

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

FAX: 301-796-9849

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1. IND NUMBER
7921
61010

2. AGENT NAME
Bevacizumab (rhuMab VEGF)
CCI-779 (tamsirolimus, Torisel™)

3. DATE
April 15, 2010

4. SPONSOR

Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION

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6. PHONE NUMBER
301-496-1196

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301-402-0428

8a. PROTOCOL NUMBER (AE #)
8233 (AE# 1746507)

8b. AE GRADE: AE
Grade 3: Hemorrhage, GI: Rectum

9. PATIENT IDENTIFICATION
PH524

10. AGE
67

11. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 67-year-old female with carcinoid tumor of the jejunum who experienced grade 3 rectal bleeding while on a phase 2 trial utilizing the investigational agents bevacizumab and tamsirolimus. She began the investigational therapy on January 27, 2010, and received only one dose of bevacizumab. The patient received the last dose of tamsirolimus on April 7, 2010. (Cycle 3, Day 8). On January 28, 2010 (Cycle 1, Day 2), the patient, who was on Coumadin®, was admitted to the hospital for an episode of GI bleed. The source of the GI bleed was not found, and it was attributed to the investigational treatment. Bevacizumab was discontinued, and the patient continued treatment with tamsirolimus. Her INR was 1.3 (reference range: 0.9-1.2) on April 7, 2010. On April 8, 2010 (Cycle 3, Day 9), she presented to the ER with several episodes of rectal bleeding, fatigue, dyspnea, and tachycardia. She appeared slightly pale and had dry mucous membranes. Her hemoglobin was 8.1 mg/dL (reference range: 12.0-15.5 mg/dL), and the hemocult was negative. The patient was admitted to the hospital and treated with 2 units of packed red blood cells. An EGD the next day showed prior pylorus-preserving Whipple with duodenojejunostomy, but was otherwise normal. Her hemoglobin was now 10.5 mg/dL. On April 10, 2010, the patient was discharged home in a stable condition. 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
Tamsirolimus: 25 mg IV 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 January 27, 2010, and received only one dose of bevacizumab. She received the last dose of tamsirolimus on April 7, 2010 (Cycle 3, Day 8).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using tamsirolimus = 1,970; and bevacizumab 25,522. There have been 4 other cases of rectal bleeding reported to the NCI through AdEERS as serious adverse events for tamsirolimus. Gastrointestinal hemorrhage is a known event for bevacizumab.

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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