

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 April 7, 2009
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4. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION L. Austin Doyle, MD-Senior Investigator for Targeted Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI	6. PHONE NUMBER 301-496-1196
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8. PROTOCOL NUMBER (AE #)
N038H (1795312)

9. PATIENT IDENTIFICATION 9046484	10. AGE 68	11. SEX Male
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12. DESCRIPTION OF ADVERSE EVENT
The patient is a 68-year-old male with mantle cell lymphoma who experienced a grade 3 left ventricular systolic dysfunction while on a phase 2 trial using the investigational agent temsirolimus in combination with rituximab. The patient began the first dose of temsirolimus on June 16, 2008, and received the last dose of temsirolimus on February 9, 2009 (Cycle 9, Day 15), and the last dose of rituximab on January 26, 2009 (Cycle 9, Day 1). On February 9, 2009 (Cycle 9, Day 15), the patient was taken off the study and placed into event monitoring due to toxicities. On February 24, 2009 (Cycle 9, Day 30), the patient presented to the clinic to remove infusaport. The patient was found to be tachycardic prior to the procedure and the tachycardia was persisted after the procedure. An echocardiogram showed severe cardiomyopathy with ejection fraction of 25-30%. Transesophageal echo revealed a left atrial thrombus so cardioversion was not a possibility and the patient was placed on anticoagulants. The patient did have a cardiac catheterization which showed coronary disease that was not amenable to intervention and he was placed on low dose aspirin, statins and beta-blockers. On admission, decompensated CHF was noted and the patient was placed on Lasix®. CT scan of the neck revealed a mass in the right posterior nasopharynx extending inferiorly. The patient was given CHF-specific instructions for activity as tolerated, no salt, and heart healthy diet. The patient was discharged from the hospital on March 2, 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
Temsirolimus 25 mg IV over 30 minutes Days 1, 8, 15, 22
Rituximab 375 mg/m² IV at an initial rate of 100 mg hour increasing by 100 mg/hour q 30 min to a max of 400 mg/hour on Day 1 of Cycles 3, 5, 7, 9, and 11 only

14. DATES OF TREATMENT
The patient began the investigational drug therapy on June 16, 2008, and received the last dose of temsirolimus on February 9, 2009 (Cycle 9, Day 15), and the last dose of rituximab on January 26, 2009 (Cycle 9, Day 1).

15. ACCRUAL AND IND EXPERIENCE
Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1546. There have been 7 other cases of left ventricular systolic dysfunction 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 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.