

FORMS PACKET

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

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✓ designates revised/new forms

*Generic forms completion instructions are available on the NCCTG web site under “the CRA link in the Remote Registration and Data Entry section and are titled “Remote Data Entry Screen Instructions (Forms Completion).”

The specific forms instructions take precedence over the generic forms instructions, so it is very important to review them in addition to the generic forms instructions.

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). 	<p>____</p> <p>____</p>
<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). 	<p>____</p> <p>____</p>
<ul style="list-style-type: none"> • Patient has given NCCTG permission to give tissue sample(s) to outside researchers. 	<p>____</p> <p>____</p>
<ul style="list-style-type: none"> • Patient has given NCCTG permission to give blood sample(s) to outside researchers. 	<p>____</p> <p>____</p>
<ul style="list-style-type: none"> • Patient has given NCCTG permission to be contacted in the future to take part in more research. 	<p>____</p> <p>____</p>
<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”. 	<p>____</p> <p>____</p>

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) ____/____/____

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

ON-STUDY FORM

ALL ITEMS MUST BE COMPLETED

Are data amended? (*check one*) Yes No
(if data are amended, please circle in red when using paper form)

Description of Primary Disease

MedDRA code: 10049010 [Hepatocellular Carcinoma]

Differentiation (Grade) (*check one*) 1 Well 2 Moderate 3 Poor 4 Undifferentiated, anaplastic

Status of Primary Tumor (*check one*) 2 Resected with known residual
3 Unresected
4 Recurrent

Distant Metastases: (*check all that apply*) Nodal Bone
 Liver Brain
 Subcutaneous Lung
 Abdominal Other, specify _____

Previous Radiotherapy: (*check one*) 1 Yes 2 No

Current Symptoms & Diseases: (*check one*) 1 Yes 2 No

If Yes:	Current Symptom/Disease	
Chronic Hepatitis	1 <input type="checkbox"/> Yes	2 <input type="checkbox"/> No
Other Liver Disease (<i>excluding cirrhosis</i>)	1 <input type="checkbox"/> Yes	2 <input type="checkbox"/> No

Child Pugh Classification

Ascites: (*check one*) 1 Absent 2 Slight 3 Moderate

Bilirubin: (*check one*) 1 <2 2 2 - 3 3 >3
__ . __ mg/dL

Albumin: (*check one*) 1 >3.5 2 2.8 - 3.5 3 <2.8
__ . __ g/dL

Prothrombin time INR: (*check one*) 1 <1.7 2 1.7 - 2.3 3 >2.3
__ . __ sec

Encephalopathy: (*check one*) 1 None 2 Grade 1 - 2 3 Grade 3 - 4

Descriptive Factors

Disease status: (*check one*) 1 Intrahepatic 2 Extrahepatic

Vascular invasion: (*check one*) 1 Yes 2 No

Fibrolamellar histology: (*check one*) 1 Yes 2 No

History of cirrhosis: (*check one*) 1 Yes 2 No

If Yes, specify: (*check one*) 1 Viral hepatitis (hepatitis B, C, other)
2 Hemachromatosis
3 Alcoholic cirrhosis
4 Other

Prior chemoembolization: (*check one*) 1 Yes 2 No

Height (cm): __ __ __ .

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

PATHOLOGY REPORTING FORM

HEPATOCELLULAR CARCINOMA

Protocol Number: N0745

Patient ID Number: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

Primary Pathologist: _____ No. of slides sent: _____

Clinic/Hospital: _____ Date sent: _____

Reviewer: _____ Slide No. _____ Sequence No. _____

I. CRA/RN

1. DATE OF OPERATIVE PROCEDURE

/ /
m m d d y y y y

_____ to _____
_____ to _____

2. OPERATIVE PROCEDURE

- 1. Fine needle aspiration
- 2. Needle biopsy
- 3. Wedge biopsy
- 4. Other (specify): _____

II. Completed by the NCCTG Pathology reviewer

3. LOCATION OF PRIMARY NEOPLASM

- LOBE
- 1. Right
- 2. Left
- 3. Caudate
- 4. Quadrate
- 5. Combination (specify): _____

4. GROSS FEATURES OF PRIMARY NEOPLASM

- 1. Unifocal
- 2. Multifocal
- 3. Diffuse

5. SIZE OF PRIMARY NEOPLASM (Enter all 3 dimensions if possible OR the GREATEST dimension)

mm x mm x mm

6. HISTOLOGIC FEATURES OF PRIMARY NEOPLASM

HISTOLOGIC TYPE

- 1. Trabecular
- 2. Acinar
- 3. Clear
- 4. Spindle
- 5. Sclerosing
- 6. Fibrolamellar
- 7. Combination (specify): _____
- 8. Other (specify): _____

DEGREE OF DIFFERENTIATION

- 1. Grade 1
- 2. Grade 2
- 3. Grade 3
- 4. Grade 4

CIRRHOSIS

- Present
- Absence of cirrhosis confirmed:
 - 1. Clinically only
 - 2. Surgical inspection only
 - 3. Histologically

7. EXTENT OF LOCAL SPREAD

- 1. Confined to liver
- 2. Extrahepatic invasion (specify organs): _____
- 3. Other (specify): _____

8. REGIONAL LYMPH NODE STATUS

Number of nodes positive (specify location): _____

Number of nodes negative

9. SOURCE(S) OF SPECIMEN (specify location)

- 1. Primary tumor
 - 2. Primary and metastatic tumor
 - 3. Metastatic tumor with clinical evidence of primary tumor in the liver
- (specify metastatic site[s]): _____

COMMENTS: _____

III. Signatures

NCCTG Pathology Reviewer

Research base Advisor

Committee Chairperson

Date

Date

Date

- 1. Agree with original local diagnosis
- 2. Minor disagreement with original local diagnosis
- 3. Substantial disagreement with original local diagnosis

- 1. Agree with original local diagnosis
- 2. Minor disagreement with original local diagnosis
- 3. Substantial disagreement with original local diagnosis

- 1. Agree with original local diagnosis
- 2. Minor disagreement with original local diagnosis
- 3. Substantial disagreement with original local diagnosis

Comments: _____

Comments: _____

Comments: _____

Block/Slide number(s) to be used for research/banking: _____

PLACE LABEL HERE

NORTHCENTRALCANCERTREATMENTGROUP

PATHOLOGY SUBMISSION FORM

Protocol Number: N0745

Patient ID: Patient Initials: L F M

Institution Number:

Institution:

(NOTE: This form is used to update the Outstanding Materials Report) (DMS: Refer to Section 17 - if no outside NCCTG reviewer, remove the above statement).

** This form must be submitted to the NCCTG Operations Office at the time slides/blocks are sent to the NCCTG reviewer (see Pathology section of the protocol) **

Date specimen shipped: (mm/dd/yyyy) _ _ / _ _ / _ _ _ _ _ _

Reviewer: (check one) [] Dr. Thomas C. Smyrk, Hilton 11, Mayo Clinic Rochester - Rochester, MN

Number of slides sent: _ _

Accession number(s) (on the slides sent):

Five pairs of horizontal lines for accession numbers.

Number of blocks sent: _ _

Accession number(s) (on the blocks sent):

Five pairs of horizontal lines for accession numbers.

COMMENTS: []

Institution Contact Information: (Please Print) Contact Person at Institution (CRA/Nurse): Institution Name: Street Address: City: State: Zip Code: Phone Number: Fax Number: E-mail Address:

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____
L F M

Institution Number: _____

Institution: _____

BASELINE
ADVERSE EVENTS FORM

ALL ITEMS MUST BE COMPLETED

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Required Baseline Adverse Events from Section 10.0 of Protocol		
CTC Adverse Events Term (CTCAE v3.0)	MedDRA Code (v. 10.0)	CTC Adverse Event Grade
Baseline number of stools per day: _____		
Rash/desquamation	10037853	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Rash: Hand-foot skin reaction	10019126	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3
Wound complication, non-infectious	10048031	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Hypertension	10020772	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Cardiac ischemia/infarction	10028601	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Fatigue (asthenia, lethargy, malaise)	10016256	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Endocrine: Other: Thyroid dysfunction	10014695	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Hemorrhage, GI - <i>Select</i>		
- Abdomen, NOS	10055291	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Proteinuria	10037020	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
CNS cerebrovascular ischemia	10023030	<input type="checkbox"/> 0 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Pain: Other: Abdominal	90004082	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Thrombosis/thrombus/embolism	10043607	<input type="checkbox"/> 0 <input type="checkbox"/> 1 <input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4
Peripheral arterial ischemia	10034578	<input type="checkbox"/> 2 <input type="checkbox"/> 3 <input type="checkbox"/> 4

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

ADVERSE EVENT FORM

ALL ITEMS MUST BE COMPLETED

Pg. 1 of 2

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Current Cycle Number (adverse events associated with this cycle): _____

Date of Evaluation: (mm/dd/yyyy) ____/____/____

CTC Adverse Event Term (CTCAE v3.0)	MedDRA Code (v. 10.0) (must be completed)	CTC Adverse Event Grade (highest grade this cycle) INCLUDE GRADE 0's	CTC AE Attribution Code (If Grade > 0) 1 = Unrelated 2 = Unlikely 3 = Possible 4 = Probable 5 = Definite	Has an adverse event expedited report been submitted?*(Enter 1 for Yes or 2 for No)
-------------------------------------	---	---	---	---

Required Adverse Events from Section 10.0 of Protocol

Rash/desquamation	10037853	0 1 2 3 4 5 (death)	1 2 3 4 5	____
Rash: Hand-foot skin reaction	10019126	0 1 2 3	1 2 3 4 5	____
Wound complication, non-infectious	10048031	0 1 2 3 4 5 (death)	1 2 3 4 5	____
Prolonged QTc interval	10053698	0 1 2 3 4 5 (death)	1 2 3 4 5	____
Hypertension	10020772	0 1 2 3 4 5 (death)	1 2 3 4 5	____
Cardiac ischemia/infarction	10028601	0 1 2 3 4 5 (death)	1 2 3 4 5	____
Cardiac general - Other: Asymptomatic decrease in LVEF and symptomatic cardiac events	10061024	0 1 2 3 4 5 (death)	1 2 3 4 5	____
Fatigue (asthenia, lethargy, malaise)	10016256	0 1 2 3 4	1 2 3 4 5	____
Endocrine: Other: Thyroid dysfunction	10014695	0 1 2 3 4 5 (death)	1 2 3 4 5	____
Hemorrhage, GI - Select				
- Abdomen, NOS	10055291	0 1 2 3 4 5 (death)	1 2 3 4 5	____
Diarrhea	10012727	0 1 2 3 4 5 (death)	1 2 3 4 5	____
Pancreatitis	10033645	0 1 2 3 4 5 (death)	1 2 3 4 5	____
Proteinuria	10037020	0 1 2 3 4 5 (death)	1 2 3 4 5	____
CNS cerebrovascular ischemia	10023030	0 2 3 4 5 (death)	1 2 3 4 5	____
Thrombosis/thrombus/embolism	10043607	0 2 3 4 5 (death)	1 2 3 4 5	____
Peripheral arterial ischemia	10034578	0 2 3 4 5 (death)	1 2 3 4 5	____

* See Section 10.0 of the protocol.

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: Patient Initials: L F M

Institution Number:

Institution:

ADVERSE EVENT FORM

ALL ITEMS MUST BE COMPLETED

Pg. 2 of 2

Are data amended? (check one) Yes No (if data are amended, please circle in red when using paper form)

Current Cycle Number (adverse events associated with this cycle):

Were (other) adverse events assessed during this report period?

1 Yes, and reportable adverse events occurred

3 Yes, but no reportable adverse events occurred (Stop here)

2 No (Stop here)

Adverse Events** beyond those required in Section 10.0 of the protocol. Record grade 2 with attribution of possible, probable or definite and all grade 3, 4 and 5 regardless of attribution.

Table with 5 columns: Other CTC Adverse Event Term not listed (CTCAE v3.0), MedDRA Code (v. 10.0) (must be completed), CTC Adverse Event Grade (highest grade this cycle), CTC AE Attribution Code (If Grade > 0), Has an adverse event expedited report been submitted?*

* See Section 10.0 of the protocol.

** Both hematologic and nonhematologic Adverse Events must be graded on this form as applicable.

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

**PRETREATMENT
RECIST MEASUREMENT FORM**

ALL ITEMS MUST BE COMPLETED

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Protocol Number: N0745
Patient ID: _____ Patient Initials: _____
L F M
Institution Number: _____
Institution: _____

INSTRUCTIONS

1. Record target lesions (per Section 11 of the protocol).
2. Measure target lesions in cm. using longest diameter (one dimension only).
3. Record measurements at pretreatment.
4. Maintain same type of assessment throughout study.
5. Record presence or absence of non-target lesions at baseline, thereafter record the status of non-target lesions at each required evaluation.

Assessment Date: (mm/dd/yyyy) / /
(Assessment date is the date reflecting type of assessment, not the physician interpretation date)

(Total) Number of Target Lesions (1-10): _____

Target Lesion Site(s)	Type of Assessment						Measurement (cm)
	PE ¹	CT ²	Spiral CT ³	PET/CT ⁴	MRI	CXR ⁵	
1	1 <input type="checkbox"/>	2 <input type="checkbox"/>	13 <input type="checkbox"/>	15 <input type="checkbox"/>	3 <input type="checkbox"/>	5 <input type="checkbox"/>	
2	1 <input type="checkbox"/>	2 <input type="checkbox"/>	13 <input type="checkbox"/>	15 <input type="checkbox"/>	3 <input type="checkbox"/>	5 <input type="checkbox"/>	
3	1 <input type="checkbox"/>	2 <input type="checkbox"/>	13 <input type="checkbox"/>	15 <input type="checkbox"/>	3 <input type="checkbox"/>	5 <input type="checkbox"/>	
4	1 <input type="checkbox"/>	2 <input type="checkbox"/>	13 <input type="checkbox"/>	15 <input type="checkbox"/>	3 <input type="checkbox"/>	5 <input type="checkbox"/>	
5	1 <input type="checkbox"/>	2 <input type="checkbox"/>	13 <input type="checkbox"/>	15 <input type="checkbox"/>	3 <input type="checkbox"/>	5 <input type="checkbox"/>	
6	1 <input type="checkbox"/>	2 <input type="checkbox"/>	13 <input type="checkbox"/>	15 <input type="checkbox"/>	3 <input type="checkbox"/>	5 <input type="checkbox"/>	
7	1 <input type="checkbox"/>	2 <input type="checkbox"/>	13 <input type="checkbox"/>	15 <input type="checkbox"/>	3 <input type="checkbox"/>	5 <input type="checkbox"/>	
8	1 <input type="checkbox"/>	2 <input type="checkbox"/>	13 <input type="checkbox"/>	15 <input type="checkbox"/>	3 <input type="checkbox"/>	5 <input type="checkbox"/>	
9	1 <input type="checkbox"/>	2 <input type="checkbox"/>	13 <input type="checkbox"/>	15 <input type="checkbox"/>	3 <input type="checkbox"/>	5 <input type="checkbox"/>	
10	1 <input type="checkbox"/>	2 <input type="checkbox"/>	13 <input type="checkbox"/>	15 <input type="checkbox"/>	3 <input type="checkbox"/>	5 <input type="checkbox"/>	
Sum of all Lesions							

Non-Target Lesions <i>(check one)</i>	1 <input type="checkbox"/> Present	2 <input type="checkbox"/> Absent
---	------------------------------------	-----------------------------------

- 1=Physical exam
- 2=CT scan
- 3=spiral CT scan
- 4=PET/CT - Only CT portion of scan can be used for measurement.
- 5=Chest x-ray

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

**ACTIVE MONITORING
RECIST MEASUREMENT FORM**

ALL ITEMS MUST BE COMPLETED

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Current Cycle Number: _____

INSTRUCTIONS

1. Record the target lesions in the same order as recorded at pretreatment (refer to Section 11 of the protocol).
2. Measure target lesions in cm. using longest diameter (one dimension only).
3. Record measurements at scheduled evaluations and progression (refer to protocol Section 4).
4. Maintain same type of assessment throughout study.
5. Record presence or absence of non-target lesions at baseline, thereafter record the status of non-target lesions at each required evaluation.
6. Overall objective status is determined by combining status of target lesions, non-target lesions and new lesions (refer to protocol Section 11).

Assessment Date: (mm/dd/yyyy) __ __ / __ __ / __ __ __ __

(Assessment date is the date reflecting type of assessment, not the physician interpretation date. If tumor measurements are not required this cycle per Section 4.0, Assessment Date is the date the patient was evaluated.)

Overall Response Status at This Assessment: (check one)

- 19 NA (not applicable this cycle) - End Form
- 1 CR*
- 2 PR*
- 5 SD
- 6 PD* (Complete End of Active Treatment and Event Monitoring Forms)

Was the appearance of any new lesions documented? (check one) 1 Yes 2 No

Symptomatic Deterioration? (check one) 1 Yes 2 No

NOTE: If PD is selected for Overall Response Status, and Yes is selected for "Was the appearance of any new lesions

Target Lesion Site(s) Measurement (cm)	
1.	
2.	
3.	
4.	
5.	
6.	
7.	
8.	
9.	
10.	
Sum of all Lesions:	
Nontarget Lesions	Change: (check one) 1 <input type="checkbox"/> CR 2 <input type="checkbox"/> SD 3 <input type="checkbox"/> NonPD 4 <input type="checkbox"/> PD 5 <input type="checkbox"/> Not Done 9 <input type="checkbox"/> Not Applicable

*Submit documentation to verify CR,PR, PD.

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

BLOOD SPECIMEN SUBMISSION FORM

ALL ITEMS MUST BE COMPLETED

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Protocol Number: N0745
Patient ID: _____ Patient Initials: _____
L F M
Institution Number: _____
Institution: _____

Baseline _____ OR Current Cycle Number: _____

ENTER ONE FORM FOR EACH TIME POINT

INSTRUCTIONS:

- Complete this form **for all patients** and enter into the remote data entry system within 7 days of specimen collection.
- See Section 14 of the protocol for specimen requirements and shipment.
- Include a copy of this form with blood submission (see Section 14).

- Time Point: (check one)
- 1 Baseline
 - 2 Prior to treatment Cycle 1, Day 3
 - 3 Prior to treatment Cycle 1, Day 15
 - 4 Prior to treatment Cycle 2
 - 5 Prior to treatment Cycle 3
 - 6 Prior to treatment Cycle 4
 - 7 Prior to treatment Cycle 5
 - 8 Prior to treatment Cycle 6
 - 9 Prior to treatment Cycle 7
 - 10 At disease progression

Was a research blood specimen collected? (check one)

- 1 Yes. If Yes: Date of collection: (mm/dd/yyyy) ___/___/_____
Date Specimen Shipped: (mm/dd/yyyy) ___/___/_____
2 No. If No, reason: _____

<p>Institution Contact Information: (Please Print)</p> <p>Contact Person at Institution (CRA/Nurse): _____</p> <p>Institution Name: _____</p> <p>Street Address: _____ _____</p> <p>City: _____</p> <p>State: _____</p> <p>Zip Code: _____</p> <p>Phone Number: _____</p> <p>Fax Number: _____</p> <p>E-mail Address: _____</p>
--

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

**BASELINE
TISSUE SPECIMEN SUBMISSION FORM**

ALL ITEMS MUST BE COMPLETED

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Protocol Number: N0745
Patient ID: _____ Patient Initials: _____
L F M
Institution Number: _____
Institution: _____

INSTRUCTIONS:

- Complete this form **for all patients** and enter into the remote data entry system within 30 days of study entry.
- See Section 17 of the protocol for specimen requirements and shipment.
- Include a copy of this form with tissue submission (see Section 17).

Did this patient provide written consent to give tissue specimen (s) for research? (check one)

1 Yes. If Yes, complete rest of form.

2 No. If No, end form.

Was a research tissue specimen collected? (check one)

1 Yes. If Yes: Date of collection: (mm/dd/yyyy) ___/___/___

Date Specimen Shipped: (mm/dd/yyyy) ___/___/___

2 No. If No, reason: _____

Institution Contact Information: (Please Print)

Contact Person at Institution (CRA/Nurse):

Institution Name: _____

Street Address: _____

City: _____

State: _____

Zip Code: _____

Phone Number: _____

Fax Number: _____

E-mail Address: _____

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

**CONCURRENT TREATMENT FORM
(BASELINE)**

ALL ITEMS MUST BE COMPLETED

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

Date of evaluation: (mm/dd/yyyy) ___/___/_____

Is the patient taking any concomitant medications? (check one)

1 Yes 2 No (Stop here)

If Yes, enter all medications (including prescription, over-the-counter, and alternative medications)

Concomitant Medication	Dose	Schedule

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

**CONCURRENT TREATMENT FORM
(ACTIVE MONITORING PHASE)**

ALL ITEMS MUST BE COMPLETED

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

Current Cycle Number: _____

Date of evaluation: (mm/dd/yyyy) ___/___/___

Has there been any change in medications since the previous visit? (check one)

1 Yes 2 No (Stop here)

If Yes, enter medications (including prescription, over-the-counter, and alternative medications) that have not been previously reported, no longer being taken or have a dose and/or schedule change.

Concomitant Medication	Concomitant Medication Reason: 1= New medication 2= Medication no longer being taken 3= Dose and/or schedule change	Dose	Schedule

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: Patient Initials: L F M

Institution Number:

Institution:

ARM C - PHASE II
EVALUATION/TREATMENT FORM

ALL ITEMS MUST BE COMPLETED

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Use one form per cycle, one column per agent.

Current Cycle Number:

Weight (kg):
(used for this cycle, round to the nearest tenth)

ECOG Performance Status: (check one) 0 1 2 3 4
(used for this cycle)

BSA (m²): (used for this cycle)

Was this cycle of treatment held (Day 1)? (check one) 1 Yes, planned 2 No 3 Yes, unplanned

(If Yes, planned or unplanned) Primary reason treatment held: (check one)

- 35 Blood/Bone Marrow 154 Metabolic/Laboratory
79 Cardiac General 45 Dermatology/Rash/Skin
159 Cardiac Arrhythmia 38 Other Nonhematologic
99 Other (not per protocol), Specify

Table with 2 columns: Agent (Sorafenib 439006) and various clinical data points including Agent Start Date, Initial Dose, Total Dose, Dose modification, Reason Modified, and Was agent omitted.

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

ARM A - PHASE I
EVALUATION/TREATMENT FORM

ALL ITEMS MUST BE COMPLETED

Pg. 1 of 2

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Use one form per cycle, one column per agent.

Current Cycle Number: _____

Weight (kg): _____
(used for this cycle, round to the nearest tenth)

ECOG Performance Status: (check one) 0 1 2 3 4
(used for this cycle)

BSA (m²): (used for this cycle) _____

Was this cycle of treatment held (Day 1)? (check one) 1 Yes, planned 2 No 3 Yes, unplanned

(If Yes, planned or unplanned) Primary reason treatment held: (check one)

- 35 Blood/Bone Marrow 154 Metabolic/Laboratory
79 Cardiac General 38 Other Nonhematologic
159 Cardiac Arrhythmia 99 Other (not per protocol), Specify _____

Did patient have dose limiting toxicity (per Section 7.14) this cycle? (check one) 1 Yes 2 No

If Yes, check all that apply: Hematologic Other Nonhematologic
 Gastrointestinal Other (not per protocol), Specify _____

Agent	Bevacizumab (AVASTN)
Agent Start Date (this cycle) (mm/dd/yyyy)	___/___/___
Initial Dose (dose level day one this cycle) (If agent was not given this cycle, enter the dose level received on last day of treatment.)	_____ mg/Kg
Total Dose of Agents/Drugs for this cycle (If agent was not given this cycle, enter 0 for total dose.)	_____ mg
Dose (Level) modification (Day 1, 15)	1 <input type="checkbox"/> Yes, planned 3 <input type="checkbox"/> Yes, unplanned 2 <input type="checkbox"/> No
Reason Modified (If Yes, planned or unplanned, Primary Reason for Dose (Level) modification per Section 8.0). Not BSA changes. (Check one)	35 <input type="checkbox"/> Blood/Bone Marrow 79 <input type="checkbox"/> Cardiac General 159 <input type="checkbox"/> Cardiac Arrhythmia 154 <input type="checkbox"/> Metabolic/Laboratory 38 <input type="checkbox"/> Other Nonhematologic 99 <input type="checkbox"/> Other (not per protocol), Specify _____
Was (agent) omitted this cycle?	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
If Yes, which days were omitted? (check all that apply)	<input type="checkbox"/> 1 <input type="checkbox"/> 15

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

ARM A - PHASE I
EVALUATION/TREATMENT FORM

ALL ITEMS MUST BE COMPLETED

Pg. 2 of 2

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Agent	Sorafenib (439006)
Agent Start Date (this cycle) (mm/dd/yyyy)	___/___/___
Initial Dose (dose level day one this cycle) (If agent was not given this cycle, enter the dose level received on last day of treatment.)	_____ mg
Total Dose of Agents/Drugs for this cycle (If agent was not given this cycle, enter 0 for total dose.)	_____ mg
Dose (Level) modification	1 <input type="checkbox"/> Yes, planned 3 <input type="checkbox"/> Yes, unplanned 2 <input type="checkbox"/> No
Reason Modified (If Yes, planned or unplanned, Primary Reason for Dose (Level) modification per Section 8.0). Not BSA changes. (Check one)	35 <input type="checkbox"/> Blood/Bone Marrow 79 <input type="checkbox"/> Cardiac General 159 <input type="checkbox"/> Cardiac Arrythmia 154 <input type="checkbox"/> Metabolic/Laboratory 38 <input type="checkbox"/> Other Nonhematologic 99 <input type="checkbox"/> Other (not per protocol), Specify _____
Was (agent) omitted this cycle?	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

ARM B - PHASE II
EVALUATION/TREATMENT FORM

ALL ITEMS MUST BE COMPLETED

Pg. 1 of 2

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Use one form per agent, one column per agent.

Current Cycle Number: _____

Weight (kg): _____ . _____

(used for this cycle, round to the nearest tenth)

ECOG Performance Status: (check one) 0 1 2 3 4

(used for this cycle)

BSA (m²): (used for this cycle) _____ . _____

Was this cycle of treatment held (Day 1)? (check one) 1 Yes, planned 2 No 3 Yes, unplanned

(If Yes, planned or unplanned) Primary reason treatment held: (check one)

- 35 Blood/Bone Marrow
- 79 Cardiac General
- 159 Cardiac Arrythmia
- 60 Gastrointestinal
- 201 Vascular
- 154 Metabolic/Laboratory
- 193 Hemorrhage/bleeding
- 45 Dermatology/Rash/Skin
- 38 Other Nonhematologic
- 99 Other (not per protocol), Specify _____

Agent	Bevacizumab (AVASTN)
Agent Start Date (this cycle) (mm/dd/yyyy)	___/___/____
Initial Dose (dose level day one this cycle) (If agent was not given this cycle, enter the dose level received on last day of treatment.)	mg/Kg
Total Dose of Agents/Drugs for this cycle (If agent was not given this cycle, enter 0 for total dose.)	mg
Dose (Level) modification (Day 1, 15)	1 <input type="checkbox"/> Yes, planned 3 <input type="checkbox"/> Yes, unplanned 2 <input type="checkbox"/> No
Reason Modified (If Yes, planned or unplanned, Primary Reason for Dose (Level) modification per Section 8.0). Not BSA changes. (Check one)	35 <input type="checkbox"/> Blood/Bone Marrow 79 <input type="checkbox"/> Cardiac General 159 <input type="checkbox"/> Cardiac Arrythmia 154 <input type="checkbox"/> Metabolic/Laboratory 187 <input type="checkbox"/> Allergy/Immunology 38 <input type="checkbox"/> Other Nonhematologic 99 <input type="checkbox"/> Other (not per protocol), Specify _____
Was (agent) omitted this cycle?	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No
If Yes, which days were omitted? (check all that apply)	<input type="checkbox"/> 1 <input type="checkbox"/> 15

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

ARM B - PHASE II
EVALUATION/TREATMENT FORM

ALL ITEMS MUST BE COMPLETED

Pg. 2 of 2

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Agent	Sorafenib (439006)
Agent Start Date (this cycle) (mm/dd/yyyy)	___/___/___
Initial Dose (dose level day one this cycle) (If agent was not given this cycle, enter the dose level received on last day of treatment.)	mg
Total Dose of Agents/Drugs for this cycle (If agent was not given this cycle, enter 0 for total dose.)	mg
Dose (Level) modification	1 <input type="checkbox"/> Yes, planned 3 <input type="checkbox"/> Yes, unplanned 2 <input type="checkbox"/> No
Reason Modified (If Yes, planned or unplanned, Primary Reason for Dose (Level) modification per Section 8.0). Not BSA changes. (Check one)	35 <input type="checkbox"/> Blood/Bone Marrow 79 <input type="checkbox"/> Cardiac General 159 <input type="checkbox"/> Cardiac Arrhythmia 154 <input type="checkbox"/> Metabolic/Laboratory 45 <input type="checkbox"/> Dermatology/Rash/Skin 38 <input type="checkbox"/> Other Nonhematologic 99 <input type="checkbox"/> Other (not per protocol), Specify _____
Was (agent) omitted this cycle?	1 <input type="checkbox"/> Yes 2 <input type="checkbox"/> No

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

END OF ACTIVE TREATMENT/CANCEL NOTIFICATION FORM

Patient ID: _____ Patient Initials: _____

Submit Once Per Patient

L F M

ALL ITEMS MUST BE COMPLETED

Institution Number: _____

Are data amended? (check one) Yes No

Institution: _____

(if data are amended, please circle in red when using paper form)

Last Date (any modality of) protocol therapy was given: (mm/dd/yyyy) ___/___/_____
(date of last treatment dose on this study or date decision made not to initiate protocol treatment)

Off Treatment Date: (mm/dd/yyyy) ___/___/_____
(date decision was made to end active treatment or not to initiate protocol treatment)

This patient will now go to: (check one)
(See Schema and Section 13.0 of the protocol)

2 Event Monitoring (follow Event Monitoring schedule)

9 Off Study (cancels only)

Reason Treatment Ended <i>(check one)</i>	COMMENTS
1 <input type="checkbox"/> Treatment Completed Per Protocol Criteria	
2 <input type="checkbox"/> Patient Withdrawal/Refusal After Beginning Protocol Therapy	Specify:
24 <input type="checkbox"/> Patient Withdrawal/Refusal Prior To Beginning Protocol Therapy <i>(cancel)</i>	Specify:
3 <input type="checkbox"/> Adverse Event/Side Effects/Complications	Specify:
4 <input type="checkbox"/> Disease Progression, Relapse During Active Treatment*	Complete Event Monitoring Form
10 <input type="checkbox"/> Disease Progression Before Active Treatment	
5 <input type="checkbox"/> Alternative Therapy	Specify:
6 <input type="checkbox"/> Patient Off-Treatment For Other Complicating Disease	Specify:
7 <input type="checkbox"/> Death On Study	Complete Event Monitoring Form
8 <input type="checkbox"/> Other	Specify:

* Submit documentation to verify progression. See Section 11.0 and Section 18.0 of protocol.

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

EVENT MONITORING FORM

ALL ITEMS MUST BE COMPLETED

Pg. 1 of 2

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

Were you able to obtain any information about the patient since the last report?*

- 1 Yes. If Yes, complete rest of form.
- 2 No. If No, date of last attempt to contact patient: (mm/dd/yyyy) ___/___/_____ (End form)

Vital Status

- 1 Alive Date of last contact or date of death: (mm/dd/yyyy) ___/___/_____
- 2 Dead
 - Primary Cause of Death: (check one)
 - 1 Due to this disease
 - 2 Due to other cause, specify _____
 - 4 Due to protocol treatment
(adverse event related to treatment)

Disease Follow-up Status

- Has the patient had a documented clinical assessment for this cancer (since submission of the last event monitoring form)?*
- 2 No. If No, Go to Notice of New Primary.
- 1 Yes. If Yes, Cancer Follow-up Status Date: (mm/dd/yyyy) ___/___/_____

Notice of First Relapse/Progression in the Event Monitoring Phase

- Has the patient developed a first relapse or progression that has not been previously reported (in event monitoring phase)?
- 2 No 1 Yes. If Yes, Date of Relapse/Progression:** (mm/dd/yyyy) ___/___/_____
- Site(s) of Relapse/Progression: Intrahepatic Extrahepatic
(check all that apply)

Notice of First Subsequent Treatment

- Has the patient received subsequent treatment for this cancer that has not been previously reported?
- 2 No 3 Unknown 1 Yes. If Yes, Start date of subsequent treatment: (mm/dd/yyyy) ___/___/_____
- Specify subsequent treatment: _____

Notice of New Primary

- Has a new primary cancer or MDS (myelodysplastic syndrome) been diagnosed that has not been previously reported?
- 2 No 3 Unknown 1 Yes. If Yes, New Primary Cancer Date: (mm/dd/yyyy) ___/___/_____
- Site of New Primary: _____

Late Adverse Event (post completion of active monitoring)

- Has the patient experienced (prior to treatment for progression or relapse or a second primary, and prior to non-protocol treatment) any severe (grade ≥ 3) long term toxicity that has not been previously reported:
 - Adverse events at least possibly attributed to treatment on this study.
 - Death within 30 days of treatment.
 - Death any time at least possibly treatment related.
- 2 No 3 Unknown/Not evaluated 1 Yes. If Yes, Submit page 2 of the Event Monitoring Form for Late Adverse Event Reporting.

*If this is the first event monitoring form check yes, enter cancer follow-up status date and complete the rest of the form.

**Submit documentation to verify PD.

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

**EVENT MONITORING FORM
(LATE ADVERSE EVENT REPORTING)**

ALL ITEMS MUST BE COMPLETED

Pg. 2 of 2

Are data amended? (check one) Yes No
(if data are amended, please circle in red when using paper form)

The CTC AE v.3.0 will be used to evaluate the following adverse events:

CTC Adverse Event Term	MedDRA Code (v. 10.0) (must be completed)	CTC Adverse Event Grade (Highest Grade)	CTC AE Attribution Code 1 = Unrelated 2 = Unlikely 3 = Possible 4 = Probable 5 = Definite	Late Adverse Event Onset Date (mm/dd/yyyy)
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____
	<input type="text"/>	<input type="text"/> <input type="text"/> <input type="text"/> (death)	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	___/___/_____

PLACE LABEL HERE

NORTH CENTRAL CANCER TREATMENT GROUP

Protocol Number: N0745

Patient ID: _____ Patient Initials: _____

L F M

Institution Number: _____

Institution: _____

NOTIFICATION FORM
Grade 4 or 5 Non-AER Reportable Events/Hospitalization
ALL ITEMS MUST BE COMPLETED

INSTRUCTIONS:

- Use this form to report all known information on non-AER reportable grade 4 or 5 adverse events or any hospitalization during active treatment.
- Verify reporting requirements listed within the study protocol, prior to entering into the remote data entry system.
- If AER has been submitted for this event do not enter this form.
- Fill out all information known.
- Enter into the remote data entry system within 5 working days of notification.
- These events must also be reported on the Nadir/Adverse Event Form.

Date membership CRA aware of event(s): (mm/dd/yyyy) ___/___/_____

Name of Person Completing Form: _____ Phone: (_____) _____ - _____

Current Cycle Number: _____ Assigned Treatment Arm: _____

Event ≥ Grade 4: (check one) 1 Yes 2 No

Date of First Occurrence of Adverse Event (mm/dd/yyyy)	CTC Adverse Event Term (only one event per line)	CTC Adverse Event Grade	In your opinion, is this related to the study medication?*
___/___/_____		<input type="checkbox"/> 4 <input type="checkbox"/> 5	4 <input type="checkbox"/> Yes: Unlikely 1 <input type="checkbox"/> Yes: Possible, probable, or definite 2 <input type="checkbox"/> No 3 <input type="checkbox"/> Unknown
___/___/_____		<input type="checkbox"/> 4 <input type="checkbox"/> 5	4 <input type="checkbox"/> Yes: Unlikely 1 <input type="checkbox"/> Yes: Possible, probable, or definite 2 <input type="checkbox"/> No 3 <input type="checkbox"/> Unknown
___/___/_____		<input type="checkbox"/> 4 <input type="checkbox"/> 5	4 <input type="checkbox"/> Yes: Unlikely 1 <input type="checkbox"/> Yes: Possible, probable, or definite 2 <input type="checkbox"/> No 3 <input type="checkbox"/> Unknown
___/___/_____		<input type="checkbox"/> 4 <input type="checkbox"/> 5	4 <input type="checkbox"/> Yes: Unlikely 1 <input type="checkbox"/> Yes: Possible, probable, or definite 2 <input type="checkbox"/> No 3 <input type="checkbox"/> Unknown
___/___/_____		<input type="checkbox"/> 4 <input type="checkbox"/> 5	4 <input type="checkbox"/> Yes: Unlikely 1 <input type="checkbox"/> Yes: Possible, probable, or definite 2 <input type="checkbox"/> No 3 <input type="checkbox"/> Unknown

*Answer YES if attribution is unlikely, possible, probable or definite; answer NO if unrelated; answer UNKNOWN if you are not sure. Verify if expedited reporting (e.g. ADEERS) is required (see protocol), based on relationship to study treatment.

Hospitalization: (check one) 1 Yes 2 No

If Yes: Hospital Admission Date: (mm/dd/yyyy) ___/___/_____

Reason(s) for Hospitalization:

- 1 Adverse Event, specify type and grade: _____
- 2 Prophylactic, specify: _____
- 3 Other reason, specify _____

Biospecimen Accessioning Processing
Fax Supply Order Form – No Cover Sheet Necessary
Fax to Research Kit Building @ 507-538-4103

NOTE: Form must be either typed or printed legibly and filled out completely.
Study ID: N0745

Investigator: _____

Order Placed By: _____ Phone #: () _____

Email: _____ Fax #: () _____

Complete Address (kits sent to):

ALLOW AT LEAST TWO WEEKS TO RECEIVE THE KITS.

NOTE: Kits will be sent via FedEx® Ground at no additional cost to the participating institutions. Kits will not be sent via rush delivery service unless the participating institution provides their own FedEx® account number or alternate billing number for express service. **The study will not cover the cost for rush delivery of kits.**

Date Needed: _____
(Please be specific)

Fed Ex account number (Rush deliveries only) _____

<u>Type of Kits</u>	<u># of Kits Needed</u>
Custom Kit #1 (For Baseline, Cycle 1 Day 3, and pre-tx Cycle 2)	_____
Custom Kit #2 (Pre-treatment Cycles 1 Day 15, 3, 4, 5, 6, and 7)	_____
Kit #3 (For Disease Progression)	_____
Total Kits	_____

Questions? Contact the Biospecimen Resource Manager listed on the Protocol Resource page of the protocol.