

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
June 17, 20114. 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, Investigational
Drug Branch, CTEP, DCTD, NCI**6. PHONE NUMBER
301-496-11967. FAX NUMBER
301-402-04288a. PROTOCOL NUMBER (AE#)
RTOG-0825 (AE# 1956122)8b. AE GRADE: AE
Grade 5: Sudden death9. PATIENT IDENTIFICATION
90510. AGE
69 years11. SEX
Male

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 69-year-old male with glioblastoma multiforme who suddenly died 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 April 14, 2011, and received the last dose of bevacizumab/placebo on June 1, 2011 (Cycle 1, Day 49), the last dose of temozolomide and radiation treatment on May 25, 2011 (Cycle 1, Day 42). On June 9, 2011, the patient's wife called the treating physicians stating that the patient had altered mental status. Instructions were given that the patient needed to go to the local hospital for evaluation. The patient called back stating that he was "fine", his wife was "over-reacting", and he was not going to the emergency room. On June 11, 2011, the patient was found dead on the floor by his wife. The patient was not taken to the hospital; the coroner came to the home and the patient was taken directly to the funeral home. No autopsy was performed. 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 April 14, 2011, receiving the last dose of bevacizumab on June 1, 2011, (Cycle 1, Day 49), the last dose of temozolomide and radiation treatment on May 25, 2011 (Cycle 1, Day 42).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 33,125. There have been 57 other cases of sudden death and 167 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.

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