

North Central Cancer Treatment Group

N083E, Phase II Safety Study of Docetaxel and Carboplatin in Combination with Trastuzumab and Lapatinib in Early Breast Cancer

Addendum 4 – January 7, 2011

Summary

- In compliance with the NCI/CTEP mandate (dated May 28, 2010), expedited adverse event reporting requirements were converted from CTCAE v3.0 to CTCAE v4.0 (affected sections 10.1 and 10.11) while routine data collection via Case Report Forms (which includes the Notification Form: Grade 4 or 5 Non-AER Reportable Events/Hospitalization Form) will remain using CTCAE v3.0 (clarifications added to sections 8.2, 8.3, 8.6, 10.22, 10.3, and 10.31). Effective April 1, 2011, expedited reporting via AdEERS must use CTCAE v4.0 while the remainder of the data collection for legacy trials will continue to use CTCAE v3.0.
- Per NCI, the Secondary AML/MDS Report Form will no longer be used. Therefore, Sections 10 and 18 have been revised accordingly.

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

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

Section 8.0 **Dosage Modification Based on Adverse Events**
 Pages 24-26: The first column headers in Sections 8.2 and 8.3 tables have been revised for clarification as follows:

CTCAE v3.0 CATEGORY

Section 10.0 **Adverse Event (AE) Reporting and Monitoring**
 Page 35: Section 10.1 and Section 10.11 have been revised as follows to update the required AE reporting from CTCAE v3.0 to CTCAE v4.0:

~~This study will utilize the Common Terminology Criteria for Adverse Events (CTCAE) v3.0 for adverse event (AE) monitoring and reporting. The CTCAE v3.0 can be accessed from the CTEP home page (<http://ctep.cancer.gov>).~~
CTCAE term (AE description) and grade: The descriptions and grading scales found in the revised NCI Common Terminology Criteria for Adverse Events (CTCAE) version 3.0 will be utilized until March 31, 2010. CTCAE version 4.0 will be utilized for expedited adverse event reporting only, beginning April 1, 2011. All appropriate treatment areas should have access to a copy of the CTCAE v3.0. **A copy of the CTCAE version 4.0 can be downloaded from the CTEP web site (<http://ctep.cancer.gov>).**

10.11 Adverse event monitoring and reporting is a routine part of every clinical trial...

Expedited adverse event reporting requires submission of an Adverse Event Expedited Reporting System (AdEERS)...

Effective with Addendum 4, and beginning April 1, 2011, expedited AdEERS reporting for this protocol has been updated by the NCI/CTEP to use CTCAE v4.0. Therefore;

- 1) Events requiring expedited reporting through AdEERS must be reported through the AdEERS system in CTCAE v4.0.**
- 2) The events reported via AdEERS must ALSO be reported through routine reporting (i.e., Case Report Forms) using CTCAE v3.0.**
- 3) Routine data collection via Case Report Forms, including the “Notification Form: Grade 4 or 5 Non-AER Reportable Events/Hospitalization Form,” will remain using CTCAE v3.0 for this study.**

Page 36:

Due to the removal of the Secondary AML/MDS Report Form, a new third bullet has been added under the table in Section 10.21 as follows:

- **SECONDARY MALIGNANCIES (defined as “cancer caused by treatment for a previous malignancy,” e.g., treatment with radiation or chemotherapy) are to be reported through AdEERS, as noted in Section 10.22. Secondary malignancies are not considered metastasis of the initial neoplasm. Secondary malignancy is unrelated to the first cancer that was treated, and may occur months or even years after initial treatment.**

Note: Second Primary malignancy (malignancy not due to prior treatment) should not be reported through AdEERS.

The second bullet under the Additional Instructions section in Section 10.21 has been updated to reflect current submission procedures as follows:

~~In the rare event when Internet connectivity is disrupted, a report may be prepared using the Adverse Event Expedited Report—Single Agent or Multiple Agents paper template (available on the CTEP Home Page at <http://ctep.cancer.gov>) and faxed to 301-230-0159. Contact the NCCTG SAE Coordinator (as identified on the NCCTG Protocol Resources page) for additional back-up submission instructions~~ **24-hour notification is to be made to NCI by telephone at: 301-897-7497. An electronic report MUST be submitted immediately upon re-establishment of internet connection. Please note that all paper AdEERS forms have been removed from the CTEP web site and will NO LONGER be accepted.**

Page 37: Due to the removal of the Secondary AML/MDS Report Form, the second column for the “Secondary AML/MDS” section has been revised as follows:

Reporting for this event required during and after completion of study treatment **via AdEERS**.

Through March 31, 2011, continue using CTCAE v3.0: Report Myelodysplasia as “Blood/Bone Marrow – Myelodysplasia” and Leukemias as “Blood/Bone Marrow – Other (Specify, _____).”

Beginning April 1, 2011, AdEERS will only accept CTCAE v4.0 for this study. Report these events using “Neoplasms benign, malignant and unspecified (incl. cysts and polyps)” and including the appropriate adverse event:

- Leukemia secondary to oncology chemotherapy OR
- Myelodysplastic syndrome OR
- Treatment related secondary malignancy

~~Submit the NCI/CTEP Secondary AML/MDS Report form within 15 days via fax or mail to the NCCTG SAE Coordinator, NCCTG Operations Office, 200 First Street SW, Rochester, MN 55905, Fax (507)284-9628. The Operations Office will submit to NCI.~~

The second column for “Other Grade 4 or 5 Events...” section in Section 10.22 has been revised for clarification as follows:

Complete a Notification Form: Grade 4 or 5 Non-AER Reportable Events/Hospitalization Form within 5 working days, **using CTCAE v3.0**.

If an AdEERS report has been submitted, this form does not need to be submitted.

You must use CTCAE v3.0 for data submission with this form. The events reported on this form must also appear on the Case Report Forms (i.e., routine data) for this study.

Submit the Non-AER form electronically via the NCCTG Remote Data Entry System within 5 working days of the date the CRA is aware of the event(s) necessitating the form.

The NCCTG SAE Coordinator will notify the NCCTG IND Coordinator who will submit to the FDA IND as warranted by the event and stipulated in the U.S. Code of Federal Regulations.

Pages 38-39: Section 10.3 and Section 10.31 have been revised for clarification. In Section 10.3, the first column header in the table has added **(CTCAE v3.0)** and Section 10.31 has been revised as follows:

Submit to the NCCTG Research Base via the Nadir/AE Log the following AEs **using CTCAE v3.0** experienced by a patient and not specified in Section 10.3:

Section 18.0 Records and Data Collection Procedures

Page 72: With the removal of the Secondary AML/MDS Report Form, the row for the “NCI/CTEP Secondary AML/MDS Report Form” has been deleted. Secondary AML/MDS is now reported through AdEERS, see Section 10.22).