

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
February 5, 2010

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

5. REPORTER=S NAME, TITLE, AND INSTITUTION
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6. PHONE NUMBER
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7. FAX NUMBER
301-402-0428

8. PROTOCOL NUMBER (AE #)
CALGB-10502 (AE# 1617319)

9. PATIENT IDENTIFICATION
115609

10. AGE
63

11. SEX
Male

12. DESCRIPTION OF ADVERSE EVENT
The patient was a 63-year-old male with acute myeloid leukemia who expired while on a phase 2 study using the investigational agent bortezomib in combination with daunorubicin and cytarabine. He began the first course of the remission induction therapy on April 24, 2009, and he received the last dose of bortezomib on May 4, 2009 (Cycle 1, Day 11). He also received the last doses of daunorubicin on April 26, 2009, (Cycle 1, Day 3), and cytarabine on August 6, 2009. He started the consolidation course with cytarabine on August 3, 2009, but was non-compliant; he received only 3 of 5 doses of Cycle 1, and 4 of 5 doses of Cycle 2. He did not show up for the 5th scheduled day of treatment and was reported to have died in an outside hospital on September 16, 2009. 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:
Bortezomib 1.3 mg/m² IVB over 3-5 seconds on Days 1, 4, 8, and 11
Remission Consolidation Therapy (max = 2 cycles):
Bortezomib: 0.7mg/m² IVB over 3-5 seconds on Days 1, 4, 8, and 11**

14. DATES OF TREATMENT
The patient began the investigational therapy on April 24, 2009, and received the last dose of bortezomib on May 4, 2009 (Cycle 1, Day 11).

15. ACCRUAL AND IND EXPERIENCE
**Number of patients enrolled in NCI-sponsored clinical trials using bortezomib = 3040.
There have been 19 other cases of death NOS and 10 cases of sudden death reported to the NCI through AdEERS as serious adverse events for bortezomib.**

16. COMMENTS
**The following was also administered on this protocol:
Remission induction Therapy:
Daunorubicin: 60 mg/m² IV on Days 1-3
Cytarabine: 100 mg/m² IV CIV on Days 1-7
Remission Consolidation Therapy:
Cytarabine: 2gm/m² IV over 3 hours 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.