

**IND SAFETY REPORT: FOLLOW-UP #1**TO: *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  
May 29, 20094. SPONSOR  
Division of Cancer Treatment and Diagnosis, National Cancer Institute5. REPORTER'S NAME, TITLE, AND INSTITUTION  
Kevin Conlon, MD – Senior Investigator, Investigational Therapeutic III,  
Investigational Drug Branch, CTEP, DCTD, NCI6. PHONE NUMBER  
301-496-11967. FAX NUMBER  
301-402-04288. PROTOCOL NUMBER (AE #)  
GOG-0218 (1968432)9. PATIENT IDENTIFICATION  
083-0218-07710. AGE  
7811. SEX  
Female

## 12. DESCRIPTION OF ADVERSE EVENT

The patient is a 78-year-old female with ovarian epithelial cancer who experienced grade 3 syncope and vein injury of the left lower extremity 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 March 4, 2009, and received the last doses of bevacizumab/placebo, carboplatin, and paclitaxel on March 25, 2009, (Cycle 2, Day 1). On March 30, 2009 (Cycle 2, Day 6), the patient presented to the emergency room via ambulance after experiencing a syncopal episode when standing from a seated position which lasted only a few seconds. The patient denied loss of consciousness. She reported persistent nausea, weakness, fatigue, and a 2-day history of diarrhea. Given the patient's history of newly diagnosed deep venous thrombosis (DVT) and treatment with Lovenox<sup>®</sup>, a CT angiogram of the chest with contrast revealed bilateral pulmonary embolism (PE). She denied chest pain, back pain, or dyspnea. The patient was admitted to the hospital for further evaluation of the syncope and PE. A DVT scan of the lower extremities and upper left extremity showed evidence of DVT of the right common femoral vein and the right great saphenous vein. The patient had an IVC filter placed and her condition improved. She was discharged home on April 4, 2009 (Cycle 2, Day 11), only to be re-admitted on April 8, 2009 (Cycle 2, Day 15) with complaints of left lower extremity pain. A CT scan of the left lower extremity showed femoral pseudoaneurysm. The patient remains hospitalized for further evaluation and management of her symptoms. 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/Placebo 15 mg/kg IV over 30-90 minutes on Day 1 starting with Cycle 2 × 5 cycles

## 14. DATES OF TREATMENT

The patient began the investigational therapy on March 4, 2009, and received the last dose of bevacizumab/placebo on March 25, 2009 (Cycle 2, Day 1).

## 15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21,394. There have been 90 other incidences of syncope and no other incidences of vein injury reported to the NCI through AdEERS as serious adverse events for bevacizumab.

## 16. COMMENTS

The following was also administered:

Carboplatin AUC 6 IV over 30 minutes on Day 1 and Paclitaxel: 175 mg/m<sup>2</sup> IV over 3 hours on Day 1, every 21 days × 6 cycles; Last doses administered on March 25, 2009 (Cycle 2, Day 1).**FOLLOW-UP:****Based upon further investigation, the Senior Investigator at the Investigational Drug Branch has decided not to file this adverse event expeditiously.**

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