



# NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

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**Date:** October 3, 2008

**To:** NCCTG Primary Clinical Research Associates

**From:** Sara Braun

**Re:** N0775, A Randomized Phase II Trial of Temozolomide (TMZ) and Avastin® or ABI-007/Carboplatin (CBDCA) and Avastin® in Patients with Unresectable Stage IV Malignant Melanoma

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\_1506455**

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 Sara Braun at [braun.sara@mayo.edu](mailto:braun.sara@mayo.edu) or 507-538-8226.

SB/kjm  
enclosure

**IND SAFETY REPORT: INITIAL WRITTEN REPORT**

No. 35

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

**FAX: 301-796-9849**

**1. IND NUMBER**  
7921

**2. AGENT NAME**  
Bevacizumab (rhuMAb VEGF)

**3. DATE**  
September 18, 2008

**4. SPONSOR**  
Division of Cancer Treatment and Diagnosis, National Cancer Institute

**5. REPORTER-S NAME, TITLE, AND INSTITUTION**  
Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics III, Investigational Drug Branch, CTEP, DCTD, NCI

**6. PHONE NUMBER**  
301-496-1196

**7. FAX NUMBER**  
301-402-0428

**8. PROTOCOL NUMBER (AE #)**  
CALGB-90401 (AE # 1506455)

**9. PATIENT IDENTIFICATION**  
110301

**10. AGE**  
68

**11. SEX**  
Male

**12. DESCRIPTION OF ADVERSE EVENT**  
The patient was a 68-year-old male with prostate cancer who died suddenly while on a phase 3 study using the investigational agent bevacizumab/placebo in combination with dexamethasone, docetaxel, and prednisone. He began his first course of treatment on November 15, 2007, and received the last doses of bevacizumab/placebo, docetaxel, dexamethasone, and prednisone on September 4, 2008 (Cycle 15, Day 1). On the morning of September 13, 2008, the patient's wife found the patient dead having died in his sleep. She called emergency services. The patient was not able to be resuscitated and he was pronounced dead by the deputy coroner. He was taken directly to the mortuary and no autopsy was performed. 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**  
Bevacizumab/Placebo 15 mg/kg IV over 30 to 90 minutes on day 1, every 21 days.

**14. DATES OF TREATMENT**  
The patient started began his first course of treatment on November 15, 2007, and received the last doses of bevacizumab/placebo, docetaxel, dexamethasone, and prednisone on September 4, 2008 (Cycle 15, Day 1).

**15. ACCRUAL AND IND EXPERIENCE**  
Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 17,088. There have been 41 other cases of sudden death and 57 cases of death not otherwise specified reported to the NCI through AdEERS as serious adverse events for bevacizumab.

**16. COMMENTS**  
The following was also administered every cycle (21 days):  
Dexamethasone 8 mg PO 12 hours, 3 hours, and 1 hour prior to docetaxel on day 1  
Docetaxel 75 mg/m<sup>2</sup> IV over 1 hour on day 1  
Prednisone 5 mg PO twice daily

**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.**