

**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  
**May 20, 2009**4. SPONSOR  
**Division of Cancer Treatment and Diagnosis, National Cancer Institute**5. REPORTER=S NAME, TITLE, AND INSTITUTION  
**Kevin Conlon, MD-Senior Investigator for Investigational Therapeutics III, Investigational Drug Branch, CTEP, DCTD, NCI**6. PHONE NUMBER  
**301-496-1196**7. FAX NUMBER  
**301-402-0428**8. PROTOCOL NUMBER (AE #)  
**CALGB-40502 (AE # 1192440)**9. PATIENT IDENTIFICATION  
**115173**10. AGE  
**70**11. SEX  
**Female**

12. DESCRIPTION OF ADVERSE EVENT

**The patient was a 70-year-old female with invasive breast carcinoma who experienced a grade 5 peritoneal cavity infection, a grade 4 GI perforation of the colon, a grade 4 GI abscess while on a phase 3 study using the investigational agent bevacizumab in combination with nab-paclitaxel. She began her first course of treatment on March 31, 2009, and received the last doses of bevacizumab and nab-paclitaxel on April 14, 2009, (Cycle 1, Day 15). The patient presented to the emergency room on April 27, 2009 (Cycle 1, Day 28), with severe abdominal pain. A CT scan of the abdomen and pelvis showed free intraperitoneal air, a large abscess in the pelvis, free fluid in the abdomen, diverticulosis, and a large hiatal hernia. An emergency surgical consult was ordered. Upon a physical examination, the patient was tachycardic, clammy, sweaty, and short of breath while on oxygen. The trunk of her body was mottled, and her extremities were cool. Her abdomen was distended and tender. On April 27, 2009, the patient was taken to surgery where the following procedures were performed: sigmoid colon resection, colostomy and Hartmann pouch procedure, and JP drain placement into the pelvic cavity where the abscess was located. She was then admitted to the intensive care unit. While recovering, the patient developed respiratory failure and was placed on BiPAP. On May 4, 2009 (Cycle 1, Day 34), the patient returned to her room after having a repeat CT scan, went into cardiac arrest and expired. No resuscitative efforts were performed as the patient was a DNR/DNI. Additional information has been requested from the investigational site. There is a reasonable possibility that the adverse event may have been caused by the drug.**

13. DOSE, ROUTE, AND SCHEDULE  
**Bevacizumab 10 mg/kg IV over 30-90 min on Days 1 and 15**14. DATES OF TREATMENT  
**The patient began the investigational therapy on March 31, 2009, and received the last dose of bevacizumab on April 14, 2009 (Cycle 1, Day 15).**15. ACCRUAL AND IND EXPERIENCE  
**The number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21394. There have been 2 GI abscess incidences reported to the NCI through AdEERS as serious adverse events for bevacizumab. Infection of the peritoneal cavity and GI perforation are known to be associated with the investigational agent, bevacizumab.**16. COMMENTS **The following was also administered:**  
**Nab-paclitaxel 150 mg/m<sup>2</sup> IV over 30 min on Days 1, 8, and 15 (last administered on April 14, 2009).**

**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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