

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 63383	2. AGENT NAME OSI-774 (erlotinib; Tarceva®)	3. DATE January 11, 2010
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 3, CTEP, DCTD, NCI		6. PHONE NUMBER 301-496-1196
		7. FAX NUMBER 301-402-0428
8. PROTOCOL NUMBER (AE #) S0727 (AE# 1727021)		
9. PATIENT IDENTIFICATION 220820	10. AGE 73	11. SEX Female
12. DESCRIPTION OF ADVERSE EVENT The patient was a 73-year-old female with adenocarcinoma of the pancreas who experienced grade 4 hyperglycemia and grade 3 muscle weakness while on a phase I/II trial utilizing the investigational agent erlotinib in combination with gemcitabine. She began the investigational therapy on November 23, 2009, and received her last dose of erlotinib on December 23, 2009 (Cycle 2, Day 3), and her last dose of gemcitabine hydrochloride on December 21, 2009 (Cycle 2, Day 1). On December 23, 2009, the patient was admitted to the hospital complaining of extreme weakness, fatigue, poor appetite and weight loss. She had a known history of diabetes mellitus, hypertension and hypercholesterolemia. The laboratory findings revealed a glucose level of 624 mg/dL (reference range: 70-105 mg/dL) and a creatinine level of 2.0 (reference range: 0.5-1.7 mg/dL). The urinalysis revealed a urinary tract infection. Because the patient had hypokalemia and acute renal insufficiency, her ACE inhibitors were held. She received IV fluids, antibiotics and IV and subcutaneous insulin. While in the hospital, the patient developed large, rapidly-accumulating pleural effusions. A CT scan of the chest on December 29, 2009, revealed an ill-defined nodularity throughout the lungs and an enlarged left pleural effusion. On December 31, 2009, she underwent a bronchoscopy with right and left video-assisted thoracoscopy with talc pleurodesis bilaterally and placement of the chest tubes bilaterally. On January 2, 2010, the patient experienced hypotension. The patient and her family decided not to have any further aggressive treatment. She expired on January 3, 2010, and it was felt that the cause of death was due to disease progression. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.		
13. DOSE, ROUTE, AND SCHEDULE Cycle =28 Days Erlotinib 100 mg PO daily		
14. DATES OF TREATMENT The patient began the investigational therapy on November 23, 2009, and received the last dose of erlotinib on December 23, 2009 (Cycle 2, Day 3).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using erlotinib = 2916. There have been 15 other cases of hyperglycemia and 10 other cases of muscle weakness, generalized or specific area: Whole body/generalized reported to the NCI through AdEERS as serious adverse events for erlotinib.		
16. COMMENTS Also administered on this protocol: Gemcitabine hydrochloride 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 21CFR312.32(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.		