

IND SAFETY REPORT: INITIAL WRITTEN REPORT**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 January 16, 2009
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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 Targeted Therapeutics III, Investigational Drug Branch, CTEP, DCTD, NCI**6. PHONE NUMBER**
301-496-1196**7. FAX NUMBER**
301-402-0428**8. PROTOCOL NUMBER (AE #)**
GOG-0218 (AE # 1996104)**9. PATIENT IDENTIFICATION**
035-0218-021**10. AGE**
50**11. SEX**
Female**12. DESCRIPTION OF ADVERSE EVENT**
The patient is a 50-year-old female with ovarian epithelial cancer who experienced grade 4 vertigo 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 October 2, 2008, and received the last doses of bevacizumab/placebo, paclitaxel, and carboplatin on December 30, 2008, (Cycle 5, Day 6). The patient presented to the clinic on December 4, 2008 (Cycle 4, Day 1), and reported debilitating dizziness, nausea, and vomiting following any type of head movement, which was not relieved by antiemetics. On January 2, 2009, (Cycle 5 Day 9), she was admitted to the hospital for worsening symptoms. Her vital signs upon admission were as follows: temperature 97.6° F, pulse 57 bpm, respiratory rate 20 per minute, blood pressure 155/88 mmHg and oxygen saturation was 98% on room air. Physical examination was insignificant for neurological deficits. Laboratory results showed: WBC $3.9 \times 10^3/\mu\text{L}$ (reference range: $4.5 - 13.0 \times 10^3/\mu\text{L}$), hemoglobin 10.4 g/dL (reference range: 12.0 - 16 g/dL), and glucose 132 mg/dL (reference range: 74-106 mg/dL). An MRI of the patient revealed no acute deficits. The patient is currently undergoing treatment related to this adverse event. There is a reasonable possibility that the adverse event may have been caused by the drug.**13. DOSE, ROUTE, AND SCHEDULE**
Bevacizumab/Placebo 15 mg/kg IV on Day 1, every 21 days, starting with cycle 2, for 5 cycles**14. DATES OF TREATMENT**
The patient started Cycle 1, Day 1 of therapy on October 2, 2008, and received the last doses of bevacizumab/placebo, paclitaxel, and carboplatin on December 30, 2008, (Cycle 5, Day 6).**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 every cycle (21 days):
Paclitaxel: 175 mg/m² IV over 3 hours on day 1 × 6 cycles
Carboplatin: AUC 6 IV over 45 minutes on day 1 × 6 cycles**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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