

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 1 – December 26, 2008

Summary

- Contact for “Protocol document, consent form, regulatory issues” has been added to protocol resource page
- Section 8.5 has a dose modification correction for PLT level in the Blood/Bone Marrow row of “Retreatment”
- Revisions in Section 15.0 and Consent Form based on Carboplatin Package Insert dated January 2004
- Editorial/Administrative changes

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

Title page The title page reflects the addition of Addendum 1 and a new NCI version date.

Protocol Resource Page

Page 2: Contact information has been revised for “Protocol document, consent form, regulatory issues” and a new contact has been added, as follows:

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Section 4.0 **Test Schedule**

Page 14: In the eighth row entitled “Urinalysis for proteinuria/ UPC ratio,” an **X⁶** has been added to the “Weekly during treatment” column for clarification

New footnote 11 has been added for clarification and is annotated in the ninth row entitled “Brain MRI (or CT if MRI cannot be performed).” The new footnote reads as follows:

≤28 days prior to registration.

New footnote 12 has been added and is annotated in the eleventh row entitled “Mandatory Research blood samples” in the “Prior to each cycle of treatment” column. The new footnote reads as follows:

Done ≤ 48 hours prior to each cycle of treatment.

Page 15: Footnote 7 has been revised as follows for consistency:

~~May be done up to~~ **Done ≤ 48 hours prior to treatment on (days 1, 8, and 15 of each cycle)**

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

Page 22: In the dose modification table for Temozlomide (Section 8.5), an editorial error has been corrected as follows:

Use Common Terminology Criteria for Adverse Events (CTCAE) v3.0 unless otherwise specified.			
CTCAE CATEGORY	ADVERSE EVENT	AGENT	DOSAGE CHANGE
<i>BASED ON INTERVAL ADVERSE EVENT</i>			
Blood/Bone Marrow	Hematologic: ANC <1000 or PLT <75,000	TMZ	Reduce dose by one dose level.
<i>AT SCHEDULED RETREATMENT</i>			
Blood/Bone Marrow	Hematologic: ANC <1500 or PLT < 50,000 75,000	TMZ	Hold Rx until blood counts are above these levels then reduce by one dose level. If not recovered in 4 weeks, proceed to observation <u>and then event monitoring</u>
Other	Grade 3 or 4		Hold Rx until resolved to ≤ grade 1 then reduce by one dose level. If not resolved in 4 weeks, proceed to observation and then event monitoring.

Section 14.0 Body Fluid Biospecimens

Page 39: In Section 14.241 text has been revised and Footnote 2 has been added for clarification, as follows:

Indicate if specimen is mandatory or optional	Collection tube description and/or additive (color of tube top)	Volume to collect per tube (number of tubes to be collected)	Blood product being processed	Pretreatment and prior to treatment, day 1 of each cycle ²	At PD or at end of active treatment	Process at site?	Storage/shipping conditions ¹
Mandatory	Heparin (dark green)	10 mL (9)	Whole Blood	X	X	No	Ambient

1. After all samples have been processed according to kit instructions, ship all specimens according to shipping instructions (see Section 14.25 for detailed shipping instructions).

2. **Done ≤ 48 hours prior to treatment.**

Page 40: In Section 14.4124 the 3rd sentence has been revised for an editorial correction as follows:

After 7 days of culture, cells will be....

Section 15.0 Drug Information

Page 41: In Section 15.1, the following editorial correction has occurred to the IND status:

IND: **EXEMPT** *application pending*

Pages 44/45: In Section 15.22, the following revisions have been made to the carboplatin section based on review of carboplatin package insert dated January 2004:

Known potential toxicities: Myelosuppression, nausea, vomiting, and electrolyte loss are most common. Hypocalcemia, hypokalemia, hypomagnesemia, and hyponatremia may occur, although these are rarely associated with symptoms. Peripheral neuropathies, diarrhea, constipation, mucositis, change in taste, hypotension, **hypertension**, visual disturbances, ototoxicity, changes in taste, CNS symptoms, rare bronchospasms, abnormal kidney and liver tests, possible kidney failure, pain, **fever, change in appetite and weight**, and alopecia may occur...

Page 54: The statement at the end of Section 15.35 has been replaced for an editorial correction as follows:

~~Return any outdated or remaining drug to the research base pharmacy.~~
Destroy any outdated or remaining drug on-site as per policies and procedures in place at your institution.

Page 58: The statement at the end of Section 15.49c has been replaced for an editorial correction as follows:

~~Return any outdated or remaining drug to the research base pharmacy.~~
Destroy any outdated or remaining drug on-site as per policies and procedures in place at your institution.

Appendix I

Consent Form

Page 5:

The following bolded text has been added for clarification in “During the study,” under the subheading “Groups A and B” in the third paragraph:

This study also has research laboratory tests that will be performed to study small samples of blood. A blood sample will be drawn from a vein just before starting treatment, **prior to each cycle during treatment and at the end of active treatment.** The blood will be sent to a laboratory...

Page 9:

The following revisions have been made to the risk section for carboplatin based on package insert dated January 2004:

Carboplatin

Likely (events that occur greater than 20% of the time):

- Nausea (~~Feeling sick to your stomach~~) (**nausea**)
- Vomiting (~~Throwing up~~) (**vomiting**)
- **Change in appetite or weight (newly added)**
- Constipation or difficult bowel movements (*moved to less likely*)
- Mouth sores (*moved to less likely*)
- Hearing problems (*moved to less likely*)
- Low white blood cell counts leading to an increased risk of infections with or without fever
- Low platelet count leading to an increased risk of bleeding
- Low red blood cell count causing anemia
- Fever (*moved to less likely*)
- Numbness and/or tingling of the hands and feet, usually this goes away after the drug is stopped, however for some patients this may not ever go away (*moved to less likely*)
- Hair loss (*moved to less likely*)
- **Change in blood tests, particularly loss of magnesium (newly added)**
- Diarrhea (~~loose stools~~) (*moved to less likely*)

Less Likely (events that occur less than or equal to 20% of the time):

- **Numbness and/or tingling of the hands and feet, usually this goes away after the drug is stopped, however for some patients this may not ever go away** (*moved from likely*)
- **Hearing problems** (*moved from likely*)
- Abnormal kidney tests ~~and~~ (*separated from liver tests*)
- **Abnormal** liver tests (*separated from kidney tests*)
- Low **or high** blood pressure
- **Mouth sores** (*moved from likely*)
- Change in taste
- **Fever** (*moved from likely*)
- Vision problems
- Allergic reactions (rash, hives, redness, itching, swelling, and difficulty in breathing with wheezing)
- Other skin rashes
- **Difficult bowel movements (constipation)** (*moved from likely*)
- **Loose stools (diarrhea)** (*moved from likely*)
- **Hair loss or thinning** (*moved from likely and added “thinning”*)

Page 11: Near the end of the section “What side effects or risks can I expect from being in the research study?” the reproductive risks have been revised as follows:

Reproductive risks: You should not become pregnant or father a baby while on this study **and for up to 6 months after your last dose of study drugs**. ~~because~~ The drugs in this study can affect an unborn baby. Women should not breastfeed a baby while on this study. It is important you understand that you need to use birth control while on this study **and for up to 6 months after your last dose of study drugs**. Check with your health care provider about what kind of birth control methods to use and how long to use them. Some methods might not be approved for use in this study.

Page 13: In the section entitled “About using biological samples for research” the last sentence of the first paragraph has added text for clarification, as follows:

The blood will be taken just before treatment starts, **prior to each cycle during treatment and at the end of active treatment**.

In the section entitled “About using biological samples for research” the first sentence of the second paragraph has been revised for clarification, as follows:

The blood will be sent to ~~Dr. Markovic’s~~ laboratories associated with...