

**IND SAFETY REPORT: INITIAL WRITTEN REPORT**

<b>TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA</b> <b>Division of Drug Oncology Products, Center for Drug Evaluation and Research, FDA</b>		<b>FAX: 301-796-9849</b> <b>FAX: 301-796-9845</b>
1. IND NUMBER <b>100947</b> <b>61010</b>	2. AGENT NAME <b>IMC-A12 (HuMab IGF-1R)</b> <b>CCI-779 (temsirrolimus, Torisel™)</b>	3. DATE <b>May 13, 2011</b>
4. SPONSOR <b>Division of Cancer Treatment and Diagnosis, National Cancer Institute</b>		
5. REPORTER'S NAME, TITLE, AND INSTITUTION <b>Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics 3, Investigational Drug Branch, CTEP, DCTD, NCI</b>  <b>L. Austin Doyle, MD-Senior Investigator for Investigational Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI</b>		6. PHONE NUMBER <b>301-496-1196</b> 7. FAX NUMBER <b>301-402-0428</b>
8a. PROTOCOL NUMBER (AE #) <b>ADVL0813 (AE# 1413345)</b>	8b. AE GRADE: AE <b>Grade 4: Wound complication, non-infectious</b>	
9. PATIENT IDENTIFICATION <b>800079</b>	10. AGE <b>18 yrs</b>	11. SEX <b>Male</b>
12. DESCRIPTION OF ADVERSE EVENT <b>The patient is an 18-year-old male with epithelioid sarcoma who experienced grade 4 non-infectious wound complication while on a phase 1 trial utilizing the investigational agents IMC-A12 and CCI-779. He began the investigational therapy on March 10, 2010, and received his last doses of IMC-A12 and CCI-779 on April 1, 2011 (Cycle 11, Day 1). On February 11, 2011 (Cycle 10, Day unconfirmed), the patient, who had soft tissue necrosis on his right forearm at study entry which necessitated holding the investigational treatments, underwent wound debridement and Apligraf® placement. On March 11, 2011, he was re-instated on the investigational treatments, and continued on to Cycle 11. During week one of Cycle 11, another debridement was planned and the study drugs were again held. On April 11, 2011, a MRI of the right proximal upper extremity revealed increasing T2 signal and enhancement in the soft tissues along the distal aspect of the humeral shaft and elbow. Another MRI of the forearm that day was consistent with cellulitis and osteomyelitis. On April 19, 2011, the patient underwent a debridement of the necrotic bone, jet irrigation, and a dressing change, which was repeated after 3 days, and subsequently continued. On April 29, 2011, an amputation of the arm was recommended after discussion with the patient's family. He was removed from the protocol 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.</b>		
13. DOSE, ROUTE, AND SCHEDULE <b>Cycle = 28 Days</b> <b>IMC-A12: 6 mg/kg IV over 1 hour on Days 1, 8, 15, and 22</b> <b>CCI-779: 15 mg/m<sup>2</sup> IV over 30 minutes on Days 1, 8, 15, and 22</b>		
14. DATES OF TREATMENT <b>The patient began the investigational therapy on March 10, 2010, and received the last doses of IMC-A12 and CCI-779 on April 1, 2011 (Cycle 11, Day 1).</b>		
15. ACCRUAL AND IND EXPERIENCE <b>Number of patients enrolled in NCI-sponsored clinical trials using IMC-A12 = 1015, and CCI-779 = 2679. There has been one other case of non-infectious wound complication reported to the NCI through AdEERS as a serious adverse event for IMC-A12. Non-infectious wound complications are expected events for CCI-779.</b>		
16. COMMENTS <b>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).</b> <b>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.</b>		