

North Central Cancer Treatment Group

N0775: A Randomized Phase II Trial of Temozolomide (TMZ) and Avastin® or ABI-007/Carboplatin (CBDCA) and Avastin® in Patients with Unresectable Stage IV Malignant Melanoma

Addendum 13 – December 10, 2010

**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 8.1, 8.2, 8.5, 8.7, 10.22, 10.3, 10.31, and 16.3). Effective January 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.
- Administrative changes.

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

**Title Page** Reflects the addition of Addendum 13 and a new NCI version date.

**Section 8.0** **Dosage Modification Based on Adverse Events**

Pages 21-24: The first column headers in the Sections 8.1, 8.2, 8.5, and 8.7 tables have been revised to add CTCAE v3.0 for clarification.

**Section 10.0** **Adverse Event (AE) Reporting and Monitoring**

Page 30: 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.

- 10.1 ~~This study will utilize the Common Terminology Criteria for Adverse Events (CTCAE) v3.0 for adverse event 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 December 31, 2010 for AE reporting. CTCAE v4.0 will be utilized for expedited adverse event reporting only, beginning January 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 ...

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

**Effective with Addendum 13, and beginning January 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 31: The third bullet has been corrected 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 using ~~“Neoplasms benign, malignant and unspecified (incl. cysts and polyps) —Other, specify”~~ **as noted in Section 10.22.**

Page 32: With the removal of the Secondary AML/MDS Report Form text has been revised in Section 10.22 for clarification as follows:

EVENT TYPE	REPORTING PROCEDURE
Secondary AML/MDS	Reporting for this event required during and after completion of study treatment via AdEERS <del>using CTCAE v3.0.</del> <b>Through December 31, 2010, continue using CTCAE v3.0:</b> Report Myelodysplasia as “Blood/Bone Marrow - Myelodysplasia” and Leukemias as “Blood/Bone Marrow - Other (Specify, __)”. <b>Beginning January 1, 2011, AdEERS will only accept CTCAE v4.0 for this study:</b> Report these events using “Neoplasms benign, malignant and unspecified (incl cysts and polyps) <del>—Other, specify”</del> <b>and including the appropriate adverse event:</b> - <b>Leukemia secondary to oncology chemotherapy OR</b> - <b>Myelodysplastic syndrome OR</b> - <b>Treatment related secondary malignancy</b>

<p>Other Grade 4 or 5 Events and/or Any Hospitalizations During Treatment Not Otherwise Warranting an Expedited Report</p>	<p>Complete a Notification Form: Grade 4 or 5 Non-AER Reportable Events/Hospitalization Form within 5 working days <b>using CTCAE v3.0</b> of the date the clinical research associate (CRA) is aware of the event(s) necessitating the form.</p> <p>If an AdEERS report has been submitted, this form does not need to be submitted.</p> <p>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.</p> <p><b>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.</b></p>
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Pages 33-34

Section 10.3 and Section 10.31 have been revised for clarification. In Section 10.3 the first column header in the chart has added **(CTCAE v3.0)** after the word (Category) and Section 10.31 has been revised as follows:

10.31 Submit to the NCCTG Research Base via the Adverse Event Form the following AEs **using CTCAE v3.0** experienced by a patient and not...

**Section 16.0**

**Statistical Considerations and Methods**

Page 60:

A new sentence has been added to Section 16.3 for clarification as follows:

**CTCAE v3.0 will be used to determine grading for these stopping rules.**