

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 8 – April 1, 2005

**Summary**

- The title of the study has been revised to reflect a Pilot and Phase II study rather than a Phase I/II as our community memberships have preferred the word Pilot be used in the title as opposed to a Phase I.
- Protocol resource personnel updates.
- Additional translational research with regard to other potential molecular markers and MGMT assays will now be performed on this study.
- Pneumocystis carinii pneumonia has developed in patients when taking temozolomide and steroids. Due to the concern for lymphopenic patients, this has been added to the Ancillary Treatment section of the protocol.
- Conjunctivitis (eye infections) has been identified as an expected adverse event associated with study drug OSI-774. This has been added to the Drug Information section of the protocol and the consent forms.
- Taste changes, heartburn, and hair loss have been identified as adverse events as a result of an updated Comprehensive Adverse Events and Potential Risks List (CAEPR) associated with OSI-774. These have been added to the Drug Information section of the protocol and the consent forms.
- Monitor unit calculations data are needed for RTQC data collection. This has been added to footnote #3 in Section 18.2.
- Editorial/administrative changes.

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

Title page: The title of the study has been revised to reflect a **Pilot and** Phase II study rather than a Phase I/II study.

Reflects addition of Addendum 8 and revised NCI version date.

Page 2: The following revisions have been made to the Protocol Resource page:

- Now reflects current formatting guidelines.
- The fax number for Butch Kvittem has been changed to 507/266-7240.
- Vicki Bryhn has been added as the NCCTG *Research Base* Protocol Administration Specialist.

Page 14: Section 2.21 (Goals), a new last sentence has been added to reflect additional molecular markers that will be studied “**Also, to correlate these same efficacy endpoints with other potential molecular markers of response assessed in pre-treatment tumor tissue.**”

Page 15: New Section 2.22 (Goals) has been added to reflect additional translational research being done on this study.

Previous Section 2.22 now becomes Section 2.23.

- Page 17: Section 4.0 (Test Schedule), the last column heading has been revised for clarification to read “**(6 months and beyond after RT, i.e., after 6 cycles TMZ [completed])**” rather than (~~Second 6 months after RT~~).”
- Section 4.0 (Test Schedule), “**MGMT assay in blood**” has been added and will be performed  $\leq 14$  days prior to registration
- Page 19: Section 6.5 (Registration/Randomization Procedures), the bulleted items have been separated for clarification that patients have given their permission to store both **blood** and **tissue** for future research and permission to give the sample(s) to outside researchers.
- Page 21: The dose level labeling has been corrected to reflect **1D, 1DR, and 2DR** rather than 1A, 1AR, and 2AR in Sections 7.221, 7.222, and 7.223 (Protocol Treatment) as reflected in the dose scheme (Section 7.22).
- Page 22: The dose level labeling has been corrected to reflect **1E, 1ER, 2E, 2ER, 3E, and 3ER** rather than 1B, 1BR, 2B, 2BR, 3B, and 3BR in Sections 7.321, 7.322, and 7.323 (Protocol Treatment) as reflected in the dose escalating scheme (Section 7.32)
- Page 28: Section 9.6 (Ancillary Treatment) is newly added to reflect pneumocystis carinii pneumonia.
- Page 39: Section 14.12 (Translational/Pharmacologic Studies), the second paragraph has been revised to reflect reference to Section 14.17 rather than 14.16 due to a new Section 14.16 being added.
- Page 40: New Section 14.16 (Translational/Pharmacologic Studies) has been added to reflect the additional translational research being done on this study. Previous Section 14.16 now becomes Section 14.17.
- Page 42: Section 14.24 (Translational/Pharmacologic Studies) is newly added to reflect the additional translational research being done on this study.
- Pages 40-45: Due to additional text being added to Section 14.0, repagination has occurred.
- Page 43: Section 15.152 (Drug Information) has been revised to include **conjunctivitis (eye infection), taste alterations, heartburn, and hair loss** as additional adverse events for OSI-774.
- Page 56: Section 18.0 (Records and Data Collection Procedures), item c under footnote #3 has been revised to include **monitor unit calculations**.
- Appendix IA: The title for Study 1 has been revised to read “**A Pilot and Phase II Study of OSI-774 and Temozolomide in Combination with Radiation Therapy in Glioblastoma Multiforme.**”
- Per Addendum 6, the sample size for this study has increased. At that time, the increase was not reflected in the section “How many people will take part in the study?” This has now been corrected to reflect **36** people rather than 18.

Appendix IA  
Con't: Due to the additional translational research being done on this study, the fifth paragraph under “What will happen in the study?” on page 1 has been revised to read “Brain tumor specimens collected during surgery will be analyzed for variations in EGFR content and type, **and other molecular features.**”

On page 3, under the section titled “Will any biological sample(s) be stored and used in the future by the North Central Cancer Treatment Group (NCCTG)?” the questions have been separated in order for the patients to give their permission for each **blood** and/or **tissue** sample to be stored and used for future research.

On page 4, under the section titled “How do outside researchers get the sample?” the questions have been separated in order for the patients to give their permission for either **blood** and/or **tissue** sample to be given to outside researchers.

**Eye infections, taste changes, heartburn, and hair loss** have been added as additional side effects to the “Rare side effects” section for OSI-774 on page 4.

Under “What are the risks of the study?” section, a new first sentence has been added to the fifth paragraph on page 4 as a result of the updated CAEPR listing for OSI-774 and reads “**OSI-774 when given with other drugs could cause more severe side effects associated with the other drug (i.e., temozolomide) or result in side effects not associated with either drug.**”

Appendix IB: The title for Study 2 has been revised to read “A **Pilot and Phase III** Study of OSI-774 and Temozolomide in Combination with Radiation Therapy in Glioblastoma Multiforme.”

Due to the additional translational research being done on this study, the last sentence of the fourth paragraph under “What will happen in the study?” on page 2 has been revised to read “Brain tumor specimens collected during surgery will be analyzed for variations in EGFR content and type, **and other molecular features.**”

On page 3, under the section titled “Will any biological sample(s) be stored and used in the future by the North Central Cancer Treatment Group (NCCTG)?” the questions have been separated in order for the patients to give their permission for each **blood** and/or **tissue** sample to be stored and used for future research.

On page 4, under the section titled “How do outside researchers get the sample?” the questions have been separated in order for the patients to give their permission for either **blood** and/or **tissue** sample to be given to outside researchers.

**Eye infections, taste changes, heartburn, and hair loss** have been added as additional side effects to the “Rare side effects” section for OSI-774 on page 4.

Under “What are the risks of the study?” section, a new first sentence has been added to the fifth paragraph on page 4 as a result of the updated CAEPR listing for OSI-774 and reads “**OSI-774 when given with other drugs could cause more severe side effects associated with the other drug (i.e., temozolomide) or result in side effects not associated with either drug.**”

Appendix IC: The title for Study 3 has been revised to read “A **Pilot and Phase III** Study of OSI-774 and Temozolomide in Combination with Radiation Therapy in Glioblastoma Multiforme.”

Due to the additional translational research being done on this study, the last sentence of the third paragraph under “What will happen in the study?” on page 1 has been revised to read “Brain tumor specimens collected during surgery will be analyzed for variations in EGFR content and type, **and other molecular features.**”

On page 3, under the section titled “Will any biological sample(s) be stored and used in the future by the North Central Cancer Treatment Group (NCCTG)?” the questions have been separated in order for the patients to give their permission for each **blood** and/or **tissue** sample to be stored and used for future research.

On page 4, under the section titled “How do outside researchers get the sample?” the questions have been separated in order for the patients to give their permission for either **blood** and/or **tissue** sample to be given to outside researchers.

**Eye infections, taste changes, heartburn, and hair loss** have been added as additional side effects to the “Rare side effects” section for OSI-774 on page 4.

Under “What are the risks of the study?” section, a new first sentence has been added to the fifth paragraph on page 4 as a result of the updated CAEPR listing for OSI-774 and reads “**OSI-774 when given with other drugs could cause more severe side effects associated with the other drug (i.e., temozolomide) or result in side effects not associated with either drug.**”