

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 13, 2009
4. SPONSOR Division of Cancer Treatment and Diagnosis, National Cancer Institute		
5. REPORTER'S NAME, TITLE, AND INSTITUTION Kevin Conlon, MD – Senior Investigator, Investigational Therapeutic III, Investigational Drug Branch, CTEP, DCTD, NCI		6. PHONE NUMBER 301-496-1196
		7. FAX NUMBER 301-402-0428
8. PROTOCOL NUMBER (AE #) E5103 (1950915)		
9. PATIENT IDENTIFICATION 50874	10. AGE 67	11. SEX Female
12. DESCRIPTION OF ADVERSE EVENT The patient is a 67-year-old female with invasive breast cancer who developed grade 3 hemolysis while on a phase 3 study utilizing the investigational agent bevacizumab/placebo in combination with doxorubicin, cyclophosphamide, pegfilgrastim, and paclitaxel. She began her first course of the investigational therapy on August 27, 2008, and received the last dose of bevacizumab/placebo on March 4, 2009, (Cycle 10, Day 1), the last doses of doxorubicin and cyclophosphamide on October 22, 2008 (Cycle 4, Day 1), the last dose of pegfilgrastim on October 23, 2008 (Cycle 4, Day 2), and the last dose of paclitaxel on December 17, 2008 (Cycle 6, Day 8). The study drug was held at various intervals due to other adverse events. On April 12, 2009, the patient presented to the emergency room of the local hospital via ambulance with complaints of chest pain. A cardiac evaluation showed no coronary artery disease or acute coronary event. The patient was dehydrated and laboratory report showed a urinary tract infection. The patient was started on IV fluids and IV antibiotic therapy to which she responded. She was subsequently transferred to another facility for admission and further management of her symptoms. On admission, the patient appeared chronically ill, confused, and lethargic with a pulse of 102 bpm. On April 13, 2009, her hemoglobin decrease to 9.7 g/dL (reference range: 11.7-16.1 g/dL) from a value of 13.6 g/dL on the previous day and urine cultures grew <i>E. coli</i>. She received 2 units of PRBCs, and was continued on IV fluid and antibiotic therapy. The patient's condition gradually improved, her hemoglobin recovered to 11.6 g/dL, and she was discharged home on April 24, 2009. 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 Cycles 1-4, Cycle = 14 days: Bevacizumab/Placebo 10 mg/kg IV over 30-90 minutes on Day 1; Cycles 5-8, Cycle = 21 days: Bevacizumab/Placebo 15 mg/kg IV over 30-90 minutes on Day 1; Cycle 9-18, Cycle = 21 days: Bevacizumab/Placebo 15 mg/kg IV over 30-90 minutes on Day 1 with concurrent hormonal therapy		
14. DATES OF TREATMENT The patient started the investigational therapy on August 27, 2008, and received the last dose of bevacizumab/placebo on March 4, 2009 (Cycle 10, Day 1).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21,344. There have been two other incidences of hemolysis reported to the NCI through AdEERS as serious adverse events for bevacizumab.		
16. COMMENTS The following was also administered: Cycles 1-4: Doxorubicin: 60 mg/m² IVP on Day 1 and Cyclophosphamide: 600 mg/m² IV over 20-30 minutes on Day 1; Last administered on October 22, 2008 (Cycle 4, Day 1). Pegfilgrastim: 6 mg SQ on Day 2; Last administered on October 23, 2008 (Cycle 4, Day 2). Cycles 5-8: Paclitaxel: 80 mg/m² IV over 1 hour on Days 1, 8, and 15; Last administered on December 17, 2008 (Cycle 6, Day 8).		
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.		