

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 December 22, 2010
4. SPONSOR Division of Cancer Treatment and Diagnosis, National Cancer Institute		
5. REPORTER'S NAME, TITLE, AND INSTITUTION L. Austin Doyle, M.D., 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 #) GOG-0248 (AE# 1666032)	8b. AE GRADE: AE Grade 4: Magnesium, serum-low (hypomagnesemia)	
9. PATIENT IDENTIFICATION 070-0248-007	10. AGE 66 years	11. SEX Female
12. DESCRIPTION OF ADVERSE EVENT The patient is a 66-year-old female with stage III endometrial cancer who experienced grade 4 hypomagnesemia while on a phase 2 trial utilizing the investigational agent temsirolimus. The patient began the first course of the investigational therapy on November 11, 2010, and received her last dose of temsirolimus on December 9, 2010 (Cycle 1, Day 29). On December 11, 2010 (Cycle 1, Day 31), the patient, who was previously hospitalized on September 21, 2010 for hypocalcemia secondary to hypomagnesemia and discharged, called the clinic complaining of nausea and vomiting. She was given a prescription for Compazine® which was helpful. On December 14, 2010 (Cycle 1, Day 34), the patient presented to the ER with nausea, a 2-day history of vomiting, and some mental confusion. As a result of her symptoms, she was unable to take her medications, especially magnesium tablets, for the past 3 days. An ECG showed wide complex tachycardia, ventricular bigeminy, and an old left bundle branch block. Her magnesium was 0.3 mg/dL (reference range: 1.8-2.4 mg/dL), her troponin was 0.30 ng/mL (reference: <0.04 ng/mL), her calcium was 5.0 mg/dL (reference range: 8.6-10.2 mg/dL), and her albumin was 2.7 g/dL (reference range: 3.4-5.0 g/dL) which corrected her calcium level to 6.0 mg/dL. Of note, the patient has a history of renal tubular disease and has difficulty retaining magnesium. The patient was started on IV magnesium and calcium, and frequent oral magnesium supplements which increased her level to 1.4 mg/dL. She also received Zofran® and Ativan®, and was started on IV Nexium®. The patient remained hospitalized as of December 15, 2010. 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 = 6 weeks Temsiroliimus 25 mg IV over 30 minutes on weekly.		
14. DATES OF TREATMENT The patient began the investigational therapy on November 11, 2010, and received her last dose of temsirolimus on December 9, 2010 (Cycle 1, Day 29).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 2357. There have been 4 other cases of hypomagnesemia 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 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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