

**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****77782**

2. AGENT NAME

**CCI-779 (temsirolimus, Torisel™)****AZD6244 Hydrogen sulfate**

3. DATE

**December 1, 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 #)

**8412 (AE# 1797555)**

8b. AE GRADE: AE

**Grade 3: Nervous system disorders-Other, specify: Numbness**

9. PATIENT IDENTIFICATION

**PAS-001**

10. AGE

**56 years**

11. SEX

**Female**

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 56-year-old female with metastatic uterine leiomyosarcoma who experienced grade 3 numbness of the left upper extremity while on a phase 2 trial utilizing the investigational agents temsirolimus and AZD6244 Hydrogen sulfate. The patient began the investigational therapy on October 15, 2010, and received her last dose of temsirolimus on October 29, 2010 (Cycle 1, Day 15) and her last dose of AZD6244 Hydrogen sulfate on November 1, 2010 (Cycle 1, Day 18). On November 1, 2010 (Cycle 1, Day 18), the patient, who has prior history of a cerebrovascular accident, was admitted to the hospital with left upper extremity weakness and numbness, associated with bilateral lower extremity discoordination, right eye visual disturbance and a slight headache. The study drugs were held. A CT scan of the head showed small areas of low density in the right frontal white matter and left centrum semiovale that were concerning for small infarcts. A MRI scan of the brain performed on November 2, 2010, revealed: no focal acute intracranial abnormality, no evidence of intracranial metastasis, a few old deep white matter lacunar infarcts, and moderately extensive leukoaraiosis due to the combination of normal aging and chronic small-vessel ischemic disease. A MRA of the brain was normal. Coagulation test results were within normal range. During the course of the patient's hospital stay, her symptoms improved. On November 3, 2010, the patient was discharged with the numbness of her arm resolved. During a follow-up visit on November 5, 2010, the patient did not have extremity numbness and the investigational agents were resumed. 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 = 28 days****Temsirolimus: 25 mg IV over 30-60 minutes on Days 1, 8, 15, and 22****AZD6244 Hydrogen sulfate: 50 mg PO twice daily**

14. DATES OF TREATMENT

The patient began the investigational therapy on October 15, 2010, and received his last doses of temsirolimus on October 29, 2010 (Cycle 1, Day 15) and his last dose of AZD6244 Hydrogen sulfate on November 1, 2010 (Cycle 1, Day 18).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 2307, and AZD6244 Hydrogen sulfate = 303.

There have been 8 other cases of sensory neuropathy reported to the NCI through AdEERS as serious adverse events for temsirolimus and 1 other case of sensory neuropathy reported to the NCI through AdEERS as serious adverse events for AZD6244 Hydrogen sulfate.

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.**

0002