

IND SAFETY REPORT: INITIAL WRITTEN REPORT

TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA		FAX: 301-796-9849
Division of Drug Oncology Products, Center for Drug Evaluation and Research, FDA		FAX: 301-796-9845
1. IND NUMBER 7921 74019	2. AGENT NAME Bevacizumab (rhuMAb VEGF) Sunitinib malate (SU011248 L-malate; Sutent®)	3. DATE November 24, 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 Pamela Harris, MD –Senior Investigator for Investigational Therapeutics I, Investigational Drug Branch, CTEP, DCTD, NCI		6. PHONE NUMBER 301-496-1196 7. FAX NUMBER 301-402-0428
8. PROTOCOL NUMBER (AE #) 7537 (AE # 1939558)		
9. PATIENT IDENTIFICATION 045	10. AGE 38	11. SEX Female
12. DESCRIPTION OF ADVERSE EVENT The patient was a 38-year-old female with metastatic adrenal carcinoma who developed grade 5 disease progression and expired while on a phase 1 study using the investigational agents bevacizumab and sunitinib. She began her first course of treatment on October 30, 2009, and received only one dose of bevacizumab and only two doses of sunitinib with the last dose given on October 31, 2009 (Cycle 1, Day 2). On November 1, 2009 (Cycle 1, Day 3), the patient presented to the emergency department with complaints of dyspnea, severe abdominal pain and constipation. Upon physical examination she was lethargic and had extremity edema. Her vital signs included a BP of 149/110 mmHg, respiratory rate of 22 per minute and oxygen saturation of 97%. During the course of her hospital stay she developed respiratory distress and became severely dyspneic. The patient was placed on DNR with comfort care measures and expired on November 12, 2009 (Cycle 1, Day 14). Additional information has been requested from the investigative site. There is a reasonable possibility that the experience may have been caused by the drugs.		
13. DOSE, ROUTE, AND SCHEDULE Cycle = 42 days Bevacizumab: 5 mg/kg IV over 90 - 30 minutes on Days 1, 15, and 29 SU11248: 37.5 mg PO once daily on Days 1-28		
14. DATES OF TREATMENT The patient started the investigational therapy on October 30, 2009, and received her last dose of bevacizumab on October 30, 2009 (Cycle 1, Day 1), and sunitinib on October 31, 2009 (Cycle 1, Day 2).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 23,774 and using sunitinib = 2,066. There has been 152 other case of disease progression reported to the NCI through AdEERS as serious adverse events for bevacizumab and 48 other cases of disease progression reported to the NCI through AdEERS as serious adverse events for sunitinib.		
16. COMMENTS 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). <u>DISCLAIMER per 21 CFR 312.32(e):</u> 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.		