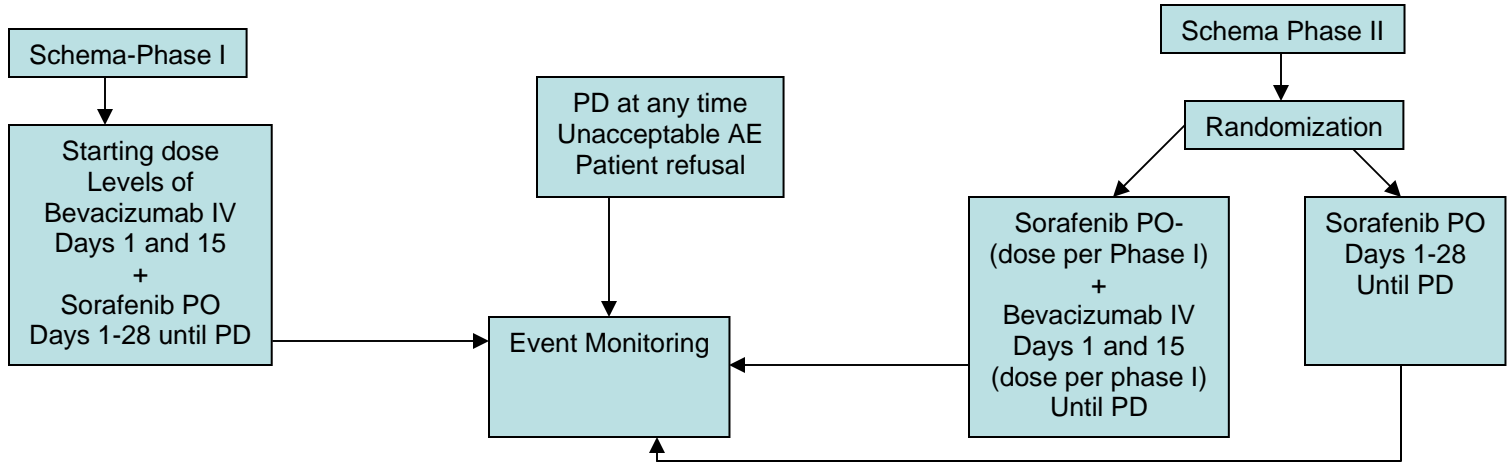


N0745-Phase I/II Randomized Study of Sorafenib and Bevacizumab as First-Line Therapy in Patients with Locally Advanced or Metastatic Hepatocellular Carcinoma



The current study evaluates the use of bevacizumab and sorafenib as first line therapy in locally advanced or metastatic HCC. The phase II portion of this study will all a real time comparator of bevacizumab/sorafenib versus sorafenib alone.

Major Inclusion Criteria:

- Histologically or cytologically confirmed diagnosis of hepatocellular carcinoma that is locally advanced or metastatic and is not amenable to treatment with surgery or orthotopic liver transplant.
- Child Pugh class A or B7 liver disease ¹.
- Patients must have measurable disease by RECIST.
- ≥6 weeks for chemoembolization, RFA or other local ablative therapy with evidence of progression or new metastatic disease, if applicable.
- EGD for evaluation and treatment of known or suspected esophageal varicies ≤6 months prior to registration, if applicable.
- ECOG PS of 0 or 1.
- Adequate hematologic values (Hgb ≥ 9.0 g/dL; ANC ≥1200; PLT ≥ 75,000).
- Adequate renal function (Urine protein ≤1+ by dipstick or UPC ratio1) and liver function (total bili ≤1.5 xULN; AST ≤5 xULN; Alk Phos ≤5x ULN)
- Willing to provide mandatory blood samples (research purposes) and tissue specimen (for central review of diagnosis).
- Life expectancy ≥3 months.

Major Exclusion Criteria

- Mixed cholangiocarcinoma/HCC.
- Current or previously resected brain metastases.
- Prior systemic chemotherapy for HCC.
- Prior external beam radiation to the primary site.
- Radiation to ≥25% of bone marrow.
- Biologic, hormone or immune therapy ≤4 weeks prior to registration.
- Uncontrolled HTN defined as systolic BP >150 or diastolic BP >100 despite optimal medical management.
- CHF- NYHA class III or IV ¹.
- Ventricular arrhythmias requiring anti-arrhythmic therapy.
- Any of the following ≤6 months if surgical or medical intervention was required: TIA, CVA, cardiac arrhythmia, unstable angina, clinically significant PAD, arterial thrombotic event ¹.
- Serious or non-healing wound, ulcer or bone fracture.
- Major surgical procedure, open biopsy, or traumatic injury ≤4 weeks or need for major surgical procedure during course of study.
- No pregnant or nursing women, or those unwilling to employ adequate contraception.
- Co-morbid systemic illnesses or conditions that would make the patient inappropriate for study ¹.
- Receiving any investigational agent as treatment for the primary neoplasm
- Active other malignancy ≤3 years ¹.
- Patients on anticoagulant therapy ¹.
- History of abdominal fistula, GI perforation, or intra-abdominal abscess ≤6 months prior to registration.
- Evidence of bleeding diathesis or coagulopathy.
- Active or recent hemoptysis ≤ 30 days prior to registration ¹.
- Core biopsy or other minor surgical procedures ≤7 days prior to registration ¹.
- Significant vascular disease or recent peripheral arterial thrombosis ≤ 6 months prior to registration ¹.
- History of hypertensive crisis or hypertensive encephalopathy.
- Any of the following risk factors for decreased LVEF: prior anthracyclines, prior central thoracic RT, history of MI within last 12 months.

¹ See protocol for more details