

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 January 15, 2010
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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 #)**
CALGB-10502 (AE# 1649799)**9. PATIENT IDENTIFICATION**
118347**10. AGE**
69**11. SEX**
Female**12. DESCRIPTION OF ADVERSE EVENT**

The patient was a 69-year-old female with acute myeloid leukemia who experienced grade 4 adult respiratory distress syndrome, grade 4 hypoxia, grade 4 catheter-related infections while on a phase 2 study using the investigational agent bortezomib in combination with daunorubicin and cytarabine. She began the first course of the remission induction therapy on November 20, 2009, and she received the last dose of bortezomib on November 30, 2009 (Cycle 1, Day 11), and the last dose of daunorubicin on November 22, 2009 (Cycle 1, Day 3) and cytarabine on November 27, 2009 (Cycle 1, Day 8). On November 24, 2009 (Cycle 1, Day 5), the patient developed chest heaviness, dyspnea, hypoxia with an oxygen saturation of 80% on room air, and was placed on 2L of supplemental oxygen. By November 25, 2009 (Cycle 1, Day 6), the dyspnea and hypoxia had resolved. The patient was treated with Zofran[®], Questran[®], posaconazole and valacyclovir because of nausea, vomiting, diarrhea, and fatigue. The patient developed left upper extremity weakness and a left facial droop. The results of brain imaging were inconclusive. On December 2, 2009 (Cycle 1, Day 13), the patient became unresponsive, collapsed and was discovered to have agonal respirations. She was transferred to the ICU, intubated, and placed on a ventilator. She had a fever of 103 °F and positive catheter and blood cultures showing gram-negative and gram-positive bacilli. She was treated with Amikacin[®], Caspofungin[®], Zosyn[®] and Vancomycin[®]. She expired on the same 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**Remission Induction Therapy****Cycle 1: Bortezomib: 1.3 mg/m² IVB over 3-5 seconds on Days 1, 4, 8, and 11****Cycle 2: Bortezomib: 1.3 mg/m² IVB over 3-5 seconds on Days 1 and 4****14. DATES OF TREATMENT****The patient began the investigational therapy on November 20, 2009, and received the last dose of bortezomib on November 30, 2009 (Cycle 1, Day 11).****15. ACCRUAL AND IND EXPERIENCE****Number of patients enrolled in NCI-sponsored clinical trials using bortezomib = 3027.****There have been 5 other cases of adult respiratory distress syndrome, 5 other cases catheter related infections and 57 cases of hypoxia reported to the NCI through AdEERS as serious adverse events for bortezomib.****16. COMMENTS****The following was also administered on this protocol:****Cycle 1: Daunorubicin: 60 mg/m² IV on Days 1-3; Cytarabine: 100 mg/m² CIV on Days 1-7****Cycle 2: Daunorubicin: 60 mg/m² IV on Days 1-2; Cytarabine: 100 mg/m² 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.**

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