

## 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  
April 18, 2011

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, Investigational Drug Branch, CTEP, DCTD, NCI

6. PHONE NUMBER  
301-496-1196

7. FAX NUMBER  
301-402-0428

8a. PROTOCOL NUMBER (AE #)  
E5103 (AE# 1751032)

8b. AE GRADE: AE  
Grade 4: Wound complication

9. PATIENT IDENTIFICATION  
54789

10. AGE  
57 years

11. SEX  
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 57-year-old female with invasive breast carcinoma who experienced a grade 4 wound complication while on a phase 3 trial utilizing the investigational agent bevacizumab/placebo in combination with doxorubicin, cyclophosphamide, filgrastim/pegfilgrastim, and paclitaxel. She began her first course of treatment on December 29, 2010, and received the last doses of bevacizumab/placebo, cyclophosphamide, and doxorubicin on December 29, 2010 (Cycle 1, Day 1), and the last dose of pegfilgrastim December 30, 2010 (Cycle 1, Day 2). On January 8, 2011 (Cycle 1, Day 11), the patient started to experience abdominal pain, nausea, and vomiting. The following day, she presented to the emergency department with continued pain and abdominal bulging from a baseline hernia. She was given normal saline as well as IV Zofran<sup>®</sup> and Dilaudid<sup>®</sup>. She was admitted, and continued monitoring and serial abdominal exams were performed. A CT scan of the abdomen and pelvis revealed an incarcerated ventral hernia. The patient was unblinded on January 10, 2011, pending surgical intervention. A repeat abdominal and pelvic CT scan on January 11, 2011, revealed a fairly large anterior abdominal wall hernia containing multiple loops of the small bowel which were slightly increased from the previous exam. It also confirmed a left adrenal adenoma. On January 12, 2011, a ventral hernia repair with biological mesh was performed. Postoperatively, the patient had a slow return of GI function and strength. She was able to ambulate without difficulty, her pain was controlled with oral medications and she was discharged to home on January 20, 2011. On January 26, 2011, the patient was re-admitted for an enteric leak status post the ventral hernia repair. Exploratory laparoscopy with removal of the infected mesh and oversewing of the enterotomy was performed. The patient subsequently developed an enterocutaneous fistula in the middle of an open wound which required further surgery. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.

13. DOSE, ROUTE, AND SCHEDULE

Cycle = 14 days (Cycles 1-4)  
Bevacizumab/Placebo: 10 mg/kg IV over 30-90 minutes on Day 1  
Cycle = 21 days (Cycles 5-8)  
Bevacizumab/Placebo: 15 mg/kg IV over 30-90 minutes on Day 1

14. DATES OF TREATMENT

The patient began the investigational therapy on December 29, 2010, and received the last dose of bevacizumab on December 29, 2010 (Cycle 1, Day 1).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 32,044. There have been 88 other cases of wound complication, non infectious reported to the NCI through AdEERS as serious adverse events for bevacizumab.

16. COMMENTS The following were also administered:

Cycle = 14 days (Cycles 1-4): Doxorubicin: 60 mg/m<sup>2</sup> IVP on Day 1, cyclophosphamide: 600 mg/m<sup>2</sup> IV over 20-30 minutes on Day 1, filgrastim: 5 mcg/kg SQ on Days 2-11 or pegfilgrastim: 6 mg SQ on Day 2.  
Cycle = 21 days (Cycles 5-8): Paclitaxel: 80 mg/m<sup>2</sup> IV over 1 hour on Days 1, 8, and 15

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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