

IND SAFETY REPORT: FOLLOW-UP #1

TO: Division of Oncology Products 2, Center for Drug Evaluation and Research, FDA		FAX: 301-796-9849
1. IND NUMBER 113916	2. AGENT NAME Bevacizumab (rhuMAb VEGF)	3. DATE December 22, 2011
4. SPONSOR Division of Cancer Treatment and Diagnosis, National Cancer Institute		
5. 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 301-496-1196
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8a. PROTOCOL NUMBER (AE#) E1305 (AE# 1455510)	8b. AE GRADE: AE Grade 5: Bronchopulmonary hemorrhage	
9. PATIENT IDENTIFICATION 13148	10. AGE 58 years	11. SEX Male
12. PROTOCOL SPECIFIED Cycle = 21 days Bevacizumab: 15 mg/kg IV over 30-90 minutes on Day 1 Docetaxel: 75 mg/m ² IV over 1 hour on Day 1 Cisplatin: 75 mg/m ² IV over 1-2 hours on Day 1		
13. TREATMENT RECEIVED AND DATES The patient began the investigational therapy on November 2, 2011, and received the last doses of bevacizumab, docetaxel, and cisplatin on November 23, 2011 (Cycle 2, Day 1).		
14. DESCRIPTION OF ADVERSE EVENT The patient was a 58-year-old male with head and neck squamous cell carcinoma who expired from a bronchopulmonary hemorrhage while on a phase 3 trial utilizing the investigational agent bevacizumab in combination with docetaxel and cisplatin. Of note, the patient had a pre-existing cavitation of the tumor site causing a fistulous tract at the time of the event. On November 28, 2011 (Cycle 2, Day 6), he presented to the radiology unit for a PEG tube insertion, and was noted to have tachycardia and sent to the ER. In the ER, the patient had a pulse of 160 beats per minute for which he was given adenosine with no improvement. He also received IV Cardizem [®] , and was admitted for monitoring. His ECG was normal. On December 2, 2011 (Cycle 2, Day 10), the patient had a coughing spell while being prepared for discharge from the hospital. He initially coughed out clear sputum, but developed hemoptysis and gagged up fresh blood with sponge-sized gelatinous blood clots thereafter. The rapid response team was notified; the patient coded and died later that 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.		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 35,453. Bronchopulmonary hemorrhage is an expected event for bevacizumab; however, this event is being reported because it is a rare event with increased severity.		
16. ASSESSMENT In this case, a probable relationship exists between the event and bevacizumab.		
_____	_____	Bronchopulmonary hemorrhage
Bevacizumab	_____	Probable
Cisplatin	_____	Unrelated
Docetaxel	_____	Unrelated
Head and neck squamous cell carcinoma	_____	Possible
Cavitation of tumor site, causing a fistula tract	_____	Probable
17. COMMENTS Medications taken at the time of the event are not available at this time.		
FOLLOW-UP: BASED UPON FURTHER INVESTIGATION, THE SENIOR INVESTIGATOR HAS DECIDED THAT THIS EVENT IS EITHER EXPECTED OR NOT SERIOUS AND THUS DOES NOT REQUIRE EXPEDITED REPORTING.		