

North Central Cancer Treatment Group

N0177: A Pilot and Phase II Study of OSI-774 and Temozolomide in Combination with Radiation Therapy in Glioblastoma Multiforme

Addendum 12 – June 15, 2007

Summary

- Edition #10 of the investigator brochure for erlotinib (OSI-774) has been received. Even though new risks were not identified, it was recognized from the review that several events were missing from the consent and some event categories needed to be changed. Therefore, Section 15.15 and the risk section of the consent form have been revised accordingly. Consent for Study 1 will not be updated as patients are no longer receiving treatment.
- The investigator brochure for temozolomide dated December 2006 has been received. Even though new risks were not identified, it was recognized that several events were missing from the consent and some event categories needed to be changed. Therefore, the risk section of the consent form has been revised accordingly. Consent for Study 1 will not be updated as patients are no longer receiving treatment.
- Administrative/editorial changes

A replacement protocol is provided. Please replace the current copy with the one attached. Please keep this addendum with your protocol.

Title page Now reflects Addendum 12 and revised NCI version date.

Wenting Wu, Ph.D. replaces ~~Karla Ballman, Ph.D.~~ as the study statistician.

Protocol Resources

Page 2: **Christine R. Maszk** has been added as a NCCTG *Research Base* Pathology Coordinator.

The “Questions” column for the NCCTG *Research Base* Pathology Coordinators has been updated as follows:

Paraffin-embedded Tissue Pathology

Jacqueline M. Lafky replaces ~~Brenda J. Booth~~ as the laboratory contact for non-paraffin biospecimens.

The title and e-mail address for Vicki Bryhn has been updated as follows:

NCCTG *Research Base* ~~Protocol Administration~~ **Data Management** Specialist
bryhn.vicki@mayo.edu

Section 14.0 Translational/Pharmacologic Studies

Page 40:

The contact information and address for specimen submissions in Section 14.17 has been updated as follows:

Paraffin blocks submitted from outside hospitals besides Mayo Clinic Rochester should be sent to ~~Helen Tollefson~~ **the NCCTG Pathology Coordinator** at the following address:
 NCCTG Operations Office
ATTN: NCCTG PC Office
RO_FF_03_24-CC/NW Clinic 3-24
 200 First Street SW
 Rochester, MN 55905
 ATTN: ~~Helen Tollefson~~

The NCCTG Pathology Coordinator ~~Helen Tollefson~~ will forward the materials to: Dr. Robert B. Jenkins' laboratory at Mayo Clinic Rochester.

Page 41:

The address and contact information for the Biospecimens Accessioning and Processing laboratory in Section 14.232 has been updated and reformatted as follows:

Blood samples will be processed into serum by NCCTG participants. Serum samples should be transferred to individual collection tubes and frozen to -20°C within 4 hours. Do not store serum in a frost-free freezer as cycling freezers subject the specimen to repeated freeze-thaw cycles. Ship on dry ice within 24 hours to

~~the~~ **Biospecimens Accessioning and Processing (BAP)**
Stabile 13-10A Guggenheim 1034
 Mayo Clinic, **221 4th Avenue** ~~200 First Street~~ SW
 Rochester, MN 55905
 Attention **BAP Supervisor** ~~Brenda Booth~~

BAP will record receipt of specimens in the Research Accessioning Tracking System, then forward the specimens to Dr. Joon Uhm's laboratory (Guggenheim 638) for temporary storage until the end of the study, or upon request. who will process the sample and forward to Lori Carria, At the end of the study, or upon request, Dr. Uhm will forward the specimens to Dr. Maihle's Laboratory, Yale University – School of Medicine, 300 George Street, Suite 8100, New Haven, CT 06511 for sEGFR determination, within 2 hours of receipt. The samples will be transferred to -must be stored at -70°C at all times storage immediately. These stringent steps are absolutely essential to ensure that serum protein degradation does not occur, since the sEGFR that will be measured in the serum is extremely sensitive to temperature fluctuations and must be kept frozen solid.

Page 42:

For clarification purposes, the last paragraph in Section 14.2 has been revised as follows to include the location of where the MGMT expression will be performed:

Each of these measures of MGMT expression will be correlated with time to progression and survival to evaluate whether they can serve as predictive markers for outcome. **Analyses of MGMT status will be performed in the laboratory of Jann N. Sarkaria, M.D., Guggenheim 6-02.**

Section 15.0 Drug Information

Page 44:

Due to the updated investigator brochure for erlotinib, additional risks have been outlined at the end of Section 15.15 as follows:

Other adverse events as per OSI-774 Investigator Brochure, Edition #10, dated February 3, 2006: Weight loss, depression, chills or shakes, chest pain, coughing up blood, constipation

Section 17.0 Pathology Considerations

Page 55:

The contact information has been updated in the 5th sentence of Section 17.0 as follows:

If materials have been previously submitted to Dr. B. Scheithauer for a consult review or to a cooperative group pathologist for central pathology review for another cooperative group protocol, fax a copy of this review to ~~Helen Tollefson~~ **the pathology coordinator** (507/284-9628) to verify grade 4 astrocytoma.

Section 18.0 Records and Data Collection Procedures

Page 57:

Contact information in footnote #1 has been updated as follows:

A call needs to be made to ~~Helen Tollefson~~ **the NCCTG Pathology Coordinator** (507/266-0724 or **507/266-8919**) prior to forwarding the following material:

Contact information in the first paragraph of footnote #2 has been updated as follows:

Within 30 days of registration, submit the paraffin block to ~~Helen Tollefson~~ **NCCTG Operations Office, ATTN: NCCTG PC Office, RO_FF_03_24-CC/NW Clinic 3-24, 200 First Street SW, Rochester, MN 55905.**

Contact information in the third paragraph of footnote #2 has been updated as follows:

Following patient registration, submit the packaged blocks/slides to the NCCTG Operations Office, ~~Helen Tollefson~~ **ATTN: NCCTG PC Office.**

Further clarification has been made to letter f in footnote 3 as follows regarding the submission of CT/MRI scans:

Copies of CT/MRI scans used for treatment planning (indicate whether pre-op or post-op).
NOTE: When films are submitted on CD(s), they must include a viewing tool.

Appendices IB-IC Consent Forms

Due to the review of the investigator brochure for erlotinib, the risk section of the consent forms have been revised as follows:

OSI-774

Likely side effects (events that occur greater than 20% of the time) (newly added due to IB review):

- Diarrhea
- Skin rash
- Nausea
- **Vomiting** (moved from *Less Likely* due to IB review)
- **Loss of appetite** (moved from *Less Likely* due to IB review)
- **Tiredness or fatigue** (expanded wording and moved from *Less Likely* due to IB review)
- **New or worse** shortness of breath (expanded wording and moved from *Less Likely* due to IB review)
- **Infections** (moved from "not proven" due to IB review)
- **Weight loss** (newly added due to IB review)
- **Dry cough** (moved from *Less Likely* due to IB review)
- Dizziness
- Skin dryness
- Itchiness

Less likely side effects (*events that occur less than or equal to 20% of the time*) (newly added due to IB review):

- Mouth dryness
- ~~Vomiting~~ (moved to Likely due to IB review)
- Headache
- ~~Fatigue~~ (moved to Likely due to IB review)
- ~~Loss of appetite~~ (moved to Likely due to IB review)
- Fever
- Hair loss or **thinning** (expanded wording due to IB review)
- Heartburn, **gas, or upset stomach** (expanded wording due to IB review)
- Mouth sores or **mouth ulcers** (expanded wording due to IB review)
- Taste changes
- Dry, **red, irritated** eyes ~~dryness~~ (expanded wording due to IB review)
- ~~Dry cough~~ (moved to Likely due to IB review)
- ~~Shortness of breath~~ (moved to Likely due to IB review)
- Eye pain
- Eye infections
- ~~Liver injury~~ (reworded and moved to Rare but serious due to IB review)
- **Dehydration (loss of too much body fluid)** (moved from “not proven” due to IB review)
- **Stomach pain** (was in CAEPR but not in consent and moved from “not proven” due to IB review)
- **Nose bleeds** (was in CAEPR but not in consent and moved from “not proven” due to IB review)
- **Neuropathy (nerve damage resulting in numbness or tingling)** (newly added due to IB review)
- **Peeling skin rash** (was in the CAEPR but not in the consent)
- **Mouth pain** (was in the CAEPR but not in the consent)
- **Depression** (newly added due to IB review)
- **Chills or shakes** (newly added due to IB review)
- **Chest pain** (newly added due to IB review)
- **Coughing up blood** (newly added due to IB review)
- **Constipation** (newly added due to IB review)

Rare but serious side effects (*events that occur less than 2-3% of the time*) (newly added due to IB review):

- ~~Lung damage~~ **irritation (this may be life threatening)** (expanded wording due to IB review)
- Skin sores/ulcers
- ~~Stomach or intestine ulcers~~ **Irritation of stomach or bowel, which may lead to ulcers (lining breakdown) or bleeding** (reworded and moved from “not proven” due to IB review)
- ~~Bleeding~~ **Increased risk of bleeding in patients who have low platelet count, are taking blood thinners, or are taking certain drugs for pain called NSAIDS (aspirin or ibuprofen)** (reworded and moved from “not proven” due to IB review)
- ~~Liver injury~~ **Changes in liver function tests, which may indicate liver damage, this may be life threatening** (reworded and moved from Less Likely due to IB review)
- ~~Kidney damage~~ **Decreased kidney function** (reworded and moved from “not proven” due to IB review)
- ~~Eye inflammation and blurred vision~~ **Damage to the front of the eye, which may lead to changes in vision** (reworded and moved from “not proven” due to IB review)
- **Infection, which may be life threatening** (newly added due to IB review)

The category of “Side effects reported by patients, but not proven to be caused by OSI-774” has been deleted as follows:

~~Side effects reported by patients, but not proven to be caused by OSI-774:~~

~~Dehydration (moved to Less Likely due to IB review)~~

~~Stomach or intestine ulcers (reworded and moved to Rare but serious due to IB review)~~

~~Bleeding (reworded and moved to Rare but serious due to IB review)~~

~~Infections (moved to Likely due to IB review)~~

~~Kidney damage (reworded and moved to Rare but serious due to IB review)~~

~~Eye inflammation and blurred vision (reworded and moved to Rare but serious due to IB review)~~

Appendices IB-IC Consent Forms

Due to the review of the investigator brochure for temozolomide, the risk section of the consent forms have been revised as follows:

Temozolomide (TMZ)

~~More common side effects~~ **Likely** (*events occurring greater than 20% of the time*):

- Nausea, and/or vomiting
- Headache
- Constipation
- Drowsiness/Fatigue
- Decrease in appetite (*moved from Less Likely*)
- Fever (*moved from Less Likely*)
- **Headache** (*newly added*)

~~Less common side effects~~ **Less Likely** (*events occurring less than or equal to 20% of the time*):

- ~~Decrease in blood counts that may result in infection, bleeding or anemia (broken into the following 3 separate entries)~~
- **Fall in the white blood cell counts that leads to a higher risk of infection**
- **Fall in the platelet count leading to a higher risk of bleeding**
- **Fall in the red blood cell count leading to anemia (feeling tired and low energy)**
- **Decreased** ability to carry out daily activities
- Pneumonia
- Loss of appetite
- **Diarrhea**
- ~~Fever (moved to Likely)~~
- Weight loss and/or decrease in appetite (*moved to Likely*)
- **Weakness**
- **Sores** in your mouth
- Hair loss
- Numbness or tingling **or burning in your arms or legs** (*expanded wording*)
- **Abdominal** pain/jaw pain
- **Skin** rash
- Weakness of hands and feet
- **Change in liver function tests (tests that show how the liver is working)** (*expanded wording*);
Liver damage
- **Arm** and leg swelling
- **Itchiness** (*newly added*)
- **Dizziness** (*newly added*)
- **Anxiety** (*newly added*)
- **Depression** (*newly added*)
- **Memory loss** (*newly added*)

- **Muscle or joint pain** (*newly added*)
- **Shortness of breath** (*newly added*)
- **Cough** (*newly added*)
- **Increased need to pass urine** (*newly added*)

Rare side effects but serious (*events occurring less than 2-3% of the time*):

- Secondary (a different) cancer
- **Myelodysplastic syndrome (problem with the bone marrow that causes decreased production of red cells, white cells, or platelets that can sometimes turn into blood cancer)** (*newly added*)
- **Convulsions** (*newly added*)
- **Weakness on one side of the body** (*newly added*)
- **Abnormal coordination** (*newly added*)
- **Paralysis** (*newly added*)
- **Severe skin reaction** (*newly added*)
- **Allergic reaction** (*newly added*)