



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: January 30, 2009

To: NCCTG Primary Clinical Research Associates

From: Lynn Flickinger
Protocol Development Coordinator

Re: N0735, Phase II Trial of Albumin-Bound Paclitaxel in Combination with Gemcitabine and Bevacizumab in Patients with Metastatic Breast Cancer

The purpose of this memorandum is to provide investigators with a recent report of an adverse event that has occurred in association with Bevacizumab 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_1205368

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 Lynn Flickinger at Flickinger.lynn@mayo.edu or 507-538-7034.

LF/kjm
enclosure

IND SAFETY REPORT: INITIAL WRITTEN REPORT #42

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

FAX: 301-796-9849

1. IND NUMBER 61010 7921	2. AGENT NAME CCI-779 (temsirolimus, Torisel™) Bevacizumab (rhuMAb VEGF)(704865)	3. DATE November 19, 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 #)
E2804 (AE# 1205368)

9. PATIENT IDENTIFICATION 28070	10. AGE 69	11. SEX Female
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12. DESCRIPTION OF ADVERSE EVENT
The patient is a 69-year-old female with renal cell carcinoma who experienced a grade 3 left ventricular systolic dysfunction while on a phase 2 trial utilizing the investigational agents bevacizumab and temsirolimus. She began the investigational therapy on September 11, 2008, and received her last dose of bevacizumab on September 25, 2008 (Cycle 1, Day 15), and the last dose of temsirolimus on October 16, 2008 (Cycle 2, Day 8). On October 22, 2008 (Cycle 2, Day 14), the patient presented to the emergency room complaining of headache, weakness, dyspnea, nausea, and vomiting. She had a temperature of 99.2° F, pulse 94 bpm, blood pressure 165/104 mmHg, and an oxygen saturation of 93% on room air. The patient was treated with Zofran® and morphine for her headache, started on IV fluids, and admitted to the hospital for observation. A CT scan of the chest showed bilateral effusions and areas of atelectasis with some pulmonary nodules. The patient later developed multifocal atrial tachycardia (MAT). An echocardiogram showed a mildly depressed left ventricular function with an estimated ejection fraction of less than 50%. It was felt that her cardiomyopathy likely developed following chemotherapy. She was treated with Solu-Medrol®, Lasix®, and antibiotics. The patient's condition gradually improved and she was discharged home on October 29, 2008 (Cycle 2, Day 21). 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 =28 Days. Temsirolimus 25 mg IV over 30 minutes on Days 1, 8, 15, and 22
Bevacizumab 10 mg/kg IV over 30-90 minutes on Days 1 and 15**

14. DATES OF TREATMENT
The patient began the investigational therapy on September 11, 2008, and received the last dose of bevacizumab on September 25, 2008 (Cycle 1 Day 15), and temsirolimus on October 16, 2008 (Cycle 2, Day 8).

15. ACCRUAL AND IND EXPERIENCE
Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1372 and for bevacizumab = 18130. There have been no other incidences of left ventricular systolic dysfunction reported to the NCI through AdEERS as a serious adverse event for temsirolimus; and 105 other incidences of left ventricular systolic dysfunction 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.