

IND SAFETY REPORT: INITIAL WRITTEN REPORT

TO: <i>Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA</i> <i>Division of Drug Oncology Products, Center for Drug Evaluation and Research, FDA</i>		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 March 5, 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	
8. PROTOCOL NUMBER (AE #) S0727 (AE # 1203166)			
9. PATIENT IDENTIFICATION 220735	10. AGE 59	11. SEX Female	
12. DESCRIPTION OF ADVERSE EVENT <p>The patient is a 59-year-old female with metastatic adenocarcinoma of the pancreas who experienced grade 3 cardiac ischemia/infarction and grade 3 cardiac troponin I while on a phase 1 and phase 2 study utilizing the investigational agents IMC-A12 and OSI-774 in combination with gemcitabine. She began her first course of treatment on November 16, 2009, and received her last doses of IMC-A12 and gemcitabine on December 23, 2009 (Cycle 2, Day 8) and the last dose of OSI-774 on December 28, 2009 (Cycle 2, Day 13). On December 28, 2009 (Cycle 2, Day 13), the patient presented to the local ER with nausea, vomiting and severe retrosternal chest pain. An ECG showed normal sinus rhythm, and her troponin was 0.07 ng/mL (reference range: 0-0.3 ng/mL). She was treated with sublingual nitroglycerin, which relieved her chest pain. On December 29, 2009 (Cycle 2, Day 14), the patient was transferred to another hospital for further therapy, where her initial troponin on arrival was 0.59 ng/mL, the repeat value was 0.92 ng/mL, and she was started on beta blockers, ACE inhibitors and statins. A 2-D echocardiogram showed normal left ventricular systolic function and motion with estimated ejection fraction of 60-65% and normal right ventricular function. However, mild aortic insufficiency and trace tricuspid valve regurgitation were also reported. A cardiac stress test with nuclear imaging done on December 30, 2009 (Cycle 2, Day 15) was negative. By December 31, 2009 (Cycle 2, Day 16), the patient continued to be chest pain free and her troponins had trended down. She was discharged home on the same day to be followed up at the cardiology and oncology clinics. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.</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 OSI-774: 100 mg PO daily			
14. DATES OF TREATMENT The patient started the investigational therapy on November 16, 2009, and received the last dose of IMC-A12 on December 23, 2009 (Cycle 2, Day 8), and the last dose of OSI 774 on December 28, 2009 (Cycle 2, Day 13).			
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using IMC-A12= 336 and using OSI-774 = 2992. There has been 1 other case of cardiac ischemia/infarction and 1 other case of cardiac troponin I reported to the NCI through AdEERS as serious adverse events for IMC-A12; and 10 other cases of cardiac ischemia/infarction and 4 other cases of cardiac troponin I 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).			
<u>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.</u>			