

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 7921	2. AGENT NAME Bevacizumab (rhuMab VEGF)	3. DATE June 21, 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		6. PHONE NUMBER 301-496-1196
		7. FAX NUMBER 301-402-0428
8a. PROTOCOL NUMBER (AE #) CALGB-90601 (AE # 1546701)	8b. AE GRADE: AE Grade 5: Sudden death NOS	
9. PATIENT IDENTIFICATION 126292	10. AGE 63 yrs	11. SEX Male
12. DESCRIPTION OF ADVERSE EVENT The patient was a 63-year-old male with transitional cell carcinoma of the urothelial tract who expired while on a phase 3 trial utilizing the investigational agent bevacizumab/placebo in combination with cisplatin and gemcitabine. He began the first dose of the investigational therapy on June 1, 2011, and received the first and only dose of bevacizumab/placebo and cisplatin on June 1, 2011 (Cycle 1, Day 1), and the last dose of gemcitabine on June 8, 2011 (Cycle 1, Day 8). On June 8, 2011 (Cycle 1, Day 8), the patient presented to the clinic to receive scheduled dose of gemcitabine as per protocol. He complained of constipation and was later hospitalized for rehydration and palliative care. A CT scan of the abdomen and pelvis revealed generalized dilation of the colon, right colon more than the left colon and the appearance of the large bowel was compatible with an ileus or possibly colonic pseudo-obstruction. This was followed by an abdominal obstruction series with posterior-anterior chest X-ray on June 10, 2011, which revealed markedly dilated gastrointestinal tract with air levels, predominantly involving the small bowel and the right colon, probably related to the ileus. On June 11, 2011 (Cycle 1, Day 11), his WBC was 2.6 K/μL (reference level: 4.0-11.0 K/μL) and his platelet count was 87 K/μL (reference level: 160-375 K/μL). Two units of platelets were administered on June 16, 2011. On June 17, 2011 at 2:00 PM, the site was notified from the hospital floor that the patient was taken for emergency surgery and expired during surgery. No further details are available at this moment. 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 1		
14. DATES OF TREATMENT The patient began the first dose of the investigational therapy on June 1, 2011, and received the first and only dose of bevacizumab/placebo on June 1, 2011 (Cycle 1, Day 1).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 33,125. There have been 167 other cases of death NOS and 57 cases of sudden death reported to the NCI as serious adverse events through AdEERS for bevacizumab.		
16. COMMENTS The following was also administered: Cisplatin 70 mg/m² IV 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.		

0002