

North Central Cancer Treatment Group

N0177: Pilot and Phase II Trial of OSI-774 and Radiation in Glioblastoma Multiforme Patients

Addendum 2 – May 30, 2003

Summary

1. Mouth sores has been identified as a side effect of OSI-774 associated with ADEERs reports #1862928 and #1028056.
2. Lung damage has been identified as a side effect of OSI-774 associated with ADEERs report 1862928.
3. Registration section 6.4 has been revised to reflect current IRB approval submission.

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

Title page: Reflects addition of Addendum 2.

Page 16: Section 6.4 has been revised to reflect that the CTSU IRB certification form needs to be faxed to CTSU and reads as follows:

~~A signed HHS 310 form must be on file in the Randomization Center before an investigator may register any patient.~~ **IRB approval(s) is required for each treating site. A signed Clinical Trials Support Unit (CTSU) IRB Certification Form is to be on file at the CTSU Regulatory Office (fax 215-569-0206). This form can be found at the following Web site: www.ctsu.org/rss2_page.asp. Guidelines can be found under Quick Fact Sheets.**

Page 41: Section 15.152 (Drug Information), the first sentence has been revised to include the risk of mouth sores and now reads as follows:

Treatment-related, adverse events in $\geq 10\%$ of subjects receiving OSI-774 on Phase 1 studies include asthenia, headache, diarrhea, dry mouth, anorexia, nausea, vomiting, dry skin, exfoliative dermatitis, pruritus, rash, **mouth sores**, ~~and~~ dry eyes, **and lung damage**.

Appendix IA: Additional rare side effects for OSI-774 have been added to section “What are the risks of the study?” and reads as follows:

Eye dryness, eye pain, fever, dry cough, shortness of breath, **lung damage**, **mouth sores**, and liver injury.

Appendix IB: Additional rare side effects for OSI-774 have been added to section “What are the risks of the study?” and reads as follows:

Eye dryness, eye pain, fever, dry cough, shortness of breath, **lung damage**, **mouth sores**, and liver injury.

Appendix IC: Additional rare side effects for OSI-774 have been added to section “What are the risks of the study?” and reads as follows:

Eye dryness, eye pain, fever, dry cough, shortness of breath, **lung damage**, **mouth sores**, and liver injury.

Adverse Event Expedited Report

Protocol Number : N0177 **Title :** A Phase I/II Study of OSI-774 in Combination with Radiation Therapy in
Giblastoma Multiforme

Institution : Mayo Clinic **PI :** Paul D Brown **Report Type :** Original **Ticket # :** 1862928 **Amendment # :** 0

AE Created Date : 03/26/2003 11:47:56 AM

Date Submitted to Group : 03/27/2003 08:47:16 AM **Reviewer :** Patricia McNamara

Date Submitted to NCI (Electronic) : 03/27/2003 09:20:37 AM

Reporter Information

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Submitter Name : Jill K Burton
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Physician Name : Paul D Brown
Phone : (507)284-2949 **Email :** brown.paul@mayo.edu

Patient Information

Patient ID : 3651975 **Birth Date :** 08/1927

Race : White **Gender :** Female

Height(cm) : 152.6 **Weight(kg) :** 52.5 **Body Surface Area :** 1.4808

Baseline performance status at initiation of protocol - ECOG/Zubrod scale : 1

Disease Name : Astrocytoma malignant NOS
Disease Name Not Listed :

Primary Site of Disease : Cerebrum
Date of Initial Diagnosis : 01/2003

Course Information

Treatment Assignment Code : 1A

Description : Study 1:
OSI-774 100 mg PO qd.
RT 5 days/week, Weeks 2-7.

Start date of first course : 01/29/2003

Start date of course associated with Expedited Report : 01/29/2003

Start date of primary AE : 03/18/2003

End date of AE : 03/18/2003

Course Number on which event(s) occurred : 1

Total number of courses to date : 1

Was Investigational Agent(s) administered on this protocol?: Yes

Description of Event

Description and Treatment of Event(s): patient d/c OSI-774 on 2/10 due to gr 3 stomatitis but did continue with Radiation. on 3/17 call from family. patient incoherent, not eating, unresponsive. Steroid increased and patient placed in hospice care. Family decided not to proceed with final 2 radiation treatments. Patient died 3/18/03 due to progressive

Adverse Event Expedited Report

Protocol Number : N0177 **Title :** A Phase I/II Study of OSI-774 in Combination with Radiation Therapy in
Giloblastoma Multiforme

Institution : Mayo Clinic **PI:** Paul D Brown **Report Type :** Amended **Ticket #:** 1028056 **Amendment #:** 1

AE Created Date : 03/26/2003 10:23:54 AM

Date Submitted to Group : 03/26/2003 10:45:40 AM **Reviewer :** Patricia McNamara

Date Submitted to NCI (Electronic) : 03/26/2003 11:11:10 AM

Reporter Information

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Physician Name : Patrick A Burch
Phone : 507-284-8440 **Email :** burton@mayo.edu

Patient Information

Patient ID : 3651975 **Birth Date :** 08/1927

Race : White **Gender :** Female

Height(cm) : 152.6 **Weight(kg) :** 52.5 **Body Surface Area :** 1.4808

Baseline performance status at initiation of protocol - ECOG/Zubrod scale : 1

Disease Name : Astrocytoma malignant NOS
Disease Name Not Listed :

Primary Site of Disease : Cerebrum
Date of Initial Diagnosis : 01/2003

Course Information

Treatment Assignment Code : 1A

Description : Study 1:
OSI-774 100 mg PO qd.
RT 5 days/week, Weeks 2-7.

Start date of first course : 01/29/2003

Start date of course associated with Expedited Report : 01/29/2003

Start date of primary AE : 02/10/2003

End date of AE :

Course Number on which event(s) occurred : 1

Total number of courses to date : 1

Was Investigational Agent(s) administered on this protocol?:

Description of Event

Description and Treatment of Event(s): admitted to hospital for Supratherapeutic INR. Recent hospitalization 2/6 for DVT and anticoag initiation.

Present Status : Not recovered/Not resolved **Date of Recovery or Death :**

Adverse Event Expedited Report

Protocol Number : N0177 **Title :** A Phase I/II Study of OSI-774 in Combination with Radiation Therapy in Glioblastoma Multiforme
Institution : Mayo Clinic **PI :** Paul D Brown **Report Type :** Amended **Ticket # :** 1028056 **Amendment # :** 1
AE Created Date : 03/26/2003 10:23:54 AM
Date Submitted to Group : 03/26/2003 10:45:40 AM **Reviewer :** Patricia McNamara
Date Submitted to NCI (Electronic) : 03/26/2003 11:11:10 AM

Adverse Events (CTC)

Category	Adverse Event	Grade	Hospitalization/ Prolongation of Hospitalization	Comments
COAGULATION	Prothrombin time (PT)	3	Yes	prottime 2/7 was 11.1 - prottime 2/10 >240
COAGULATION	Partial thromboplastin time (PTT)	3	Yes	dvt diagnosed 2/6/03 started anticoagulation
GASTROINTESTINAL	Diarrhea patients without colostomy	2	Yes	
GASTROINTESTINAL	Stomatitis/pharyngitis (oral/pharyngeal mucositis)	3	Yes	patient not eating due to painful stomatitis, given IV fluids.

Attribution for Adverse Events

Attribute to	Diarrhea patients without colostomy	Partial thromboplastin time (PTT)	Prothrombin time (PT)	Stomatitis/phary ngitis (oral/pharyngeal mucositis)
OSI-774(718781)	Probable	Definite	Definite	Probable
Astrocytoma malignant NOS	Unrelated	Unrelated	Unrelated	Unrelated
Colace	Possible	Unrelated	Unrelated	Unrelated
Coumadin	Unrelated	Probable	Probable	Unrelated
Dexamethasone	Unrelated	Unrelated	Unrelated	Unrelated
Diffucan	Unrelated	Possible	Possible	Unrelated
Lovenox	Unrelated	Probable	Probable	Unrelated
Protonix	Unrelated	Unrelated	Unrelated	Unrelated
Senokot	Possible	Unrelated	Unrelated	Unrelated
Verapamil	Unrelated	Unrelated	Unrelated	Unrelated

Abnormal and Relevant Normal Lab Results

Lab	Baseline date	Value	Worst Date	Value	Recovery/Latest Date	Value	Microbiology Date Site	Infectious Agent
International normalised ratio (INR)	02/07/2003	1.1 number	02/10/2003	18.8 number	02/17/2003	1.2 number		
Prothrombin time (PT)	02/07/2003	11.1 seconds	02/10/2003	240 seconds	02/17/2003	12.4 seconds		

