

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
March 8, 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, CTEP, DCTD, NCI6. PHONE NUMBER
301-496-11967. FAX NUMBER
301-402-04288. PROTOCOL NUMBER (AE #)
S0518 (AE # 1236502)9. PATIENT IDENTIFICATION
21560610. AGE
6111. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 61-year-old female with carcinoid tumor who experienced grade 5 small bowel obstruction while on a phase 3 trial utilizing the investigational agent bevacizumab in combination with octreotide. She began the first course of the investigational therapy on March 13, 2009, and received the last dose of bevacizumab on December 18, 2009 (Cycle 13, Day 1), and the last dose of octreotide on January 8, 2010 (Cycle 14, Day 1). On January 8, 2010, during the clinic visit, the patient complained of severe abdominal pain with new onset of numbness and weakness in the lower extremities. Bevacizumab was held and she was admitted for observation and evaluation of her symptoms. A CT scan of the abdomen and pelvis revealed findings consistent with either an early complete small bowel obstruction or exacerbation of partial small bowel obstruction and progressive disease. The patient was treated with Cipro[®], MS Contin[®], lactulose, MiraLax[®], and a clear liquid diet. Her condition improved, and she was discharged home on January 12, 2010. The patient, shortly thereafter, was admitted and treated for an occlusive DVT of the right lower extremity and discharged. On February 2, 2010, she presented to the local ER complaining of lower extremity edema, cold to touch left lower extremity, generalized weakness, and weight loss. She was admitted for observation, and a consult for hospice care was obtained. On February 4, 2010, the patient became hypoglycemic with suspected aspiration and respiratory arrest requiring intubation and mechanical ventilation. After discussions with the patient's family, the patient was placed on do not resuscitate (DNR) status, and she expired later that evening. 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: 15 mg/kg IV over 30-90 minutes on Day 114. DATES OF TREATMENT **The patient began the investigational therapy on March 13, 2009, and received the last dose of bevacizumab on December 18, 2009 (Cycle 13, Day 1).**

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 25,462. There have been 122 other cases of small bowel obstruction reported to the NCI as serious adverse events through AdEERS for bevacizumab.

16. COMMENTS **The following was also administered:****Cycle = 21 Days****Octreotide Test Dose: short-acting octreotide 100 mcg SQ, Day 1, Cycle 1 only****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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