

North Central Cancer Treatment Group

N0321: Phase I/II Study of PS-341 in Combination with Paclitaxel, Carboplatin, and Concurrent Thoracic Radiation Therapy for Non-small Cell Lung Cancer (NSCLC)

Addendum 1 – February 11, 2005

**Summary**

- Dr. Kendrith M. Rowland, Jr. has been added as NCCTG Study Chair.
- Update to protocol resource personnel.
- Changes have been made throughout the document to clarify treatment days and patient follow-up.
- Clarification to the Test Schedule with regard to monitoring toxicity and chemistries during the observation phase of the study.
- Clarification to the Protocol Treatment section to reflect that the NCCTG operations office is to be contacted as soon as any dose-limiting toxicity occurs.
- Editorial/administrative changes.

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

Title page: Reflects Addendum 1 and revised NCI version date.

Dr. Kendrith M. Rowland has been added as NCCTG Study Chair.

Page 2: The Protocol Resource page has been revised as follows:

- Paula Stellmaker replaces Jennifer Frank as the NCCTG Research Base Quality Control Specialist resource person.
- Janis Gjervik replaces Jeannine Hadley as the NCCTG Research Base Protocol Development Coordinator resource person.
- Wanda L. DeKrey, R.N. replaces Nancy Pierson, R.N. as the NCCTG Member Nurse resource person.

Pages 4: The schema for the Phase I Component now reflects a **4-week post RT evaluation** rather than a 4 week observation for consistency with the Test Schedule, Section 4.0. The boxes were reformatted for clarity.

- Page 5: The schema for the Phase II Component now reflects a **4-week post RT evaluation** rather than a 4-week observation for consistency with the Test Schedule, Section 4.0. At the time of this 4-week post RT evaluation, if the patient is CR, PR, or SD, they go to observation (per Section 4.0) and the schema now reflects this flow. Asterisks \*\*\* and \*\*\*\* have been deleted.
- Page 12: Section 3.19c (Patient Eligibility) has been deleted as questionnaires are not being used in this study. Section 3.19d now becomes Section 3.19c.
- Page 14: Section 4.0 (Test Schedule), the heading for the fourth column has been clarified to read “Prior to drug administration on day 23, **cycle 2** of Taxol/CBDCA.”
- Section 4.0 (Test Schedule), the heading for the last column has been revised for clarification and now reads “**Phase II patients CR, PR, SD** Observation – q3 months for up to 2 yrs from time of registration.”
- Section 4.0 (Test Schedule), X’s have been added for clarification to the “Observation – q3 months for up to 2 yrs from time of registration” column for Toxicity assessment, the Hematology group, and Chemistry group.
- Section 4.0 (Test Schedule), the last sentence in footnote #3 has been deleted as it is clearly reflected at the beginning of footnote #3 that a CT chest scan is to be done.
- Pages 15-17: The following revisions have been made to Section 6.0 (Registration/Randomization Procedures):
- Sections 6.12 and 6.22 have been clarified that the translational research component is optional.
  - Sections 6.14 and 6.24, reference to “~~randomization~~” has been deleted as patients are registered to this study, not randomized.
  - The protocol reflected two Sections 6.24. Therefore, the second Section 6.24 has now become 6.25 and all remaining sections have been renumbered.
  - Section 6.29, previously Section 6.28 (Registration/Randomization Procedures), reference to the “on-study form” has been deleted.
- Page 18: Section 7.11 (Protocol Treatment) has been revised to clarify that either RANIT can be given at 50 mg, CIMET can be given at 300 mg, or Pepcid® can be given at 20 mg 30 minutes pretaxol.
- Pages 18 & 21: Sections 7.12 and 7.42 (Protocol Treatment), now indicate **Day** rather than d for consistency within the tables.

- Page 19: Section 7.17 (Protocol Treatment) is newly added for clarification: NCCTG should be notified as soon as any dose-limiting toxicity is seen.
- Page 21: Section 7.41 (Protocol Treatment) has been revised to clarify that either RANIT can be given at 50 mg, CIMET can be given at 300 mg, or Pepcid® can be given at 20 mg 30 minutes pretaxol. The route for Pepcid has also now been identified (**IV**).
- Page 22: Section 7.5 (Protocol Treatment), the first sentence of the opening paragraph has been revised for clarification “Radiation Therapy (**Phase I and II Components**) – Use of IMRT is not allowable
- Section 12.5 (Descriptive Factors) has been revised for clarification and now reads “Stage IIIA vs. IIIB vs. **IIIB with pleural effusion.**”
- Pages 35 & 36: Section 13.0 (Treatment/Follow-up Decision at Evaluation of Patient) has been revised for clarification as follows:
- Section 13.21 – acute toxicity will be **evaluated** rather than ~~determined~~
  - Section 13.22 now reads “Patients with progressive disease **during treatment** will go to....”
  - Sections 13.26 and 13.27 have been relocated and renumbered to sections 13.23 and 13.24. All remaining sections have been renumbered
  - Section 13.25, previously Section 13.23 now reads “After the completion of the study treatment, all patients will **be evaluated at four weeks post radiation therapy** ~~go to the observation phase for a minimum of 4 weeks~~ unless the patient has progressed, refused further treatment, or had unacceptable toxicity”
  - Section 13.26, previously Section 13.24 now reads “**Phase II component only:** If the patient has achieved CR, PR, or SD, **at the 4 week post-RT evaluation** ~~after the completion of all study treatment~~, the patient will stay ~~in~~ ~~be observed~~ ~~ation~~ **every 3 months for up to two years from time of registration and then will go to event monitoring. Patients** ~~and~~ may receive adjuvant treatment....”

- Page 37: The following editorial revisions have been made to Section 14.3 (Translational/Pharmacologic Studies):
- The name of the Pathology Coordinator has been added “**Helen Tollefson**” and **NCCTG** has been added to the Pathology Coordinator’s title.
  - The first bulleted item now reflects **unstained** charged slides rather than regular charged slides
  - The third bullet is newly added “Specimen submission form.”
  - **NCCTG** has been added to the Pathology Coordinator’s title and the room number for the Guggenheim building has been corrected in the second paragraph.
- Page 37: Section 15.1 has been revised to reflect contact information for the investigator brochure.
- Page 50: Section 17.1 (Pathology Considerations for Quality Control) has been revised for clarification as follows:
- 17.1 **Central pathology review is required for confirmation of diagnosis. Within 30 days, submit the following material:**
- ~~Required materials~~
- The first sentence of Section 17.2 (Pathology Considerations for Quality Control) has been deleted as this statement is reflected in Section 17.1.
- Page 51: The following revisions have been made to Section 18.1 (Records and Data Collection Procedures):
- The heading for the “Pathology Submission Form (see Section 17)” has been revised for clarification to read “Pathology Materials (See Section 17.0).”
  - The row for “Lung Pathology Reporting Form” has been deleted as this is covered in “Pathology Materials.”
  - “**Monitor unit calculations**” has been added to “c” under footnote #1.
  - Footnote #4 has been revised to read “Required if  $\geq$ grade 4 hematologic,  $\geq$ grade 3 esophagitis,  **$\geq$ grade 3 pneumonitis**, or  $\geq$ grade 4 nonhematologic other than esophagitis, pneumonitis, dyspnea, or radiation dermatitis ~~only~~.”

Appendix IA: The timing of when PS-341 will be given has been corrected and now reads “days 1, 4, 8, 11, 22, 25, 29, ~~31~~ **32**” in the first sentence of the second paragraph under “What will happen in this research study?” section.

The last sentence of the second paragraph under “What will happen in this research study?” section has been added for clarification.

The third and fourth paragraphs under “What will happen in this research study?” have been relocated to page 2 directly under the treatment schedule table for better readability.

The treatment table under “What will happen in this research study?” has been revised for clarification as follows:

Before Study Entry:

- The third bullet now reads “History and ~~E~~examination”
- The fourth bullet now reads “**CT chest scan**” rather than “Chest x-ray”

During Treatment:

- The heading for the During Treatment section now reads “During Treatment ~~You will complete 2 cycles and then have 4 weeks of observation 1 cycle = 6 weeks treatment~~”
- The first column of the first row now reads “Days M-F x **6 weeks**”
- The first column of the second row now reads “Days 1, 4, 8, 11, 22, 25, 29, ~~31~~, **32**”
- The first column of the third row now reads “Days 2, ~~23~~”
- The second column of the third row now reads “Paclitaxel ~~will be given into the vein over 3 hours will follow the Paclitaxel~~ **followed by Carboplatin given** over 30 minutes”
- A new fourth row has been added for Day 23 because bloods are also taken
- Previous fourth row is now the fifth row
- The second bullet of the fifth row now reads “History and ~~E~~examination”

4 Weeks Post Radiation:

- The heading of the third section now reads “**4 Weeks Post Radiation Therapy**” rather than “~~After Treatment is Complete~~”
- Text in the first column has been deleted
- The first bullet in the second column now reads “History and ~~E~~examination”
- The second bullet, previously the second bullet in the second column now reads “**CT chest scan**” rather than “~~Chest x-ray~~”
- A new third bullet in the second column has been added “**Routine blood tests**”

Appendix IA Con't: The words “left over” have been added to the first sentence of the first paragraph under the “Will any biological sample(s) be stored and used in the future by the North Central Cancer Treatment Group (NCCTG)?” section for clarification.

The following revisions have been made to the “What are the risks of the study?” section in order to be consistent throughout both consent forms:

- **Loss of appetite** has been added under “More common side effects” section for paclitaxel on page 4.
- A typographical error has been corrected “closedly” in the last sentence of the tenth bulleted item under “Less common side effects” for paclitaxel on page 4.
- “**Loss of appetite**” has been added under “More common side effects” section for carboplatin on page 5.
- “Neurologic effects such as numbness, tingling or weakness in the arms and legs” has been moved from the “Anemia” category and replaces “Numbness and tingling in hands and feet” category for PS-341 on page 5.
- “Problems with the central nervous system (the brain and spinal cord) which controls mental activities, movements and nerves” has been moved to it’s own category for PS-341 on page 6 as this does not belong with “Abnormal tests of liver function.”
- ~~Altered mental status and CNS changes~~ have been deleted for PS-341 on page 6 as this is covered under “Problems with the central nervous system (the brain and spinal cord) which controls mental activities, movements and nerves.”
- “**Clotting abnormalities**” has been added for PS-341 on page 6.

Appendix IB: The timing of when PS-341 will be given has been corrected and now reads “days 1, 4, 8, 11, 22, 25, 29, ~~31~~ 32” in the first sentence of the second paragraph under “What will happen in this research study?” section.

The last sentence of the second paragraph under “What will happen in this research study?” section has been added for clarification.

The third and fourth paragraphs under “What will happen in this research study?” have been relocated to page 2 directly under the treatment schedule table for better readability.

Appendix IB  
Con't:

The treatment table under “What will happen in this research study?” has been revised for clarification as follows:

Before Study Entry:

- The third bullet now reads “History and ~~E~~examination”
- The fourth bullet now reads “**CT chest scan**” rather than “Chest x-ray”

During Treatment:

- The heading for the During Treatment section now reads “During Treatment-~~You will complete 2 cycles and then have 4 weeks of observation 1 cycle = 6 weeks treatment~~”
- The first column of the first row now reads “Days M-F x **6 weeks**”
- The first column of the second row now reads “Days 1, 4, 8, 11, 22, 25, 29, ~~31,~~ **32**”
- The first column of the third row now reads “Days 2, ~~23~~”
- The second column of the third row now reads “Paclitaxel ~~will be given into the vein over 3 hours will follow the Paclitaxel~~ **followed by Carboplatin given** over 30 minutes”
- A new fourth row has been added for Day 23 because bloods are also taken
- Previous fourth row is now the fifth row
- The second bullet of the fifth row now reads “History and ~~E~~examination”

4 Weeks Post Radiation:

- The heading of the third section now reads “**4 Weeks Post Radiation Therapy**” rather than “~~After Treatment is Complete~~”
- Text in the first column has been deleted
- The first bullet in the second column now reads “History and ~~E~~examination”
- A new second bullet in the second column has been added “**Routine blood tests**”
- The third bullet, previously the second bullet in the second column now reads “**CT chest scan**” rather than “~~Chest x-ray~~”

After Treatment is Done and Disease is the Same or Better:

- This section has been added

The words “left over” have been added to the first sentence of the first paragraph under the “Will any biological sample(s) be stored and used in the future by the North Central Cancer Treatment Group (NCCTG)?” section for clarification.

Appendix IB  
Con't:

The following revisions have been made to the “What are the risks of the study?” section in order to be consistent throughout both consent forms:

- “(feeling sick to your stomach)” has been moved from the “Loss of appetite” category to the “Nausea” category under “More common side effects” section for paclitaxel on page 4.
- “**Vomiting**” has been added for paclitaxel on page 4 and “(throwing up)” has been moved from the “Nausea” category to the “Vomiting” category under “More common side effects” section for paclitaxel on page 4.
- A typographical error has been corrected “closedly” in the last sentence of the tenth bulleted item under “Less common side effects” for paclitaxel on page 4.
- “(feeling sick to your stomach)” has been moved from the “Loss of appetite” category to the “Nausea” category under “More common side effects” section for carboplatin on page 5.
- “**Vomiting**” has been added under “More common side effects” section and “(throwing up)” has been moved from the “Nausea” category to the “Vomiting” category for carboplatin on page 5.
- “**As with any medication, allergic reactions are a possibility**” has been added as a new paragraph after the “Less common side effects” section for carboplatin on page 5.
- There were two “Loss of appetite” listed under the “More common side effects” section for PS-341 on page 5. One has now been deleted.
- “Neurologic effects such as numbness, tingling or weakness in the arms and legs” has been moved from under the “More common side effects” section for the “Anemia” category and replaces “Numbness and tingling in hands and feet” category for PS-341 on page 5.
- “Problems with the central nervous system (the brain and spinal cord) which controls mental activities, movements and nerves” has been moved to its own category for PS-341 on page 6 as this does not belong with “Abnormal tests of liver function.”