

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

February 19, 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

8. PROTOCOL NUMBER (AE #)

CALGB-90601 (AE # 1900497)

9. PATIENT IDENTIFICATION

118685

10. AGE

66

11. SEX

Male

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 66-year-old male with transitional cell carcinoma of the urothelial tract who suddenly expired while on a phase 3 trial utilizing the investigational agent bevacizumab/placebo in combination with cisplatin and gemcitabine. He began the first course of the investigational therapy on December 23, 2009, and received the only doses of bevacizumab/placebo and cisplatin on December 23, 2009 (Cycle 1, Day 1), and the last dose of gemcitabine on December 30, 2009 (Cycle 1, Day 8). The patient was earlier hospitalized between January 11-15, 2010 for ischemic stroke, pulmonary embolism and pleural effusion. He was treated with Lovenox[®], had therapeutic thoracentesis done and was discharged. On January 26, 2010, he presented to the ER with a new-onset seizure-like activity and worsening dyspnea on exertion. The CT scan of the head showed no intracranial hemorrhage or infarcts. The chest X-ray showed worsening left pleural effusion with atelectasis and multiple nodules in the right lung. The possibilities of alcohol withdrawal seizures, infection, brain metastasis and CVA were considered. The patient was admitted. An EEG revealed status epilepticus. He was started on 2L oxygen, Keppra[®], Ativan[®], thiamine, folate, fosphenytoin and empiric antibiotics. He also underwent a therapeutic thoracentesis. The patient's family decided that he should be transitioned to comfort care, and he was discharged home with hospice services on January 29, 2010. On February 4, 2010, the patient was restless and dyspneic. He was given Roxanol[®] and atropine and he expired on the same day. 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/placebo 15 mg/kg IV over 30-90 minutes on Day 1

14. DATES OF TREATMENT The patient began the investigational therapy on December 23, 2009, and received the only dose of bevacizumab/placebo on that day.

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 25,441. There have been 49 other cases of sudden death and 68 other cases of death NOS reported to the NCI as serious adverse events through AdEERS for bevacizumab.

16. COMMENTS The following was also administered:

Cisplatin 70 mg/m² IV over 1 hour on Day 1 and Gemcitabine 1000 mg/m² IV over 30 minutes on Days 1 and 8 for Cycles 1-6.

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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