

**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**

**FAX: 301-796-9845**

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1. IND NUMBER

**61010**

**100947**

2. AGENT NAME

**CCI-779 (temsirolimus, Torisel™)**

**IMC-A12 (HuMab IGF-1R)**

3. DATE

**November 17, 2009**

4. SPONSOR

**Division of Cancer Treatment and Diagnosis, National Cancer Institute**

5. REPORTER'S NAME, TITLE, AND INSTITUTION

**L. Austin Doyle, MD-Senior Investigator for Investigational Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI**

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6. PHONE NUMBER

**301-496-1196**

7. FAX NUMBER

**301-402-0428**

8. PROTOCOL NUMBER (AE #)

**8109 (AE# 1586021)**

9. PATIENT IDENTIFICATION

**23**

10. AGE

**57**

11. SEX

**Female**

12. DESCRIPTION OF ADVERSE EVENT

**The patient was a 57-year-old female with metastatic uterine carcinoma who developed grade 3 renal failure, grade 3 pneumonitis, and died while on a phase 1 trial utilizing the investigational agents IMC-A12 and temsirolimus. She began the first course of the investigational therapy on April 28, 2009, and received her last doses of temsirolimus and IMC-A12 on June 30, 2009 (Cycle 3, Day 8). The patient had previously been admitted in early June 2009, for right-sided malignant pleural effusion which improved with thoracentesis, and she was discharged on June 19, 2009. On July 6, 2009, the patient was admitted to the hospital with a 2-day history of progressive dyspnea, nausea, dizziness, and increase upper extremity swelling. A chest X-ray revealed moderate bilateral pleural effusions with adjacent pulmonary opacities consistent with compressive subsegmental atelectasis. Laboratory results included a potassium of 6.1 mEq/L (reference range: 3.2-5 mEq/L) and a creatinine of 2.2 mg/dL (reference range: 0.5-1.7 mg/dL), down from a value of 2.6 mg/dL within the last week. The patient was started on IV fluids, and an ultrasound-guided intrapleural catheter drained 850 cc of yellow fluid which improved her dyspnea. Pathology again revealed high grade carcinoma. She was started on hemodialysis. Her condition deteriorated, and she was made DNR after discussions with her and her family. The patient was discharged home in guarded condition on July 30, 2009. On August 5, 2009, the staff was informed by the family that the patient died that morning. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drugs.**

13. DOSE, ROUTE, AND SCHEDULE

**Cycle =28 Days; Temsirolimus 25 mg IV over 30 minutes weekly; IMC-A12 6 mg/kg IV over 60 minutes weekly**

14. DATES OF TREATMENT

**The patient began the investigational therapy on April 28, 2009, and received the last doses of temsirolimus and IMC-A12 on June 30, 2009 (Cycle 3, Day 8).**

15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1796 and using IMC-A12 = 218. There have been 19 other cases of renal failure, 52 other cases of pneumonitis, 20 other cases of death NOS, and 4 other cases of sudden death reported to the NCI through AdEERS as serious adverse events for temsirolimus; and 2 other cases of renal failure, 1 other cases of pneumonitis, 2 other cases of death NOS, and no other cases of sudden death reported to the NCI through AdEERS as serious adverse events for IMC-A12.**

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 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.**