



# NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

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**Date:** December 26, 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\_1567424**

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

## 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  
**58443**

2. AGENT NAME  
**PS-341 (bortezomib; Velcade)**

3. DATE  
**December 2, 2008**

4. SPONSOR

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

5. REPORTER=S NAME, TITLE, AND INSTITUTION

**John Wright, MD, Ph.D. – 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**

8. PROTOCOL NUMBER (AE #)

**AAML07P1 (AE# 1567424)**

9. PATIENT IDENTIFICATION

**784586**

10. AGE

**19**

11. SEX

**Male**

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 19-year-old male with treatment related acute myeloid leukemia who experienced hypokalemia, and adult respiratory distress syndrome (ARDS), and died from renal failure while on a phase 2 pilot study using the investigational agents bortezomib combined with reinduction chemotherapy. He began the first course of the investigational therapy on October 1, 2008 (Day 0), receiving the first dose of bortezomib on October 2, 2008 (Cycle 1, Day 1), and the last dose of bortezomib on October 5, 2008 (Cycle 1, Day 4). On October 3, 2008 (Cycle 1, day 2), while hospitalized for treatment, the patient became febrile and was started on antibiotics. On October 7, 2008, he was transferred to the ICU for worsening symptoms of respiratory distress and renal failure. His potassium level was 2.3 mEq/L, his creatinine level was 1.4 mg/dL, his renal ultrasound was normal, and a chest X-ray showed small pleural effusions. On October 10, 2008, he was intubated, his creatinine level increased to 3.3 mg/dL, and he was started on dialysis. His condition continued to decline and after discussions with the family, on October 20, 2008, dialysis was discontinued, and he died the following day. 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 = 28 days**

**Bortezomib 1 mg/m<sup>2</sup> IVP over on days 1, 4, and 8**

14. DATES OF TREATMENT

**The patient began the investigational therapy on October 1, 2008 (Cycle 1, Day 0), and received the last dose of bortezomib on October 5, 2008 (Cycle 1, Day 4).**

15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using bortezomib = 2621.**

**Other incidences of the events reported to the NCI through AdEERS as serious adverse events for PS-341: renal failure = 17; hypokalemia = 26; ARDS = 1; and respiratory distress = 1.**

16. COMMENTS

**The following was also administered on this protocol:**

**Cytarabine IT: 30-70 mg/m<sup>2</sup> (age - based dosing) on Day 0; administered on October 1, 2008**

**Etoposide: 150 mg/m<sup>2</sup> IV over 1 hour on days 1-5; last administered on October 6, 2008**

**Cytarabine: 1000 mg/m<sup>2</sup> IV over 1 hour, Q12 hours, on days 1-5; last administered on October 6, 2008**

**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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