

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 13, 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, NCI6. PHONE NUMBER
301-496-11967. FAX NUMBER
301-402-04288. PROTOCOL NUMBER (AE #)
E5103 (AE # 1809441)9. PATIENT IDENTIFICATION
5123610. AGE
4511. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 45-year-old female with invasive breast carcinoma who developed a grade 2 pneumothorax 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 October 27, 2008, and received the last dose of bevacizumab/placebo on February 24, 2009 (Cycle 8, Day 1). On February 28, 2009 (Cycle 8, Day 5), the patient presented to the ER after being awakened by left-sided radiating chest pain. Her oxygen saturation was 96% on room air, blood pressure 112/80 mm/Hg, respiratory rate 20 per minute, pulse 114 bpm, and temperature was 97.6°F. Upon physical examination, the patient's lung sounds were decreased in the left base. A chest x-ray revealed a large left-sided apical pneumothorax and atelectasis, and a chest tube was placed. The patient was then admitted to the hospital. On March 5, 2009 (Cycle 8, Day 10), the patient's chest tube was removed. A portable chest x-ray was performed afterwards, which revealed no evidence of a pneumothorax and minimal basilar atelectasis. The patient remains in the hospital for treatment of left herpes zoster ophthalmicus, which developed on the day of her admission. 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 = 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 October 27, 2008, and received the last dose of bevacizumab/placebo on February 24, 2009 (Cycle 8, Day 1).**15. ACCRUAL AND IND EXPERIENCE **Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 19819. There have been 14 other incidences of pneumothorax 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
Cycles 5-8: paclitaxel: 80 mg/m² IV over 1 hour on Days 1, 8, and 15 (last administered February 24, 2009 (Cycle 8, 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.**

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