

IND SAFETY REPORT: INITIAL WRITTEN REPORT

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

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1. IND NUMBER 61010 100947	2. AGENT NAME CCI-779 (temsirrolimus, Torisel™) IMC-A12 (HuMab IGF-1R)	3. DATE July 15, 2010
4. SPONSOR Division of Cancer Treatment and Diagnosis, National Cancer Institute		
5. REPORTER'S NAME, TITLE, AND INSTITUTION L. Austin Doyle, M.D., Senior Investigator for Investigational Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI Helen Chen, M.D., 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 #) 8121 (AE# 1097524)	8b. AE GRADE: AE Grade 3: Dysphagia	
9. PATIENT IDENTIFICATION MSK-000044	10. AGE 78 years	11. SEX Male
12. DESCRIPTION OF ADVERSE EVENT The patient is a 78-year-old male with adrenal leiomyosarcoma who experienced grade 3 dysphagia while on a phase 2 trial utilizing the investigational agents temsirolimus and IMC-A12. The patient began the investigational therapy on May 27, 2010, and received his last doses of temsirolimus and IMC-A12 on June 17, 2010 (Cycle 1, Day 22). On June 24, 2010 (Cycle 1, Day 29), the patient presented to the clinic with fatigue and tumor-related pain in the abdomen, back, and scalp. The study drugs were held, and he was treated with IV hydration, oxycodone, and Tylenol®. On June 28, 2010 (Cycle 1, Day 33), he reported worsening of his symptoms, early satiety, and difficulty in swallowing. The patient was admitted and started on IV fluids and low-dose Marinol®. An upper gastrointestinal endoscopy the next day revealed mucosal abnormality in the duodenum, which was considered unrelated to the study drugs. However, the dysphagia was deemed possibly related to treatment or inflammation, and the patient was removed from the protocol on June 30, 2010 (Cycle 1, Day 35). Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug temsirolimus.		
13. DOSE, ROUTE, AND SCHEDULE Cycle = 6 weeks Temsirolimus: 25 mg IV over 30 minutes weekly IMC-12: 6 mg/kg IV over 60 minutes weekly		
14. DATES OF TREATMENT The patient began the investigational therapy on May 27, 2010, and received his last doses of temsirolimus and IMC-A12 on June 17, 2010 (Cycle 1, Day 22).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 2137, and IMC-A12 = 485. There have been 4 other cases of dysphagia reported to the NCI through AdEERS as serious adverse events for temsirolimus and no other cases of dysphagia reported to the NCI through AdEERS as serious adverse events for IMC-A12.		
16. COMMENTS 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.		

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