

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
79212. AGENT NAME
Bevacizumab (rhuMAb VEGF)3. DATE
May 1, 20094. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute5. REPORTER=S NAME, TITLE, AND INSTITUTION
**Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics
3, IDB, CTEP, DCTD, NCI**6. PHONE NUMBER
301-496-11967. FAX NUMBER
301-402-04288. PROTOCOL NUMBER (AE #)
E1505 (AE # 1391765)9. PATIENT IDENTIFICATION
1530010. AGE
6211. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 62-year-old female with invasive breast carcinoma who experienced a Grade 2 CNS hemorrhage and Grade 2 seizure while on a phase 3 study utilizing the investigational agent bevacizumab in combination with gemcitabine and cisplatin. She began her first course of treatment on January 26, 2009, and received her last dose of bevacizumab on March 9, 2009 (Cycle 3, Day 1). On March 13 (Cycle 3, Day 5), the patient stated that while in the clinic lobby she was "passing out, felt dehydrated, nauseated, and had a headache." When the patient arrived to the emergency room, she was awake, oriented, and complained of a headache and nausea. A CT scan was performed, which revealed an intracranial bleed and subarachnoid hemorrhage. The patient was transferred and admitted to the intensive care unit at St. Mary's Hospital on March 13, 2009 (Cycle 3, Day 5) for further evaluation. After a neurology consult, a cerebral angiogram was performed which was negative for an aneurysm. On March 20, 2009 (Cycle 3, Day 12), a CT scan of the brain without contrast showed a slight decrease in the amount of subarachnoid blood with no new hemorrhage and the patient was discharged home in stable 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**
Bevacizumab 15 mg/kg IV over 30-90 minutes on Day 1 (Cycles 1-4);
Bevacizumab 15 mg/kg IV over 30-90 minutes on Day 1 every 3 weeks , for up to 1 year (Cycles 4+)14. DATES OF TREATMENT **The patient started the investigational therapy on January 26, 2009, and received the last dose of bevacizumab on March 9, 2009 (Cycle 3, Day 1).**15. ACCRUAL AND IND EXPERIENCE **Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 20524. There have been 30 other incidences of CNS hemorrhage and 45 other incidences of seizure reported to the NCI through AdEERS as serious adverse events for bevacizumab.**16. COMMENTS **The following was also administered:**
Cycles 1-4: gemcitabine: 1200 mg/m² /day IV over 30 minutes on Days 1 and 8, cisplatin: 75 mg/m² IV over 60 minutes on Day 1 (last administered on March 9, 2009 [Cycle 3, 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.**

0002