

**IND SAFETY REPORT: INITIAL WRITTEN REPORT**

**TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA**  
**Division of Drug Oncology Products, Center For Drug Evaluation and Research, FDA**

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1. IND NUMBER <b>7921</b> <b>61010</b>	2. AGENT NAME <b>Bevacizumab (rhuMAb VEGF)(704865)</b> <b>CCI-779 (temsirolimus, Torisel<sup>TM</sup>)</b>	3. DATE <b>April 3, 2009</b>
4. SPONSOR <b>Division of Cancer Treatment and Diagnosis, National Cancer Institute</b>		
5. REPORTER'S NAME, TITLE, AND INSTITUTION <b>Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics 3, CTEP, DCTD, NCI</b> <b>L. Austin Doyle, MD-Senior Investigator for Targeted Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI</b>		6. PHONE NUMBER <b>301-496-1196</b>
		7. FAX NUMBER <b>301-402-0428</b>
8. PROTOCOL NUMBER (AE #) <b>E2804(AE# 1994045)</b>		
9. PATIENT IDENTIFICATION <b>28048</b>	10. AGE <b>50</b>	11. SEX <b>Male</b>
12. DESCRIPTION OF ADVERSE EVENT <b>The patient is a 50-year-old male with renal cell carcinoma who experienced grade 2 osteonecrosis while on a phase 2 trial utilizing the investigational agents bevacizumab and temsirolimus. He began the investigational therapy on July 15, 2008, and received his last dose of bevacizumab and temsirolimus on March 16, 2009 (Cycle 9, Day 18). On March 15, 2009, the patient presented to the clinic complaining of sore glands on the neck and was placed on amoxicillin 500 md tid x 10 days. On the next day the patient called the clinic, he had a very painful area of about 1 cm on his inner left lower jaw that was white and sharp to touch. The patient has not been on bisphosphonates. He has stable swelling of the bilateral neck area. On March 20, 2009, the patient was referred to an oral surgeon for osteonecrosis of left jaw. The investigational agents were held. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.</b>		
13. DOSE, ROUTE, AND SCHEDULE <b>Cycle = 28 Days.</b> <b>Temsirolimus 25 mg IV over 30 minutes on Days 1, 8, 15, and 22</b> <b>Bevacizumab 10 mg/kg IV over 30-90 minutes on Days 1 and 15</b>		
14. DATES OF TREATMENT <b>The patient began the investigational therapy on July 15, 2008, and received the last dose of bevacizumab and temsirolimus on March 16, 2008 (Cycle 9 Day 18).</b>		
15. ACCRUAL AND IND EXPERIENCE <b>Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 19819, and for temsirolimus = 1546. There have been 10 other incidences of osteonecrosis reported to the NCI through AdEERS as serious adverse events for bevacizumab; and no other incidences of osteonecrosis reported to the NCI through AdEERS as a serious adverse event for temsirolimus.</b>		
COMMENTS <b>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 21CFR312.32(d)(2).</b> <b>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.</b>		

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