

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 7921 61010	2. AGENT NAME Bevacizumab (rhuMAb VEGF) CCI-779 (tamsirolimus, Torisel™)	3. DATE May 10, 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# 1367114)	8b. AE GRADE: AE Grade 3: Ulcer, Gastrointestinal: Anus	
9. PATIENT IDENTIFICATION PH1479	10. AGE 52	11. SEX Male
12. DESCRIPTION OF ADVERSE EVENT The patient is a 52 year-old male with carcinoid tumor who experienced a grade 3 anal ulcer while on a phase 2 trial utilizing the investigational agents bevacizumab and tamsirolimus. He began the investigational therapy on February 12, 2010, and received the last dose of bevacizumab on March 26, 2010 (Cycle 2, Day 15), and the last dose of tamsirolimus on April 16, 2010 (Cycle 3, Day 8). On April 23, 2010 (Cycle 3, Day 15), the patient presented to the ER with a history of worsening rectal pain with hematochezia of 3 weeks prior to presentation. He also complained of oral ulcer. He had no nausea, vomiting, abdominal pain, or fever. The patient was admitted, started on a mouth wash, and had a surgical consultation. His rectal examination revealed a posterior midline fissure with a hypertrophic anal papilla and sentinel tag which was exquisitely tender to palpation. His hemoglobin was normal, and his stool cultures were negative. The surgeon recommended a high-fiber diet, fiber supplements, increase water intake, sitz baths, and rectal applications of hydrocortisone cream. On April 24, 2010 (Cycle 3, Day 16), the patient reported better controlled rectal pain, and he was discharged on the same day to be followed up at the clinic. 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 February 12, 2010, and received the last dose of bevacizumab on March 26, 2010 (Cycle 2, Day 15), and the last dose of tamsirolimus on April 16, 2010 (Cycle 3, Day 8).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab=26,427; and tamsirolimus=1,983. There has been 1 other case of ano-rectal ulcer failure reported to the NCI through AdEERS as serious adverse events for bevacizumab, and no other cases of ano-rectal ulcer reported to the NCI through AdEERS as serious adverse events for tamsirolimus.		
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). <u>DISCLAIMER per 21 CFR 312.32(e)</u> : 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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