

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 7921 61010	2. AGENT NAME Bevacizumab (rhuMab VEGF) CCI-779 (temsirolimus, Torisel™)	3. DATE April 11, 2011
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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, Investigational Drug Branch, CTEP, DCTD, NCI 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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8a. PROTOCOL NUMBER (AE #) E2804 (AE# 1792675)	8b. AE GRADE: AE Grade 3: Left ventricular systolic dysfunction
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9. PATIENT IDENTIFICATION 28303	10. AGE 71 years	11. SEX Male
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12. DESCRIPTION OF ADVERSE EVENT
The patient is a 71 year-old male with clear cell renal adenocarcinoma who experienced a grade 3 left ventricular systolic dysfunction while on a phase 2 trial utilizing the investigational agents bevacizumab and temsirolimus. He began the investigational therapy on May 15, 2010, and received the last doses of bevacizumab and temsirolimus on March 25, 2011 (Cycle 10, Day 15). On March 31, 2011 (Cycle 10, Day 21), as per site, the patient experienced new onset of congestive heart failure, hyperkalemia, acute renal failure, and was admitted to the hospital for volume management. 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 May 15, 2010, and received the last doses of bevacizumab and temsirolimus on March 25, 2011 (Cycle 10, Day 15).

15. ACCRUAL AND IND EXPERIENCE
Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab=31,760 and temsirolimus=2,640. There have been 18 other cases of left ventricular systolic dysfunction reported to the NCI through AdEERS as serious adverse events for temsirolimus. Left ventricular systolic dysfunction is an expected event 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 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.