

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 22, 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 3, CTEP, DCTD, NCI****6. PHONE NUMBER
301-496-1196****7. FAX NUMBER
301-402-0428****8. PROTOCOL NUMBER (AE #)
E5103 (AE # 1333814)****9. PATIENT IDENTIFICATION
52252****10. AGE
32****11. SEX
Female****12. DESCRIPTION OF ADVERSE EVENT**

The patient is a 32-year-old female with invasive breast carcinoma who developed a grade 4 cardiopulmonary arrest, cause unknown, while on a phase 3 study using the investigational agent bevacizumab/placebo in combination with doxorubicin, cyclophosphamide, and paclitaxel. She began her first course of treatment on April 3, 2009, and received the first and the last dose of bevacizumab/placebo on that drug (Cycle 1, Day 1). On April 17, 2009 (Cycle 1, Day 15), the patient presented to the ER with chest pain, palpitations. The patient was seated in the chair and had her port accessed but not yet given medications, she said "faint, faint", became pale and passed out and was taken to the ER. Apparently, the patient developed rapid heart rate which was followed by a period of asystole. She had atrial fibrillation with a rapid ventricular response. Upon physical examination, the patient had a normal mood, affect, and behavior. Her judgment and thought content were normal. She went home on April 17, 2009. Additional information has been requested. There is a reasonable possibility that the experience may have been caused by the drug.

**13. DOSE, ROUTE, AND SCHEDULE Cycle = 14 days
Bevacizumab/Placebo 10 mg/kg IV over 30-90 minutes on Day 1 (Cycles 1-4)****14. DATES OF TREATMENT The patient started the investigational therapy on April 3, 2009, and received the first and the last dose of bevacizumab/placebo on that drug.****15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21394. There have been 3 other incidences of cardiopulmonary arrest, cause unknown reported to the NCI through AdEERS as serious adverse events for bevacizumab.****16. COMMENTS : 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
Filgrastim: 5 mcg/kg SQ on Days 2-11 OR
Pelfilgrastim: 6 mg on Day 2****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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