



# 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\_1843518**

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](mailto:braun.sara@mayo.edu) or 507-538-8226.

SB/kjm  
enclosure

INITIAL IND SAFETY REPORT COMMUNICATION # 64

**TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA**

**FAX: 301-796-9849**

|   |   |  |
|---|---|--|
| 1. IND NUMBER<br><b>7921</b>  | 2. AGENT NAME<br><b>Bevacizumab (rhuMAb VEGF)</b> | 3. DATE<br><b>October 14, 2008</b>     |
| 4. SPONSOR<br><b>Division of Cancer Treatment and Diagnosis, National Cancer Institute</b>  |   |  |
| 5. REPORTER=S NAME, TITLE, AND INSTITUTION<br><b>Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics 3, CTEP, DCTD, NCI</b>  |   | 6. PHONE NUMBER<br><b>301-496-1196</b> |
|   |   | 7. FAX NUMBER<br><b>301-402-0428</b>   |
| 8. PROTOCOL NUMBER (AE #)<br><b>GOG-0218 (AE # 1843518)</b>   |   |  |
| 9. PATIENT IDENTIFICATION<br><b>023-0218-022</b>  | 10. AGE<br><b>43</b>                              | 11. SEX<br><b>Female</b>               |
| 12. DESCRIPTION OF ADVERSE EVENT<br><b>The patient was a 43-year-old female with stage IV epithelial ovarian cancer who experienced grade 4 cerebellar syndrome 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 4, 2007, and received the last doses of bevacizumab/placebo, on August 29, 2008, (Cycle 12, Day 1). She received her last doses of paclitaxel, and carboplatin on March 28, 2008 (Cycle 7, Day 16). The patient presented to the clinic August 29, 2008 (Cycle 12, Day 1). Within three hours of receiving her treatment she developed a headache, tremor, nystagmus, dizziness, and ataxia. Her anti-purkinje fiber antibody test was positive, and it was thought she was experiencing a paraneoplastic syndrome. She was treated with steroids which did not improve her symptoms. She was removed from protocol on August 29, 2008. Additional information has been requested. There is a reasonable possibility that the experience may have been caused by the drug.</b> |   |  |
| 13. DOSE, ROUTE, AND SCHEDULE<br><b>Cycle = 21 days</b><br><b>Bevacizumab/Placebo 15 mg/kg IV on Day 1 , starting on Cycle 7 x 16 Cycles</b>  |   |  |
| 14. DATES OF TREATMENT<br><b>The patient started the investigational therapy on December 4, 2007, and received the last dose of bevacizumab/placebo on August 29, 2008.</b>   |   |  |
| 15. ACCRUAL AND IND EXPERIENCE<br><b>Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 14,552. There have been no other cases of cerebellar syndrome reported to the NCI through AdEERS as serious adverse events for bevacizumab.</b>   |   |  |
| 16. COMMENTS<br><b>The following was also administered every cycle (21 days): paclitaxel: 175 mg/m<sup>2</sup> IV over 3 hours on Day 1 x 6 cycles, and carboplatin: AUC 6 IV over 30 minutes on Day 1 x 6 cycles, and her last doses of paclitaxel and carboplatin were administered on March 28, 2008.</b>  |   |  |
| <b>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).</b>  |   |  |
| <b>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.</b>   |   |  |