

IND SAFETY REPORT: INITIAL WRITTEN REPORT

TO: Division of Drug Oncology Products, Center for Drug Evaluation and Research, FDA

FAX: 301-796-9845

1. IND NUMBER

70116

58443

2. AGENT NAME

CC-5013 (lenalidomide, Revlimid[®])

PS-341 (bortezomib; Velcade[®])

3. DATE

August 16, 2011

4. SPONSOR

Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION

Howard Streicher, MD - Senior Investigator for Investigational Therapeutics 3, Investigational Drug Branch, CTEP, DCTD, NCI

John Wright, MD, PhD - Associate Branch Chief for Investigational Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI

6. PHONE NUMBER

301-496-1196

7. FAX NUMBER

301-402-0428

8a. PROTOCOL NUMBER (AE #)

S0777 (AE# 1506930)

8b. AE GRADE: AE

Grade 5: Multi-organ failure

9. PATIENT IDENTIFICATION

230641

10. AGE

52 years

11. SEX

Male

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 52-year-old male with multiple myeloma who died from multi-organ failure while on a phase 3 study utilizing the investigational agents lenalidomide and bortezomib. He began the investigational therapy on June 9, 2011, and received his last dose of lenalidomide on June 18, 2011 (Cycle 1, Day 10), and the last dose of bortezomib on June 16, 2011 (Cycle 1, Day 8). The patient had a history of hypercalcemia which was treated with pamidronate on May 26, 2011. On June 10, 2011, the patient was transferred to the emergency room from an infusion center due to significantly low blood pressure and weakness. He was admitted to the intensive care unit for probable sepsis of an unknown source, respiratory failure related to metabolic acidosis, acute renal failure, anemia, and hypernatremia. An echocardiogram did not show any evidence of heart failure or pulmonary embolism. The patient's condition continued to deteriorate. He developed worsening respiratory failure, circulatory failure, renal failure, CNS failure, and metabolic failure. Blood cultures were positive for *Staphylococcus aureus*. His treatment included dialysis, mechanical ventilation, vasopressors, antibiotics, and steroids. He expired on June 19, 2011. Additional information has been requested from the investigational site. There is a reasonable possibility that the event may have been caused by the drugs.

13. DOSE, ROUTE, AND SCHEDULE:

Cycle = 21 Days

Lenalidomide: 25 mg PO QD on Days 1-14

Bortezomib: 1.3 mg/m² IV over 3-5 seconds on Days 1, 4, 8, and 11

14. DATES OF TREATMENT

The patient began the investigational therapy on June 9, 2011, and received his last dose of lenalidomide on June 18, 2011 (Cycle 1, Day 10), and his last dose of bortezomib on June 16, 2011 (Cycle 1, Day 8).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using lenalidomide = 2988 and bortezomib = 3881. There have been 5 other cases of multi-organ failure reported to the NCI through AdEERS as a serious adverse event for lenalidomide and 8 other cases of multi-organ failure reported to the NCI through AdEERS as a serious adverse event for bortezomib.

16. COMMENTS: **Also administered on this protocol: Dexamethasone: 20 mg PO on Days 1, 2, 4, 5, 8, 9, 11, and 12;**

Aspirin: 325 mg PO daily

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.