

IND SAFETY REPORT: INITIAL WRITTEN REPORT**TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA****FAX: 301-796-9849**1. IND NUMBER
79212. AGENT NAME
Bevacizumab (rhuMAb VEGF)3. DATE
January 13, 20104. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute5. REPORTER'S NAME, TITLE, AND INSTITUTION
Kevin Conlon, MD-Senior Investigator for Investigational Therapeutics 3, CTEP, DCTD, NCI6. PHONE NUMBER
301-496-11967. FAX NUMBER
301-402-04288. PROTOCOL NUMBER (AE #)
CALGB-90601 (AE # 1070874)9. PATIENT IDENTIFICATION
11821110. AGE
6411. SEX
Male

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 64-year-old male with transitional cell carcinoma of the urothelial tract who suddenly expired while on a phase 3 trial utilizing the investigational agent bevacizumab/placebo in combination with cisplatin and gemcitabine. He began the first of the investigational therapy on November 18, 2009, and received the last dose of bevacizumab/placebo on December 16, 2009 (Cycle 2, Day 1), and the last doses of cisplatin and gemcitabine on January 6, 2010 (Cycle 3, Day 1). On January 6, 2010 (Cycle 3, Day 1), the bevacizumab/placebo was held due to symptomatic hypertension. On January 12, 2010, the patient's son left a message for the research staff informing them of the patient's death at home on January 11, 2010 (Cycle 3, Day 6). The staff has been unable to contact the patient's son. At this time, there is no other information about the cause of the patient's death. 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 = 21 days**
Bevacizumab/placebo 15 mg/kg IV over 30-90 minutes on Day 114. DATES OF TREATMENT **The patient began the investigational therapy on November 18, 2009, and received the last dose of bevacizumab/placebo on December 16, 2009 (Cycle 2, Day 1), and the last doses of cisplatin and gemcitabine on January 6, 2010 (Cycle 3, Day 1).**15. ACCRUAL AND IND EXPERIENCE **Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 24,655. There have been 48 other cases of sudden death and 67 other cases of death NOS reported to the NCI as serious adverse events through AdEERS for bevacizumab.**16. COMMENTS **The following was also administered:**
Cisplatin 70 mg/m² IV over 1 hour on Day 1 and Gemcitabine 1000 mg/m² IV over 30 minutes on Days 1 and 8 for Cycles 1-6.**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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