



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: November 4, 2011

To: Primary Clinical Research Associates

From: Sanna McKinzie
Research Protocol Specialist III

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

CRF Title	Brief Description of Edit
Pathology Submission Form	<ul style="list-style-type: none">Deleted Rhonda Boblett as reviewer

If you have any questions, please feel free to contact me.

Enclosure

North Central Cancer Treatment Group

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

Addendum 8 – November 4, 2011

Summary

- Dr. Shaji Kumar, Research Base Laboratory Cochair has been removed from title page.
- Dr. Zoran Gatalica, Pathology – NCCTG has been removed from the title page and Section 17.
- Administrative changes.

Replacement pages are included. Please incorporate into the protocol and keep this with your protocol.

Title page Addendum 8 has been added and the NCI version date has been updated.

Drs. Shaji Kumar and Zoran Gatalica have been removed.

Section 14.0 **Body Fluid Biospecimen Submission**

Page 54: Sections 14.255 and 14.256 have been updated to reflect current shipping instructions as follows:

14.254 Use kit **shippers with** mailing labels for shipment to BAP.

14.255 BAP ~~Receiving Freezer~~ will forward specimens immediately to the NCCTG Research Base Biospecimens Accessioning and Processing (BAP) Shared Resource, ~~Stable 13-10A~~ **Hilton CL-21**, Attention: BAP Supervisor.

Section 17.0 **Pathology Considerations/Tissue Biospecimens**

Page 95: Due to the removal of Dr. Zoran Gatalica from the protocol, Section 17.25 has been revised as follows:

17.25 Review is being performed ~~by an external reviewer not located~~ at the NCCTG Research Base at Mayo Clinic Rochester. Please ship specimens and appropriate materials as indicated below:

17.251 ~~The Pathology Submission Form must be sent to the NCCTG Operations Office at Mayo Clinic Rochester. Please do not send this form to the external reviewer listed below~~ **Mayo Clinic Rochester (MCR) patients only: please forward pathology material to Dr. Thomas C. Smyrk, Hilton 11, for review.**

- 17.252 ~~Mayo Clinic Rochester (MCR) patients only: please forward pathology material to Dr. Thomas C. Smyrk, Hilton 11, for review~~ **For all other NCCTG memberships, including MCJ AND MCA, materials should be sent to the NCCTG Research Base:**

**NCCTG Operations Office
Attn: PC Office (Study N0745)
RO_FF_03_24-CC/NW Clinic
200 First Street SW
Rochester, MN 55905**

- 17.253 ~~For all other NCCTG memberships, including MCJ and MCA, materials should be sent to the Caris Life Sciences Primary CRA:~~ **The NCCTG Operations Office will forward the diagnostic slides to Dr. Thomas C. Smyrk, Hilton 11, for central review to confirm diagnosis of Hepatocellular carcinoma.**

~~Rhonda Boblett
N0745 NCCTG Pathology Review
Caris Life Sciences
4207 East Cotton Center Blvd.
Phoenix, AZ 85040~~

- ~~17.254 Rhonda Boblett will accession the pathology materials and forward the materials to Dr. Thomas C. Smyrk for central review to confirm diagnosis of hepatocellular carcinoma.~~

North Central Cancer Treatment Group

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

*For any communications regarding this protocol,
please call the protocol resource person on the following page.*

Study Chairs: Steven R. Alberts, MD MPH (Research Base)*
Mayo Clinic
200 First Street, SW
Rochester, MN 55905
507/284-4918 (Quality Assurance Specialist)
507/284-5280 (FAX)
Alberts.steven@mayo.edu

William S. Loui, M.D. (NCCTG)

Study Cochairs: Lewis R. Roberts, MD PhD (Research Base)
Thomas C. Smyrk, M.D. (Pathology - Research Base) ✓

Statistician: Michelle Mahoney MS✓
507/284-8803 (Secretary)

Drug Availability

DCTD or DCP Supplied Investigational Agents: None

Commercial Agents: Sorafenib, bevacizumab

Drug Company Funded: Bevacizumab (funded by Bayer, Inc.)

Available through the REACH Program: Sorafenib

IND# if investigational: IND exempt

***Investigator having NCI responsibility for this protocol**

✓Study contributor(s) not responsible for patient care.

Document History	(Effective Date)	Document History	(Effective Date)
Activation	April 10, 2009	Addendum 6	April 15, 2011
Addendum 1	July 3, 2009	Update 1	April 15, 2011
Addendum 2	January 15, 2010	Addendum 7	July 8, 2011
Addendum 3	October 8, 2010	Addendum 8	November 4, 2011
Addendum 4	October 8, 2010		
Addendum 5	November 19, 2010		

Study (a) Date Activated**Participants**

Entire NCCTG April 10, 2009

NCI Version Date: October 26, 2011

14.25 Shipping

- Add 1,3 14.251 Verify ALL sections of the Blood Specimen Submission Form, Biospecimen Accessioning and Processing (BAP) Requisition Form, and specimen collection labels are completed and filled in correctly. Enter information from the Blood Specimen Submission Form into the remote data entry system ≤14 days of specimen collection (see Forms Packet).
- 14.252 Specimens must be shipped the same day they are drawn.
- 14.253 Specimens will be shipped in a dual-temperature shipping container. Place the refrigerated whole blood EDTA tubes with a properly prepared cold pack in one compartment. See kit instructions for specific details for cold pack preparation (i.e., frozen or refrigerated) and proper packing of blood and cold pack to avoid freezing of specimen. Place the frozen plasma samples with dry ice in the other compartment of the dual-temperature shipping container.
- Add 1,3 14.254 Ship specimens via Priority Overnight service, **Monday – Thursday ONLY**, to BAP. **Do not send samples on weekends or holidays.**
- Add 1,3,8 14.255 Use kit shippers with mailing labels for shipment to BAP.
- Add 1,3,8 14.256 BAP Freezer will forward specimens immediately to the NCCTG Research Base Biospecimens Accessioning and Processing (BAP) Shared Resource, Hilton CL-21, Attention: BAP Supervisor.
- 14.257 BAP will process specimens according to Appendix IX instructions.
- 14.3 Other Body Fluids: None.

Add 8

17.25 Review is being performed at the NCCTG Research Base at Mayo Clinic Rochester. Please ship specimens and appropriate materials as indicated below:

17.251 Mayo Clinic Rochester (MCR) patients only: please forward pathology material to Dr. Thomas C. Smyrk, Hilton 11, for review.

17.252 For all other NCCTG memberships, including MCF and MCA, materials should be sent to the NCCTG Research Base:

NCCTG Operations Office
Attn: PC Office (Study N0745)
RO_FF_03_24-CC/NW Clinic
200 First Street SW
Rochester, MN 55905

Update 1

17.253 The NCCTG Operations Office will forward the diagnostic slides to Dr. Thomas C. Smyrk, Hilton 11, for central review to confirm diagnosis of Hepatocellular carcinoma.

Add 6

17.26 After central review is completed, the pathologist will return all pathology materials to:

NCCTG Operations Office
Attn: PC Office (Study N0745)
RO_FF_03_24-CC/NW Clinic
200 First Street SW
Rochester, MN 55905

17.27 One or two slides will be identified by the reviewing pathologist for inclusion in the pathology files for this study. These slides are being stored for quality assurance purposes only and no future research will be conducted on them. All remaining diagnostic slides will be returned to the submitting institution.

17.3 Paraffin Embedded Tissue Blocks/Slides

17.31 Submit one formalin fixed paraffin-embedded (FFPE) tumor tissue block with representative tumor from each surgical biopsy. Material obtained at the time of recurrence is preferred. **A corresponding H&E slide for each submitted block must be provided** to permit quality assessment (QA) of each tissue block. Once the QA is completed, all H&E slides will be returned, unless specified otherwise in Section 17.27.

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

- Contents:
- Eligibility checklist *(11/19/10)*
 - * Forms completion instructions
 - On-study form *(12/10/08)*
 - Pathology reporting form hepatocellular carcinoma *(12/10/08)*
 - ✓ Pathology submission form *(10/26/11)*
 - Baseline adverse events form *(8/3/10)*
 - Adverse event form *(8/3/10)*
 - Pretreatment Recist measurement form *(4/1/09)*
 - Active monitoring Recist measurement form *(4/1/09)*
 - Blood specimen submission form *(1/5/10)*
 - Baseline tissue specimen submission form *(12/10/08)*
 - Concurrent treatment form (baseline) *(12/10/08)*
 - Concurrent treatment form (active monitoring phase) *(12/10/08)*
 - Arm C-Phase II evaluation/treatment form *(4/1/09)*
 - Arm A-Phase I evaluation/treatment form *(7/30/10)*
 - Arm B-Phase II evaluation/treatment form *(4/1/09)*
 - End of active treatment/cancel notification form *(12/10/08)*
 - Event monitoring form *(12/10/08)*
 - Notification form Grade 4 or 5 non-AER reportable events/hospitalization form *(12/10/08)*
 - Fax supply order form

✓ 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.

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: