

## IND SAFETY REPORT: INITIAL WRITTEN REPORT

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

**FAX: 301-796-9845**

1. IND NUMBER  
**61010**

2. AGENT NAME  
**CCI-779 (temsirolimus, Torisel™)**

3. DATE  
**January 12, 2011**

4. SPONSOR  
**Division of Cancer Treatment and Diagnosis, National Cancer Institute**

5. REPORTER'S NAME, TITLE, AND INSTITUTION  
**L. Austin Doyle, M.D., 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 #)  
**GOG-0248 (AE# 1487991)**

8b. AE GRADE: AE  
**Grade 3: Obstruction, GI, Small bowel NOS**

9. PATIENT IDENTIFICATION  
**074-0248-003**

10. AGE  
**69 years**

11. SEX  
**Female**

**12. DESCRIPTION OF ADVERSE EVENT**

The patient is a 69-year-old female with stage II metastatic endometrioid endometrial adenocarcinoma who experienced a grade 3 small bowel obstruction while on a phase 2 trial utilizing the investigational agent temsirolimus. She began the first course of the investigational therapy on October 27, 2010, and received her last dose of temsirolimus on December 22, 2010 (Cycle 2, Day 8). On December 27, 2010 (Cycle 2, Day 13), the patient presented to the ER with a 2-day history of nausea, vomiting green bile, diarrhea, and abdominal pain. She reported that her laboratory and abdominal tests were negative, she was given Compazine® and Immodium®, and was discharged. On December 29, 2010 (Cycle 2, Day 15), the patient presented to the clinic with persistent nausea, vomiting, diarrhea, and abdominal bloating and pain. She reported being unable to eat for 3 days. Her abdomen was soft, distended, and tender with palpation, with hypoactive bowel sounds. She was admitted to the hospital, IV fluids were started, and she was made NPO. An NG tube was inserted with an immediate output of 700 mL of bilious drainage, and it was left in place with low suction. A proton pump inhibitor (PPI), anti-emetics, and morphine sulfate for pain were also ordered. Her stool cultures were negative. An abdominal and pelvic CT scan revealed new moderate abdominal pelvic ascites, new moderate dilatation of the stomach, and small bowel with long segment mild decrease in caliber and wall thickening in the distal ileum, probably representing enteritis causing partial small bowel obstruction. No pneumatosis was noted. A small hiatal hernia with new circumferential wall thickening of the distal esophagus was noted, possibly representing esophagitis. On December 30, 2010 (Cycle 2, Day 16), the patient's NG tube continued to drained large amounts of greenish fluid. She denied any nausea or vomiting, and reported that she had a very small bowel movement. She was started on IV Cipro® and Flagyl®. On January 1, 2011 (Cycle 2, Day 18), the patient's NG tube was clamped and a clear liquid diet was started, with no complaints of nausea, vomiting, or abdominal pain; however, she did have multiple loose stools. On January 2, 2011 (Cycle 2, Day 19), the patient tolerated removal of her NG tube. On January 4, 2011 (Cycle 2, Day 21), the patient's condition was improved, and she was discharged. 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**  
**Temsirolimus: 25 mg IV over 30 minutes weekly.**

**14. DATES OF TREATMENT**

**The patient began the investigational therapy on October 27, 2010, and received her last dose of temsirolimus on December 22, 2010 (Cycle 2, Day 8).**

**15. ACCRUAL AND IND EXPERIENCE**

**Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 2429**  
**There have been 33 other cases of small bowel obstruction reported to the NCI through AdEERS as serious 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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