Cancer Research Consortium of West Michigan
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FAST FACTS

EA2222: A Randomized Phase III Study of Systemic Therapy With or Without Hepatic Arterial Infusion for Unresectable Colorectal Liver Metastases: The PUMP Trial

ELIGIBILITY CRITERIA

1. Patient must be ≥ 18 years of age.

2. Patient must have confirmed unresectable liver confined metastatic colorectal cancer (CRC).

   - Patient must not have radiographically or clinically evident extrahepatic disease (including but not limited to radiographically positive periportal lymph nodes).

     NOTE: Patients found to have positive periportal nodes at the time of HAI placement can remain on study.

   - Patient may have calcified pulmonary nodules, and/or ≤ 5 indeterminate and stable (for a minimum of 3 months on chemotherapy) pulmonary nodules each measuring ≤ 6 mm in maximal axial dimension.

   - Patient's primary tumor may be in place.

3. Patient must have received 3-6 months of previous first-line chemotherapy that meet one of the following three 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.

   NOTE: First-line chemotherapy may have included any of the following regimens as listed in the NCCN Guidelines: FOLFOX (or equivalent), FOLFIRI (or equivalent), FOLFOXIRI, each with or without any of the following: bevacizumab, cetuximab, or panitumumab.

4. Patient must have stable or responding disease on first-line chemotherapy by RECIST 1.1 criteria

5. Patient must meet the following criteria for technical unresectability:

   - A margin-negative resection requires resection of three hepatic veins, both portal veins, or the retrohepatic vena cava OR a resection that leaves less than two adequately perfused and drained segments.

     NOTE: Institutional multidisciplinary review is required to confirm unresectability and rule out radiographically positive extrahepatic disease.

6. Patient must undergo CT angiography (chest/abdomen/pelvis) to confirm acceptable hepatic arterial anatomy for HAI and to rule out extrahepatic disease within 4 weeks prior to randomization.

7. Patient must have an ECOG Performance Status 0-1 and be clinically fit to undergo surgery as determined by the pre-operative evaluation.

8. Patient must not have a liver tumor burden exceeding 70% of total liver volume.

9. Patient must not have had prior radiation to the liver (prior radiation therapy to the pelvis is acceptable if completed at least 2 weeks prior to randomization).

10. Patient must not have had prior trans-arterial bland embolization, chemoembolization (TACE) or radioembolization (TARE).

11. Patient must not have had prior treatment with HAI/FUDR.

12. Patient must not have microsatellite instability-high (MSI-H) colorectal cancer.

13. Patient must not have CRLM that could be resected with 2-stage hepatectomy, including associating liver partition and portal vein ligation (ALPPS).

14. Patient must not have an active infection, serious or non-healing active wound, ulcer, or bone fracture.

15. Patient must not have any serious medical problems which would preclude receiving the protocol treatment or would interfere with the cooperation with the requirements of this trial.

16. Patient must not have cirrhosis and/or clinical or radiographic evidence of portal hypertension.

17. Patient must not be pregnant or breast-feeding due to the potential harm to an unborn fetus and possible risk for adverse events in nursing infants with the treatment regimens being used.

    All patients of childbearing potential must have a blood test or urine study within 14 days prior to randomization to rule out pregnancy.

    A patient of childbearing potential is defined as anyone, regardless of sexual orientation or whether they have undergone tubal ligation, who meets the following criteria: 1) has achieved menarche at some point, 2) has not undergone a hysterectomy or bilateral oophorectomy; or 3) has not been naturally postmenopausal (amenorrhea following cancer therapy does not rule out childbearing potential) for at least 24 consecutive months (i.e., has had menses at any time in the preceding 24 consecutive months).

    Patient of child bearing potential? _____ (Yes or No)
    Date of blood test or urine study: _____

18. Patient must not expect to conceive or father children by using accepted and effective method(s) of contraception or by abstaining from sexual intercourse for the duration of their participation in the study.

19. Patient must have adequate organ and marrow function as defined below (these labs must be obtained ≤ 14 days prior to protocol randomization):

    Leukocytes ≥ 3,000/mcL

    Leukocytes:_____ Date of Test:_____

    Absolute neutrophil count (ANC) ≥ 1,500/mcL

    ANC:_____ Date of Test:_____

    Platelets ≥ 100,000/mcL

Platelets:_____ Date of Test:_____

Total Bilirubin ≤ 1.5 mg/dL

Total Bilirubin:_____

Date of Test:_____

AST(SGOT)/ALT(SGPT) ≤ 3.0 × institutional upper limit of normal (ULN)

AST:_____ Institutional ULN:_____

Date of Test:_____

ALT: _____Institutional ULN:_____

Date of Test:_____

Creatinine ≤ 1.5 x institutional ULN

OR

Creatinine clearance ≥ 50 mL/min calculated by the Cockcroft-Gault method as follows:

- Male creatinine clearance = (140 –age in years) x (weight in Kg) / (serum Cr in mg/dl x 72)
- Female creatinine clearance = (140 – age in years) x (weight in Kg) x 0.85 / (serum Cr in mg/dl x 72)

Creatinine _____ Institutional ULN:_____

Date of Test:_____

Creatinine clearance:_____Date of Test:_____

Calcium ≥ institutional lower limit of normal (LLN)

Calcium:_____ LLN:_____

Date of Test:_____

20. Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

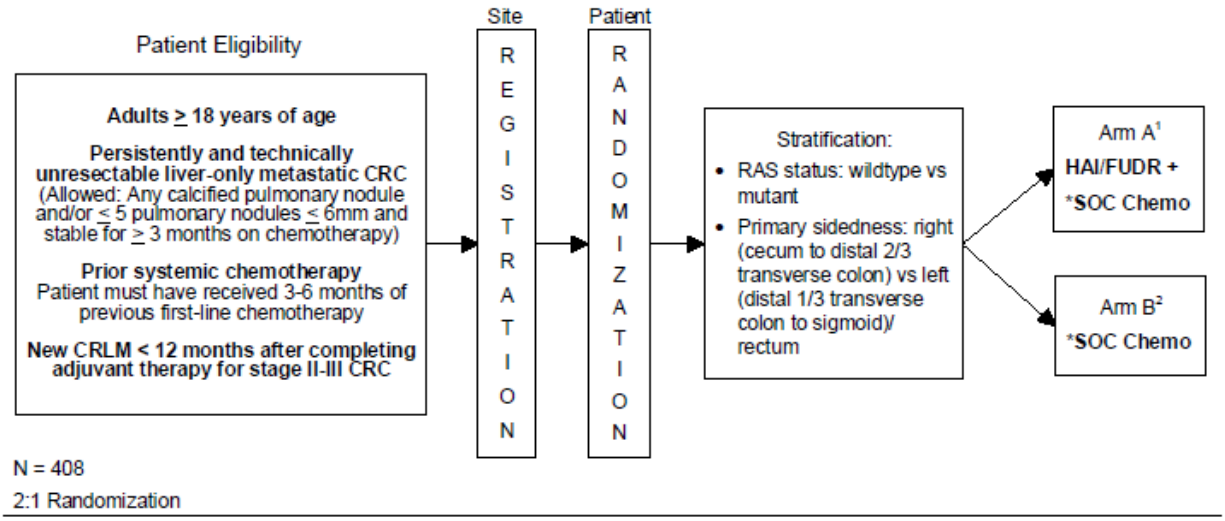
21. Human immunodeficiency virus (HIV)-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months of randomization are eligible for this trial. Testing for HIV is not required for entry onto the study.

_____ _____

Physician Signature Date

OPTIONAL: This signature line is provided for use by institutions wishing to use the eligibility checklist as source documentation.

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.