

**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  
301-496-1196****7. FAX NUMBER  
301-402-0428****8. PROTOCOL NUMBER (AE #)  
E1305 (AE # 1390754)****9. PATIENT IDENTIFICATION  
13009****10. AGE  
50****11. SEX  
Male****12. DESCRIPTION OF ADVERSE EVENT**

**The patient is a 50-year-old male with head and neck squamous cell carcinoma who developed a grade 3 esophageal fistula while on a phase 3 study using the investigational agent bevacizumab in combination with cisplatin and 5-fluorouracil (5-FU). He began his first course of treatment on April 20, 2009, and this was his first and only dose of bevacizumab. He received his last dose of cisplatin also on April 20, 2009, and his last dose of 5-FU on April 24, 2009 (Cycle 1, Day 5). On May 4, 2009 (Cycle 1, Day 15), while the patient was eating, his food contents exited out of his tracheostomy site. The patient was diagnosed with a tracheal-esophageal fistula and admitted to the hospital. IV fluids were started, and patient was evaluated for a PEG tube placement for nutrition and hydration. A laryngectomy tube was successfully placed. On May 5, 2009 (Cycle 1, Day 16), a percutaneous endoscopic gastrostomy tube was unable to be placed. As a result of this, on May 6, 2009 (Cycle 1, Day 17), an open gastrostomy with placement of a gastrostomy tube was placed. On May 9, 2009 (Cycle 1, Day 20), the patient developed aspiration pneumonia and was placed on IV antibiotics. The patient was discharged home on May 12, 2009 (Cycle 1, Day 23), and was instructed to follow up with the ENT. 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/Placebo 15 mg/kg IV over 30-90 minutes on Day 1****14. DATES OF TREATMENT The patient started the investigational therapy on April 20, 2009, and this 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. Gastrointestinal fistulas are known to be associated with bevacizumab.****16. COMMENTS The following was also administered:  
cisplatin 100 mg/m<sup>2</sup> IV over 1-2 hours on Day 1 and 5-FU 1000 mg/m<sup>2</sup>/day CIV over 4 days, starting on 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.**

0002