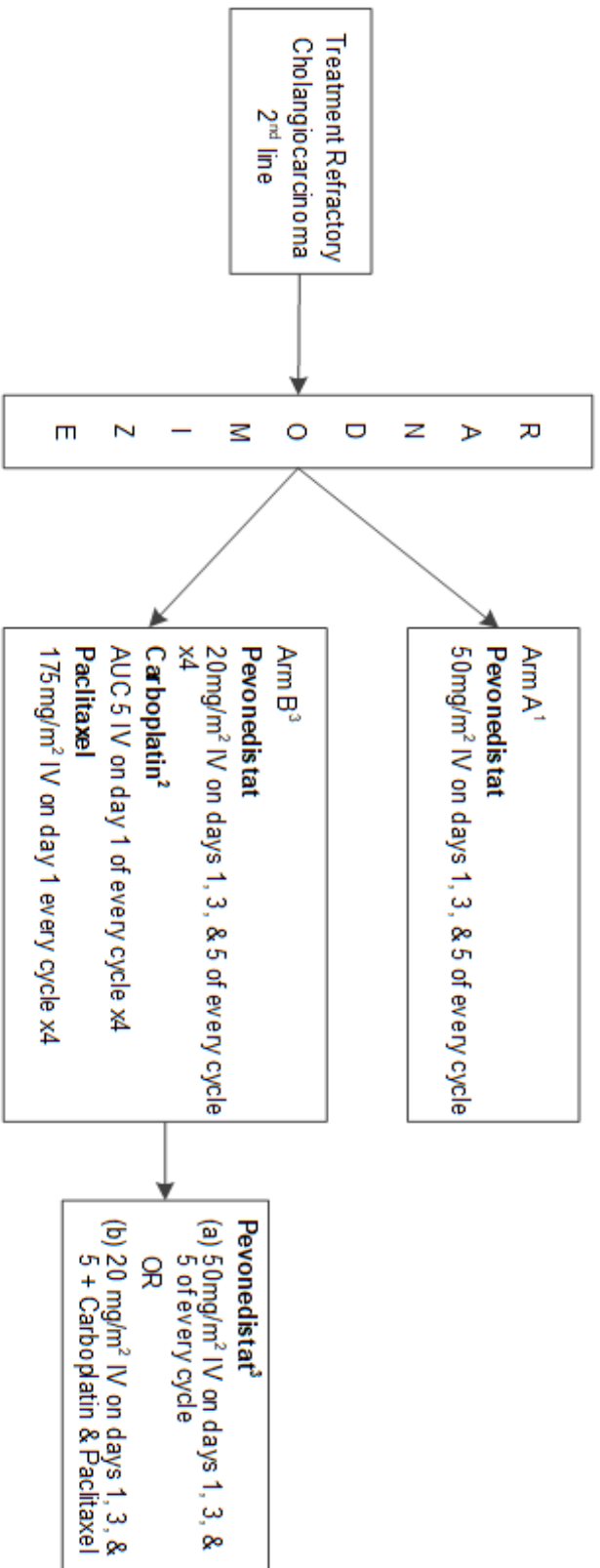
Please Enroll Your Eligible Patients!

Study Chair:
Dustin Deming, MD

Co-Chair:
Anita Turk, MD

EA2187

Schema



Cycle: 21 days

Accrual Goal: 52

1. For Arm A, treatment will continue until disease progression, unacceptable toxicity, or patient desire to discontinue study therapy.
2. Refer to section 5.1.2.2 for carboplatin dose specifics.
3. For Arm B at any time after 4 cycles of combination therapy, the treating physician is given discretion to continue combination therapy or switch to pevonedistat monotherapy. Treatment will continue on Arm B until disease progression, unacceptable toxicity or patient desire to discontinue study therapy.