

IND SAFETY REPORT: FOLLOW-UP #1

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 29, 2009
4. SPONSOR Division of Cancer Treatment and Diagnosis, National Cancer Institute		
5. REPORTER'S NAME, TITLE, AND INSTITUTION Kevin Conlon, MD-Senior Investigator 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 # 1823741)		
9. PATIENT IDENTIFICATION 021-0218-020	10. AGE 60	11. SEX Female
12. DESCRIPTION OF ADVERSE EVENT The patient is a 60year-old female with ovarian epithelial cancer who experienced grade 2 fistula, GI: colon/cecum/appendix 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 February 6, 2009, and received the last doses of bevacizumab/placebo, paclitaxel, and carboplatin on April 13, 2009, (Cycle 4, Day 1). On April 20, 2009 (Cycle 4, Day8), the patient was admitted to the hospital with a history of having air as well as increasing diarrhea and dehydration. The patient was having bowel movements every 20-30 min. She received IV fluids as well as Lomotil® on the second day of the admission. On April 21, 2009 (Cycle 4, Day 9), a gastrografin enema showed a focal colonic perforation. The patient developed neutropenia and received broad spectrum antibiotics on the second day. Her condition returned to baseline, and she was discharged from the hospital on April 22, 2009 (Cycle 5, Day 10). The patient will be followed up as an outpatient regarding the fistula. Additional information has been requested from the investigational site. 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 began the investigational therapy on the February 6, 2009, and received the last dose of bevacizumab/placebo, paclitaxel, and carboplatin on April 13, 2009 (Cycle 4, Day 1).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21394. There have been 13 incidences of fistula: GI colon/cecum/appendix reported to the NCI through AdEERS as serious adverse events for bevacizumab.		
16. COMMENTS The following was also administered: Paclitaxel: 175 mg/m ² IV over 3 hours on day 1 × 6 cycles Carboplatin: AUC 6 IV over 30 minutes on day 1 × 6 cycles		
<p><u>Follow-up # 1:</u> Based upon further investigation, the Senior Investigator at the Investigational Drug Branch has decided not to file this report expeditiously to the FDA.</p>		

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