

**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  
**October 26, 2010**

4. SPONSOR  
**Division of Cancer Treatment and Diagnosis, National Cancer Institute**

5. REPORTER'S NAME, TITLE, AND INSTITUTION  
**John Wright, MD, PhD-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**

8a. PROTOCOL NUMBER (AE #)  
**CALGB-10502 (AE# 1762261)**

8b. AE GRADE: AE  
**Grade 4: Adult Respiratory Distress Syndrome**

9. PATIENT IDENTIFICATION  
**116639**

10. AGE  
**71**

11. SEX  
**Male**

12. DESCRIPTION OF ADVERSE EVENT

**The patient is a 71-year-old male with acute myeloid leukemia (AML) who experienced grade 4 adult respiratory distress syndrome while on a phase 2 study utilizing the investigational agent bortezomib in combination with cytarabine. He began the investigational therapy on July 14, 2009, and received his last dose of bortezomib on November 13, 2009 (Cycle 3, Day 11), and cytarabine on November 7, 2009 (Cycle 3, Day 5). On November 19, 2009 (Cycle 3, Day 17), the patient was admitted to the hospital for neutropenic fever. Shortly after the admission, the patient developed respiratory failure, which required intubation. A chest X-ray on November 20, 2009, revealed interval worsening aeration of the chest with a development of patchy bibasilar airspace opacities, which was concerning for pneumonia or aspiration pneumonitis. A CT scan on November 26, 2009, revealed new right lower lobe consolidation concerning for pneumonia as well as new moderate right and small left pleural effusions. On the same day, respiratory culture found *Enterococcus faecium*. During his hospitalization, the patient was aggressively managed for typhlitis, acute renal failure, and cardiovascular compromise. Treatment included broad-spectrum antibiotics and hemodialysis. His condition slowly improved. He was discharged on January 6, 2010, when a repeat chest CT revealed interval decrease in the small amount of residual opacity in the right middle lobe, favoring scarring from prior infection; no new opacities were noted. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drug.**

13. DOSE, ROUTE, AND SCHEDULE:

**Bortezomib: 0.7 mg/m<sup>2</sup> IV on Days 1, 4, 8, and 11**

14. DATES OF TREATMENT

**The patient began the investigational therapy on July 14, 2009, and received his last dose of bortezomib on November 13, 2009 (Cycle 3, Day 11).**

15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using bortezomib = 3,281. There have been 10 other cases of adult respiratory distress syndrome reported to the NCI through AdEERS as serious adverse events for bortezomib.**

16. COMMENTS:

**The following was also administered on this protocol:  
Cytarabine: 2 g/m<sup>2</sup> IV 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.**