



# NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

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**Date:** March 13, 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\_1433885**

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 SAFETY REPORT: INITIAL WRITTEN REPORT**

**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  
**December 12, 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  
**301-496-1196**

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

8. PROTOCOL NUMBER (AE #)  
**E5103 (AE # 1433885)**

9. PATIENT IDENTIFICATION  
**50752**

10. AGE  
**61**

11. SEX  
**Female**

12. DESCRIPTION OF ADVERSE EVENT  
**The patient is a 61-year-old female with breast carcinoma who experienced grade 3 pulmonary infiltrates while on a double-blind phase 3 study using the investigational agent bevacizumab/placebo in combination with paclitaxel, doxorubicin, and cyclophosphamide. She began her first course of treatment on August 5, 2008, and received the last dose of bevacizumab/placebo on October 21, 2008 (Cycle 6, Day 1). The patient presented to the hospital to receive her 7<sup>th</sup> cycle of chemotherapy on November 11, 2008 (Cycle 6, Day 22). The patient presented with chronic dry cough during that day, with daily expectoration of white phlegm mixed with blood as well as watery non-bloody diarrhea. The patient appeared depressed although she did not specifically express this. Chest X-rays showed bilateral diffuse opacities consistent with possible pneumonia. She developed a fever and had an O2 saturation of 94% on room air. The patient was hospitalized and went off the investigation study. She was receiving Sertaline® for depression and aciclovir for a possible HSV pneumonitis. On November 23, 2008, she was having chest pain with negative troponin. Her medical condition improved and she was discharged home on November 24, 2008. 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 30-90 minutes on Day 1 (Cycles 1-4) Cycle=14 days**  
**Bevacizumab/Placebo 15 mg/kg IV on Day 1 (Cycles 5-8) Cycle=21 days**

14. DATES OF TREATMENT **The patient started the investigational therapy on August 05, 2008, and received the last dose of bevacizumab/placebo on October 21, 2008 (Cycle 6, Day 1).**

15. ACCRUAL AND IND EXPERIENCE  
**Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 18177.**  
**There have been 105 other cases of pulmonary infiltrates reported to the NCI though AdEERS as serious adverse events for bevacizumab.**

16. COMMENTS  
**Also administered on this protocol:**  
**Doxorubicin 60 mg/m<sup>2</sup> IVP on Day 1 (last administered dose: September 16, 2008)**  
**Cyclophosphamide 600 mg/m<sup>2</sup> over 20-30 min on Day 1 (last administered dose: September 16, 2008)**  
**Paclitaxel 80 mg/m<sup>2</sup> over 1 hr on Days 1, 8, and 15 (last administered dose: November 04, 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.**