

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 2 – July 29, 2005

**Summary**

**This amendment is in response to the revised Adverse Event Reporting Requirements that were distributed by CTEP in a communication from Mike Montello, PharmD. in January 2005.**

- Change in the reporting timeframes for AdEERS reports: The timeframe for submitting a fully detailed AdEERS report for events which require AdEERS notification within 24 hours has changed from seven (7) working days to three (3) calendar days. The timeframe for other events requiring AdEERS reporting has been changed from seven (7) working days to seven (7) calendar days.
- Clarification of the requirement for an AdEERS report for certain serious events that occur >30 days following agent administration: A fully detailed AdEERS report is to be submitted for grade 3 (with hospitalization/prolongation of hospitalization) or grade 4 when the event occurs more than 30 days after receiving an agent under a CTEP IND. For a complete discussion and breakdown of the revised requirements, refer to the “CTEP, NCI Guidelines: Adverse Event Reporting Requirements (December 15, 2004 version)” which is accessible from the CTEP home page at <http://ctep.cancer.gov>.
- Section 10.3 (Adverse Event [AE] Reporting and Monitoring) has been revised to reflect a change in the NCCTG routine adverse event reporting requirements.

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

Title page: Reflects Addendum 2 and revised NCI version date.

Page 27: The second sentence of Section 10.1 (Adverse Event [AE] Reporting and Monitoring) has been revised to reflect the correct CTEP web site to access the CTCAE as follows:

The CTCAE v3.0 can be ~~downloaded~~ **accessed** from the CTEP home page (<http://ctep.cancer.gov/reporting/etc.html>).

Page 27: The first and second paragraphs of Section 10.11 (Adverse Event[AE] Reporting and Monitoring) have been revised to reflect the current CTEP mandated adverse event reporting guidelines as follows:

Adverse event monitoring and reporting is a routine part of every clinical trial. First, identify and grade the severity of the event using the CTCAE. Next, determine whether the event is expected or unexpected (~~refer to protocol and/or product literature~~ **see Section 10.12**) and if the adverse event is related to the medical treatment or procedure (see Section ~~10.12~~ **10.13**). With this information, determine whether ~~an adverse~~ **the event should must** be reported as an expedited report (see Section 10.2) ~~or as part of the routinely reported clinical data.~~ **Important: All AEs reported via expedited mechanisms must also be reported via the routine data reporting mechanisms defined by the protocol (see Sections 10.3 and 18.0).**

Expedited adverse event reporting requires submission of an Adverse Event Expedited Reporting System (AdEERS) report(s). ~~Electronic 24-hour notification of NCI and NCCTG may also be required~~ **Other expedited reporting requirements and systems may also apply.** ~~Electronic 24-hour notification and AdEERS~~ **Expedited and routine reports are to be completed within the timeframes and via the mechanisms specified in Section 10.2. All expedited adverse event AE reports should must** also be submitted to the local Institutional Review Board (IRB) **according to local IRB's policies and procedures.**

Page 28: New Section 10.12 (Expected vs. Unexpected Events) has been added to reflect the current CTEP mandated adverse event reporting guidelines and remaining sections have been renumbered.

Previous Section 10.12 has now become Section 10.13.

Page 28: Previous Section 10.13, now Section 10.14 (Additional instructions) has been revised to reflect the current CTEP mandated adverse event reporting guidelines as follows:

~~When a study includes both investigational and commercial agents, the following applies~~ **Additional instructions for trials that include both investigational agent(s) (those under an IND) and a commercial agent(s):**

- When an investigational agent (**an agent under an IND**) is used in combination with a commercial agent(s) **on the same treatment arm**, the combination is considered investigational. Expedited reporting of ~~adverse events~~ **will** follows the ~~guidelines~~ **requirements** for investigational agents.

Pages 29-31: Section 10.2 (Expedited Reporting Requirements) has been replaced in its entirety to reflect the current CTEP mandated adverse event reporting guidelines.

Page 33: Sections 10.312 and 10.313 have been revised to reflect a change in the NCCTG routine adverse event reporting requirements as follows:

~~10.312 Grade 3, and 4, and 5 AEs and deaths within 30 days of the patient's last treatment~~ **10.312** Grade 3, and 4, and 5 AEs and deaths within 30 days of the patient's last ~~treatment~~ **treatment** regardless of attribution to the study treatment or procedure, ~~with the exception of signs or symptoms definitely related to the patient's disease or disease progression.~~

**10.313 Grade 5 AEs (Deaths)**

~~10.313~~ **10.313** **Any death within 30 days after the patient's last treatment, regardless of relationship to study treatment or procedure.**

~~10.313~~ **10.313** **Any death more than 30 days after the patient's last study treatment or procedure that is felt to be at least possibly treatment related must also be submitted as a Grade 5 AE, with a CTCAE type and attribution assigned.**

Pages 30-55: Repagination only.