

## 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  
61010**

2. AGENT NAME

**Bevacizumab (rhuMab VEGF)  
CCI-779 (tamsirolimus, Torisel™)**

3. DATE

**April 9, 2010**

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  
L. Austin Doyle, MD-Senior Investigator for Investigational Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI**

6. PHONE NUMBER

**301-496-1196**

7. FAX NUMBER

**301-402-0428**

8a. PROTOCOL NUMBER (AE #)

**8233 (AE# 1670473)**

8b. AE GRADE: AE

**Grade 3: Dehydration  
Grade 3: Phosphate (hypophosphatemia)  
Grade 3: Potassium (hypokalemia)**

9. PATIENT IDENTIFICATION

**PH1501**

10. AGE

**75**

11. SEX

**Female**

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 75-year-old female with ovarian cancer who experienced grade 3 dehydration, grade 3 hypophosphatemia, and grade 3 hypokalemia while on a phase 2 trial utilizing the investigational agents bevacizumab and temsirolimus. She began the investigational therapy on March 1, 2010, and received her last dose of bevacizumab on March 15, 2010 (Cycle 1, Day 15), and the last dose of temsirolimus on March 22, 2010 (Cycle 1, Day 22). On March 29, 2010, the patient presented to the clinic with anorexia, nausea, vomiting, dizziness, shoulder pains, oral mucositis, and fatigue. She appeared pale and fatigued with a pulse rate of 112 bpm, and dry mucous membranes. Her potassium was 2.7 mmol/L (reference range: 3.6-5.1 mmol/L), and her phosphorus was 1.5 mg/dL (reference range: 2.5 – 4.6 mg/dL). The patient was admitted and started on IV fluids, IV acyclovir, and analgesics. On March 30, 2010, her potassium increased to 3.5 mmol/L, and her phosphorus rose to 1.7 mg/dL. The patient remains hospitalized as the intervention for these adverse events continues. 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 = 28 Days.  
Temsirolimus: 25 mg IV over 30 minutes on Days 1, 8, 15, and 22  
Bevacizumab: 10 mg/kg IV over 30-90 minutes on Days 1 and 15**

14. DATES OF TREATMENT

**The patient began the investigational therapy on March 1, 2010, and received the last dose of bevacizumab on March 15, 2010 (Cycle 1, Day 15), and the last dose of temsirolimus on March 22, 2010 (Cycle 1, Day 22).**

15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1,966; and bevacizumab 25,513. There have been 63 other cases of dehydration reported to the NCI through AdEERS as serious adverse events for temsirolimus, and 645 other cases of dehydration, 43 other cases of hypophosphatemia, and 124 other cases of hypokalemia reported to the NCI through AdEERS as serious adverse events for bevacizumab. Hypophosphatemia and hypokalemia are known adverse events 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 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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