

NORTH CENTRAL CANCER TREATMENT GROUP
Eligibility Checklist

11/19/2010
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N0745: Phase I/II Randomized Trial of Sorafenib and Bevacizumab as First-Line Therapy in Patients with Locally Advanced or Metastatic Hepatocellular Carcinoma

Phase II patients only: To register a patient, access the NCCTG web page at <https://ncctg.mayo.edu/training> and enter the remote registration/randomization application.

Has the patient ever been on a prior study entered through this Randomization Center? Yes No

If yes: Prior study number _____; prior patient study ID number _____

Registration date (date on) (mm/dd/yyyy) ___/___/_____

Patient study ID number (provided at time of Reg/Random) _____

NCCTG member (participant sponsor) _____

NCCTG treating location _____

NCCTG treating physician _____

Institution patient number (local subject number) _____

IRB approval date (mm/dd/yyyy) ___/___/_____

Person Completing Form:

Last Name: (print) _____ First Name: (print) _____

Phone: _____ Fax: _____ Email: _____

Patient initials (last, first, middle) _____
(For Mayo Rochester patients, include first four letters of last name.)

Gender (check one) Male Female Unknown

Date of birth (mm/dd/yyyy) ___/___/_____

ZIP code _____

Country of Residence _____

Race (check all that apply)

- White
- Black or African American
- Native Hawaiian or Other Pacific Islander
- Asian
- American Indian or Alaska Native
- Not reported: Patient refused or not available
- Unknown: Patient unsure

Method of payment (check one)

- PI (Private Insurance)
- MR (Medicare)
- MRP (Medicare and Private Insurance)
- MD (Medicaid)
- MM (Medicaid and Medicare)
- MVA (Military or Veterans Sponsored,
Not Otherwise Specified (NOS))
- MS (Military Sponsored [including CHAMPUS & TRCARE])
- MV (Veterans Sponsored)
- SP (Self pay [no insurance])
- NP (No means of payment [no insurance])
- OTH (Other)
- UNK (Unknown)

Ethnicity (check one)

- Not Hispanic or Latino
- Hispanic or Latino
- Not reported: Refused or data not available
- Unknown: Unsure of their ethnicity

Patient study ID number _____

Grouping Factor

Phase
 _____ I (dose escalation)
 _____ II (at MTD)

Eligibility Check - Answer questions below (yes/no). All requirements must be confirmed. All dates are to be *mm/dd/yyyy*.

Inclusion Criteria

Yes No NA

Inclusion Criteria	Yes	No	NA
≥18 years of age. Age = _____.	_____	_____	_____
Histologically or cytologically confirmed diagnosis of hepatocellular carcinoma that is locally advanced or metastatic and is not amenable to treatment with surgery or to orthotopic liver transplant.	_____	_____	_____
Child Pugh class A or B7 liver disease (see Appendix VI).	_____	_____	_____
Patients must have measurable disease as defined in Section 11.0.	_____	_____	_____
Prior chemoembolization, radioembolization, radiofrequency ablation (RFA), or other local ablative therapies are permissible if ≥6 weeks from procedure with evidence of progression or new metastatic disease, if applicable. If not applicable, check "NA".	_____	_____	_____
Esophagogastroduodenoscopy (EGD) for evaluation and treatment of known or clinically suspected esophageal varices ≤6 months prior to registration, if applicable. If not applicable, check "NA".	_____	_____	_____
Phase I only: ECOG Performance Status (PS) 0 or 1. PS (Performance Status) = _____. If not applicable, check "NA".	_____	_____	_____
The following laboratory values obtained ≤14 days prior to registration. Earliest laboratory test date ___/___/_____; latest laboratory test date ___/___/_____. PhaNOTE: These dates pertain to the following labs only.	_____	_____	_____
• ANC ≥1200/mm ³ (cells/uL). ANC = _____.	_____	_____	_____
• PLT ≥75,000/mm ³ . PLT = _____.	_____	_____	_____
• Hgb ≥9.0 g/dL. Hgb = _____.	_____	_____	_____
• Total bilirubin ≤1.5 x UNL. Total bilirubin = _____ . UNL = _____.	_____	_____	_____
• SGOT (AST) ≤5 x UNL. SGOT (AST) = _____ . UNL = _____.	_____	_____	_____
• Alkaline phosphatase ≤5 x UNL. Alkaline phosphatase = _____ . UNL = _____.	_____	_____	_____
• Urine protein ≤1+ by Urine Protein Creatinine (UPC) ratio (see appendix VIII) or urine dip stick. If >1+, 24-hour urine collection should be performed. If <1 gm of protein, the patient is eligible.	_____	_____	_____
Negative pregnancy test done ≤7 days prior to registration, for women of childbearing potential only. If not a woman of childbearing potential or male (<i>check NA</i>) If a woman of childbearing potential – Negative pregnancy test date ___/___/_____	_____	_____	_____
Men or women of childbearing potential must agree to use adequate contraception (barrier method of birth control) prior to study entry and for the duration of study participation. Men and women should continue to use adequate birth control for at least 2 weeks after the last administration of sorafenib alone or for at least 6 months after the last administration of combined sorafenib and bevacizumab. This study involves agents whose genotoxic, mutagenic and teratogenic effects on the developing fetus and newborn are unknown.	_____	_____	_____
Ability to understand and the willingness to sign a written informed consent.	_____	_____	_____
Willing to return to NCCTG enrolling institution for follow-up every 4 weeks.	_____	_____	_____
Willing to provide mandatory blood samples for research purposes (see Sections 6.33 and 14.0).	_____	_____	_____
Willing to provide mandatory tissue specimen for central review of diagnosis.	_____	_____	_____
Life expectancy of ≥3 months.	_____	_____	_____

All responses in above section must be "Yes" unless specified as "NA."

Patient study ID number _____

Exclusion Criteria	Yes	No
Mixed cholangiocarcinoma/hepatocellular carcinoma.	_____	_____
Current or previously resected brain metastases.	_____	_____
History of allergic reactions attributed to compounds of similar chemical or biologic composition to bevacizumab or sorafenib.	_____	_____
Prior systemic chemotherapy regimens for hepatocellular carcinoma.	_____	_____
Prior external beam radiation to the primary site.	_____	_____
Radiation (if given for another malignancy) to ≥ 25 percent of the bone marrow.	_____	_____
Prior biologic, hormone, or immune therapy ≤ 4 weeks prior to registration.	_____	_____
Uncontrolled hypertension defined as systolic blood pressure > 150 mmHg or diastolic blood pressure > 100 mmHg despite optimal medical management.	_____	_____
Congestive heart failure (New York Heart Association classification III or IV). NOTE: Patients classified as NYHA class II controlled with treatment may participate with increased monitoring as outlined in Section 4.0, footnote 10.	_____	_____
Cardiac ventricular arrhythmias requiring anti-arrhythmic therapy ≤ 6 months.	_____	_____
Any of the following ≤ 6 months if surgical or medical intervention was required: transient ischemic attack, cerebrovascular accident, unstable angina or angina. Patients with clinical significant peripheral artery disease (i.e., claudication in less than one block) or any other arterial thrombotic event are also ineligible.	_____	_____
QTC interval > 500 msec on baseline EKG.	_____	_____
Serious or non-healing wound, ulcer or bone fracture.	_____	_____
Major surgical procedure, open biopsy, or significant traumatic injury ≤ 4 weeks prior to registration or anticipation of need for major surgical procedure during the course of the study.	_____	_____
Any of the following: <ul style="list-style-type: none"> • Pregnant women • Nursing women • Men or women of childbearing potential who are unwilling to employ adequate contraception for the duration of study participation. Men and women should continue to use adequate birth control for at least 3 months after the last administration of sorafenib and 6 months after the last administration of bevacizumab. This study involves agents whose genotoxic, mutagenic and teratogenic effects on the developing fetus and newborn are unknown. 	_____	_____
Co-morbid systemic illnesses or other severe concurrent disease which, in the judgment of the investigator, would make the patient inappropriate for entry into this study or interfere significantly with the proper assessment of safety and toxicity of the prescribed regimens.	_____	_____
Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, or psychiatric illness/social situations that would limit compliance with study requirements.	_____	_____
Receiving any investigational agent which would be considered as a treatment for the primary neoplasm.	_____	_____
Active other malignancy ≤ 3 years prior to registration, excepting non-melanotic skin cancer or carcinoma-in-situ of the cervix. If there is a history of prior malignancy, they must not be receiving other specific treatment (other than hormonal therapy) for their cancer.	_____	_____
Patients on any anticoagulant except those receiving low-dose warfarin or heparin for deep venous thrombosis prophylaxis [not treatment].)	_____	_____
History of abdominal fistula, gastrointestinal perforation, or intra-abdominal abscess ≤ 6 months prior to registration.	_____	_____
Evidence of bleeding diathesis (greater than normal risk of bleeding) or coagulopathy (in the absence of therapeutic anticoagulation).	_____	_____
Active or recent history of hemoptysis ($\geq \frac{1}{2}$ teaspoon of bright red blood per episode) ≤ 30 days prior to registration.	_____	_____
Core biopsy or other minor surgical procedures ≤ 7 days prior to registration. NOTE: Placement of a vascular access device is allowed.	_____	_____
Significant vascular disease (e.g. aortic aneurysm, aortic dissection) or recent peripheral arterial thrombosis ≤ 6 months prior to registration.	_____	_____

All responses in above section must be "No."

Patient study ID number

Exclusion Criteria – continued

Yes No

History of hypertensive crisis or hypertensive encephalopathy.	_____
Any of the following risk factors for decreased left ventricular ejection fraction (LVEF): <ul style="list-style-type: none"> • Prior treatment with anthracyclines • Prior central thoracic radiation therapy (RT), including RT to the heart • History of myocardial infarction (MI) within last 12 months 	_____

All responses in above section must be “No.”

Registration Check – Answer questions below (yes/no). All requirements must be confirmed. All dates are to be *mm/dd/yyyy*.

Yes No NA

A mandatory translational research component for blood is part of this study. The patient will be automatically registered separately to this translational component of the study (Sections 3.19f and 14.0).	_____
Consent form signed and dated. Date informed consent signed _____ - _____ - _____	_____
Authorization for use and disclosure of protected health information (<i>U.S.A. institutions only</i>) signed and dated. If not a USA institution (<i>check NA</i>); If a USA institution – Date of authorization _____ / _____ / _____	_____
Treatment on this protocol must commence at the accruing membership under the supervision of an NCCTG member physician.	_____
Treatment cannot begin prior to registration and must begin ≤14 days after registration.	_____
Pretreatment tests/procedures must be completed ≤14 days prior to registration (see Section 4.0). Earliest pretreatment test date _____ - _____ - _____; latest pretreatment test date _____ - _____ - _____ NOTE: The earliest pretreatment test date must be less than or equal to the earliest laboratory test date and the latest pretreatment test date must be greater than or equal to the latest laboratory test date.	_____
<p><u>Exceptions to the above dates:</u></p> <ul style="list-style-type: none"> • CT or MRI for tumor measurement must be performed within 28 days prior to registration (see Section 4.0). Earliest tumor measurement date _____ / _____ / _____; latest tumor measurement date _____ / _____ / _____ • PT/INR, activated partial thromboplastin time (aPTT), fibrinogen to be done only for patients taking warfarin and should be done within 21 days prior to registration (see Section 4.0). Is patient taking warfarin? (this question may be answered yes or no) _____ No → Go to next question. _____ Yes → PT/INR, activated partial thromboplastin time (aPTT), fibrinogen date (within 21 days prior to pre-registration) _____ / _____ / _____ 	_____
All required baseline symptoms (see Section 10.3) must be documented and graded.	_____
Study drug availability checked.	_____
Blood draw kit availability checked.	_____
Phase II only: Randomization Procedures Treatment assignment will be calculated using a dynamic allocation procedure that balances the marginal distributions of the stratification factors between the treatment arms (Pocock-Simon). The factors defined in Section 5.0, together with the membership, will be used as stratification factors If not applicable, check “NA”.	_____

All responses in above section must be “Yes” unless specified as “NA.”

Yes No

An optional translational research component for tissue is part of this study. The Registration Office/Remote Registration application will register patients separately to the translational research component of this study (see Section 17.3). The following will be recorded. <ul style="list-style-type: none"> • Patient has given permission to give tissue sample(s) for research testing. 	_____
At the time of registration/randomization, the following will also be recorded: <ul style="list-style-type: none"> • Patient has given permission to keep tissue sample(s) for use in future research to learn about, prevent, or treat cancer. 	_____
<ul style="list-style-type: none"> • Patient has given permission to keep blood sample(s) for use in future research to learn about, prevent, or treat cancer. 	_____

Patient study ID number _____

Registration continued

Yes No

<ul style="list-style-type: none"> • Patient has given permission to keep tissue sample(s) for use in future research to learn about, prevent, or treat other health problems (for example: diabetes, Alzheimer’s disease, or heart disease). 	_____	_____
<ul style="list-style-type: none"> • Patient has given permission to keep blood sample(s) for use in future research to learn about, prevent, or treat other health problems (for example: diabetes, Alzheimer’s disease, or heart disease). 	_____	_____
<ul style="list-style-type: none"> • Patient has given NCCTG permission to give tissue sample(s) to outside researchers. 	_____	_____
<ul style="list-style-type: none"> • Patient has given NCCTG permission to give blood sample(s) to outside researchers. 	_____	_____
<ul style="list-style-type: none"> • Patient has given NCCTG permission to be contacted in the future to take part in more research. 	_____	_____
<ul style="list-style-type: none"> • Patient has agreed to be enrolled on N0392 entitled “Assessment of Patient Satisfaction with Participation in Phase II/III NCCTG Clinical Trials”. 	_____	_____

All responses in above section may be “Yes” or “No”.

Stratification Factors (Phase II only)

Gender
 _____ Female
 _____ Male

Child-Pugh class
 _____ A
 _____ B7

ECOG Performance Status (PS):
 _____ 0
 _____ 1

Descriptive Factor

Dose Level (Phase 1 dose escalation only)

_____ +2
 _____ +1
 _____ 0
 _____ -1
 _____ -2a
 _____ -2
 _____ -3b
 _____ -3a
 _____ -3

Assigned Treatment

_____ Arm B: AVASTN + Sorafenib (Phase II)
 _____ Arm C: Sorafenib (Phase II)

Person registering Signature _____ Registration Office specialist initials _____

Physician Signature _____ Date (mm/dd/yyyy) ____/____/____