



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: December 12, 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_1354425

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 or 507-538-8226.

SB/kjm
enclosure

INITIAL IND SAFETY REPORT COMMUNICATION # 666

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

October 20, 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 # 1354425)

9. PATIENT IDENTIFICATION

50623

10. AGE

51

11. SEX

Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 51-year-old female with stage II-A infiltrating ductal breast cancer who experienced grade 3 adult respiratory distress syndrome (ARDS) while on a phase 3 study using the investigational agent bevacizumab/placebo in combination with paclitaxel, doxorubicin and cyclophosphamide. She began her first course of treatment on July 3, 2008, and received the last dose of bevacizumab/placebo, on September 19, 2008, (Cycle 6, Day 1). She received her last dose of paclitaxel on September 25, 2008 (Cycle 6, Day 8). The patient presented to the clinic October 1, 2008 (Cycle 6, Day 13) with cough, fever, dyspnea and a CXR consistent with RML pneumonia. She was treated with Avelox[®] but continued to have worsening dyspnea and recurrence of fevers. She was admitted to the hospital on October 4, 2008, with worsening pulmonary infiltrates and oxygen requirements consistent with ARDS and was transferred to the ICU. Her condition continued to deteriorate and she required BIPAP for respiratory failure; however, after treatments with steroids her condition began to improve. She was removed from protocol on October 7, 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 Cycle = 21 days

Bevacizumab/Placebo 10 mg/kg IV over 30-90 minutes on Day 1, (Cycles 1-4)

Bevacizumab/Placebo 15 mg/kg IV on Day 1, starting on Cycle 5 x 4 Cycles

14. DATES OF TREATMENT The patient started the investigational therapy on July 3, 2008, and received the last dose of bevacizumab/placebo on September 19, 2008.

15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 17,261. There have been 11 other cases of adult respiratory distress syndrome (7 unlikely related and 4 unrelated) reported to the NCI through AdEERS as serious adverse events for bevacizumab.

16. COMMENTS The following was also administered every cycle (14 days) Cycle 1-4: doxorubicin: 60 mg/m² IVP on Day 1, cyclophosphamide: 600 mg/m² IV over 20-30 min on Day 1; cycle (21 days) Cycle 5-8: paclitaxel: 80 mg/m² IV over 1 hours on Day 1, 8 and 15. Her last dose of paclitaxel was administered on September 25, 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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