

IND SAFETY REPORT: INITIAL WRITTEN REPORT

To: *Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA*
Division of Drug Oncology Products, Center for Drug Evaluation and Research, FDA

FAX: 301-796-9849

FAX: 301-796-9845

1. IND NUMBER 100947 63383	2. AGENT NAME IMC-A12 (Humab, IGF-1R) OSI-774 (erlotinib, Tarceva®)	3. DATE June 4, 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, Investigational Drug Branch, CTEP, DCTD, NCI		6. PHONE NUMBER 301-496-1196
		7. FAX NUMBER 301-402-0428
8a. PROTOCOL NUMBER (AE #) S0727 (AE# 1398066)	8b. AE GRADE: AE Grade 5: Hypoxia Grade 3: Pneumonitis/pulmonary infiltrates	
9. PATIENT IDENTIFICATION 222971	10. AGE 65 years	11. SEX Female
12. DESCRIPTION OF ADVERSE EVENT <p>The patient was a 65-year-old female with metastatic adenocarcinoma of the pancreas who experienced grade 5 hypoxia and grade 3 pneumonitis, while on a phase 1/2 study utilizing the investigational agents IMC-A12 and OSI-774 in combination with gemcitabine. She began her first course of treatment on February 11, 2010, and received the last doses of IMC-A12 and gemcitabine on May 20, 2010 (Cycle 4, Day 15), and the last dose of OSI-774 on May 22, 2010 (Cycle 4, Day 17). On May 22, 2010 (Cycle 4, Day 17), the patient, who had previously experienced recurrent pleural effusions which necessitated continuous positive airway pressure (CPAP) therapy, contacted the clinic with complaints of increasing dyspnea of 2-3 weeks duration. She was instructed to discontinue her OSI-774 medication and report to the emergency room, which she declined. On May 25, 2010 (Cycle 4, Day 20), she presented to the clinic with complaints of dyspnea, abdominal pain, and back pain. Her oxygen saturation was 84% on room air. She was admitted and started on oxygen and intravenous fluids. A chest X-ray revealed bilateral interstitial infiltrates. Her arterial blood gases showed a PO₂ of 50 mmHg (reference range: 67.5-84.4 mmHg), a PCO₂ of 45.3 mmHg (reference range: 38.0-42.0 mmHg), and a pH of 7.383 (reference range: 7.380-7.420). A CT scan of the chest also revealed pleural effusion with diffuse interstitial infiltrates. The patient was transferred to the ICU and continued on intravenous fluids with Solu-Medrol^(R). It was felt that the interstitial lung disease could have been a reaction to the OSI-774 versus the progression of pancreatic cancer. On May 28, 2010 (Cycle 4, Day 23), the patient's condition continued to deteriorate, and she subsequently died the same 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.</p>		
13. DOSE, ROUTE, AND SCHEDULE Cycle = 28 Days; IMC-A12: 6 mg/kg/dose IV over 60 minutes on Days 1, 8, 15 and 22 and OSI-774: 100 mg PO daily		
14. DATES OF TREATMENT The patient began the investigational therapy on February 11, 2010, and received the last dose of IMC-A12 on May 20, 2010 (Cycle 4, Day 15), and the last dose of OSI-774 on May 22, 2010 (Cycle 4, Day 17).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using IMC-A12=466 and using OSI-774=3,097. There have been 4 other cases of hypoxia and 2 case of pneumonitis reported to the NCI through AdEERS as serious adverse events for IMC-A12; and 45 cases of hypoxia and 45 cases of pneumonitis 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.		