



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_1477246

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

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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 3, 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 #)
GOG-0218 (AE # 1477246)

9. PATIENT IDENTIFICATION
064-0218-007

10. AGE
58

11. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT
The patient was a 58-year-old female with primary peritoneal carcinoma who experienced grade 5 sudden death while on a phase 3 study using the investigational agent bevacizumab/placebo in combination with paclitaxel and carboplatin. She began her first course of treatment on March 31, 2008, with paclitaxel and carboplatin only, and received the last dose of bevacizumab/placebo, and her last doses of paclitaxel and carboplatin on July 28, 2008 (Cycle 6, Day 1). The patient's son called the clinic on August 5, 2008, to say his mother would not be keeping her appointment for follow-up blood work because she had diarrhea and weakness. On August 6, 2008, the family notified the clinic that the patient had died suddenly of a cardiac arrest shortly after the initial phone call cancelling the appointment on August 5, 2008. EMS attempted resuscitation at her home and continued efforts were unsuccessfully in the ambulance and the emergency room. 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 on Day 1 , starting on Cycle 2 x 5 Cycles

14. DATES OF TREATMENT
The patient started the investigational therapy on April 21, 2008, and received the last dose of bevacizumab/placebo on July 28, 2008.

15. ACCRUAL AND IND EXPERIENCE
Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 18,109. There have been 40 other cases of sudden death reported to the NCI through AdEERS as serious adverse events for bevacizumab.

16. COMMENTS
The following was also administered every cycle (21 days): paclitaxel: 175 mg/m² IV over 3 hours on Day 1 × 6 cycles, and carboplatin: AUC 6 IV over 30 minutes on Day 1 × 6 cycles, and her last doses of paclitaxel and carboplatin were administered on July 28, 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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