

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 21, 2009

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, CTEP, DCTD, NCI

6. PHONE NUMBER

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8. PROTOCOL NUMBER (AE #)

S0518 (AE # 1687519)

9. PATIENT IDENTIFICATION

215483

10. AGE

53

11. SEX

Male

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 53-year-old male with a carcinoid tumor who died of disease progression while on a phase 3 study using the investigational agent bevacizumab in combination with octreotide. He began his first course of treatment on March 10, 2009, receiving bevacizumab on March 11, 2009 (Cycle 1, Day 2). This was his first and only dose of bevacizumab. He received his first and only dose of octreotide on March 10, 2009 (Cycle 1, Day 1). On March 29, 2009 (Cycle 1, Day 20), the patient presented to the ER with complaints of nausea, vomiting, headache, dizziness, confusion, and dysphagia and was admitted to the ICU. A CT scan of the head revealed a right tentorial subdural hematoma as well as an acute bleed in the right inferior cerebellum and a slight mass effect on the fourth ventricle. His INR was 4.7 (reference range: 0.9-1.1). Note that he was on Coumadin and Plavix. The patient received Vitamin K and Factor VII. An ultrasound of the abdomen was performed which showed metastatic disease of the liver along with ascites and gallbladder stones. The patient was started on tube feedings and antibiotics for possible aspiration pneumonia. He was eventually transferred out of the ICU, though his mental status had not changed. A repeat CT scan revealed no changes from the previous scans. There was the possibility of sepsis when his white count began to rise. The family requested for the patient to be placed under comfort measures. The patient's clinical condition continued to worsen, and on April 10, 2009 (Cycle 1, Day 32), the patient died from cardiorespiratory failure. Additional information has been requested. There is a reasonable possibility that the experience may have been caused by the drug.

13. DOSE, ROUTE, AND SCHEDULE **Cycle = 21 days****Bevacizumab 15 mg/kg IV over 30-90 minutes on Day 1**14. DATES OF TREATMENT **The patient started the investigational therapy on March 10, 2009, and March 11, 2009 was his first and only dose of bevacizumab.**15. ACCRUAL AND IND EXPERIENCE **Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21,394. There have been 62 deaths due to disease progression reported to the NCI through AdEERS as serious adverse events for bevacizumab.**16. COMMENTS **The following was also administered:****octreotide test dose: short acting octreotide 100 mcg SQ, Day 1, Cycle 1 only and octreotide LAR depot: 20 mg IM, Day 1.****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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