

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 57004	2. AGENT NAME Bevacizumab (rhuMAb VEGF) OXALIplatin (Eloxatin)	3. DATE March 4, 2009
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 III, Investigational Drug Branch, CTEP, DCTD, NCI S. Percy Ivy, MD -Associate Chief for Targeted Therapeutics 1, Investigational Drug Branch, CTEP, DCTD, NCI		6. PHONE NUMBER 301-496-1196 7. FAX NUMBER 301-402-0428
8. PROTOCOL NUMBER (AE #) E5204 (AE # 1201753)		
9. PATIENT IDENTIFICATION 52300	10. AGE 53	11. SEX Male
12. DESCRIPTION OF ADVERSE EVENT The patient is a 53-year-old male with adenocarcinoma of the rectum who experienced grade 4 allergic reaction/hypersensitivity while on a phase 3 study using the investigational agents bevacizumab and OXALIplatin in combination with leucovorin and 5-fluorouracil. He began his first course of treatment on January 13, 2009, and received his first and last doses of bevacizumab and OXALIplatin on that day (Cycle 1, Day 1). He was sent home with a portable pump for continuous 5-FU infusion. In the early morning of January 14, 2009, the patient's wife called 911 and he was transported to the Emergency Room where he presented with angioedema and upper airway obstruction. This wife reported that he experienced 3 or 4 bouts of vomiting immediately upon returning home from after his first infusion, but later went to bed and slept well until he woke up with a swollen tongue and difficulty breathing. The 5-FU continuous infusion pump was discontinued, and the patient received epinephrine, Benadryl®, and Solu-Medrol without relief of symptoms. He was intubated with a nasopharyngeal airway and given humidified oxygen. O2 saturation remained greater than 90%. He was admitted to the ICU and was placed on steroids and Benadryl® and the Lisinopril® that he had been taking for years was stopped. The swelling went down promptly. The patient was extubated and observed for 24 hours. He experienced hypertension throughout the hospital stay. He was discharged on January 17, 2009, and as of January 21, 2009, still had difficulty talking. He will not receive any additional chemotherapy at this time and will be re-evaluated at the next office visit. Additional information has been requested. There is a reasonable possibility that the experience may have been caused by the drugs.		
13. DOSE, ROUTE, AND SCHEDULE (Cycle = every two weeks for a total of 12 cycles) Bevacizumab 5 mg/kg IV over 30 to 90 minutes on Day 1 OXALIplatin 85mg/m ² infusion over 2 hours on Day 1		
14. DATES OF TREATMENT The patient received his first and last doses of bevacizumab and OXALIplatin on January 13, 2009.		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 19,771 and using OXALIplatin = 19,688. There have been 42 other cases of allergic reaction/hypersensitivity reported to the NCI through AdEERS as serious adverse events for bevacizumab and 57 other cases of allergic reaction/hypersensitivity reported to the NCI through AdEERS as serious adverse events for OXALIplatin.		
16. COMMENTS Also administered on this protocol: Luecovorin 400 mg/m ² IV infusion over 2 hours on Day 1 followed by 5-FU 400 mg/m ² IV bolus on Day 1; 5-FU 2.4 g/m ² continuous infusion over 46 hours immediately following bolus 5-FU on Days 1&2, every two weeks for a total of 12 cycles. First and last doses administered on January 13, 2009. 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.		