Version 10/20/23 (Add. #3)

NCI National Clinical Trials Network

EA2222/PUMP

For Patients with Colorectal Liver Metastases

EA2222 Available Through ECOG-ACRIN Cancer Research Group

A Randomized Phase III Study of Systemic Therapy with or without Hepatic Arterial Infusion for Unresectable Colorectal Liver Metastases: The PUMP Trial

Patient Population

See Section 3 for Complete Eligibility Details

- Age ≥ 18 years; adequate lab values
- ECOG PS 0-1; clinically fit to undergo surgery
- Must have confirmed unresectable liver confined metastatic colorectal cancer (CRC)
  - ◊ No radiographically/clinically evident extrahepatic disease; may have pulmonary nodules per protocol
  - ◊ No MSI-H colorectal cancer
- Must have received 3-6 months of previous first-line chemotherapy that meet 1 of 3 criteria: a) have received at least 6 but no more than 12 cycles of first-line cytotoxic chemotherapy (where 1 cycle = 14 days), OR b) have received at least 4 but no more than 8 cycles of first-line cytotoxic chemotherapy (where 1 cycle = 21 days), OR c) have developed new colorectal liver metastases (CRLM) within 12 months of completing adjuvant systemic therapy for stage II-III colorectal cancer
- Must have stable/responding disease on first-line chemotherapy (RECIST 1.1)
- Must meet the protocol criteria for technical unresectability
- Must not have liver tumor burden exceeding 70% of total liver volume; no prior radiation to the liver
- No prior trans-arterial bland embolization, chemoembolization (TACE), or radioembolization (TARE)
- No prior treatment with HAI/FUDR
- Must not have CRLM that could be resected with 2-stage hepatectomy (including ALPPS)
- No active infection, serious/non-healing active wound, ulcer or bone fracture
- Must not have cirrhosis and/or clinical /radiographic evidence of portal hypertension
- Patients with HIV are eligible per protocol

Note: See Section 4 for protocol-specific requirements for site registration

Treatment Plan

See Section 5 for Complete Treatment Details

Arm A

- **Surgery:** Insertion of the hepatic artery infusion pump by open or minimally invasive (robotic) techniques within 6 weeks of randomization
  - ◊ Cholecystectomy, unless performed previously
  - ◊ Wedge biopsy of a representative hepatic lesion, when risk considered minimal
  - ◊ Core biopsy of representative tumor when resection deemed inappropriate
  - ◊ Selected patients may have the primary tumor resected/diverted, based on multidisciplinary recommendations
- **HAI:** Postoperatively, patients will undergo single photon emission computed tomography (SPECT) with/without CT per institutional standard to confirm hepatic-only perfusion prior to initiating HAI/FUDR
  - ◊ Treatment to begin within 12 weeks of randomization
  - ◊ HAI/FUDR given on Days 1-14 of each cycle, followed by heparinized saline on Days 15-28
  - ◊ Patients will administer oral proton pump inhibitor daily (physician's choice of agent)
- **Systemic Therapy:** One of the allowable standard of care regimens (physician's choice– FOLFOX, FOLFIRI, OX/IRI – may include anti-EGFR)
  - ◊ Chemotherapy to initiate within 16 weeks of randomization (given Day 1 and 15)

Arm B

- **Systemic Therapy:** One of the allowable standard of care regimens (physician's choice– FOLFOXIRI, FOLFOX, FOLFIRI, OX/IRI – may include anti-VEGF or EGFR therapies)
  - ◊ Chemotherapy to initiate within 6 weeks of randomization (given Day 1 and 15)
  - ◊ Selected patients may have the primary tumor resected/diverted

Study Chair:
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Patient Enrollment

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

Protocol Information

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

Please Enroll Your Eligible Patients!

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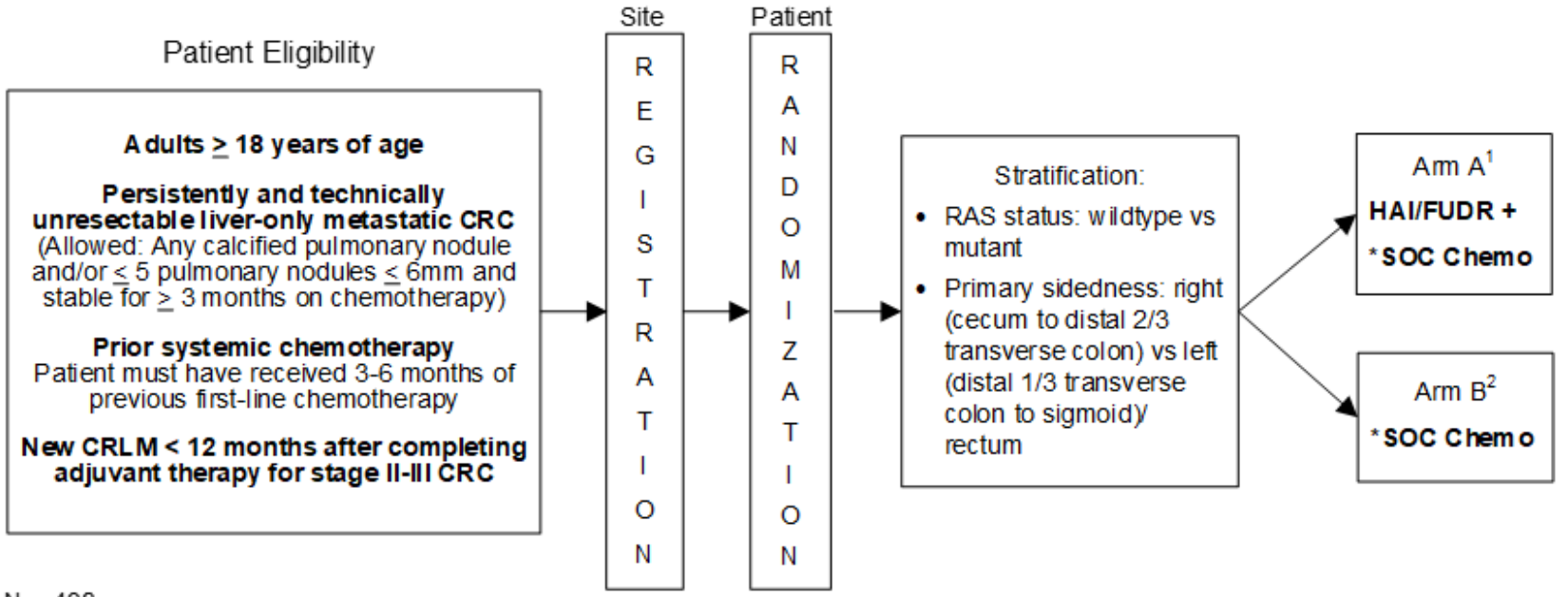
ECOG-ACRIN cancer research group

EA2222

Schema



N = 408

2:1 Randomization

1. Arm A consists of HAI/FUDR (Hepatic arterial infusion/ floxuridine) plus standard of care chemotherapy options that are outlined in Section 5.1.1.3.
2. Arm B consists of standard of care chemotherapy options that are outlined in Section 5.1.2.1.