

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
74019**

2. AGENT NAME

**BAY 43-9006 tosylate (BAY 54-9085; sorafenib tosylate)
Sunitinib malate (SU011248 L-malate; Sutent[®])**

3. DATE

January 15, 2010

4. SPONSOR

Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION

**John Wright, MD, PhD-Senior Investigator for Targeted Therapeutics 1,
Investigational Drug Branch, CTEP, DCTD, NCI**

6. PHONE NUMBER

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7. FAX NUMBER

301-402-0428

8. PROTOCOL NUMBER (AE #)

E2805 (AE# 1222406)

9. PATIENT IDENTIFICATION

29284

10. AGE

67

11. SEX

Male

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 67-year-old male with renal cell carcinoma who experienced a grade 4 pulmonary embolism while on phase 3 trial comparing adjuvant sorafenib tosylate/placebo and sunitinib malate/placebo. The patient began the investigational therapy on April 13, 2009, and received the last doses of sorafenib tosylate/placebo, or sunitinib malate/placebo on August 14, 2009, (Cycle 3, Day 39). On August 14, 2009, the patient presented to the clinic for a routine CT scan of the chest which was reported as unremarkable. A repeat chest CT scan done on December 18, 2009, showed a small segmental pulmonary embolism. A venous Doppler[®] ultrasound of both lower extremities was negative but D-dimer done on December 22, 2009, was 1.1 ug/mL (reference: < 0.35 ug/mL). The patient was placed on Coumadin[®] on December 23, 2009. Additional information has been requested from the investigative site. There is a reasonable possibility that the event may have been caused by the drug.

13. DOSE, ROUTE, AND SCHEDULE (Cycle = 42 days)

Sorafenib/Placebo 400 mg PO twice daily for a maximum of 9 cycles.**Sunitinib malate/Placebo 50 mg PO once daily for Weeks 1-4.**

14. DATES OF TREATMENT

The patient started the investigational drug therapy on April 13, 2009, and received the last doses of sorafenib/placebo and sunitinib malate/placebo on August 14, 2009 (Cycle 3, Day 39).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using sorafenib tosylate = 5597, and using sunitinib malate = 2114. Pulmonary embolism is an expected adverse event for sorafenib tosylate.**There have been 24 other cases of pulmonary embolism reported to the NCI through AdEERS as serious adverse events for sunitinib malate.**

AT THIS TIME, NO OTHER INFORMATION IS AVAILABLE. IF UPON FURTHER INVESTIGATION RELEVANT INFORMATION BECOMES AVAILABLE, THEN A FOLLOWUP REPORT WILL BE SUBMITTED IN ACCORDANCE WITH 21CFR312.32(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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