

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
October 14, 20104. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute5. REPORTER'S NAME, TITLE, AND INSTITUTION
Kevin Conlon, MD-Senior Investigator for Investigational Therapeutics 3, Investigational Drug Branch, CTEP, DCTD, NCI6. PHONE NUMBER
301-496-11967. FAX NUMBER
301-402-04288a. PROTOCOL NUMBER (AE#)
RTOG-0825 (AE# 1584360)8b. AE GRADE: AE
Grade 5: Sudden Death9. PATIENT IDENTIFICATION
52810. AGE
72 years11. 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/m² 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/m² PO on Days 1-5

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.