

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 July 21, 2010
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# 1164386)	8b. AE GRADE: AE Grade 2: Osteonecrosis (avascular necrosis)	
9. PATIENT IDENTIFICATION 221713	10. AGE 67 years	11. SEX Male
12. DESCRIPTION OF ADVERSE EVENT The patient is a 67-year-old male with myeloma who experienced grade 2 vascular necrosis while on a phase 3 study utilizing the investigational agents CC-5013 and bortezomib in combination with dexamethasone and aspirin. He began the investigational therapy on January 11, 2010, and received his last dose of CC-5013 on July 13, 2010 (maintenance therapy Cycle 1, Day 16), the last dose of bortezomib June 17, 2010 (Cycle 8, Day 11), and the last dose of dexamethasone on July 12, 2010 (maintenance therapy Cycle 1, Day 15). On June 28, 2010 (maintenance therapy Cycle 1, Day 1), the patient presented to the clinic with an exposed jaw bone. A diagnosis of osteonecrosis without associated infection was made by the oral surgeon. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drugs.		
13. DOSE, ROUTE, AND SCHEDULE: Cycle = 21 days Lenalidomide 25 mg PO daily on Days 1-14 Bortezomib: 1.3 mg/m² IVP on Days 1, 4, 8, and 11		
14. DATES OF TREATMENT The patient began the investigational therapy on January 11, 2010, and received his last dose of CC-5013 on July 13, 2010 (maintenance therapy Cycle 1, Day 16), and the last dose of bortezomib on June 17, 2010 (Cycle 8, Day 11).		
15. ACCRUAL AND IND EXPERIENCE Number of patients enrolled in NCI-sponsored clinical trials using CC-5013 = 2192 and bortezomib = 3204. There have been 2 other cases of osteonecrosis reported to the NCI through AdEERS as serious adverse events for CC-5013 and no other cases of osteonecrosis reported to the NCI through AdEERS as serious adverse events 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.		