

**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 <b>61010</b>	2. AGENT NAME <b>CCI-779 (temsirrolimus, Torisel™)</b>	3. DATE <b>December 18, 2009</b>
4. SPONSOR <b>Division of Cancer Treatment and Diagnosis, National Cancer Institute</b>		
5. REPORTER'S NAME, TITLE, AND INSTITUTION <b>L. Austin Doyle, MD-Senior Investigator for Targeted Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI</b>		6. PHONE NUMBER <b>301-496-1196</b>
		7. FAX NUMBER <b>301-402-0428</b>
8. PROTOCOL NUMBER (AE #) <b>N038H (AE#1548651)</b>		
9. PATIENT IDENTIFICATION <b>9047085</b>	10. AGE <b>75</b>	11. SEX <b>Male</b>
12. DESCRIPTION OF ADVERSE EVENT <b>The patient is a 75-year-old male with mantle cell lymphoma who experienced grade 4 testicular atrophy while on a phase 2 trial using the investigational agent temsirolimus in combination with rituximab. The patient received the first dose of temsirolimus on September 12, 2008, and received the last doses of temsirolimus and rituximab on August 18, 2009 (Cycle 12, Day 29). On February 3, 2009, the patient reported that he was getting weaker and was losing muscle mass. It was noticed that he had testicular atrophy. The laboratory findings were significant for a testosterone level of 440 ng/dL (reference range: 270-1070 ng/dL), and at that range the patient was not eligible for hormonal replacement. On July 21, 2009, the testicular atrophy rose to a grade 4. The laboratory levels revealed a testosterone level of 112 ng/dL. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.</b>		
13. DOSE, ROUTE, AND SCHEDULE <b>Cycle =4 weeks: Temsirolimus 25 mg IV over 30 minutes Days 1, 8, 15, 22</b>		
14. DATES OF TREATMENT <b>The patient began the investigational drug therapy on September 12, 2008, and received the last dose of temsirolimus on August 18, 2009 (Cycle 12, Day 29).</b>		
15. ACCRUAL AND IND EXPERIENCE <b>Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1815. There has been no other case of testicular atrophy reported to the NCI through AdEERS as serious adverse events for temsirolimus.</b>		
16. COMMENTS. Also administered on this protocol: <b>Cycle 1(Cycle = 4 weeks): Rituximab 375 mg/m<sup>2</sup> IV at an initial rate of 50 mg/hour increasing by 50 mg/hour every 30 minutes to a maximum of 400 mg/hour on Day 1. Rituximab 375 mg/m<sup>2</sup> IV at an initial rate of 100/mg hour increasing by 100 mg/hour every 30 minutes to a maximum of 400 mg/hour on Days 8, 15, 22. (The last administered dose of rituximab on August 18, 2009 (Cycle 12, Day 29) Cycle 2+(Cycle = 4 weeks): Rituximab 375 mg/m<sup>2</sup> IV at an initial rate of 100 mg/hour increasing by 100 mg/hour every 30 minutes to a maximum of 400 mg/hour on Day 1 of Cycles 3, 5, 7, 9, and 11 only.</b> <b>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).</b> <b>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.</b>		

0002