

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
701162. AGENT NAME
Bevacizumab (rhuMAb VEGF)
CC-5013 (lenalidomide, Revlimid)3. DATE
April 7, 20094. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute5. REPORTER=S NAME, TITLE, AND INSTITUTION
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301-496-11967. FAX NUMBER
301-402-04288. PROTOCOL NUMBER (AE #)
7313 (AE # 1277486)9. PATIENT IDENTIFICATION
2510. AGE
6711. SEX
Male

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 67-year-old male with myeloma who developed grade 3 pneumonitis/pulmonary infiltrates and atrial fibrillation while on a phase 2 study using the investigational agent bevacizumab in combination with lenalidomide and dexamethasone. He began his first course of treatment on August 11, 2008, and received the last dose of bevacizumab on March 9, 2009 (Cycle 8, Day 15). On March 14, 2009 (Cycle 8, Day 20), the patient presented to the ER with dyspnea and a cough. Vital signs upon admission were as follows: temperature 98.2° F, pulse 82 bpm, respiratory rate 22 per minute, blood pressure 171/89 mmHg and oxygen saturation was 92% on room air. While in the hospital, he developed atrial fibrillation, and was started on an amiodarone drip and Ranexa®, and converted to normal rhythm. The patient was started on Avelox® and a CT scan without contrast revealed bilateral alveolar infiltrates. He was started on nebulizer, inhaler, and steroid treatments. On March 20, 2009 (Cycle 8, Day 26), the patient was discharged home on oxygen. On March 23, 2009 (Cycle 8, Day 29), the patient was removed from protocol. On March 24, 2009, the patient presented back to the ER with dyspnea and cough. Vital signs upon admission were as follows: temperature 97.4° F, pulse 56 bpm, respiratory rate 24 per minute, blood pressure 167/85 mmHg and oxygen saturation was 96%. A CT scan of the lungs showed- improvement in alveolar infiltrates. The patient was started on Lasix® and Avelox®. On March 27, 2009, he was discharged home on oxygen. Additional information has been requested. There is a reasonable possibility that the experience may have been caused by the drugs.

13. DOSE, ROUTE, AND SCHEDULE Cycle = 28 days
Bevacizumab 10 mg/kg IV over 30-90 minutes on Day 1 and 15
CC-5013 25 mg PO QD on Days 1-21

14. DATES OF TREATMENT The patient started the investigational therapy on August 11, 2008, and received the last dose of bevacizumab on March 9, 2009 (Cycle 8, Day 15) and the last dose of CC-5013 on March 15, 2009 (Cycle 8, Day 21).

15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 19819 and using CC-5013 = 1541. There have been 120 pneumonitis/pulmonary infiltrates incidences reported to the NCI through AdEERS as serious adverse events for bevacizumab; and 42 pneumonitis/pulmonary infiltrate incidences reported to the NCI through AdEERS as serious adverse events for CC-5013, excluding this report.

16. COMMENTS The following was also administered:

Dexamethasone 40 mg PO on Days 1, 8, 15, and 22; Last administered on March 9, 2009.**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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