

## 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>March 13, 2009</b>
4. SPONSOR <b>Division of Cancer Treatment and Diagnosis, National Cancer Institute</b>		
5. REPORTER=S NAME, TITLE, AND INSTITUTION <b>John Wright, MD, Ph.D. – 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 #) <b>CALGB-10502 (AE# 1073953)</b>		
9. PATIENT IDENTIFICATION <b>114432</b>	10. AGE <b>74</b>	11. SEX <b>Male</b>
12. DESCRIPTION OF ADVERSE EVENT <b>The patient was a 74-year-old male with acute myeloid leukemia who experienced adult respiratory distress syndrome (ARDS), and subsequently died while on a phase 2 dose escalation study using the investigational agent bortezomib added to standard daunorubicin and cytarabine therapy. He began the first course of the investigational therapy on January 29, 2009, and received the last dose of bortezomib on February 1, 2009 (Cycle 1, Day 4). On January 26, 2009, the patient was admitted to the hospital to receive the investigational treatment. After receiving induction, he developed pancytopenia and multiple complications including pneumonia, congestive heart failure, and respiratory failure requiring ventilator support. He was transferred to the intensive care unit where he remained on ventilator support and despite treatment got progressively worse. On February 19, 2009, at the request of the patient's family, he was extubated, and placed on comfort measures only. He expired later that day. No autopsy was performed. Additional information has been requested. There is a reasonable possibility that the experience may have been caused by the drug.</b>		
13. DOSE, ROUTE, AND SCHEDULE <b>Cycle = 28 days</b> <b>Bortezomib 1.3 mg/m<sup>2</sup> IVP over 3-5 seconds on days 1, 4, 8, and 11 for cycle 1</b>		
14. DATES OF TREATMENT <b>The patient began the investigational therapy on January 29, 2009 (Cycle 1, Day 0), and received the last dose of bortezomib on February 1, 2009 (Cycle 1, Day 4).</b>		
15. ACCRUAL AND IND EXPERIENCE <b>Number of patients enrolled in NCI-sponsored clinical trials using bortezomib = 2731.</b> <b>There were 2 other incidences of ARDS reported to the NCI through AdEERS as serious adverse events for PS-341.</b>		
16. COMMENTS <b>The following was also administered on this protocol:</b> <b>Cytarabine 100 mg/m<sup>2</sup> CIV on Days 1-7; administered on January 29, 2009</b> <b>Daunorubicin 60 mg/m<sup>2</sup> IV on days 1-3; last administered on January 31, 2009</b>		
<b>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).</b>		
<b>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.</b>		

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