



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: October 10, 2008

To: NCCTG Primary Clinical Research Associates

From: Janis Wobschall
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_1859262

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 Janis Wobschall at wobschall.janis@mayo.edu or 507-284-4852.

JW/kjm
enclosure

IND SAFETY REPORT: INITIAL WRITTEN REPORT

18

TO: Division of Drugs Oncology Products, Center for Drug Evaluation and Research, FDA

FAX: 301-796-9845

1. IND NUMBER
63383
7921

2. AGENT NAME
OSI-774 (erlotinib; Tarceva)
Bevacizumab (rhuMAb VEGF)

3. DATE
October 2, 2008

4. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION
Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics III,
Investigational Drug Branch, CTEP, DCTD, NCI

6. PHONE NUMBER
301-496-1196

7. FAX NUMBER
301-402-0428

8. PROTOCOL NUMBER (AE #)
7024 (AE # 1859262)

9. PATIENT IDENTIFICATION
PH971

10. AGE
32

11. SEX
Male

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 32-year-old male with cholangiocarcinoma who experienced pneumomediastinum while on a phase 2 study using the investigational agent bevacizumab in combination with erlotinib. He began his first course of treatment on August 28, 2007, and received the last dose of erlotinib on September 23, 2008 (Cycle 14, Day 29), and his last dose of bevacizumab on August 26, 2008 (Cycle 14, Day 1). On September 23, 2008, the patient presented to the clinic with increasing chest and epigastric pain. The previous day the patient had a restaging CT of the chest, abdomen and pelvis which demonstrated a pneumomediastinum and bilateral anterior pneumothoraces. He was admitted to the hospital. The patient reported a "weird sensation" in his throat and chest that was accompanied by a sharp pain in his lower neck 2 days prior to his admission to the hospital. Boerhaave's syndrome was suspected but never proven. The patient's pneumomediastinum resolved spontaneously and he was discharged on September 25, 2008. Additional information has been requested. There is a reasonable possibility that the experience may have been caused by the drugs.

13. DOSE, ROUTE, AND SCHEDULE
(Cycle = 28 days)

Erlotinib 150 mg PO daily, and bevacizumab 5 mg/kg IV over 30 to 90 minutes on days 1 and 15.

14. DATES OF TREATMENT

The patient began his first course of treatment with erlotinib in combination with bevacizumab on August 28, 2007, and received his last dose of erlotinib on September 23, 2008 (Cycle 14, Day 29), and the last dose of bevacizumab on August 26, 2008 (Cycle 14, Day 1).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 17,088 and the number using erlotinib = 2644. There have been no other cases of pneumomediastinum reported to the NCI through AdEERS as serious adverse events for bevacizumab or erlotinib, and 22 and 6 other cases of pneumothorax reported for bevacizumab and erlotinib respectively.

16. COMMENTS

AT THIS TIME, NO OTHER INFORMATION IS AVAILABLE. IF UPON FURTHER INVESTIGATION RELEVANT INFORMATION BECOMES AVAILABLE, THEN A FOLLOW-UP REPORT WILL BE SUBMITTED IN ACCORDANCE WITH 21CFR 312.32(d)(2).

DISCLAIMER per 21 CFR 312.32(e): THIS SAFETY REPORT DOES NOT NECESSARILY REFLECT A CONCLUSION OR ADMISSION BY THE CTEP IDB SENIOR INVESTIGATOR/ SPONSOR THAT THE INVESTIGATIONAL AGENT/THERAPY CAUSED OR CONTRIBUTED TO THE ADVERSE EXPERIENCE BEING REPORTED.

0002