

**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 2, 2009**

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 Investigational Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI**

6. PHONE NUMBER  
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7. FAX NUMBER  
**301-402-0428**

8. PROTOCOL NUMBER (AE #)  
**GOG-0248 (AE# 1963044)**

9. PATIENT IDENTIFICATION  
**087-0248-002**

10. AGE  
**63**

11. SEX  
**Female**

12. DESCRIPTION OF ADVERSE EVENT

**The patient is a 63-year-old female with endometrioid endometrial adenocarcinoma who developed grade 3 carbon monoxide diffusion capacity (DL(co)) and grade 2 FEV (1) while on a phase 2 trial utilizing the investigational agent temsirolimus. She began the first course of the investigational therapy on June 26, 2009, and received her last dose of temsirolimus on July 31, 2009 (Cycle 1, Day 36). On August 3, 2009, a restaging CT scan of the chest with contrast revealed interval development of the lower lobe predominant lung disease which was thought to represent drug reaction, aspiration or infection. The patient presented to the Pulmonary Clinic on August 6, 2009 for further investigation and reported dyspnea on exertion with climbing a flight of stairs since the initiation of the investigational therapy. She also reported the beginning of an upper respiratory illness with a 5-day history of productive cough. The study drug was held pending results of a pulmonary function test (PFT). On August 10, 2009, the PFT showed a reduced diffusing capacity and a significant underestimation of the total lung capacity which suggested that airflow obstruction was present. She was seen for a follow-up evaluation on August 20, 2009, at which time she complained of fatigue and chills with continued dyspnea on exertion. On physical examination, there were decreased breath sounds at the lung bases and she appeared to be in no apparent distress. A repeat PFT on August 21, 2009, showed declining total lung capacity and diffusing capacity. The patient was removed from the protocol. She returned on October 8, 2009 reporting significant increase in her symptoms and a 4 lbs weight loss since her last visit. Her oxygen saturation was 90-91% on room air and she desaturated to 79% after walking 600 feet in the clinic. She was started on home oxygen at 3 liters and prednisone for 4 weeks. A repeat CT scan of the chest with contrast on October 14, 2009, showed significant progressive interval increase in the lower zone hypersensitivity and drug related interstitial pneumonitis. On November 5, 2009, the patient was noted to be improving on the prednisone and oxygen therapy. The patient continues on periodic evaluation. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drugs.**

13. DOSE, ROUTE, AND SCHEDULE

**Cycle = 6 weeks  
Temsiroliimus 25 mg IV over 30 minutes weekly**

14. DATES OF TREATMENT

**The patient began the investigational therapy on June 26, 2009, and received the last dose of temsirolimus on July 31, 2009 (Cycle 1, Day 36).**

15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1813. There have been no other cases of carbon monoxide diffusion capacity and FEV (1) 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.**

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