

## 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 <b>7921</b>	2. AGENT NAME <b>Bevacizumab (rhuMAb VEGF)</b>	3. DATE <b>February 18, 2011</b>
4. SPONSOR <b>Division of Cancer Treatment and Diagnosis, National Cancer Institute</b>		
5. REPORTER'S NAME, TITLE, AND INSTITUTION <b>Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics 3, Investigational Drug Branch, CTEP, DCTD, NCI</b>		6. PHONE NUMBER <b>301-496-1196</b>
		7. FAX NUMBER <b>301-402-0428</b>
8a. PROTOCOL NUMBER (AE #) <b>GOG-0252 (AE# 1523186)</b>	8b. AE GRADE: AE <b>Grade 5: Infection with unknown ANC: Blood Grade 4: Infection – Other: Necrotic skin infection</b>	
9. PATIENT IDENTIFICATION <b>835-0252-010</b>	10. AGE <b>73 yrs</b>	11. SEX <b>Female</b>
12. DESCRIPTION OF ADVERSE EVENT <b>The patient was a 73-year-old female with stage III-C serous adenocarcinoma of the fallopian tube who developed a grade 4 necrotic skin infection and died while on a phase 3 trial utilizing the investigational agent bevacizumab in combination with paclitaxel and carboplatin. She began the first course of the investigational therapy on October 18, 2010 and received the last doses of bevacizumab, paclitaxel, and carboplatin on January 12, 2011 (Cycle 5, Day 1). On January 12, 2011 (Cycle 5, Day 1), the patient presented to the office for treatment and complained of multiple areas of progressive skin breakdown, persistent diarrhea, progressive weakness, decreased appetite, and failure to thrive. She was found to have lost 6 kgs from a weight of 65.4 kg on October 22, 2010 (Cycle 1, Day 5). The patient had superficial lesions on the abdomen, coccyx, and hands. She was treated as planned and admitted to the hospital for failure to thrive and anemia. The patient was started on IV fluids and transfused with 3 units of packed red blood cells. On January 14, 2011 (Cycle 5, Day 3), her WBC was 0.3 K/mm<sup>3</sup> and her lactic acid was 3.4mg/dL (reference range: 0.5-2.2 mg/dL). The patient became increasingly less arousable and developed atrial fibrillation. She was transferred to the ICU for closer monitoring. On January 15, 2011 (Cycle 5, Day 4), infectious disease diagnosed the patient with necrotic ulcers on her posterior right thigh and sacral area, nonhealing percutaneous endoscopic gastrostomy tube site, and ascites. A chest X-ray revealed pulmonary congestion with perihilar edema, marginal edema as well as increasing lower lung opacities. Blood cultures were positive for <i>Escherichia coli</i>. She was started on vancomycin, Invanz<sup>®</sup>, Diflucan<sup>®</sup>, and the peritoneal fluid was aspirated. The patient's condition deteriorated and she died later that day. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.</b>		
13. DOSE, ROUTE, AND SCHEDULE <b>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.</b>		
14. DATES OF TREATMENT <b>The patient began the investigational therapy on October 18, 2010, and received the last dose of bevacizumab on January 12, 2011 (Cycle 5, Day 1).</b>		
15. ACCRUAL AND IND EXPERIENCE <b>Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 31,448. Infections are known events for bevacizumab.</b>		
16. COMMENTS <b>Also administered on this protocol: Phase A (Cycle 1-6): Paclitaxel: 80 mg/m<sup>2</sup> IV over 1 hour on Days 1, 8, and 15; Carboplatin: AUC 6 IV on Day 1.</b>		
<b>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.</b>		

0002