

**IND SAFETY REPORT: INITIAL WRITTEN REPORT**

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

**FAX: 301-796-9845**  
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1. IND NUMBER <b>61010</b> <b>7921</b>	2. AGENT NAME <b>CCI-779 (temsirolimus, Torisel)</b> <b>Bevacizumab (rhuMab VEGF)</b>	3. DATE <b>December 17, 2009</b>
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4. SPONSOR  
**Division of Cancer Treatment and Diagnosis, National Cancer Institute**

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, M.D., Senior Investigator for Investigational 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 #)  
**GOG-0229G (AE # 1448075)**

9. PATIENT IDENTIFICATION <b>083-0229G-030</b>	10. AGE <b>69</b>	11. SEX <b>Female</b>
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12. DESCRIPTION OF ADVERSE EVENT  
**The subject is a 69-year-old female with recurrent endometrial cancer who developed grade 4 fatigue and grade 4 cognitive disturbance while on a phase 2 study utilizing the investigational agents bevacizumab and temsirolimus. She began her first course of treatment on December 3, 2008, and received her last doses of bevacizumab and temsirolimus on September 1, 2009 (Cycle 10, Day 1). A chest CT scan on August 28, 2009 (Cycle 9, Day 25), showed no evidence of metastatic disease in the chest, no new lesions and no evidence of progressive disease. Her original mass of 3.8 cm went down to 2.5 cm. In a clinic visit on August 31, 2009 (Cycle 9, Day 28), the patient had a fever, pelvic pain and was feeling fatigued. Vitals included a BP of 126/68 mmHg and a temperature of 99°F. A hematology panel was significant for low platelet counts. In a follow-up clinic visit on September 25, 2009 (Cycle 10, Day 25), she was completely non-functional, unable to communicate and non-ambulatory. It was noted not to be due to toxicity; however, she was removed from the study due to failure to thrive. The patient elected to receive hospice care. 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 = 4 weeks**  
**Bevacizumab 10 mg/kg IV over 30-90 minutes on Days 1 and 15;**  
**Temsirolimus 25 mg IV over 30 minutes on Days 1, 8, 15 and 22.**

14. DATES OF TREATMENT  
**The patient started the investigational therapy on December 3, 2008, and received her last doses of bevacizumab and temsirolimus on September 1, 2009 (Cycle 10, Day 1).**

15. ACCRUAL AND IND EXPERIENCE:  
**Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 23,852; and temsirolimus = 1,815. Fatigue is a known event for bevacizumab and temsirolimus. There have been 10 other cases of cognitive disturbance for bevacizumab and 1 other case for temsirolimus.**

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 21CFR312.32(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.**