



**Date:** March 6, 2009

**To:** NCCTG Primary Clinical Research Associates

**From:** Janis Wobschall  
Protocol Development Coordinator

**Re:** N0572, A Phase I/II Study of Sorafenib and CCI-779 in Patients with Recurrent Glioblastoma

The purpose of this memorandum is to provide investigators with a recent report of an adverse event that has occurred in association with BAY 43-9006 for a study where the Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI) is distributing this agent. You may have also received this communication directly from DCTD.

**AE\_1434562**

Please note that all risks currently cited in the NCCTG consent form cannot be omitted; it is at the discretion of your local IRB as to whether they wish to add risks based on the enclosed information. If a determination has been made by the NCCTG Research Base that a protocol amendment is necessary, you will receive the NCI-approved protocol addendum at a later date; for purposes of cross-reference, this communication will cite the adverse event noted above.

**Please submit this adverse event to your Institutional Review Board.**

If you have any questions concerning this communication, please contact Janis Wobschall at [wobschall.janis@mayo.edu](mailto:wobschall.janis@mayo.edu) or 507/284-4852.

JW/kjm  
enclosure

**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<sup>®</sup>)**

3. DATE

**December 1, 2008**

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 Targeted Therapeutics 2,  
Investigational Drug Branch, CTEP, DCTD, NCI**

6. PHONE NUMBER

**301-496-1196****S. Percy Ivy, MD - Associate Branch Chief for Targeted Therapeutics 1,  
Investigational Drug Branch, CTEP, DCTD, NCI**

7. FAX NUMBER

**301-402-0428**

8. PROTOCOL NUMBER (AE #)

**E2805 (1434562)**

9. PATIENT IDENTIFICATION

**28587**

10. AGE

**73**

11. SEX

**Male**

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 73-year-old male with renal cell carcinoma who experienced a grade 4 thrombosis and grade 3 chest pain while on phase 3 trial comparing adjuvant sorafenib tosylate or placebo and sunitinib malate or placebo. The patient began the investigational therapy on December 28, 2007, and received the last doses of sorafenib tosylate or placebo, or sunitinib malate or placebo on May 22, 2008 (Cycle 4, Day 22). On May 23, 2008, the patient presented to the emergency room with shortness of breath and right pleuritic chest pain. He claims calluses of his hands and pain in his feet when walking due to study therapy. The patient denies nausea, vomiting, diaphoresis, abdominal pain or leg pain. Computed tomography angiography (CAT) of the chest performed while he was to the ER, showed saddle pulmonary embolus. The patient was admitted to the hospital for further evaluation and management. The patient was started on heparin drip and Flomax<sup>®</sup>. The investigational agent was discontinued and the patient was taken off the study on May 23, 2008. Venous Doppler's in both extremities was normal. There was no evidence of pneumonia on chest x-rays or CAT scan. On June 1, 2008, the patient was discharged home on 5 mg of Coumadin<sup>®</sup> orally at bedtime. There is a reasonable possibility that the experience is related to the investigation therapy. Additional information has been requested from the investigative site.

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

**Sorafenib or Placebo 400 mg PO twice a day x 6 weeks for 9 cycles, or  
Sunitinib malate or Placebo 50 mg PO daily x 4 weeks followed by rest for 2 weeks for 9 cycles**

14. DATES OF TREATMENT

**The patient started the investigational drug therapy on December 28, 2007, and received the last doses of sorafenib or placebo, or sunitinib malate or placebo on May 22, 2008 (Cycle 4, Day 22).**

15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using BAY 43-9006 tosylate = 4604, and using sunitinib malate = 1475.**

**There have been 105 other cases of thrombosis and 29 other cases of chest pain reported to the NCI though AdEERS as serious adverse events for BAY 43-9006, and 19 other cases of thrombosis and 2 other cases of chest pain reported to the NCI though 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.**

0002