

IND SAFETY REPORT: INITIAL WRITTEN REPORT

TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA

FAX: 301-796-9849

1. IND NUMBER
7921

2. AGENT NAME
Bevacizumab (rhuMab VEGF)

3. DATE
December 31, 2008

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

5. REPORTER=S NAME, TITLE, AND INSTITUTION
**Helen Chen, MD-Associate Branch Chief for Investigational Therapeutics
3, CTEP, DCTD, NCI**

6. PHONE NUMBER
301-496-1196

7. FAX NUMBER
301-402-0428

8. PROTOCOL NUMBER (AE #)
E1505 (AE # 1580693)

9. PATIENT IDENTIFICATION
15245

10. AGE
71

11. SEX
Male

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 71-year-old male with non-small cell lung cancer who expired while on a phase 3 trial utilizing the investigational agent bevacizumab in combination with vinorelbine and cisplatin. He began the first course of the investigational therapy on October 30, 2008, and received the last doses of bevacizumab and cisplatin on December 10, 2008 (Cycle 3, Day 1), and the last dose of vinorelbine on December 16, 2008 (Cycle 3, Day 7). On December 23, 2008 (Cycle 3, Day 14), the research staff was informed that the patient was admitted to a local hospital and had expired. Additional information has been requested from the investigational site. There is a reasonable possibility that the patient's death may have been caused by the drug.

13. DOSE, ROUTE, AND SCHEDULE

**Cycle = 21 days
Bevacizumab/Placebo 15 mg/kg IV over 30-90 minutes on Day 1**

14. DATES OF TREATMENT

The patient started therapy on October 30, 2008, and received his last dose of bevacizumab on December 10, 2008.

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 18,356. There have 61 other incidences death NOS and 40 other incidences of sudden death reported to the NCI through AdEERS as serious adverse events for bevacizumab.

16. COMMENTS

The following were also administered every 21 days: Vinorelbine: 30 mg/m² IV over 10 minutes on Days 1 and 8; Last administered on December 16, 2008, and Cisplatin: 75 mg/m² IV over 60 minutes on Day 1; Last administered on December 10, 2008.

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.