

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 June 23, 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	
		7. FAX NUMBER 301-402-0428	
8a. PROTOCOL NUMBER (AE#) RTOG-0825 (AE# 1226625)	8b. AE GRADE: AE Grade 3: Acute kidney injury		
9. PATIENT IDENTIFICATION 0825-450	10. AGE 57 years	11. SEX Female	
12. DESCRIPTION OF ADVERSE EVENT The patient is a 57-year-old female with glioblastoma multiforme who experienced grade 3 acute kidney injury while on a phase 3 trial utilizing the investigational agent bevacizumab/placebo in combination with temozolomide and radiation. Her baseline creatinine was 0.94 mg/dL (reference range: 0.44-1.03 mg/dL) and urea nitrogen was 21 mg/dL (reference range: 8-20 mg/dL). She began her first course of treatment on July 1, 2010, and received the last dose of bevacizumab/placebo on April 7, 2011 (Cycle 7, Day 15), the last dose of temozolomide on March 29, 2011 (Cycle 7, Day 6), and the last dose of radiation treatment on August 13, 2010 (Cycle 1, Day 44). On May 5, 2011 (Cycle 7, Day 42), the patient was admitted to the hospital for acute renal failure with a creatinine level of 12.6 mg/dL and urea nitrogen level of 63 mg/dL. Her urine protein was negative. Renal ultrasounds did not show evidence of hydronephrosis or renal artery stenosis. The patient was started with high-dose steroids and placed on dialysis several times. On May 11, 2011, her urea nitrogen and creatinine were 32 mg/dL and 3.3 mg/dL, respectively. Her kidney function slowly improved. The dialysis was discontinued and the steroids were slowly tapered. At the time of discharge, her creatinine level had returned close to normal. 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 = 6 weeks: Bevacizumab/Placebo: 10 mg/kg of actual body weight IV over 30-90 minutes on Day 1 of Weeks 4 and 6 Cycle = 4 weeks: Bevacizumab/Placebo: 10 mg/kg of actual body weight IV over 30-90 minutes at the beginning of Week 2 Cycle = 4 weeks (maximum of 12 cycles): Bevacizumab/Placebo: 10 mg/kg of actual body weight IV over 30-90 minutes on Days 1 and 15			
14. DATES OF TREATMENT The patient began the investigational therapy on July 1, 2010, receiving the last dose of bevacizumab on April 7, 2011 (Cycle 7, Day 15), the last dose of temozolomide on March 29, 2011 (Cycle 7, Day 6), and the last dose of radiation treatment on August 13, 2010 (Cycle 1, Day 44).			
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 33,125. Acute kidney injury is a known event for bevacizumab.			
16. COMMENTS Cycle = 6 weeks: Temozolomide 75 mg/m² PO daily and radiation therapy 60 Grays (delivered in 2 Gray fractions on Days 1-5 every week) Cycle = 4 weeks: (maximum of 12 cycles): Temozolomide 150-200 mg/m² PO on Days 1-5			
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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