

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

77782

61010

2. AGENT NAME

AZD6244 Hydrogen sulfate

Temsirolimus (CCI-779, Torisel®)

3. DATE

August 3, 2011

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

301-496-1196

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8a. PROTOCOL NUMBER (AE #)

8412 (AE# 1396035)

8b. AE GRADE: AE

Grade 3: Paronychia

9. PATIENT IDENTIFICATION

COH-014

10. AGE

69 years

11. SEX

Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 69-year-old female with metastatic endometrial stromal sarcoma who experienced grade 3 paronychia while on a phase 2 trial utilizing the investigational agents AZD6244 Hydrogen sulfate and temsirolimus. The patient began the investigational therapy on March 17, 2011, and received the last dose of AZD6244 Hydrogen sulfate on July 19, 2011 (Cycle 5, Day 13) and the last dose of temsirolimus on July 14, 2011 (Cycle 5, Day 8). She started the investigational treatment on a treatment arm receiving only AZD6244 Hydrogen sulfate but crossed over to a treatment arm receiving both AZD6244 Hydrogen sulfate and temsirolimus on May 12, 2011. At a follow-up visit on July 14, 2011, the patient was noted to have paronychia of the left thumb. She refused an incision and drainage at that time, and the event was managed with salt water baths. On July 16, 2011, she presented to urgent care due to progression in the size of the lesion and increased tenderness of the left thumb. She was referred to the emergency room to be managed by a hand specialist. She was admitted and started on IV antibiotics. 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

AZD6244 Hydrogen sulfate: 50 mg PO twice daily

Temsirolimus: 20 mg IV over 30-60 min on Days 1, 8, 15, and 22

14. DATES OF TREATMENT

The patient began the investigational therapy on March 17, 2011, and received the last dose of AZD6244 Hydrogen sulfate on July 19, 2011 (Cycle 5, Day 13) and the last dose of temsirolimus on July 14, 2011 (Cycle 5, Day 8).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using AZD6244 Hydrogen sulfate = 475, AZD6244 = 183, and temsirolimus = 2802. There have been no other cases of paronychia/infection reported to the NCI through AdEERS as serious adverse events for AZD6244 Hydrogen sulfate and AZD6244. Paronychia/infection is an expected event 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.