



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: October 10, 2008
To: NCCTG Primary Clinical Research Associates
From: Janis Wobschall
Re: N027D, “A Phase I Study of CCI-779 and Temozolomide in Combination with Radiation Therapy in Glioblastoma Multiforme”

The purpose of this memorandum is to provide investigators with a recent report of an adverse event that has occurred in association with CCI-779 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_1047408

Please note that all risks currently cited in the NCCTG consent form can not 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 or 507-284-4852.

JW/kjm
enclosure

IND SAFETY REPORT: INITIAL WRITTEN REPORT

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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 (temsirolimus, Torisel™)**

3. DATE

September 23, 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**L. Austin Doyle, MD-Senior Investigator for Targeted Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI**

6. PHONE NUMBER

301-496-1196

7. FAX NUMBER

301-402-0428

8. PROTOCOL NUMBER (AE #)

E2804 (1047408)

9. PATIENT IDENTIFICATION

28062

10. AGE

77

11. SEX

Male

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 77-year-old male with renal cell carcinoma who died suddenly while on a phase 2 trial using the investigational agents: bevacizumab, sorafenib, and temsirolimus. He began the investigational therapy on August 13, 2008, and received the last dose of sorafenib on September 12, 2008 (Cycle 2, Day 2), and the last dose of temsirolimus on September 11, 2008 (Cycle 2, Day 1). On September 12, 2008, the patient was found on the bathroom floor of the nursing home without spontaneous respirations or pulse. After the patient was intubated and given atropine and epinephrine, he went into ventricular tachycardia. He was defibrillated with a pulseless electrical activity response and then went into asystole. Upon arrival to the emergency room resuscitation efforts were continued but the patient did not recover. Additional information has been requested. There is a reasonable possibility that the experience may have been caused by the drug.

13. DOSE, ROUTE, AND SCHEDULE

Cycle =28 days**Sorafenib 200 mg or placebo PO twice daily****Temsirolimus 25 mg IV over 30 minutes on days 1, 8, 15, and 22**

14. DATES OF TREATMENT

The patient started the investigational therapy on August 13, 2008, and received the last dose of sorafenib on September 12, 2008 (Cycle 2, Day 2) and the last dose of temsirolimus on September 11, 2008 (Cycle 2, Day 1).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using sorafenib = 4367, temsirolimus = 1312. There have been 20 other incidences of sudden death, and 26 incidences of death NOS reported to the NCI through AdEERS as serious adverse events for sorafenib and 3 other incidences of sudden death and 14 incidences of death NOS reported to the NCI through AdEERS as serious adverse events for temsirolimus.

16. COMMENTS

Bevacizumab was not administered on this treatment arm.

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.