

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 March 4, 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 #) GOG-0252 (AE# 1694292)	8b. AE GRADE: AE Grade 5: Infection with normal ANC or grade 1 or 2 neutrophils: Blood Grade 3: Infection with normal ANC or grade 1 or 2 neutrophils: Peritoneal cavity	
9. PATIENT IDENTIFICATION 835-0252-006	10. AGE 69 yrs	11. SEX Female
12. DESCRIPTION OF ADVERSE EVENT The patient was a 69-year-old female with stage III ovarian carcinoma who developed a grade 3 peritoneal cavity infection and subsequently expired from blood infection while on a phase 3 trial utilizing the investigational agent bevacizumab in combination with paclitaxel and carboplatin. The patient had a total abdominal hysterectomy and bilateral salpingo-oophorectomy on August 9, 2010. Post surgery, persistent fluid collections in retroperitoneum and pelvis were revealed by CT scans. She began the first course of the investigational therapy on September 7, 2010 and received the last doses of bevacizumab and carboplatin on December 30, 2010 (Cycle 6, Day 1), and the last dose of paclitaxel on January 12, 2011 (Cycle 6, Day 14). On January 16, 2011 (Cycle 6, Day 18), the patient was admitted to the hospital with progressive neuropathy, weakness, and anemia. On January 17, 2011, an abdomen and pelvis CT scan was performed and compared with a prior CT scan; it revealed increased quantity of air and diminished fluid collection in the left retroperitoneum, and increased fluid collection close to the infusion catheter in the right hemipelvis. The patient was started on vancomycin. On January 19, 2011, a drainage catheter was placed into the retroperitoneal fluid and gas collection of the left. The fluid culture revealed moderate growth of <i>Staphylococcus aureus</i> , <i>Enterobacter cloacae</i> , and <i>Enterococcus</i> species. On January 21, 2011, the vascular access port and intraperitoneal port were removed surgically. One day later, an abdominal X-ray showed free air suspicious for a ruptured viscus, which was further evaluated by CT scan and revealed pneumoperitoneum, but no definite source of the free air. Later on, routine drainage cultures revealed heavy growth of alpha hemolytic <i>Streptococcus</i> and gram positive cocci; anaerobic drainage culture revealed moderate growth of <i>Prevotella</i> species. On January 27, 2011, the patient made the decision to stop medical intervention. Shortly thereafter she became unresponsive. The patient was then transferred to hospice and died on January 29, 2011. 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 = 3 Weeks: Phase A (Cycles 1-6): Bevacizumab: 15 mg/kg IV over 30-90 minutes on Day 1, beginning with Cycle 2; Phase B (Cycles 7-22): Bevacizumab: 15 mg/kg IV over 30-90 minutes on Day 1		
14. DATES OF TREATMENT The patient began the investigational therapy on September 7, 2010, and received the last dose of bevacizumab on December 30, 2010 (Cycle 6, Day 1).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 31,495. Infections are known events for bevacizumab.		
16. COMMENTS Also administered on this protocol: Phase A (Cycle 1-6): Paclitaxel: 80 mg/m ² IV over 1 hour on Days 1, 8, and 15; Carboplatin: AUC 6 IP on Day 1.		
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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