

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

69896
61010

2. AGENT NAME

BAY 43-9006 tosylate (BAY 54-9085; sorafenib tosylate)
CCI-779 (temsirrolimus, Torisel™)

3. DATE

April 20, 2010

4. SPONSOR

Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION

John Wright, MD, PhD-Associate Branch Chief for Investigational Therapeutics 2,
Investigational Drug Branch, CTEP, DCTD, NCI
L. Austin Doyle, MD-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 #)

S0438 (AE# 1416121)

8b. AE GRADE: AE

Grade 5: Pancreatitis
Grade 3: Renal failure

9. PATIENT IDENTIFICATION

220041

10. AGE

74

11. SEX

Female

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 74-year-old female with metastatic melanoma who experienced grade 5 pancreatitis and grade 3 renal failure while on a phase 2 trial utilizing the investigational agents sorafenib tosylate and temsirolimus. She began the investigational therapy on October 14, 2009, and received her last dose of sorafenib tosylate on January 24, 2010 (Cycle 4, Day 24), and the last dose of temsirolimus on January 13, 2010 (Cycle 4, Day 13). On January 24, 2010, the patient presented to the clinic with an altered mental status and 2 days of constant abdominal pain. It was described as located in the right, left and lower abdomen, in the periumbilical area, and in the pelvic area. Her amylase was 173 IU/L (reference range: 30-110 IU/L), her lipase was 2111 IU/L (reference range: 114-286 IU/L), and her total CK was 357 (reference range: 21-215). A CT scan of the abdomen and pelvis revealed multiple pulmonary nodules, multiple solid liver lesions, and an unremarkable pancreas. It was felt that her pancreatitis was possibly related to the study medication. On January 25, 2010, her amylase was 547 IU/L and her lipase 5671 IU/L. The patient expired on January 25, 2010, and no autopsy was performed. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.

13. DOSE, ROUTE, AND SCHEDULE

Cycle = 28 Days.

Sorafenib tosylate: 200 mg PO twice daily

Temsirolimus: 25 mg IV over 30 minutes on Days 1, 8, 15, and 22

14. DATES OF TREATMENT

The patient began the investigational therapy on October 14, 2009, and received her last dose of sorafenib tosylate on January 24, 2010 (Cycle 4, Day 24), and the last dose of temsirolimus on January 13, 2010 (Cycle 4, Day 13).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1,970; sorafenib tosylate = 5,916. There have been 2 other cases of pancreatitis reported to the NCI through AdEERS as serious adverse events for temsirolimus, and 23 other cases of pancreatitis and 38 other cases of renal failure reported to the NCI through AdEERS as serious adverse events for sorafenib tosylate. Renal failure 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.

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