

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 7921	2. AGENT NAME CCI-779 (temsirolimus, Torisel™) Bevacizumab (rhuMab VEGF)(704865)	3. DATE February 6, 2009
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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	6. PHONE NUMBER 301-496-1196
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8. PROTOCOL NUMBER (AE #)
E2804 (AE# 1034535)

9. PATIENT IDENTIFICATION 28100	10. AGE 61	11. SEX Male
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12. DESCRIPTION OF ADVERSE EVENT
The patient is a 61-year-old male with renal cell carcinoma who experienced a grade 3 dehydration while on a phase 2 trial utilizing the investigational agents bevacizumab and temsirolimus. He began the investigational therapy on December 15, 2008, and received his last doses of bevacizumab and temsirolimus on December 31, 2008 (Cycle 1, Day 17). His Day 15 treatment was held for 2 days due to nausea. On January 5, 2009, the patient presented to the clinic for Cycle 1, Day 22 of treatment and reported having severe diarrhea. His treatment was held and he was given IV hydration, Zofran®, and Imodium®. The following day he presented to the clinic for follow-up and due to his continuing bouts of diarrhea (up to 12 times per day), vomiting, and dehydration he was admitted to the hospital. He was given IV hydration, potassium repletion, and antidiarrheals. Stool and urine cultures were negative. His symptoms improved and he was discharged on January 8, 2009. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.

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 December 15, 2008, and received the last doses of bevacizumab and temsirolimus on December 31, 2008 (Cycle 1, Day 17).

15. ACCRUAL AND IND EXPERIENCE
Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1488 and for bevacizumab = 19652. There have been 54 other incidences of dehydration reported to the NCI through AdEERS as a serious adverse event for temsirolimus; and 424 other incidences 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.