

**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**

**FAX: 301-796-9845**

1. IND NUMBER

**7921  
69896**

2. AGENT NAME

**Bevacizumab (rhuMab VEGF)  
Sorafenib (BAY 43-9006)**

3. DATE

**April 27, 2011**

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**

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6. PHONE NUMBER

**301-496-1196**

7. FAX NUMBER

**301-402-0428**

8a. PROTOCOL NUMBER (AE #)

**E2804 (AE# 1850786)**

8b. AE GRADE: AE

**Grade 5: Death not associated with CTCAE term: Death NOS**

9. PATIENT IDENTIFICATION

**28344**

10. AGE

**63 years**

11. SEX

**Male**

12. DESCRIPTION OF ADVERSE EVENT

**The patient was a 63-year-old male with clear cell renal cell adenocarcinoma who expired while on a phase 2 trial utilizing the investigational agents bevacizumab and sorafenib. He began the investigational therapy on November 3, 2010, and received the last dose of bevacizumab on January 12, 2011 (Cycle 3, Day 15) and the last dose of sorafenib on January 21, 2011 (Cycle 3, Day 24). On January 21, 2011 (Cycle 3, Day 24), the patient complained of dizziness, falling, and feelings of anxiety. At a follow-up visit on January 26, 2011, the patient complained of increased fatigue, dizziness, and transient confusion. A stat CT of the brain was unremarkable, and the lab results showed a BUN of 35 mg/dL (reference range 6-20 mg/dL) and a creatinine of 1.68 mg/dL (reference range 0.64-1.27 mg/dL). The study treatment was held and a follow-up visit in one week was scheduled. On February 3, 2011, the patient was unable to make the follow up visit because he was incoherent and unable to talk. On February 8, 2011, the site was informed that the patient had expired 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**

**Bevacizumab: 5 mg/kg IV over 30-90 minutes on Days 1 and 15**

**Sorafenib: 200 mg PO twice daily on Days 1-5, 8-12, 15-19, and 22-26**

14. DATES OF TREATMENT

**The patient began the investigational therapy on November 3, 2010, and received the last dose of bevacizumab on January 12, 2011 (Cycle 3, Day 15) and the last dose of sorafenib on January 21, 2011 (Cycle 3, Day 24).**

15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab=32,533 and sorafenib=6,679. There have been 164 other cases of death NOS and 58 other cases of sudden death reported to the NCI through AdEERS as serious adverse events for bevacizumab and 153 other cases of death NOS and 22 other cases of sudden death reported to the NCI through AdEERS as serious adverse events for sorafenib.**

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.**

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