



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: October 31, 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 industry report of an adverse event that has occurred in association with Bevacizumab at a non-NCCTG institution. You may have also received this communication directly from the drug manufacturer.

AE_1636469

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 #65

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 15, 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 # 1636469)

9. PATIENT IDENTIFICATION
120-0218-007

10. AGE
54

11. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 54-year-old female with serous ovarian adenocarcinoma who experienced grade 3 fat necrosis 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 December 13, 2007, and received the last dose of bevacizumab/placebo on September 9, 2008 (Cycle 12, Day 1). She received her last doses of paclitaxel and carboplatin on May 8, 2008 (Cycle 6, Day 1). On June 18, 2008 the patient received her Cycle 9 treatment and complained of abdominal discomfort. A palpable mass was discovered upon physical examination. A CT scan revealed a subcutaneous soft tissue mass in the fat layer located on the lower left abdomen. Surgical excision and biopsy revealed fat necrosis. On July 8, 2008 the patient was examined prior to her Cycle 10 treatment and another palpable mass was discovered on the abdomen in the epigastric region at the midline. Surgical excision and biopsy revealed another area of fat necrosis. 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 7 × 16 Cycles**

14. DATES OF TREATMENT

The patient started the investigational therapy on December 13, 2007, and received the last dose of bevacizumab/placebo on September 9, 2008 (Cycle 12, Day 1).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 17,243. There have been no other cases of fat necrosis and 2 other cases of soft tissue necrosis 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; her last doses of paclitaxel and carboplatin were administered on May 8, 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.