

IND SAFETY REPORT: INITIAL WRITTEN REPORT**To: Division of Drug Oncology Products, Center for Drug Evaluation and Research, FDA****FAX: 301-796-9845**1. IND NUMBER
633832. AGENT NAME
OSI-774 (erlotinib, Tarceva®)3. DATE
August 18, 20104. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute5. REPORTER'S NAME, TITLE, AND INSTITUTION
Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics 3, Investigational Drug Branch, CTEP, DCTD, NCI6. PHONE NUMBER
301-496-11967. FAX NUMBER
301-402-04288a. PROTOCOL NUMBER (AE #)
S0727 (AE# 1531241)8b. AE GRADE: AE
**Grade 5: Pulmonary/Upper Respiratory: Respiratory failure
Grade 4: Adult Respiratory Distress Syndrome (ARDS)**9. PATIENT IDENTIFICATION
22123810. AGE
78 years11. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 78-year-old female with metastatic adenocarcinoma of the pancreas who experienced grade 5 respiratory failure and grade 4 Adult Respiratory Distress Syndrome (ARDS) while on a phase 1/2 study utilizing the investigational agent OSI-774 in combination with gemcitabine. She began her first course of treatment on December 9, 2009, and received the last dose of OSI-774 on July 6, 2010 (Cycle 8, Day 14), and the last dose of gemcitabine on June 30, 2010 (Cycle 8, Day 8). On July 19, 2010 (Cycle 8, Day 27), the patient had a CT scan to evaluate her disease status. She complained of severe headache shortly after receiving the IV contrast, and was found unresponsive within the CT scanner. The patient was cyanotic, pale, diaphoretic, and was spitting up pinkish frothy sputum. Her arterial blood gas showed a pH of 7.01 (reference range: 7.35 - 7.45), pCO₂ of 64 mmHg (reference range: 35 - 45 mm Hg), pO₂ of 88 mmHg (reference range: 83 - 100 mm Hg), and a bicarbonate of 15.8 mEq/L (reference range: 18 - 23 mEq/L). A CT scan of the head was negative for acute hemorrhage or infarct. A portable chest X-ray revealed bilateral diffuse airspace opacities, which were concerning for acute pulmonary interstitial edema versus ARDS, pulmonary hemorrhage/edema, or diffuse multifocal pneumonia. The patient was intubated and admitted to the MICU. She was started on nitroglycerin, Lasix®, morphine, Ativan®, and Zemuron®. On July 27, 2010, the patient extubated herself, and she was made Do-Not-Resuscitate (DNR). She expired that day. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drugs.

13. DOSE, ROUTE, AND SCHEDULE

**Cycle =28 Days
OSI-774: 100 mg PO daily**

14. DATES OF TREATMENT

The patient began the investigational therapy on December 9, 2009, and received the last dose of OSI-774 on July 6, 2010 (Cycle 8, Day 14).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using OSI-774=3,208. There have been 9 other cases of respiratory failure and 5 other cases of ARDS reported to the NCI through AdEERS as serious adverse events for OSI-774.

16. COMMENTS Also administered on this protocol:

Gemcitabine: 1000 mg/m²/dose IV over 30 minutes on Days 1, 8, and 15**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