

**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**2. AGENT NAME  
**BAY 43-9006 tosylate (sorafenib tosylate)**3. DATE  
**April 4, 2011**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**6. PHONE NUMBER  
**301-496-1196**7. FAX NUMBER  
**301-402-0428**8a. PROTOCOL NUMBER (AE #)  
**CALGB-80802 (AE# 1807371)**8b. AE GRADE: AE  
**Grade 5: Cardiac Arrest**9. PATIENT IDENTIFICATION  
**124275**10. AGE  
**68 years**11. SEX  
**Male**

## 12. DESCRIPTION OF ADVERSE EVENT

The patient was a 68-year-old male with metastatic hepatocellular carcinoma who experienced grade 5 cardiac arrest while on a phase 3 trial utilizing the investigational agent sorafenib in combination with doxorubicin. He began the first course of the investigational therapy on January 28, 2011, and received his last dose of sorafenib on February 7, 2011 (Cycle 1, Day 11). The patient received his first and only dose of doxorubicin on January 28, 2011 (Cycle 1, Day 1). On February 3, 2011 (Cycle 1, Day 7), the patient called the clinic to report soreness of the scalp and sore throat. He denied having sore mouth and pain or redness of his hands and feet. He was started on minocycline. On February 7, 2011 (Cycle 1, Day 11), the EMS was called to the patient's home with reports of him being lethargic. He was transported to the local ER in cardiac arrest. While enroute to the ER, the patient was started on cardiopulmonary resuscitation, IV fluids, and oxygen. He received Narcan<sup>®</sup>, epinephrine, atropine, and D50 for a blood sugar level of 33 mg/dL (reference range: 65-120 mg/dL). On arrival at the ER at 2:55 PM, the patient had shallow respirations at a rate of 16 breaths per minute, a blood pressure of 115/21 mmHg, and a heart rate of 156 bpm. An ECG showed atrial fibrillation with rapid ventricular response and right bundle branch block. His chest X-ray revealed bilateral diffuse infiltrates which were greater in the right lung than in the left, and a questionable emphysematous pyelonephritis. His blood sugar increased to 221 mg/dL. A nasogastric tube was inserted, dopamine drip was started, and he was intubated and placed on mechanical ventilation with an oxygen saturation of 100%. At 3:30 PM, the patient's blood pressure increased to 151/110 mmHg and his respiration was 13 breaths per minute. Cardiopulmonary resuscitation was reinitiated, the dopamine drip rate was increased, and the patient was given IV bicarbonate. Despite resuscitative measures, the patient expired at 3:59 PM that day. On February 9, 2011, the site was notified by the patient's wife of his death. An autopsy was not 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 = 21 Days  
Sorafenib: 400 mg PO twice daily**

## 14. DATES OF TREATMENT

**The patient began the investigational therapy on January 28, 2011, and received his last dose of sorafenib on February 7, 2011 (Cycle 1, Day 11).**

## 15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using sorafenib = 6634  
There have been 6 other cases of cardiac arrest reported to the NCI through AdEERS as serious adverse events for sorafenib.**

## 16. COMMENTS Also administered on this protocol:

**Doxorubicin: 60 mg/m<sup>2</sup> IV on Day 1 for Cycles 1-6****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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