



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_1729567

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

INITIAL IND SAFETY REPORT COMMUNICATION # 70

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
November 19, 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 # 1729567)

9. PATIENT IDENTIFICATION
50479

10. AGE
41

11. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 41-year-old female with invasive breast carcinoma who experienced a grade 4 pulmonary embolism 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 June 9, 2008, and received the last dose of bevacizumab/placebo on September 15, 2008 (Cycle 7, Day 1). She received her last doses of paclitaxel on September 08, 2008 (Cycle 6, Day 8), cyclophosphamide and doxorubicin on July 21, 2008 (Cycle 4, Day 1), and G-CSF on July 22, 2008, (Cycle 4, Day 2). The patient presented to the hospital on September 24, 2008 (Cycle 7, Day 10), with dyspnea for 3 weeks as well as confusion and back pain. A CT chest angiogram showed extensive pulmonary emboli in the main pulmonary arteries, and an echocardiogram revealed a 5 cm right atrial thrombus. The patient was treated with heparin, Coumadin® and Lovenox®. She was unblinded, receiving bevacuzimab, and was removed from protocol on September 26, 2008. On October 11, 2008, she was discharged home. 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 10 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 June 09, 2008, and received the last dose of bevacizumab/placebo on September 15, 2008 (Cycle 7, Day 1).**

15. ACCRUAL AND IND EXPERIENCE **This adverse event is known to be associated with the investigational agent, bevacizumab.**

16. COMMENTS **The following was also administered: Cycles 1-4: Doxorubicin 60 mg/m² IV on Day 1, Cyclophosphamide 600 mg/m² IV over 20-30 min on Day 1, Filgrastim 5 mcg/kg SQ on Days 2-11 or Pegfilgrastim 6 mg SQ on Day 2; Cycles 5-8: Paclitaxel 80 mg/m² IV over 1 hour on Days 1, 8 and 15.**

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.