

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 14 – February 18, 2011

Summary

- Correction and clarification to Section 7.26 regarding CBDCA calculation
- Section 15.0 and the consent form revisions due to the review of ABI-007 (Abraxane) Investigator Brochure dated August 5, 2010
- 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 14 and a new NCI version date.

Section 7.0 **Protocol Treatment**
Page 20: The third paragraph in Section 7.26 has been corrected and expanded for clarification, as follows:

For the purposes of this protocol, the GFR... The creatinine clearance is calculated by the method of Cockcroft and Gault ($\text{CrCl [mL/min]} = (140 - \text{age}) \times \text{actual body weight [Kg]} / \text{[plasma Cr [mg/dL]} \times 72]$ x [0.85 if female]). **You can also access the carboplatin dosing (Cockcroft and Gault) calculator via the NCCTG web site at <https://ncctg.mayo.edu/ncctg/group/cra/worksheet.html#CDC>.**

Section 15.0 **Drug Information**
Page 44: Section 15.126 has been updated based on review of ABI-007 Investigator Brochure Version 13 dated August 5, 2010. The following revisions have occurred:

15.126 Other: alopecia, fatigue, dyspnea, ~~fever~~, hypotension, cardiac arrhythmia, skin changes at injection site, death, pyrexia, infection, ~~hypo~~**hyper**phosphatemia, hypoalbuminemia, hypocalcemia, hyperglycemia, hypoglycemia, hyponatremia, hyperkalemia, hypermagnesemia, ~~arrhythmia~~, heart attack, epistaxis, xerosis, rash, paronychia, mood changes, eye problems (blurred vision, watery eyes or dry eyes), liver failure, kidney damage due to imbalance of salts or chemicals in the blood, abnormal liver function tests, **allergic reaction (can include breathing difficulties, flushing, low blood pressure, rash, and itching), pulmonary edema, cough. Also, rare reports of congestive heart failure and left ventricular dysfunction have been observed among individuals receiving Abraxane. Most of the individuals were previously exposed to cardiotoxic drugs, such as anthracyclines, or had underlying cardiac history.**

Appendix I

Pages 6/7:

Consent Form

Based on review of ABI-007 Investigator Brochure Version 13 dated August 5, 2010, the following revisions have occurred:

Likely risks of ABI-007 (events occurring greater than 20% of the time)

- Fall in the number of white blood cells leading to a greater chance of infection (Leukopenia)
- Fall in the number of red blood cells leading to anemia (feeling tired and run down) (Anemia)
- Nausea (feeling sick to your stomach)
- Vomiting (throwing up)
- Diarrhea (loose stools)
- Constipation or difficult bowel movements
- Loss of appetite (Anorexia)
- Feeling of tiredness (Fatigue)
- Hair loss (Alopecia)
- Muscle pain (Myalgia)
- Joint pain (Arthralgia)
- Nerve damage with numbness and tingling, usually in the hands and feet (Peripheral neuropathy). This effect may go away when the drug is stopped but it may not go away for some patients.
- Changes in taste sensation (Dysgeusia)

Less likely risks of ABI-007 (events occurring less than or equal to 20% of the time)

- Fever (which may indicate an infection) (Pyrexia)
- Fall in the number of platelets in your blood leading to a greater chance of bleeding (Thrombocytopenia)
- Sores in the mouth and/or throat leading to painful swallowing (**Mucositis**) (*clarified*)
- Difficult or painful breathing caused by narrowing of the airways (Dyspnea)
- Abnormal liver function tests which may be a sign that your liver is not working properly
- Abnormalities in heart rhythm (abnormal electrocardiogram) (Arrhythmia)
- Infection
- ~~Decreased~~ **Increased** level of phosphorus in the blood (~~Hypophosphatemia~~ **Hyperphosphatemia**) (*revised*)
- Decreased Albumin in the blood (Hypoalbuminemia)
- Abnormally low calcium in the blood stream, that can result in muscle cramps, abdominal cramps, spasms (Hypocalcemia)
- High blood sugar (Hyperglycemia)
- Low blood sugar (Hypoglycemia)
- Decreased sodium levels in the blood (Hyponatremia)
- Elevated levels of potassium in the blood (Hyperkalemia)
- Increased magnesium in the blood (Hypermagnesemia)
- Nose bleed (Epistaxis)
- Dry skin (Xerosis)
- Rash
- An infection where the nail and skin meet at the side or the base of a finger or toenail, which can be painful (Paronychia)
- Mood changes
- Eye problems, blurred vision, watery eyes, dry eyes

Rare but serious risks of ABI-007 (events occurring less than 2-3% of the time)

- Lack of oxygen to the heart muscle which can cause damage to the heart (Heart attack)
- Liver failure
- Imbalance of salts or chemicals in the blood leading to kidney damage
- Rare reports of congestive heart failure and left ventricular dysfunction may have been observed among patients receiving Abraxane. Most of the patients were previously exposed to cardiotoxic drugs, such as anthracyclines, or had underlying cardiac history.
- **Skin changes at the site of injection** (*new*)
- **Slowing of the heart rate (Pulse)** (*new*)
- **Allergic reaction (symptoms can include difficulty breathing, flushing, low blood pressure, rash and itching)** (*new*)
- **Pulmonary edema** (*new*)
- **Cough** (*new*)

Page 14:

The tissue sample signature line has been revised as follows for correction:

I agree to provide a tissue sample(s) to: _____ ~~laboratories~~ **the laboratory of Dr. Daniel Knauer at Abraxis Health** associated with NCCTG, for research testing planned as part of this study.