

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 (temsirrolimus, Torisel™)

AZD6244 Hydrogen sulfate

3. DATE

February 25, 2011

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# 1651103)

8b. AE GRADE: AE

Grade 3: Syncope

9. PATIENT IDENTIFICATION

PAS-008

10. AGE

71 years

11. SEX

Male

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 71-year-old male with liposarcoma of the left scapula who experienced grade 3 syncope while on a phase 2 trial utilizing the investigational agents temsirolimus and AZD6244 Hydrogen sulfate. The patient began the investigational therapy on February 2, 2011, and received his last dose of temsirolimus on February 9, 2011 (Cycle 1, Day 8) and his last dose of AZD6244 Hydrogen sulfate on February 14, 2011 (Cycle 1, Day 13). On February 14, 2011 (Cycle 1, Day 13), the patient was brought to the emergency room via ambulance after being found on the floor at home. He did not remember the events, was unable to provide any kind of history as to why he fell, and he had questionable mental status changes. The patient denied headache, chest pain, and dyspnea. He had a temperature of 38.3° C, a blood pressure of 196/96 mmHg, and a pulse rate of 103 bpm. The patient, who had mild to moderate chronic dyspnea and used oxygen at home, had an oxygen saturation of 96% on 2 liters of oxygen. An ECG showed sinus tachycardia, right bundle branch block, and T-wave inversions in V3 and V4. His troponin I was 0.153 ng/mL (reference range: 0-0.390 ng/mL). He was admitted to the hospital for possible syncope associated with dehydration and mucositis. The patient was started on IV fluids, IV Rocephin®, and Tylenol®. A CT scan of the head showed mild microangiopathic white matter changes and no evidence of intracranial hemorrhage, acute territorial infarction, mass effect, or fracture. The cardiologist evaluated the patient and felt he did not have any acute cardiac issues. Blood and urine cultures were negative. The patient's condition improved. On February 16, 2011 (Cycle 1, Day 15), the patient was discharged home in stable condition to follow-up in 1-2 days. 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 February 2, 2011, and received his last dose of temsirolimus on February 9, 2011 (Cycle 1, Day 8) and his last dose of AZD6244 Hydrogen sulfate on February 14, 2011 (Cycle 1, Day 13)

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 2490, and AZD6244 Hydrogen sulfate = 339.

There have been 5 other cases of syncope reported to the NCI through AdEERS as serious adverse events for temsirolimus and no other cases of syncope 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.

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