

NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: January 28, 2005
To: NCCTG Primary Clinical Research Associates
From: Lori Kelly
Protocol Development Coordinator
Re: N0177, A Phase I/II Study of OSI-774 and Temozolomide in Combination with Radiation Therapy in Glioblastoma Multiforme

The purpose of this memorandum is to provide investigators with a recent report of an adverse event that has occurred in association with OSI-774 for a study where the Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI) is distributing this agent. You may have also received this communication directly from DCTD.

AE_1465553

Please note that all risks currently cited in the NCCTG consent form can not be omitted; it is at the discretion of your local IRB as to whether they wish to add risks based on the enclosed information. If a determination has been made by the NCCTG Research Base that a protocol amendment is necessary, you will receive the NCI-approved protocol addendum at a later date; for purposes of cross-reference, this communication will cite the adverse event noted above.

Please submit this adverse event to your Institutional Review Board.

If you have any questions concerning this communication, please contact Lori Kelly at 507-266-3549.

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enclosure



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

National Institutes of Health
National Cancer Institute

DATE: January 5, 2005
FROM: Janet Dancy, M.D., Investigational Drug Branch, CTEP, DCTD, NCI
SUBJECT: OSI-774 IND Safety Report, AE# 1465553
TO: Investigators Using OSI-774, IND 63,383

The U.S. Food and Drug Administration (FDA) regulations require sponsors of clinical studies conducted under a U.S. IND to notify the FDA and all participating investigators of any serious and unexpected adverse experiences that are possibly related to the investigational agent. Please find attached a copy of an IND Safety Report recently submitted to the FDA for the CTEP-sponsored investigational agent, OSI-774 (IND 63,383).

Please complete the following:

- Send a copy of the IND Safety Report to your Institutional Review Board (IRB) according to your local IRB's policies and procedures.
- File a copy of the IND Safety Report in your protocol file.

Please note that for Cooperative Group studies, the Cooperative Group Operations Office will provide instructions for IRB submissions, any patient notifications, etc.

CTEP's evaluation of this IND Safety Report in light of previous experience with OSI-774 does not require a change in the clinical protocols for this agent at this time.

Please continue to report events according to the adverse event reporting guidelines in your protocol(s).

The Adverse Events Assessment that describes the following adverse event is attached:

A 73-year-old male with non-small cell lung cancer developed grade 3 pulmonary fibrosis while on a phase 1 trial using the investigational agent OSI-774. Of note, the patient had a history of radiation fibrosis and had received 66 Gy to the right lung for approximately 7 weeks.

There have been no other incidences of pulmonary fibrosis reported to the NCI as serious adverse events under this IND. There have been 1165 patients enrolled in NCI-sponsored clinical trials under this IND.

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ADVERSE EVENTS ASSESSMENT

IND 63383 NSC 718781 Erlotinib (OSI-774)	ADVERSE EXPERIENCE REPORT NO. 7 IND Safety Report: Event: Gr. 3: Pulmonary fibrosis
AE: 1465553	Protocol: 5948

The patient is a 73-year-old male with non-small cell lung cancer (NSCLC) who developed pulmonary fibrosis while on a phase 1 trial using the investigational agent OSI-774. He began his first course of treatment on November 3, 2004, receiving OSI-774 150 mg PO daily, every 28 days. He started cycle two of therapy on December 1, 2004, with the last dose administered on December 8, 2004.

The patient was diagnosed with stage III NSCLC cancer in February 2004. He was initially treated with multiple agent systemic chemotherapy along with radiotherapy, but had disease progression as per a CT scan done on October 6, 2004. He was subsequently started on OSI-774 on November 3, 2004. The patient had significant respiratory disease and was on home oxygen at the time of study entry; his performance status was considered to be a 2. Of note, he had a history of radiation fibrosis, having received 66 Gy to the right lung from May 12, 2004 to June 29, 2004 to the right lung and mediastinum. A CT scan done on December 3, 2004 for worsening dyspnea, revealed an increase in the mediastinal lymphadenopathy, increase in posterior right lower lobe consolidation, increase in bilateral basilar fibrotic change in both lower lung fields, a new area of anterior left upper lobe consolidation, and a right-sided pleural effusion. On December 8, 2004, (Cycle 2, Day 8), the patient was admitted to the hospital with a 1-week to 1-month history of increasing dyspnea and chronic dry cough. He had an oxygen saturation of 77% on 6 L oxygen via nasal cannula. The patient was afebrile with a respiratory rate of 22/min and a blood pressure of 94/56 mm Hg. A chest X-ray performed that day showed diffuse bilateral coarse interstitial opacities particularly in the lower lung fields. The patient was initially treated with antibiotics, pending the results of the blood cultures. The patient was removed from the protocol and was subsequently placed on corticosteroids along with BiPAP. On December 22, 2004, he was discharged home for hospice care and was to continue on the corticosteroid treatment.

The patient's past medical history is significant for previous radiation to the lung, hypertension, and intermittent atrial fibrillation. Medications at the time of the event included Coumadin[®], lisinopril,

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Cartia® (diltiazem), Bextra® (valdecoxib), and Atrovent®.

There have been no other incidences of pulmonary fibrosis reported to the NCI as serious adverse events under this IND.

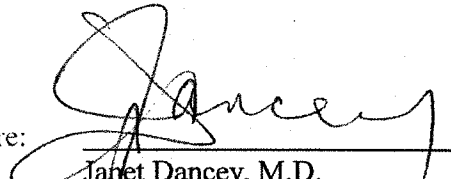
In this case, it is felt that the worsening bilateral pulmonary fibrosis is possibly related to OSI-774, the patient's NSCLC, and previous radiation to the lung. There have been 1165 patients enrolled in NCI-sponsored clinical trials under this IND.

	Pulmonary fibrosis
OSI-774	Possible
Non small cell lung cancer	Possible
Previous radiation to lung	Possible

Date:

1/5/05

Signature:


Janet Dancey, M.D.
(IDB Monitor for OSI-774)

If this assessment is changed, we will notify your office.

cc: Christine Boisclair
Brian Watson

OSI Pharmaceuticals

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2 of 2