

IND SAFETY REPORT: FOLLOW-UP #1TO: *Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA*

FAX: 301-796-9849

1. IND NUMBER
79212. AGENT NAME
Bevacizumab (rhuMAb VEGF)3. DATE
November 16, 20094. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute5. REPORTER=S NAME, TITLE, AND INSTITUTION
Kevin Conlon, MD – Senior Investigator, Investigational Therapeutic III,
Investigational Drug Branch, CTEP, DCTD, NCI6. PHONE NUMBER
301-496-11967. FAX NUMBER
301-402-04288. PROTOCOL NUMBER (AE #)
E5103 (AE # 1970713)9. PATIENT IDENTIFICATION
5110210. AGE
5911. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 59-year-old female with invasive breast carcinoma who developed a grade 3 neuropathy: motor while on a phase 3 study using the investigational agent bevacizumab/placebo in combination with doxorubicin, cyclophosphamide, and paclitaxel. She began her first course of treatment on October 8, 2008, and received the last dose of bevacizumab/placebo on March 25, 2009 (Cycle 9, Day 1). On March 29, 2009 (Cycle 9, Day 5), the patient presented to the clinic with markedly fatigue, left foot drop, week upper and lower extremity strength. The patient continued to have an extremity poor appetite and weight loss. An MRI of the lumbar spine showed mild levoconvexity of the upper spine and there is mild bilateral face hypertrophy at L3-L4 and L5-S1. MRI of the brain showed mild burden of white matter, signal abnormality and probable venous abnormality in the right hemisphere. She is not able to walk and is using a walker to walk. On April 15, 2009 (Cycle 10, Day 1), the patient presented to the clinic to start the cycle 10 of treatment. The physician decided to hold the chemotherapy due to toxicity. 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 over 30-90 minutes on Day 1 (Cycles 9-18)

14. DATES OF TREATMENT

The patient started the investigational therapy on October 8, 2008, and received the last dose of bevacizumab/placebo on March 25 (Cycle 9, Day 1).

15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21394. There have been 52 other incidences of neuropathy: motor reported to the NCI through AdEERS as serious adverse events for bevacizumab.

16. COMMENTS The following was also administered:

Cycles 1-4: doxorubicin: 60 mg/m² IVP on Day 1, cyclophosphamide: 600 mg/m² IV over 20-30 min on Day 1
Cycles 5-8: paclitaxel: 80 mg/m² IV over 1 hour on Days 1, 8, and 15**Follow-up # 1:****Based upon further investigation, the Senior Investigator at the Investigational Drug Branch has decided not to file this report expeditiously to the FDA.**

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