

**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 <b>58443</b>	2. AGENT NAME <b>PS-341 (bortezomib; Velcade®)</b>	3. DATE <b>January 15, 2010</b>
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4. SPONSOR  
**Division of Cancer Treatment and Diagnosis, National Cancer Institute**

5. REPORTER'S NAME, TITLE, AND INSTITUTION <b>John Wright, MD, PhD – Associate Branch Chief for Investigational Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI</b>	6. PHONE NUMBER <b>301-496-1196</b>
	7. FAX NUMBER <b>301-402-0428</b>

8. PROTOCOL NUMBER (AE #)  
**CALGB-10502 (AE# 1705612)**

9. PATIENT IDENTIFICATION <b>116570</b>	10. AGE <b>62</b>	11. SEX <b>Male</b>
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12. DESCRIPTION OF ADVERSE EVENT  
**The patient is a 62-year-old male with acute myeloid leukemia (AML) who experienced grade 4 respiratory failure while on a phase 2 trial using the investigational agents bortezomib in combination with cytarabine and daunorubicin. He began the first course of the investigational therapy on July 15, 2009, and received the last dose of bortezomib on July 25, 2009 (Cycle 1, Day 11). He received the last dose of daunorubicin on July 17, 2009 (Cycle 1, Day 3), and the last dose of cytarabine on July 21, 2009 (Cycle 1, Day 7). On July 14, 2009, the patient was admitted to the hospital for planned induction chemotherapy which he initially tolerated well. On July 22, 2009, the patient developed a temperature of 103.4° F, and he was started on ceftazadime. Blood cultures grew coagulase-negative *Staphylococcus*. Vancomycin and empirical Flagyl® were added to his treatment regimen. On July 30, 2009, the patient developed a temperature of 101.5° F with sharp pleuritic left upper chest pain and dyspnea requiring increased need for oxygen. The Hickman® catheter was removed due to his fever and bacteremia. A CT scan of the chest revealed scattered areas of ground glass opacity in the bilateral lobes and new left apical 3 cm consolidative nodule with surrounding ground glass opacity concerning for fungal infection particularly *Aspergillus* as compared to a prior CT scan from July 28, 2009. The patient was started on Micafungin® and he reported some improvement in his chest pain; however, the medication was later changed to AmBisome® for a broader anti-fungal therapy. On August 3, 2009, the patient was intubated, placed on mechanical ventilation, and admitted to the MICU. He remains hospitalized. 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 1 - Remission Induction Therapy: Bortezomib 1.3 mg/m<sup>2</sup> IV bolus over 3-5 seconds on Days 1, 4, 8, and 11**  
**Cycle 2 - Remission Induction Therapy (in patients with residual disease): Bortezomib 1.3 mg/m<sup>2</sup> IVB over 3-5 seconds on Days 1 and 4**

14. DATES OF TREATMENT  
**The patient began the investigational therapy on July 15, 2009, and received the last dose of bortezomib on July 25, 2009 (Cycle 1, Day 11).**

15. ACCRUAL AND IND EXPERIENCE  
**Number of patients enrolled in NCI-sponsored clinical trials using bortezomib = 3027.**  
**There has been 1 other case of respiratory failure reported to the NCI through AdEERS as a serious adverse event for bortezomib.**

16. COMMENTS **Also administered:**  
**Cycle 1 - Remission Induction Therapy: Daunorubicin 60 mg/m<sup>2</sup> IV on Days 1-3; Cytarabine 100 mg/m<sup>2</sup> CIV on Days 1-7; Cycle 2 - Remission Induction Therapy (in patients with residual disease): Daunorubicin 60 mg/m<sup>2</sup> IV on Days 1-2; Cytarabine 100 mg/m<sup>2</sup> CIV on Days 1-5**

**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.**