

IND SAFETY REPORT: INITIAL WRITTEN REPORT

To: <i>Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA</i>		FAX: 301-796-9849
1. IND NUMBER 7921	2. AGENT NAME Bevacizumab (rhuMAb VEGF)	3. DATE March 16, 2011
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 301-496-1196
		7. FAX NUMBER 301-402-0428
8a. PROTOCOL NUMBER (AE #) E5103 (AE# 1574705)	8b. AE GRADE: AE Grade 3: Arterial thrombus (brachial)	
9. PATIENT IDENTIFICATION 53411	10. AGE 54 years	11. SEX Female
12. DESCRIPTION OF ADVERSE EVENT The patient is a 54-year-old female with invasive breast carcinoma who experienced a brachial arterial thrombus while on a phase 3 trial utilizing the investigational agent bevacizumab/placebo. As reported, the patient began her first course of treatment on March 12, 2010, and received the last dose of bevacizumab/placebo on September 17, 2010 (Cycle 18, Day 1). On January 6, 2011 (Cycle 18, Day 111), the patient presented to her primary care physician with a 5-day history of right upper extremity numbness. A high resolution arterial duplex Doppler showed occlusion of the upper portion of the right brachial artery from or near its origin, approximately 2.5 cm in length. Arterial perfusion in the distal right arm appeared to be significantly reduced due to this singular lesion. Echogenicity in this area also suggested a thrombus or embolus. There was no evidence of any halo sign to indicate vasculitis. The brachial artery was reconstituted via collateral channels distal to this point. There was no evidence of obvious atherosclerosis in any of the arteries studied and the lumen caliber of the arterial vessels appeared to be satisfactory. The patient was admitted to the hospital. The hypercoagulable workup revealed negative prothrombin gene mutation. She was started on low molecular weight heparin and Coumadin [®] . The patient was discharged the following morning in good condition. 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 (Cycles 9-18) Bevacizumab/Placebo: 15 mg/kg IV over 30-90 minutes on Day 1		
14. DATES OF TREATMENT The patient began the investigational therapy on March 12, 2010, and received the last dose of bevacizumab/placebo on September 17, 2010 (Cycle 18, Day 1).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 31,563. There have been 3 other cases of arterial thromboembolic events reported to the NCI through AdEERS as serious adverse events for bevacizumab. Arterial thrombus is an expected event for bevacizumab.		
16. COMMENTS 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.		