

IND SAFETY REPORT: INITIAL WRITTEN REPORT**TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA****FAX: 301-796-9849****Division of Drug Oncology Products, Center For Drug Evaluation and Research, FDA****301-796-9845**

1. IND NUMBER 7921 61010	2. AGENT NAME Bevacizumab (rhuMAb VEGF) (704865) CCI-779 (temsirolimus, Torisel™)	3. DATE June 5, 2009
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4. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics 3, CTEP, DCTD, NCI L. Austin Doyle, MD-Senior Investigator for Targeted Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI	6. PHONE NUMBER 301-496-1196
	7. FAX NUMBER 301-402-0428

8. PROTOCOL NUMBER (AE #)
E2804 (1257729)

9. PATIENT IDENTIFICATION 28147	10. AGE 62	11. SEX Male
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12. DESCRIPTION OF ADVERSE EVENT
The patient was a 62-year-old male with renal cell adenocarcinoma who expired while on a phase 2 trial utilizing the investigational agents sorafenib, bevacizumab and temsirolimus. He had not started the sorafenib arm of the study. The patient began the investigational therapy on April 30, 2009, and received his last dose of bevacizumab on May 14, 2009 (Cycle 1, Day 15) and the last dose of temsirolimus on May 21, 2009 (Cycle 1, Day 22). On May 25, 2009 (Cycle 1, Day 26), the patient was found dead in his home by his friend. At this time, the cause of death is unknown. The result of an autopsy is pending. 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 April 30, 2009, and received the last dose of bevacizumab on May 14, 2009 (Cycle 1, Day 15) and the last dose of temsirolimus on May 21, 2009 (Cycle 1, Day 22).

15. ACCRUAL AND IND EXPERIENCE
Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21421 and for temsirolimus = 1665. There have been 15 other incidences of death NOS and 4 other incidences of sudden death reported to the NCI through AdEERS as serious adverse events for temsirolimus; and 52 other incidences of death NOS and 34 other incidences of sudden death reported to the NCI through AdEERS as serious adverse events for bevacizumab.

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 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.**