

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 18, 2011

4. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION
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6. PHONE NUMBER
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8a. PROTOCOL NUMBER (AE #)
GOG-0252 (AE# 1173562)

8b. AE GRADE: AE
Grade 5: Sudden death

9. PATIENT IDENTIFICATION
075-0252-014

10. AGE
50 yrs

11. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 50-year-old female with stage III ovarian epithelial cancer who suddenly expired while on a phase 3 trial utilizing the investigational agent bevacizumab in combination with paclitaxel and carboplatin. She began the first course of the investigational therapy on August 31, 2010 and received the last doses of bevacizumab, paclitaxel, and carboplatin on January 4, 2011 (Cycle 6, Day 1). The patient was hospitalized and treated with antibiotics for pneumonia from January 13-21, 2011. Her condition improved by the time of the discharge. On March 11, 2011 (Cycle 6, Day 67), the patient fell at home and went into asystole. Cardiopulmonary resuscitation was performed by her family member; she was then transported to the emergency room (ER) where she was intubated and resuscitated. During physical examination in ER, she was not responsive; she had no fever and her lungs were clear; her pulse returned and she had sinus tachycardia; her systolic blood pressure was kept around 120 mmHg with the application of dopamine. The laboratory results revealed troponin I level of 0.8 ng/mL (reference range: 0-0.03 ng/mL), pH < 6.8 (reference range: 7.35-7.45), PCO₂ of 78 mmHg (reference range: 35-45 mmHg), PO₂ of 54 mmHg (reference range: 80-100 mmHg), and D-dimer of 3.1 mg/L (reference range: 0.5-2.1 mg/L). A chest X-ray showed a left retrocardiac infiltrate, but the remainder of the lungs was clear and the heart was within normal limits. Noncontrast CT scan of the brain was normal and there was no evidence of acute hemorrhage, mass lesion, or findings which suggested acute infarction. The patient never regained consciousness and she passed away on March 12, 2011. Her blood culture results were not significant. The cause of her death was considered cardiac arrest. 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

Cycle = 3 Weeks: Phase A (Cycles 1-6): Bevacizumab: 15 mg/kg IV over 30-90 minutes on Day 1, beginning with Cycle 2; Phase B (Cycles 7-22): Bevacizumab: 15 mg/kg IV over 30-90 minutes on Day 1

14. DATES OF TREATMENT

The patient began the investigational therapy on August 31, 2010, and received the last dose of bevacizumab on January 4, 2011 (Cycle 6, Day 1).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 32,949. There have been 110 other cases of deaths reported to the NCI as serious adverse events through AdEERS for bevacizumab.

16. COMMENTS **Also administered on this protocol: Phase A (Cycle 1-6): Paclitaxel: 80 mg/m² IV over 1 hour on Days 1, 8, and 15; Carboplatin: AUC 6 IV on 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.