

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 42780 61010	2. AGENT NAME Bryostatin CCI-779 (temsirolimus, Torisel™)	3. DATE April 13, 2009
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4. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION S. Percy Ivy, MD -Associate Chief for Investigational Therapeutics 1, Investigational Drug Branch, CTEP, DCTD, NCI L. Austin Doyle, MD-Senior Investigator for Targeted Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI	6. PHONE NUMBER 301-496-1196
	7. FAX NUMBER 301-402-0428

8. PROTOCOL NUMBER (AE #)
5785 (AE# 1450004)

9. PATIENT IDENTIFICATION 1044041	10. AGE 55	11. SEX Male
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12. DESCRIPTION OF ADVERSE EVENT
The patient is a 55-year-old male with renal cell carcinoma who experienced a grade 3 renal failure and a grade 3 creatinine, while on a phase 1 trial utilizing the investigational agents bryostatin and temsirolimus. He began the investigational therapy on March 3, 2009, and received his last dose of bryostatin and temsirolimus on March 24, 2009 (Cycle 1, Day 22). On March 24, 2009, the patient was seen for evaluation at the cardiac rehabilitation unit. Laboratory findings showed a creatinine of 2.58 mg/dL (reference range of 0.5-1.7 mg/dL). The patient's high creatinine was thought to be related with the usage of Tylenol® which was discontinued on March 17, 2009. On March 30, 2009 (Cycle 1, Day 28), his creatinine levels was increased to 3.94 mg/dL. The patient was hospitalized the next day. An ultrasound of the right kidney was negative for obstruction. Upon nephrologist's consultation, it was thought that the patient had multifactoral acute kidney injuries, and that the patient's recent chronic use of ibuprofen and Altace® are possibly related to the events. Patient was placed on IV fluids and the creatinine /renal failure was improved. The patient also received 1 unit of packed red blood cells to correct the anemia. The patient was discharged to home on April 3, 2009. 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 1 =35 Days.
 Bryostatin-1: 20 mcg/m² IV over 1 hr on Day 1, cycle 1 only
 Bryostatin-1: 20 mcg/m² IV over 1 hr on Days 8, 15 and 2
 Temsirolimus: 37.5 mg IV over 30 min on Days 8, 15 and 22**

14. DATES OF TREATMENT
The patient began the investigational therapy on March 3, 2009, and received the last dose of bryostatin and temsirolimus on March 24, 2009 (Cycle 1, Day 22).

15. ACCRUAL AND IND EXPERIENCE
Number of patients enrolled in NCI-sponsored clinical trials using bryostatin =1285 and using temsirolimus = 1102. There have been 8 cases of renal failure and 19 cases of creatinine reported to the NCI through AdEERS as a serious adverse event for bryostatin; and 16 cases of renal failure and 20 cases of creatinine reported to the NCI through AdEERS as serious adverse events for temsirolimus.

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.**