



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: March 13, 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_1475911

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 or 507/284-4852.

JW/kjm
enclosure



Eastern Cooperative Oncology Group

Coordinating Center
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Director of Research Operations: Jean MacDonald
Director of Group Administration: Mary Steele

Group Chair: Robert L. Comis, M.D.
Group Statistician: Robert Gray, Ph.D.

MEMORANDUM

TO: ECOG Clinical Research Associates and Investigators who participate on E1305, E1404, E1804, E2501, E2603, 2804, E2805, E5203, E1105, E1505, E2100, E2104, E2204, E3501, E4203, E4599, E5103, E5202, E5204, S0438

FROM: ECOG Coordinating Center

DATE: December 10, 2008

SUBJECT: BAY 43-9006 (ECOG IND # 68,880, NCI IND # 69,896) and Bevacizumab (BB-IND's 7921, 9877, 11460 and ECOG IND 12720) Safety Report
AE# 1475911

This is a report of a Serious Adverse Event (SAE) that occurred in association with Bay 43-9006 and Bevacizumab in a study sponsored by the NCI. Attached is the actual adverse event report as received from the NCI. Should any further information related to this adverse experience become available, it will be forwarded to you as soon as possible.

Please submit this report to your Institutional Review Board (IRB)/Ethics Committee (EC) for their review within 90 days. This report, any correspondence to your IRB/EC and documentation of review should be maintained in your study files. Protocol amendments are not necessary at this point. However, the decision to amend your informed consent forms to include the possibility of the adverse events as described should be left to your individual IRB.

It is a requirement of the NCI's Clinical Trials Monitoring Branch (CTMB) that AE reports for patients on NCI sponsored trials be submitted and reviewed by the participating institution's IRB within 90 days of issue. If it is the policy of the participating institution's IRB to review such reports in a more limited manner or according to a longer time-line, this is acceptable provided that such policy is defined in the institution's IRB's Standard Operating Procedures (SOPs). A copy of the SOPs, if in variance with the CTMB requirement, must be available at the time of an ECOG sponsored audit.

If you have any questions please contact Ginny Willcox at the ECOG Coordinating Center (617-632-3610).

IND SAFETY REPORT: INITIAL WRITTEN REPORT**TO: Division of Drug Oncology Products, Center for Drug Evaluation and Research, FDA****FAX: 301-796-9845****TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA****FAX: 301-796-9849**

1. IND NUMBER

69896

2. AGENT NAME

BAY 43-9006 tosylate (BAY 54-9085; sorafenib tosylate)

3. DATE

December 2, 2008**7921****Bevacizumab (rhuMab VEGF)**

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**Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics 3, CTEP, DCTD, NCI**

7. FAX NUMBER

301-402-0428

8. PROTOCOL NUMBER (AE #)

E2804 (AE # 1475911)

9. PATIENT IDENTIFICATION

28039

10. AGE

69

11. SEX

Female

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 69-year-old female with renal cell carcinoma who died from an acute intracerebral hemorrhage while on a phase 2 trial using the investigational agents: bevacizumab, sorafenib, and temsirolimus. She began the investigational therapy on June 18, 2008, and received the last dose of sorafenib on November 10, 2008 (Cycle 6, Day 5), and the last dose of bevacizumab on November 6, 2008 (Cycle 6, Day 1). On November 12, 2008, the patient was taken to the emergency room by her husband for symptoms of a severe headache and systolic blood pressure of over 220 mmHg. En route, she lost consciousness and upon arrival at the emergency room she was intubated and placed on mechanical ventilation. A head CT scan showed two distinct areas of large intracerebral hemorrhage. She was admitted to the ICU and her hypertension was controlled with a nicardipine drip. She remained unresponsive and after discussion with the family the patient was placed on comfort care measures only. She died later that evening. 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 BID on days 1-5, 8-12, 15-19, and 22-26****Bevacizumab 5 mg/kg IV over 30-90 minutes on days 1 and 15**

14. DATES OF TREATMENT

The patient started the investigational therapy on June 18, 2008, and received the last dose of sorafenib on November 10, 2008 (Cycle 6, Day 5) and the last dose of bevacizumab on November 6, 2008 (Cycle 6, Day 1).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using sorafenib = 4,604, bevacizumab = 18,136.

CNS hemorrhage is known to be associated with bevacizumab. There have been 18 other incidences of CNS hemorrhage reported to the NCI through AdEERS as serious adverse events for sorafenib.

16. COMMENTS

Temsirolimus 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.

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