

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
September 17, 20104. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute5. REPORTER'S NAME, TITLE, AND INSTITUTION
Kevin Conlon, MD-Senior Investigator for Investigational Therapeutics 3, Investigational Drug Branch, CTEP, DCTD, NCI6. PHONE NUMBER
301-496-11967. FAX NUMBER
301-402-04288a. PROTOCOL NUMBER (AE #)
CALGB-40502 (AE# 1659292)8b. AE GRADE: AE
Grade 5: Adult Respiratory Distress Syndrome (ARDS)9. PATIENT IDENTIFICATION
12144410. AGE
80 yrs11. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient was an 80-year-old female with invasive breast carcinoma who experienced grade 5 Adult Respiratory Distress Syndrome (ARDS) while on a phase 3 study using the investigational agent bevacizumab and nab-paclitaxel. She began her first course of treatment on July 1, 2010, and this was her only dose of bevacizumab. The patient received the last dose of nab-paclitaxel on July 8, 2010 (Cycle 1, Day 8). On July 12, 2010 (Cycle 1, Day 12), the patient presented to the ER with a 2 to 3-day history of worsening dyspnea, cough, and generalized weakness. She was hypoxic with decreased breath sounds in both lung bases and an oxygen saturation of 52% on room air. The patient was started on oxygen via 100% nonrebreather mask which increased her oxygen saturation to 88%. Chest X-ray showed bilateral pleural effusions with atelectasis. She was admitted to the ICU, started on IV Levaquin[®] and ceftriaxone. Her DNR status was no intubation (only cardiac medications). The patient was also given aggressive nebulizer treatment, Lasix[®], and Lovenox[®]. On July 13, 2010 (Cycle 1, Day 13), a CT scan of the chest confirmed large bilateral pleural effusions with associated atelectasis throughout both lungs. The patient underwent left thoracentesis which improved her breathing. On July 15, 2010 (Cycle 1, Day 15), the patient developed bilateral pneumothoraces which was felt to be more related to her cancer. Bilateral chest tubes were placed and the chemotherapy was held. On July 19, 2010, a bronchoscopy with bronchoalveolar lavage showed patent bronchi without any endobronchial lesions. Mucus plugs were aspirated. On July 21, 2010, following a pleurodesis to stop drainage from the left chest tube, the patient became hypoxic requiring 24 hours of mechanical ventilation. Her condition improved and she was transferred to the floor on oxygen by nasal cannula. A repeat bronchoscopy to remove mucus plugging was successfully performed on August 2, 2010. On August 3, 2010, the patient received and tolerated chemotherapy. On August 4, 2010, the patient developed respiratory distress and morphine was given for comfort. She died later that day. Additional information has been requested from the site. There is a reasonable possibility that the experience may have been caused by the drug.

13. DOSE, ROUTE, AND SCHEDULE

Cycle: 28 Days; Bevacizumab: 10 mg/kg IV over 30-90 minutes on Days 1 and 15

14. DATES OF TREATMENT

The patient started the investigational therapy on July 1, 2010, and received her first and only dose of bevacizumab.

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 28,700. There have been 15 other cases of ARDS reported to the NCI through AdEERS as serious adverse events for bevacizumab.

16. COMMENTS Also administered on this protocol:

Nab-paclitaxel: 150 mg/m² IV over 30 minutes on Days 1, 8, and 15**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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