

IND SAFETY REPORT: FOLLOW-UP #1TO: *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
July 13, 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, CTEP, DCTD, NCI6. PHONE NUMBER
301-496-11967. FAX NUMBER
301-402-04288a. PROTOCOL NUMBER (AE #)
GOG-0252 (AE# 1190366)8b. AE GRADE: AE
Grade 5: Sudden Death9. PATIENT IDENTIFICATION
023-0252-00110. AGE
50 yrs11. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 50-year-old female with ovarian epithelial cancer who suddenly died while on a phase 3 trial utilizing the investigational agent bevacizumab in combination with paclitaxel and cisplatin. She began the first course of the investigational therapy on January 28, 2010. The patient received bevacizumab, paclitaxel, and cisplatin until Cycle 3, when she was switched to carboplatin due to renal toxicity. She received the last dose of cisplatin on February 19, 2010 (Cycle 2, Day 2), the last doses of bevacizumab and carboplatin on May 6, 2010 (Cycle 5, Day 1), and the last dose of paclitaxel on May 13, 2010 (Cycle 5, Day 8). The patient did not receive bevacizumab on Cycle 3 due to uncontrolled blood pressure and on Cycle 4 due to inadequate renal function. On April 19, 2010, she was evaluated and diagnosed with sleep apnea hypopnea syndrome (SAHS), REM sleep behavior disorder, and obesity. The patient was admitted to the hospital on April 27, 2010, for pneumonia, was treated with broad spectrum antibiotics, and she was discharged on May 1, 2010. On May 4, 2010, the patient underwent a clinical polysomnography, and it was recommended that she start using bi-PAP at a pressure of 8 cm H₂O which she did not use. On May 18, 2010, the patient presented to the clinic for evaluation of acute and chronic renal insufficiency with microalbuminuria, anemia, and hypertension. Her blood pressure was 166/102 mmHg and she reported feeling much better with minimal dyspnea on exertion. The patient was advised to follow-up in 3 months. On May 24, 2010, the patient's mother called to report that the patient was shaking and jerking, acting confused, and sleeping more than usual. The patient was coherent and denied headache, vision changes, fever, and injury. A neurological exam was scheduled for May 28, 2010. On May 25, 2010, the patient was found dead at home by her family members. The family declined an autopsy. 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 January 28, 2010, and received the last dose of bevacizumab on May 6, 2010 (Cycle 5, Day 1).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 26,872. There have been 53 other cases of sudden death and 69 other cases of death NOS 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: 135 mg/m² IV over 3 hours on Day 1; Cisplatin: 75 mg/m² IP on Day 2; and Paclitaxel: 60 mg/m² IP on Day 8. Carboplatin: AUC 5 IV over 30 minutes on Day 1 starting on Cycle 3.

FOLLOW-UP: BASED UPON FURTHER INVESTIGATION, THE SENIOR INVESTIGATOR HAS DECIDED THAT THIS EVENT IS EITHER EXPECTED OR NOT SERIOUS AND THUS DOES NOT REQUIRE EXPEDITED REPORTING.

0002