

**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  
**March 8, 2010**

4. SPONSOR  
**Division of Cancer Treatment and Diagnosis, National Cancer Institute**

5. REPORTER'S NAME, TITLE, AND INSTITUTION  
**Kevin Conlon, MD-Senior Investigator for Investigational Therapeutics 3, CTEP, DCTD, NCI**

6. PHONE NUMBER  
**301-496-1196**

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

8. PROTOCOL NUMBER (AE #)  
**GOG-0213 (AE # 1003452)**

9. PATIENT IDENTIFICATION  
**083-0213-023**

10. AGE  
**76**

11. SEX  
**Female**

12. DESCRIPTION OF ADVERSE EVENT

**The patient was a 76-year-old female with ovarian epithelial cancer who experienced grade 4 atrial fibrillation while on a phase 3 trial utilizing the investigational agent bevacizumab in combination with paclitaxel and carboplatin. She began the first course of the investigational therapy on August 18, 2009, and these were her first and only doses bevacizumab, paclitaxel, and carboplatin. On September 4, 2009 (Cycle 1, Day 18), the patient, who had a history of intermittent atrial fibrillation, hypertension, and hyperlipidemia, presented to the local hospital with complaints of rapid heart rate, weakness, and nausea. An ECG revealed atrial fibrillation with rapid ventricular response and a heart rate of 135-150 bpm. Her blood pressure was 85/36 mmHg and oxygen saturation 95% on room air. On physical examination, she had irregularly irregular rhythm. The patient was started on IV fluids and a Cardizem<sup>®</sup> drip and admitted to the acute care unit. Her dyspnea improved, the blood pressure increased to 157/79 mmHg, and her heart rate went down to 94 bpm. On September 6, 2009, the patient was transferred to a cardiac facility where she was started on Tikosin<sup>®</sup> and maintained on the diltiazem drip. A repeat ECG on September 9, 2009, showed normal sinus rhythm. The patient's condition improved and she remained in normal sinus rhythm with controlled rates. She was discharged home later that day. On September 10, 2009, the patient died at home. An autopsy was not performed. The death certificate listed the immediate cause of death as coronary artery disease. 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

**(Non-Surgical Patients) – Treatment Table Arm II; 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 August 18, 2009, and received only one dose of bevacizumab.**

15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 25,462. There have been 74 other cases of atrial fibrillation reported to the NCI as serious adverse events through AdEERS for bevacizumab.**

16. COMMENTS **The following was also administered: (Non-Surgical Patients) – Treatment Table Arm II  
Cycle = 21 Days:**

**Paclitaxel: 175 mg/m<sup>2</sup> IV over 3 hours on Day 1  
Carboplatin: AUC 5 IV over 30 minutes on Day 1**

**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.**