

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

June 23, 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-0086P (AE# 1793638)

8b. AE GRADE: AE

Grade 5: Death NOS

9. PATIENT IDENTIFICATION

073-0086P-015

10. AGE

55 years

11. SEX

Female

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 55-year-old female with Stage IV, Grade 2 endometrial adenocarcinoma who died while on a phase 2 trial utilizing the investigational agent bevacizumab in combination with paclitaxel and carboplatin. She began her first course of treatment on September 16, 2010, and received the last doses of bevacizumab, paclitaxel, and carboplatin on December 30, 2010 (Cycle 6, Day 1). On January 16, 2011(Cycle 6, Day 17), the patient was found unresponsive by her husband. He called EMS and initiated CPR. Emergency medical personnel made several unsuccessful attempts to intubate the patient. She was transported to the hospital emergency room where she expired. The patient's D dimer was > 5000 ng/ml (reference range 105-400 ng/ml), and her potassium was 7.5 mmol/L (reference range 3.5-5.1 mmol/L). The coroner's report listed the cause of death as pulmonary embolism. No autopsy was performed. A CT scan from November 15, 2010 (Cycle 3, Day 20), showed: pelvic and retroperitoneal lymph node metastases; local invasion of the sigmoid colon, cecum, and terminal ileum; omental metastases; and likely bilateral pleural metastatic disease. Other current medical problems included obesity, hypertension, and anemia. On December 30, 2010, her blood pressure was noted to be 162/81 mm/Hg and her pulse was 121 bpm, and she was started on nifedipine. 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 = 21 days:

Bevacizumab: 15 mg/kg IV over 30-90 minutes on Day 1

14. DATES OF TREATMENT

The patient began the investigational therapy on September 16, 2010, and received the last doses of bevacizumab, paclitaxel, and carboplatin on December 30, 2010 (Cycle 6, Day 1).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 33,125. There have been 167 cases of death NOS and 57 cases of sudden death reported to the NCI through AdEERS as serious adverse events for bevacizumab.

16. COMMENTS

Also administered on this protocol:

Paclitaxel: 175 mg/m² IV over 3 hours on Day 1 X 6 cycles

Carboplatin: AUC = 6 IV over 30 minutes on Day 1 X 6 cycles.

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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