

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
July 7, 20114. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute5. REPORTER'S NAME, TITLE, AND INSTITUTION
**John Wright, MD, PhD-Associate Branch Chief for Investigational Therapeutics 2,
Investigational Drug Branch, CTEP, DCTD, NCI**6. PHONE NUMBER
301-496-1196**Pamela Harris, MD-Senior Investigator for Investigational Therapeutics 1, Investigational
Drug Branch, CTEP, DCTD, NCI**7. FAX NUMBER
301-402-04288a. PROTOCOL NUMBER (AE #)
E2805 (AE# 1279979)8b. AE Grade: AE
Grade 4: Perforation, GI: Stomach9. PATIENT IDENTIFICATION
2983210. AGE
52 years11. SEX
Male

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 52-year-old male with renal cell carcinoma who experienced a grade 4 gastric perforation with sepsis and subsequently expired while on phase 3 trial comparing adjuvant sorafenib tosylate/placebo and sunitinib malate/placebo. The patient began the investigational therapy on June 16, 2010, and received the last doses of sorafenib tosylate/placebo, and sunitinib malate/placebo on May 26, 2011, (Cycle 9, Day 16). On May 28, 2011 (Cycle 9, Day 18), the patient presented to the emergency room with abdominal pain and nausea and reported that he had coffee ground emesis with a small amount of blood earlier that morning. Of note, the patient was not taking any aspirin or non-steroidal anti-inflammatory medications, and had no history of smoking or alcohol use. An abdominal CT scan revealed extensive air in the biliary system of the liver, extensive air around the abdomen, loops of bowel that were distended with pneumatosis, a large fluid collection in the pelvis, and fluid in the bowel wall. The patient was hypertensive and tachycardic but his EKG showed no acute changes. He was taken to the operating room and underwent an exploratory laparotomy, drainage of intra-abdominal abscesses, extensive lysis of adhesions, plication of gastric perforation, and application of wound VAC system for abdominal closure. He was transferred to the ICU where his condition continued to worsen due to septic shock and multi-organ failure. On May 29, 2011, his life support was withdrawn and he was given comfort care until his death later that afternoon. 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; Maximum 9 Cycles)**Sorafenib/Placebo: 400 mg PO once daily for Cycle 1 (or Cycles 1 and 2); then twice daily for Cycles 2-9 or 3-9.****Sunitinib malate/Placebo: 37.5 mg PO once daily for Weeks 1-4 for Cycle 1 (or Cycles 1 and 2); then 50 mg PO once daily for Weeks 1-4 for Cycles 2-9 or 3-9.**

14. DATES OF TREATMENT

The patient started the investigational drug therapy on June 16, 2010, and received the last doses of sorafenib/placebo and sunitinib malate/placebo on May 26, 2011 (Cycle 9, Day 16).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using sorafenib tosylate = 6,694, and using sunitinib malate = 2,917.**There has been 1 other case of stomach perforation reported to the NCI through AdEERS as a serious adverse event for sorafenib and no other cases reported to the NCI through AdEERS as serious adverse events for sunitinib malate.**

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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