



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: March 6, 2009

To: NCCTG Primary Clinical Research Associates

From: Janis Wobschall
Protocol Development Coordinator

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_1951869

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

TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA
Division of Drug Oncology Products, Center For Drug Evaluation and Research, FDA

FAX: 301-796-9849

301-796-9845

1. IND NUMBER 61010 7921	2. AGENT NAME CCI-779 (temsirolimus, Torisel™) Bevacizumab (rhuMab VEGF)(704865)	3. DATE December 5, 2008
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4. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION L. Austin Doyle , MD-Senior Investigator 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 #)
6986 (AE# 1951869)

9. PATIENT IDENTIFICATION PH1052	10. AGE 61	11. SEX Male
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12. DESCRIPTION OF ADVERSE EVENT
The patient was a 61-year-old male with renal cell carcinoma who expired while on a phase 1/2 trial utilizing the investigational agents bevacizumab and temsirolimus. He began the investigational therapy on April 1, 2008, and received his last dose of bevacizumab on June 10, 2008 (Cycle 3, Day 15), and the last dose of temsirolimus on June 17, 2008 (Cycle 3, Day 22). The patient did not show up for his scheduled visit on June 24, 2008 (Cycle 4, Day 1), due to clinical deterioration. The patient expired on June 26, 2008. An autopsy was not performed. Additional information has been requested from the investigational site. There is a reasonable possibility that the death may have been caused by the drug.

13. DOSE, ROUTE, AND SCHEDULE
Cycle =28 Days. Temsirolimus 10 mg IV over 30 minutes on Days 1, 8, 15, and 22
Bevacizumab 5 mg/kg IV over 30-90 minutes on Days 1 and 15

14. DATES OF TREATMENT
The patient began the investigational therapy on April 1, 2008, and received the last dose of bevacizumab on June 10, 2008 (Cycle 3 Day 15), and the last dose of temsirolimus on June 17, 2008 (Cycle 3, Day 22).

15. ACCRUAL AND IND EXPERIENCE
Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1375 and for bevacizumab = 18136. There have been 7 other incidences of death related to multi-organ failure, 18 other incidences of death, NOS, and 4 other incidences of sudden death reported to the NCI through AdEERS as a serious adverse events for temsirolimus; and 9 other incidences of death related to multi-organ failure, 60 other incidences of death, NOS, and 43 other incidences of sudden death reported to the NCI through AdEERS as serious adverse events for bevacizumab.

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 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.