

North Central Cancer Treatment Group

N0543: A Phase II Trial of Pharmacogenetic-Based Dosing of Irinotecan, Oxaliplatin, and Capecitabine as First-Line Therapy for Advanced Small Bowel Adenocarcinoma

Addendum 1 – October 12, 2007

Summary

- Research Base Pathology Co-Chair has been changed from Tsung-Teh Wu, M.D. to Thomas Smyrk, M.D. on the title page and in Sections 14.0 and 17.0
- Administrative/editorial changes

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

Title page Title page has been revised to include Addendum 1 and a new NCI version date.

Thomas C. Smyrk, M.D. replaces Tsung-Teh Wu, M.D., Ph.D as the Research Base Pathology Co-Chair.

Protocol Resource Page

Page 2 Carol Leonard's title of **NCCTG Quality Control Specialist** has been added, as this was previously not in the protocol.

Section 3.0

Page 11

Patient Eligibility

Section 3.29c has been removed because there are no correlative studies defined for this protocol.

~~3.29c Patient willingness to provide blood/blood product samples for research testing.~~

Section 4.0

Page 13

Test Schedule

In the row labeled "Tumor Measurement," and column "Observation...x 2 years", a double asterisk (**) has been added to the X to clarify the assessment.

In the row labeled "Serum sample for analysis of celiac disease," a superscript has been added in the first column, "Pre-registration," to refer the reader to Footnote 10 for specific information.

Page 13

The row labeled “Blood products samples for ancillary studies...” has been deleted as there are no correlative studies currently defined for this protocol. Submission for UGT1A1 and celiac testing is mandatory as part of the main study. Other unspecified future correlative studies, if defined, may utilize these same blood samples if the patient gives permission.

Blood/blood products samples drawn for ancillary studies (see section 14.0) ^{9,11,R}			X			
---	--	--	---	--	--	--

In the row labeled “Tumor tissue sent for review/translational studies (~~see sec. 14.0~~)^{12,R}”, the reference to Section 14.0 has been deleted as it is redundant to the information provided in Footnote 12.

The notation item marked by a single asterisk (*) has been revised for clarification:

If a patient has CR confirmed ~~every 2~~ **for two successive** evaluations...**If PD, unacceptable adverse events, or patient refusal, patient goes to Event Monitoring.**

The notation item marked by a double asterisk (**) has been revised for clarification of procedures during the Observation phase.

After two assessments, follow-up intervals for tumor measurement and adverse event evaluation will be at the discretion of the treating physician.
See Section 10.0....

Page 14

Footnote 9 has been revised since there are no research studies currently defined for this protocol.

Blood samples ~~and serum~~ for UGT1A1 genotyping, **and** celiac disease testing, ~~and research studies~~ are mandatory (see Sections 14.2 and 17.2). Celiac testing is a research test....

Footnote 10 has been modified to include reference to Section 14.0.

After pre-registration but prior to registration (see Sections **14.0 and 17.0**).

Section 6.0

Page 15

Registration/Randomization Procedures

Section 6.231 has been removed as there are no mandatory translational research component requiring blood/blood products. Section 6.232 has been renumbered.

~~6.231—A mandatory translational research component requiring blood/blood products is part of this study. The patient will be automatically registered onto this component (see Section 14.2).~~

Section 14.0

Page: 39

Translational/Pharmacologic Studies

The following text was revised for clarification in the first paragraph of this section:

The collection of blood/blood products is **mandatory for the UGT1A1 and celiac testing as part of the main study. No translational studies requiring blood/blood products have been defined for this protocol.** Collection of tumor blocks/slides is **optional** for the translational/pharmacologic research component of this study, but is strongly encouraged.

14.1 Sample Submission

- 14.11 Mandatory samples for **UGT1A1 and celiac testing** ~~translational/pharmacologic studies~~, regardless of treatment assignment: ~~for patients who have consented to sample submission~~, include:

In Section 14.23, instructions for labeling specimen tubes has been corrected.

Label specimen tube(s) with ~~cooperative group membership name~~, protocol number, NCCTG patient ID number, **patient initials**, and time and date blood drawn.

Page 40

In Section 14.24, the 4th column in the Summary Table has been relabeled for greater accuracy.

~~Before treatment cycle 1, day 1~~ **After pre-registration but prior to registration.**

In Section 14.251, the MCLCT Requisition Form has been added to the shipping instructions.

Verify ALL sections of the NCCTG Blood Specimen Submission Form, **MCLCT Requisition Form**, and specimen collection labels are completed and filled in correctly.

Page 41

In Section 14.31, an update has been made to the shipping information for the tissue samples. Corrections have also been made in the third bullet for clarification.

NCCTG Operations Office
 ATTN: NCCTG ~~Research Coordinator~~ **PC Office**
 RO_FF_03_24-CC/NW Clinic
 200 First Street SW
 Rochester, MN 55905

- One formalin fixed paraffin-embedded (FFPE) tumor tissue block....submit the following unstained slides: ~~4-12~~ slides with 5-um thick sections and 5 slides with 10-um thick sections...~~One~~ **The first and last** 5 um slides will be used....

Section 14.32 has been corrected.

The block/slides must be appropriately packed....Label the bag with the ~~cooperative group membership name~~, protocol number, NCCTG patient ID number, ~~surgical accession number~~, and ~~source (e.g, primary)~~ **patient initials**).

In Section 14.4212, Dr. **Thomas C. Smyrk** replaces Tsung-Teh Wu, M.D., Ph.D in the last sentence of the paragraph.

Section 17.0
 Page 71

Pathology Considerations for Quality Control
 Section 17.23 has been revised.

The slides must be appropriately packed....Label the bag with the ~~cooperative group membership name~~, protocol number, NCCTG patient ID number, ~~surgical accession number~~, and ~~source (e.g, primary)~~ **patient initials**.

Section 17.24 has been clarified and corrected.

Verify that ALL sections of the Pathology Submission Form are completed and filled in correctly. **The Pathology Submission Form must be sent to the NCCTG Operations Office at the following address:**

NCCTG Operations Office
 ATTN: NCCTG ~~Research Coordinator~~ **PC Office**
 RO_FF_03_24-CC/NW Clinic
 200 First Street SW
 Rochester, MN 55905

Page 72

In Sections 17.25 and 17.26, **Thomas C. Smyrk, M.D.** replaces Tsung-Teh Wu, M.D., Ph.D.

In Section 17.25, the following sentence has been bolded to draw the readers attention.

All other NCCTG members are to forward their materials within 30 days after registration to the following address.

In Section 17.27, an update has been made to the shipping information for the tissue samples.

NCCTG Operations Office
ATTN: NCCTG ~~Research Coordinator~~ **PC Office**
RO_FF_03_24-CC/NW Clinic
200 First Street SW
Rochester, MN 55905

Section 18.0 **Records and Data Collection Procedures**

Page 73

In the row labeled “Specimen Submission Form (blood)” the X has been moved from the column labeled “Initial Material” to the column labeled “Preregistration” to reflect the correct data submission time point.

Appendix I **Consent Form**

Page 5/6 of 19

Under “When you are finished taking the chemotherapy,...” the second paragraph has been deleted for clarification. Additional changes to this section are as follows for additional clarification, starting with the second paragraph:

~~If your disease gets worse you will continue to get treatment for 12 cycles (9 months). After 12 cycles or if the side effects are too bad or if you or your doctor decide you should not get any more treatment, you can stop chemotherapy.~~

When you stop treatment, you will need to return to the clinic for study visits every 6 weeks for two years after you stop. During those visits (every 6 weeks), you will have the following tests and procedures:

- Medical history, physical exam, including weight and a rating of how well you perform activities of daily living. ~~will be done before each chemotherapy treatment.~~
- Routine blood tests ~~will be done before each chemotherapy treatment and weekly in between treatments.~~ About 4 teaspoons of blood will be drawn from a vein in your arm for these blood tests.
- Tumor measurement done by CT scan or chest X-ray ~~every.~~

- Chest X-ray ~~about every 3 months~~ unless a CT scan is being done to measure your tumor every 6 weeks. If the CT scan is being done, the chest X-ray will not be needed.
- ~~Evaluations of the side effects you are having will be done before every chemotherapy treatment.~~

If your disease stays the same or you have partial response, you will continue to get treatment for 12 cycles (9 months). After 12 cycles or if the side effects are too bad or if you or your doctor decide you should not get any more treatment, you can stop chemotherapy.

If you decide to stop treatment and then your tumor starts to get worse, you can start treatment again without going back on the study; **if your physician agrees. None of the costs for drugs or treatment would be paid for by the study in that case.**

Page 11 of 19 The response to the question “Are there benefits to taking part in this research study?” both paragraphs have been revised as follows for an editorial change:

Taking part in this study may or may not make your health better. Currently, there is no treatment for small bowel adenocarcinoma that is considered “standard of care.” There is some preliminary evidence that a combination of irinotecan, oxaliplatin, and ~~5-fluorouracil~~ **capecitabine** may be effective in small bowel...

We do know that this study will help doctors learn more about using irinotecan, oxaliplatin, and ~~5-fluorouracil~~ **capecitabine** in treating cancer.

Page 14 of 19 Under “Additional Research Studies” the following text was revised and bulleted for clarification (the underlined text is new):

Please note: This section of the informed consent form is about additional research studies that are being done with people who are taking part in the main study.

- **Blood samples for these additional research studies are required. The blood for these studies will be taken from the samples drawn at the beginning of the study. You will not need to have any additional blood samples drawn.**
- **Tissue samples are optional, but we hope you will consider giving them for use in the research tests.**

Appendix V
Page 1 of 1

BAP Specimen Processing Instructions

The heading of the 4th column in the Summary Table has been relabeled for greater accuracy.

~~Before treatment cycle 1, day 1~~ **After pre-registration but prior to registration.**