

**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**  
**301-796-9845**

1. IND NUMBER <b>7921</b> <b>61010</b>	2. AGENT NAME <b>Bevacizumab (rhuMab VEGF)</b> <b>CCI-779 (temsirolimus, Torisel™)</b>	3. DATE <b>March 15, 2010</b>
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4. SPONSOR  
**Division of Cancer Treatment and Diagnosis, National Cancer Institute**

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>

8. PROTOCOL NUMBER (AE #)  
**E2804 (AE# 1561869)**

9. PATIENT IDENTIFICATION <b>28222</b>	10. AGE <b>56</b>	11. SEX <b>Male</b>
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12. DESCRIPTION OF ADVERSE EVENT  
**The patient is a 56-year-old male with renal cell adenocarcinoma who experienced grade 3 dehydration while on a phase 2 trial utilizing the investigational agents bevacizumab, temsirolimus and sorafenib. He began the investigational therapy on November 13, 2009, and received his last dose of bevacizumab and temsirolimus on February 19, 2010 (Cycle 4, Day 15). The patient was on an arm that did not include the sorafenib. On February 26, 2010, the patient called the clinic complaining of increased dyspnea and weakness. He was advised to go to the emergency department where the patient was admitted for further evaluation. The CT scan of the lung was negative for pulmonary emboli and no signs of progressive disease were noticed. 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 on Days 1, 8, 15, and 22**  
**Bevacizumab: 10 mg/kg IV over 30-90 minutes on Days 1 and 15**

14. DATES OF TREATMENT  
**The patient began the investigational therapy on November 13, 2009, and received the last dose of bevacizumab and temsirolimus on February 19, 2010 (Cycle 4, Day 15).**

15. ACCRUAL AND IND EXPERIENCE  
**Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1935; and bevacizumab 21,298. There have been 61 other cases of dehydration reported to the NCI through AdEERS as serious adverse events for temsirolimus and 526 other cases of dehydration reported to the NCI through AdEERS as serious adverse events for bevacizumab.**

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.**