

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
79212. AGENT NAME
Bevacizumab (rhuMAb VEGF)3. DATE
April 17, 20094. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute5. REPORTER=S NAME, TITLE, AND INSTITUTION
**Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics
3, CTEP, DCTD, NCI**6. PHONE NUMBER
301-496-11967. FAX NUMBER
301-402-04288. PROTOCOL NUMBER (AE #)
E5103 (AE # 1314985)9. PATIENT IDENTIFICATION
5137910. AGE
5111. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 51-year-old female with invasive breast carcinoma who experienced a sudden death while on a double-blind phase 3 study utilizing the investigational agent bevacizumab/placebo in combination with doxorubicin, cyclophosphamide, and paclitaxel. She began her first course of treatment on November 20, 2008, and received her last dose of bevacizumab/placebo on February 5, 2009 (Cycle 6, Day 1). On February 7, 2009 (Cycle 6, Day 3), the patient developed sudden difficulty breathing and midline chest pain. She became quickly unresponsive and CPR was initiated by EMS. A combitube and left external jugular line were placed. The patient's initial cardiac rhythm was bradycardia with a heart rate in the 20s, which then changed to ventricular fibrillation and then to asystole. Upon arrival to the ED, the patient remained unresponsive, and was unable to be resuscitated. An autopsy was not performed. 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 10 mg/kg IV over 30-90 minutes on Day 1 (Cycles 1-4);
Bevacizumab/Placebo 15 mg/kg IV over 30-90 minutes on Day 1 (Cycles 5-8)14. DATES OF TREATMENT **The patient started the investigational therapy on November 20, 2008, and received the last dose of bevacizumab/placebo on February 5, 2009 (Cycle 6, Day 1).**15. ACCRUAL AND IND EXPERIENCE **Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 20360. There have been 35 other incidences of sudden death and 53 other incidences of death NOS 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, cyclophosphamide: 600 mg/m² IV over 20-30 min on Day 1 (last administered on January 2, 2009 [Cycle 4, Day 2]).
Cycles 5-8: paclitaxel: 80 mg/m² IV over 1 hour on Days 1, 8, and 15 (last administered on February 5, 2009 [Cycle 6, 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.**

0002