

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 7, 2009

4. SPONSOR

Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION

Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics 3, Investigational Drug Branch, CTEP, DCTD, NCI

6. PHONE NUMBER

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8. PROTOCOL NUMBER (AE #)

GOG-0218 (1293580)

9. PATIENT IDENTIFICATION

046-0218-051

10. AGE

75

11. SEX

Female

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 75-year-old female with ovarian epithelial cancer who died of an opportunistic infection while on a phase 3 study utilizing the investigational agent bevacizumab/placebo in combination with carboplatin and paclitaxel. She began her first course of the investigational therapy on January 13, 2009, and received the last doses of bevacizumab/placebo, carboplatin, and paclitaxel on April 21, 2009 (Cycle 5, Day 1). On April 23, 2009 (Cycle 5, Day 3), the patient presented to the emergency room with multiple complaints including nausea and vomiting since her last treatment, and the inability to maintain any oral intake, a 2-week history of cough which had worsen over the past 2 days, dyspnea with episodes of emesis and coughing, extreme fatigue with the inability to ambulate independently over the past 2 days, increased abdominal distension from her baseline over the past 2-4 days, abdominal and severe back pain, and urinary incontinence. She described the emesis as dark brown to black but denied a coffee ground character or blood in the emesis. On physical examination, there were bilateral coarse breath sounds with decreased breathe sounds in the bases, her abdomen was distended, full, and had a positive fluid wave indicating ascites, and there was 2+ pitting edema of the knees and lower extremities. The patient reported receiving 2 units of PRBCs the previous day for anemia. Her vital signs were normal with an oxygen saturation of 92% on room air. The patient was started on 2 liters of oxygen, given Zofran[®] and morphine for pain, and admitted to the hospital for further evaluation and treatment. During the hospital course, the patient developed pancytopenia and fever; and ultimately expired of sepsis on April 26, 2009 (Cycle 5, Day 6). 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 = 21 Days****Bevacizumab/Placebo 15 mg/kg IV on Day 1 starting with Cycle 2 x 5 cycles**

14. DATES OF TREATMENT

The patient began the investigational therapy on January 13, 2009, and received the last doses of bevacizumab/placebo, carboplatin, and paclitaxel on April 21, 2009 (Cycle 5, Day 1).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21,331. There have been 7 other incidences of opportunistic infections reported to the NCI through AdEERS as serious adverse events for bevacizumab.16. COMMENTS **The following was also administered:****Paclitaxel: 175 mg/m² IV over 3 hours on Day 1 x 6 cycles, every 21 days****Carboplatin: AUC 6 IV over 30 minutes on Day 1 x 6 cycles, every 21 days****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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