



# NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

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**Date:** September 19, 2008

**To:** NCCTG Primary Clinical Research Associates

**From:** Alicia Elsing  
Protocol Development Coordinator

**Re:** N0321, Phase I/II Study of PS-341 in Combination with Paclitaxel, Carboplatin, and Concurrent Thoracic Radiation Therapy for Non-small Cell Lung Cancer (NSCLC)

The purpose of this memorandum is to provide investigators with a recent report of an adverse event that has occurred in association with PS-341 for a study where the Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI) is distributing this agent. You may have also received this communication directly from DCTD.

AE\_1358268

Please note that all risks currently cited in the NCCTG consent form cannot be omitted; it is at the discretion of your local IRB as to whether they wish to add risks based on the enclosed information. If a determination has been made by the NCCTG Research Base that a protocol amendment is necessary, you will receive the NCI-approved protocol addendum at a later date; for purposes of cross-reference, this communication will cite the adverse event noted above.

**Please submit this adverse event to your Institutional Review Board.**

If you have any questions concerning this communication, please contact Alicia Elsing at [Elsing.alicia@mayo.edu](mailto:Elsing.alicia@mayo.edu) or 507-538-3893.

AE/kjm  
enclosure



**DATE:** August 28, 2008

**FROM:** Howard Streicher, M.D., Senior Investigator, Investigational Drug Branch, CTEP, DCTD, NCI  
John Wright, M.D., Ph.D., Senior Investigator, Investigational Drug Branch, CTEP, DCTD, NCI

**SUBJECT:** CC-5013 (lenalidomide; Revlimid®) and PS-341 (bortezomib; Velcade®) NCI IND Safety Report: **Initial Written Report, AE# 1358268**

**TO:** Investigators Using CTEP-supplied Investigational lenalidomide (NSC 703813) and bortezomib (NSC 681239)

The U.S. Food and Drug Administration (FDA) regulations require sponsors of clinical studies conducted under a U.S. IND to notify the FDA and all participating investigators of any serious and unexpected adverse experiences that are possibly related to the investigational agent. Please find attached a copy of an IND Safety Report recently submitted to the FDA for the CTEP-sponsored investigational agents lenalidomide and bortezomib.

The following must be completed by all investigators using lenalidomide under NCI IND 70116 and bortezomib under NCI IND 58443:

- Send a copy of the IND Safety Report to your Institutional Review Board (IRB) according to your local IRB's policies and procedures.
- File a copy of the IND Safety Report in your protocol file.

If your study is not covered under INDs 70116 and 58443, it is strongly recommended that you follow the instructions above.

Please note that for Cooperative Group studies, the Cooperative Group Operations Office will provide instructions for IRB submissions, any patient notifications, etc.

Based on CTEP's assessment of the current information in light of previous experience with lenalidomide and bortezomib, there does not appear to be a change in the risk-benefit ratio for lenalidomide and bortezomib studies; therefore, CTEP is not requiring a protocol amendment at this time.

Please continue to report events according to the adverse event reporting guidelines in your protocol(s).

The attached Initial Written Report, which has been submitted to the FDA, describes the adverse event(s) (synopsis provided below), relevant previous experience under these INDs and/or NSCs, and the total number of patients enrolled in trials under these INDs and/or NSCs.

A 57-year-old female with multiple myeloma died suddenly while on a phase 3 study utilizing the investigational agent lenalidomide in combination with bortezomib.

**IF UPON FURTHER INVESTIGATION THIS EVENT IS CONSIDERED POSSIBLY RELATED TO THE INVESTIGATIONAL AGENT/THERAPY, WE WILL SUBMIT A FOLLOW-UP WRITTEN REPORT WITH ASSESSMENT AS SOON AS THE RELEVANT INFORMATION IS AVAILABLE IN ACCORDANCE WITH 21CFR312.32(d)(2).**

Attachment: Initial Written Report

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**IND SAFETY REPORT: INTIAL WRITTEN REPORT**

No. 46

**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 28, 2008**

4. SPONSOR

**Division of Cancer Treatment and Diagnosis, National Cancer Institute**

5. REPORTER'S NAME, TITLE, AND INSTITUTION

**Howard Streicher, MD – Senior Investigator for Biologics Evaluation, Investigational Drug Branch, CTEP, DCTD, NCI**

**John Wright, MD, Ph.D. – Senior Investigator for Targeted Therapeutics 1, Investigational Drug Branch, CTEP, DCTD, NCI**

6. PHONE NUMBER

**301-496-1196**

7. FAX NUMBER

**301-402-0428**

8. PROTOCOL NUMBER (AE #)

**S0777 (1358268)**

9. PATIENT IDENTIFICATION

**211743**

10. AGE

**57**

11. SEX

**Female**

12. DESCRIPTION OF ADVERSE EVENT

**The patient was a 57-year-old female with multiple myeloma who died suddenly while on a phase 3 trial using the investigational agent lenalidomide in combination with bortezomib. She began investigational therapy with lenalidomide and bortezomib on August 14, 2008, and received her last dose of lenalidomide on August 23, 2008 (Cycle 1, Day 10), and her last dose of bortezomib on August 21, 2008 (Cycle 1, Day 8). The patient was started at a reduced dose of lenalidomide due to an increased creatinine level and was hospitalized for days 1-8 of treatment. She was discharged on August 21, 2008. While hospitalized, in addition to the protocol treatment, she also received Lovenox® from August 11, 2008, to August 16, 2008. On August 23, 2008, at home, the patient called for her family and when they came into her room she fell backwards and was unresponsive. EMS was called and when they arrived they found the patient to be in asystole and attempted to resuscitate her. The patient was pronounced dead upon arrival to the hospital emergency room. An autopsy was performed and the results are pending. Additional information has been requested from the investigational site.**

13. DOSE, ROUTE, AND SCHEDULE

**Lenalidomide 25 mg PO on days 1-14, every 21 days**

**Bortezomib: 1.3 mg/m<sup>2</sup> IVP on days 1, 4, 8, and 11, every 21 days**

14. DATES OF TREATMENT

**The patient started investigational treatment on August 14, 2008, and received the last dose of lenalidomide on August 23, 2008 (Cycle 1, Day 10), and the last dose of bortezomib on August 21, 2008 (Cycle 1, Day 8).**

15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using lenalidomide = 1278, and bortezomib = 2512. Other incidences reported to the NCI through AdEERS as serious adverse events: 2 sudden deaths and 6 death NOS for lenalidomide; 9 sudden deaths and 16 death NOS for bortezomib.**

16. COMMENTS

**The patient started lenalidomide at 5mg PO daily; Total dose = 50 mg.**

**Also administered on this protocol: Dexamethasone 20 mg PO daily on days 1, 2, 4, 5, 8, 9, 11, and 12; Last administered August 22, 2008; 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 21CFR312.32(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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