

IND SAFETY REPORT: FOLLOW-UP #1TO: *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 October 29, 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, Investigational Drug Branch, CTEP, DCTD, NCI		6. PHONE NUMBER 301-496-1196
		7. FAX NUMBER 301-402-0428
8a. PROTOCOL NUMBER (AE#) RTOG-0825 (AE# 1584360)	8b. AE GRADE: AE Grade 5: Sudden Death	
9. PATIENT IDENTIFICATION 528	10. AGE 72 years	11. SEX Male
12. DESCRIPTION OF ADVERSE EVENT The patient was a 72-year-old male with glioblastoma multiforme who died suddenly while on a phase 3 trial utilizing the investigational agent bevacizumab/placebo in combination with temozolomide and radiation. He began his first course of treatment on August 30, 2010, and received the last dose of bevacizumab/placebo on October 5, 2010 (Cycle 1, Day 37), and the last doses of temozolomide and radiation therapy on October 11, 2010 (Cycle 1, Day 43). On October 11, 2010 (Cycle 1, Day 43), the patient presented to the clinic with extreme lethargy, poor appetite, and weight loss. He reported that he remained in bed for most of the day. He was also evaluated by the dietician. On October 13, 2010, his family reported that he entered the living room with facial expressions that suggested he was having a bowel movement, and he suddenly fell to the floor. It was felt that this may have been a vagal response. He was taken to the emergency room (ER) via ambulance, and attempts to resuscitate him were unsuccessful. He was pronounced dead in the ER. A limited autopsy report is pending. 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 = 6 weeks: Bevacizumab/Placebo: 10 mg/kg of actual body weight IV over 30-90 minutes on Day 1 of Weeks 4 and 6 Cycle = 4 weeks: Bevacizumab/Placebo: 10 mg/kg of actual body weight IV over 30-90 minutes at the beginning of Week 2 Cycle = 4 weeks (maximum of 12 cycles): Bevacizumab/Placebo: 10 mg/kg of actual body weight IV over 30-90 minutes on Days 1 and 15		
14. DATES OF TREATMENT The patient began the investigational therapy on August 30, 2010, receiving the last dose of bevacizumab on October 5, 2010 (Cycle 1, Day 37), and the last doses of temozolomide and radiation therapy on October 11, 2010 (Cycle 1, Day 43).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using Bevacizumab = 28,962. There have been 61 other cases of sudden death and 109 other cases of death NOS reported to the NCI through AdEERS as serious adverse events for bevacizumab.		
16. COMMENTS Cycle = 6 weeks: Temozolomide 75 mg/m ² PO daily and Radiation therapy 60 Grays (delivered in 2 Gray fractions on Days 1-5 every week) Cycle = 4 weeks: (maximum of 12 cycles): Temozolomide 150-200 mg/m ² PO on Days 1-5		
FOLLOW-UP: BASED UPON FURTHER INVESTIGATION, THE SENIOR INVESTIGATOR HAS DECIDED THAT THIS EVENT IS EITHER EXPECTED OR NOT SERIOUS AND THUS DOES NOT REQUIRE EXPEDITED REPORTING.		

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