



# NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

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**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\_1809808**

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](mailto:Flickinger.lynn@mayo.edu) or 507-538-7034.

LF/kjm  
enclosure

## INITIAL IND SAFETY REPORT COMMUNICATION

#41

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

FAX: 301-796-9849

1. IND NUMBER  
79212. AGENT NAME  
Bevacizumab (rhuMab VEGF)3. DATE  
November 7, 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 3, CTEP, DCTD, NCI

6. PHONE NUMBER  
301-496-11967. FAX NUMBER  
301-402-04288. PROTOCOL NUMBER (AE #)  
S0518 (AE # 1809808)9. PATIENT IDENTIFICATION  
21223210. AGE  
6811. SEX  
Male

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 68-year-old male with metastatic carcinoid tumor who experienced a grade 2 rash and grade 3 lower extremity pain while on a phase 3 study using the investigational agent bevacizumab in combination with octreotide. He began the first course of treatment on September 5, 2008, and received the only doses of bevacizumab and octreotide on that day (Cycle 1, Day 1). On the evening of September 11, 2008 (Cycle 1, Day 7), the patient was brought to the emergency room by ambulance with symptoms of extreme fatigue, weakness, and somnolence. Upon examination he was febrile, hypotensive, and had a dark violaceous rash on his inner thighs with smaller rash areas on his lower legs. He was given hydration and one dose of Zosyn<sup>®</sup> after blood cultures were drawn. A head CT scan and MRI showed no changes from prior studies or acute findings. He was admitted to the hospital and on September 12, 2008, a skin biopsy of the affected area was performed. The rash was thought to have been a hypersensitivity reaction related to a medication. His blood cultures were negative. By the following day, his somnolence and hypotension had resolved and he was discharged. On September 23, 2008, he returned for follow-up and reported a history of severe pain in his anterior thighs that started several days after receiving the investigational treatment and made rising from a sitting position and climbing stairs difficult. He also reported pedal edema that developed every afternoon. The violaceous lesions on his lower extremities were ruddier in color and smaller in appearance. He was removed from the protocol. 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 = 21 days

Bevacizumab/Placebo 15 mg/kg IV over 30-90 minutes on Day 1

14. DATES OF TREATMENT

The patient received the first and only dose of bevacizumab/placebo on September 5, 2008.

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 18,122. There have 24 other incidences of rash/desquamation and 10 other incidences of extremity pain reported to the NCI through AdEERS as serious adverse events for bevacizumab.

16. COMMENTS

The following was also administered every 21 days: Octreotide LAR depot: 20 mg IM on Day 1; Last administered on September 5, 2008.

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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