

## 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 5, 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 III, Investigational Drug Branch, CTEP, DCTD, NCI**

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7. FAX NUMBER  
**301-402-0428**

8. PROTOCOL NUMBER (AE #)  
**GOG-0218 (AE # 1836781)**

9. PATIENT IDENTIFICATION  
**004-0218-022**

10. AGE  
**54**

11. SEX  
**Female**

12. DESCRIPTION OF ADVERSE EVENT  
**The patient is a 54-year-old female with fallopian tube carcinoma who experienced grade 3 left hydronephrosis, kidney hemorrhage, and hemoglobin while on a phase 3 study using the investigational agent bevacizumab/placebo in combination with paclitaxel and carboplatin. She began her first course of treatment on December 8, 2008, and received the last doses of bevacizumab/placebo, paclitaxel, and carboplatin on March 25, 2009, (Cycle 5, Day 1). The patient presented to the emergency room on March 27, 2009 (Cycle 5, Day 3), with complaints of hematuria and left lower quadrant pain that was accompanied by nausea and vomiting. A CT scan of the abdomen and pelvis with contrast showed a mild enlargement of the left kidney with perinephric stranding and mild dilatation of the mid ureters. Her urinalysis was positive for blood and white blood cells. Laboratory results showed: glucose 142 mg/dl (reference range: 70-110 mg/dl), AST 74 u/l (reference range: 15-37 u/l), ALT 60 u/l (reference range: ≤ 31 u/l), and total bilirubin 1.6 mg/dl (reference range: 0.0-1.0 mg/dl). On March 30, 2009 (Cycle 5, Day 6), a cystoscopy was performed which showed bilateral renal bleeding. A 2.5 cm neovascularity on the posterior wall of the bladder was biopsied and found to be benign. The patient received antibiotics as well as transfusions and was discharged from the hospital on April 1, 2009 (Cycle 5, Day 8). Additional information has been requested from the investigational site. There is a reasonable possibility that the adverse event may have been caused by the drug.**

13. DOSE, ROUTE, AND SCHEDULE  
**Bevacizumab/Placebo 15 mg/kg IV on Day 1, every 21 days, starting with cycle 2, for 5 cycles**

14. DATES OF TREATMENT  
**The patient began the investigational therapy on December 8, 2008, and received the last doses of bevacizumab/placebo, paclitaxel, and carboplatin on March 25, 2009 (Cycle 5, Day 1).**

15. ACCRUAL AND IND EXPERIENCE  
**The number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21331 There have been 1 hydronephrosis and 3 kidney hemorrhage incidences reported to the NCI through AdeERS as a serious adverse events for bevacizumab. Hemoglobin is known to be associated with the investigational agent, bevacizumab.**

16. COMMENTS  
**The following was also administered:  
Paclitaxel: 175 mg/m<sup>2</sup> IV over 3 hours on day 1 × 6 cycles  
Carboplatin: AUC 6 IV over 30 minutes on day 1 × 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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