

IND SAFETY REPORT: INITIAL WRITTEN REPORT**TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA****FAX: 301-796-9849****Division of Drug Oncology Products, Center For Drug Evaluation and Research, FDA****301-796-9845**

1. IND NUMBER

7921**61010**

2. AGENT NAME

Bevacizumab (rhuMab VEGF)(704865)**CCI-779 (temsirolimus, ToriselTM)**

3. DATE

May 19, 2009

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**L. Austin Doyle, MD-Senior Investigator for Targeted Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI**

6. PHONE NUMBER

301-496-1196

7. FAX NUMBER

301-402-0428

8. PROTOCOL NUMBER (AE #)

GOG-0229 (AE# 1392926)

9. PATIENT IDENTIFICATION

049-0229G-008

10. AGE

72

11. SEX

Female

12. DESCRIPTION OF ADVERSE EVENT

The patient was a 72-year-old female with endometrioid endometrial adenocarcinoma who experienced grade 5 pneumonitis/pulmonary infiltrates while on a phase 2 trial utilizing the investigational agents bevacizumab and temsirolimus. She began the investigational therapy on January 8, 2009, and received her last dose of bevacizumab on April 2, 2009 (Cycle 4, Day 1) and the last dose of temsirolimus on April 9, 2009 (Cycle 4, Day 8). On April 2, 2009 (Cycle 4, Day 1), the patient presented to the clinic complaining that she was not feeling well for the last 3 days. She denied any history of cough, orthopnea, nocturnal dyspnea, hemoptysis, fever or chills. CT of the chest showed cystic changes as well as groundglass opacification within the lung fields and fluid minimal extend within the major fissure, compatible with the interval development of an interstitial pneumonitis. The differential diagnosis suggested a drug related hypersensitivity pneumonitis. The investigational agents were held. Correlation with the patient's chemotherapeutic agents, drug exposure, and extrinsic exposure was suggested. The patient was started on IV antibiotics. Cultures were negative, and the treatment was discontinued. Despite the aggressive treatment, her hypoxia progressively got worse and the patient was placed under hospice care after discussion with the family members. The patient died on April 21, 2009. 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

Cycle = 28 Days.**Temsirolimus 25 mg IV over 30 minutes on Days 1, 8, 15, and 22****Bevacizumab 10 mg/kg IV over 30-90 minutes on Days 1 and 15**

14. DATES OF TREATMENT

The patient began the investigational therapy on January 8, 2009, and received the last dose of bevacizumab on April 2, 2009 (Cycle 4, Day 1) and the last dose of temsirolimus on April 9, 2009 (Cycle 4, Day 8).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 21376, and for temsirolimus = 1587.

COMMENTS

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 21CFR312.32(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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