

North Central Cancer Treatment Group

N0626: Phase II Randomized Study Pemetrexed With Sorafenib versus Pemetrexed Alone as Second-line Therapy in Patients With Advanced Non-Small Cell Lung Cancer

Addendum 4 – August 15, 2008

Summary

- Sections 4.0, 17.0, 18.0 and the consent form have been modified to include central review of tissue to confirm diagnosis.
- Administrative/editorial changes.

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

Title page Updated to reflect Addendum 4 and revised NCI version date.

Marie Christine Aubry, M.D. has been added as the Research Base Pathology Co-Chair.

Protocol Resources

Page 2: **Susan Haithcox, OCN, CCRP** replaces ~~Wanda DeKrey, RN~~ as the NCCTG Member Nurse.

Jennifer S. Mentlick replaces ~~Christine R. Maszk~~ as the NCCTG *Research Base* Pathology Coordinator.

Section 4.0 **Test Schedule**

Page 20: Due to the inclusion of central review of tissue to confirm diagnosis, Footnote # 4 has been modified as follows:

Submit tissue for central review ≤30 days after registration. Submit tissue for correlative studies ≤60 days after registration.

Section 17.0 **Pathology Considerations/Tissue Biospecimens**

Pages 62-65: Due to the inclusion of central review of tissue to confirm diagnosis, Sections 17.1, 17.2, and 17.3 have been rewritten as follows:

~~17.1 Tissues being requested below are **mandatory**. An institution must provide the following pathology tissue specimens.~~

- ~~• Formalin fixed paraffin embedded (FFPE) tissue blocks/slides are being requested for correlative studies (see Section 17.3 for specimen submission information and Section 17.5 for correlative study information).~~

~~17.2 Diagnostic Slides (None)~~

~~17.3 Paraffin Embedded Tissue Blocks/Slides~~

~~17.31 Submit one formalin fixed paraffin embedded (FFPE) tumor tissue block with representative tumor. The FFPE tissue block is preferred; however, if an institution is unable to provide a tissue block, submit 8 (2 slides for H&E + 6~~

slides for correlative studies) charged and unstained glass slides cut at 5 microns. **Label the slides with NCCTG patient ID number, accession number, and order of sections.** The first and last slide will be H&E stained and reviewed centrally under the research base's quality assessment protocol. The remaining slides will be processed as described in 17.5. For samples containing less than 7 square millimeters of tumor tissue, multiple sections should be mounted onto each slide to ensure that the appropriate amount of tumor tissue is available. Ideally, each slide must have a minimum of 75% tumor tissue on the slide to be deemed adequate for study. **Do not bake or place covers slips on the slides.**

17.32—The following materials below are mandatory (unless indicated otherwise) and required for shipment:

Add 3

- Paraffin Embedded Tissue Blocks/Slides
- Tissue Specimen Submission Form
- Surgical Pathology Report
- Operative Report (*optional*)

17.33—The block/slides must be appropriately packed to prevent damage (e.g., slides should be placed in appropriate slide container) and placed in an individual plastic bag. Label the bag with the protocol number, NCCTG patient ID number, and patient initials.

17.34—Tissue specimens must be shipped before or within ≤ 60 days following registration.

Add 3

17.35—Verify that the appropriate sections of the Tissue Specimen Submission Form are completed and filled in correctly. Enter information from the Tissue Specimen Submission Form into the remote data entry system ≤ 14 days of specimen collection (see Forms Packet).

17.36—Ship all tissue specimens and accompanying materials to the NCCTG Research Base:

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

17.37—The NCCTG Operations Office will forward the block/slides to the NCCTG Research Base TACMA Laboratory, Stable 13-10B, Mayo Clinic Rochester (Attn: TACMA Supervisor) for processing as outlined in Section 17.5.

17.1 Tissue Biospecimen Submission

NOTE: It is mandatory that patients consent to submission of the tissue(s) listed in the following table. For mandatory tissues, the site must submit tissue being requested, if tissue is available.

17.11 Summary Table of Tissue Biospecimens for This Protocol

Type of tissue biospecimen to submit	Mandatory or optional	When to submit	Reason for submission (background/methodology section)	Where to find specific details for biospecimen submission
ALL diagnostic slides from original and/or recurrent tissue	Mandatory	≤30 days after registration	Confirmation of diagnosis through central review	Section 17.2
Formalin-fixed paraffin-embedded (FFPE) tissue blocks with corresponding H&E OR 7 unstained slides with 1 corresponding H&E	Mandatory	≤60 days after registration	Correlative studies (see Section 17.5)	Section 17.3

17.2 All Diagnostic Slides All Diagnostic Slides from Original and/or Recurrent Tissue

17.21 ALL original diagnostic slides used to make the diagnosis of Stage IV or Stage IIIB non-squamous cell histologic type of NSCLC should be clearly labeled and forwarded ≤30 days after registration for central review. If the original slides cannot be released, slides from the same tumor block used to make the diagnosis are acceptable. If the slides from the metastatic diagnosis are not available, slides from the original Stage IV or Stage IIIB non-squamous cell histologic type of NSCLC diagnosis will be accepted.

17.22 The following materials below are mandatory (unless indicated otherwise) and required for shipment:

- Diagnostic Slides from Original and/or Recurrent Tissue
- Pathology Reporting Form
- Pathology Submission Form
- Surgical Pathology Report
- Operative Report (*optional*)

Note: Please include the NCCTG patient ID number on all materials listed above.

- 17.23 **The diagnostic slide(s) must be appropriately packed to prevent damage (e.g., slides should be placed in appropriate slide container) and placed in an individual plastic bag. Label the bag with the protocol number, NCCTG patient ID number, and patient initials.**
- 17.24 **Verify that Section 1 of the Pathology Reporting Form is completed and filled in correctly.**
- 17.25 **Review is being performed at the NCCTG Research Base at Mayo Clinic Rochester. Ship all diagnostic slides and accompanying materials as follows:**
- 17.251 **Mayo Clinic Rochester (MCR) patients only: please forward pathology material to Dr. Marie Christine Aubry, Hilton 11, for review.**
- 17.252 **For all memberships, including MCJ and MCA, ship all specimens and accompanying materials to the NCCTG Research Base:**

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

- 17.253 **The submitting institution is responsible for the costs of shipping and handling.**
- 17.254 **The NCCTG Operations Office will forward the diagnostic slides to Dr. Marie Christine Aubry, Hilton 11, for central review to confirm diagnosis of Stage IV or Stage IIIB non-squamous cell histologic type of NSCLC.**
- 17.26 **After central review is completed, the pathologist will return all pathology materials to:**

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

17.3 Paraffin Embedded Tissue Blocks/Slides

- 17.31 **Submit one formalin fixed paraffin-embedded (FFPE) tumor tissue block with largest amount of invasive tumor (at least 1 cm of tumor) for cases of surgical resection from original and/or recurrent surgery. Biopsy material obtained at the time of recurrence is preferred, but if not available, biopsy**

material obtained at the time of initial diagnosis of non-squamous cell histologic type of NSCLC may be submitted. A corresponding H&E slide for the submitted block must be provided to permit quality assessment (QA) of the tissue block. Once the QA is completed, the H&E slide will be returned.

- 17.32** The FFPE tissue block is preferred; however, if an institution is unable to provide a tissue block, cut 8 five micron sections and mount sections on charged glass slides. Label the slides with NCCTG patient ID number, accession number, and order of sections (i.e., 1-8). H&E stain the first slide that is cut (i.e., slide labeled 1). This slide will be reviewed centrally under the research base's quality assessment protocol. The remaining slides will be processed as described in 17.5. For samples containing less than 7 square millimeters of tumor tissue, multiple sections should be mounted onto each slide to ensure that the appropriate amount of tumor tissue is available. Ideally, each slide must have a minimum of 75% tumor tissue on the slide to be deemed adequate for study. Do not bake or place covers slips on the slides.
- ~~17.32~~ **17.33** The following materials below are mandatory (unless indicated otherwise) and required for shipment:
- Paraffin Embedded Tissue Blocks/~~Slides~~ **with Corresponding H&E Slide (or 7 Unstained Slides with Corresponding H&E Slides)**
 - Tissue Specimen Submission Form
 - Surgical Pathology Report
 - Operative Report (*optional*)
- ~~17.33~~ **17.34** The block/slides must be appropriately packed to prevent damage (e.g., slides should be placed in appropriate slide container) and placed in an individual plastic bag. Label the bag with the protocol number, NCCTG patient ID number, and patient initials.
- ~~17.34~~ **17.35** Tissue specimens must be shipped before or within ≤ 60 days following registration.
- ~~17.35~~ **17.36** Verify that the appropriate sections of the Tissue Specimen Submission Form are completed and filled in correctly. Enter information from the Tissue Specimen Submission Form into the remote data entry system ≤ 14 days of specimen collection (see Forms Packet).

- ~~17.36~~ **17.37** Ship all tissue specimens and accompanying materials to the NCCTG Research Base:

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

- ~~17.37~~ **17.38** The NCCTG Operations Office will forward the block/slides to the NCCTG Research Base TACMA Laboratory, Stable 13-10B, Mayo Clinic Rochester (Attn: TACMA Supervisor) for processing as outlined in Section 17.5.

Due to the revisions made in Section 17.0, repagination has occurred throughout the remainder of the document.

Section 18.0 **Records and Data Collection Procedures**

Page 67: Due to the inclusion of central review of tissue to confirm diagnosis, 2 new rows have been added to the table and footnote #8 is also added as follows:

Op and Path Reports

Pathology Materials (see Section 17.22)

8. Submit ≤30 days after registration.

Appendix I **Consent Form**

Page 6: Due to the inclusion of central review of tissue to confirm diagnosis, the second to the last sentence of the first paragraph under the “FUTURE CYCLES Group B” table has been revised as follows:

A portion of the leftover tissue will be used for these laboratory tests **and to confirm your diagnosis.**