

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 20, 2009
4. SPONSOR Division of Cancer Treatment and Diagnosis, National Cancer Institute		
5. REPORTER=S NAME, TITLE, AND INSTITUTION Kevin Conlon, MD- Senior Investigator, Investigational Therapeutics 3, CTEP, DCTD, NCI		6. PHONE NUMBER 301-496-1196
		7. FAX NUMBER 301-402-0428
8. PROTOCOL NUMBER (AE #) E5202 (AE # 1232396)		
9. PATIENT IDENTIFICATION 53725	10. AGE 51	11. SEX Female
12. DESCRIPTION OF ADVERSE EVENT The patient is a 51-year-old female with adenocarcinoma of the colon, who experienced a grade 4 CNS hemorrhage while on a phase 3 study utilizing the investigational agent bevacizumab in combination with oxaliplatin, 5-fluorouracil, and leucovorin. She began her first course of treatment on March 18, 2009, and received her last doses of bevacizumab, oxaliplatin, 5-fluorouracil, and leucovorin were on April 15, 2009 (Cycle 2, Day 1). On April 16, 2009 (Cycle 2, Day 2), the patient was noted to have acute change in her mental status and was taken to a hospital where a CT scan showed a large left frontal hemorrhage. She subsequently underwent a left craniotomy with evacuation of the hematoma. Immediately, after extubation the patient was moving all her extremities and was alert but not oriented to time, place and person. On April 17, 2009, post operative CT scan showed pockets of pneumocephalus with small area of residual hemorrhage. There was an improvement of the midline shift with mild subarachnoid hemorrhage. She was unable to take per oral during the course of the hospitalization, and a feeding tube was placed to initiate tube feeding. Her neurological examination gradually improved through out the course of her hospitalization. She was able to speak words intermittently. At the time of discharge to acute rehabilitation on April 23, 2009, she was alert and oriented. The patient will follow up with the neurosurgery in 4 weeks. 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 = 2 weeks, 12 Cycles Bevacizumab 5 mg/kg IV over 30-90 minutes on Day 1 Bevacizumab 5 mg/kg IV over 30-90 minutes on Day 1, every 2 weeks for 12 additional cycles, after completion of first 12 cycles.		
14. DATES OF TREATMENT The patient started the investigational therapy on March 18, 2009, and received the last dose of bevacizumab on April 15, 2009 (Cycle 2, Day 1).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21,385. Hemorrhage, CNS is an expected adverse event for bevacizumab.		
16. COMMENTS The following was also administered: Oxaliplatin: 85 mg/m² IV over 2 hours on Day 1 (last administered on April 15, 2009). Leucovorin: 400 mg/m² IV over 2 hours on Day 1 ((last administered on April 15, 2009). 5-fluorouracil: 400 mg/m² IV bolus on Day 1 followed by 5-fluorouracil 2.4 gm/m² CIV over 46 hours starting on Day 1 (last administered on April 15, 2009).		
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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