

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
May 20, 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# 1631273)

8b. AE GRADE: AE
Grade 5: Neoplasms, benign, malignant and unspecified (including cysts and polyps)-
Other: Death from progressive disease
Grade 4: Colitis

9. PATIENT IDENTIFICATION
COH-009

10. AGE
55 years

11. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 55-year-old female with recurrent pelvic sarcoma who experienced grade 4 colitis, and subsequently died while on a phase 2 trial utilizing the investigational agents temsirolimus and AZD6244 Hydrogen sulfate. The patient began the investigational therapy on February 10, 2011, and received the last dose of temsirolimus on May 5, 2011 (Cycle 4, Day 1), and the last dose of AZD6244 Hydrogen sulfate on May 7, 2011 (Cycle 4, Day 3). On May 7, 2011 (Cycle 4, Day 3), the patient presented to the ER with a 2-day history of bloody diarrhea, rectal bleeding, abdominal cramps, and pain. She was given fresh frozen plasma and blood transfusions, and was admitted to the ICU. A colonoscopy (date not provided) revealed a diffusely inflamed and friable necrotic colon. On May 11, 2011, the patient underwent a subtotal colectomy with end ileostomy for ischemic colitis. On May 14, 2011, the patient was discharged from the hospital and transferred to hospice care. On May 18, 2011, the patient died at home from progressive disease. The treating physician felt that the events were related to the investigational agents. 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 10, 2011, and received the last dose of temsirolimus on May 5, 2011 (Cycle 4, Day 1), and the last dose of AZD6244 Hydrogen sulfate on May 7, 2011 (Cycle 4, Day 3)

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 2727, and AZD6244 Hydrogen sulfate = 418. There have been 4 other cases of colitis, 72 other cases of death due to disease progression, 109 other cases of death nos, and 189 other case of sudden death reported to the NCI through AdEERS as serious adverse events for temsirolimus. There have been no other cases of colitis, and 10 other cases of death nos 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.