

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
August 30, 2010

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

5. REPORTER'S NAME, TITLE, AND INSTITUTION
Kevin Conlon, MD-Senior Investigator for Investigational Therapeutics 3, CTEP, DCTD, NCI

6. PHONE NUMBER
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7. FAX NUMBER
301-402-0428

8a. PROTOCOL NUMBER (AE #)
CALGB-40502 (AE# 1803480)

8b. AE GRADE: AE
Grade 4: Infection-Other: Cerebritis
Grade 4: Adult Respiratory Distress Syndrome (ARDS)
Grade 3: Infection with normal ANC: Eye NOS

9. PATIENT IDENTIFICATION
117523

10. AGE
64 yrs

11. SEX
Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 64-year-old female with invasive breast carcinoma who experienced grade 4 cerebritis, grade 4 ARDS, and a grade 3 eye infection while on a phase 3 study using the investigational agent bevacizumab and nab-paclitaxel. She began her first course of treatment on September 21, 2009, and received the last doses of bevacizumab and nab-paclitaxel on July 1, 2010 (Cycle 10, Day 15). On July 21, 2010, the patient presented to the clinic with a tooth abscess, and she was treated with oral antibiotics. On July 29, 2010, the patient presented to the clinic for treatment, and reported a 1-week history of pain, itching, and swelling of her left eyelid that had become progressively worse. She had a markedly reddened, swollen, and draining left eyelid. She was referred to the emergency room where she underwent incision and drainage of her left eyelid abscess, and she was given clindamycin. The patient was admitted to the hospital and started on IV vancomycin and Unasyn[®]. A CT scan of the orbit, sella, and internal auditory canal later that day showed a pre-existing large destructive process at the base of the skull with destroyed left clivus and left sphenoid bone at the base of the middle cranial fossa, complete opacification or near complete opacification of the left maxillary, left ethmoid and left frontal sinuses, and an abscess in the left superior eyelid which extended into the postseptal upper orbit adjacent to the superior rectus muscle. On July 30, 2010, an MRI of the orbits also confirmed these findings. On August 4, 2010, the patient underwent a left frontal craniotomy, irrigation and debridement of the left frontal epidural and subdural abscess; excision of the left frontal pole cerebritis and early abscess formation; irrigation and debridement of the left frontal and ethmoidal sinus infection; cranialization of frontal sinus; dural patch grafting; autologous tissue harvesting of the right contralateral pericranium. The patient later developed acute respiratory failure. She was placed on mechanical ventilation and transferred to the ICU. On postoperative day 5, the patient developed septic shock and suffered a cardiac arrest. She was maintained on vancomycin, ceftriaxone, and Flagyl[®]. She was removed from the study on August 12, 2010. The patient recovered and she was discharged to a rehabilitation facility on August 19, 2010. Additional information has been requested from the site. There is a reasonable possibility that the experience may have been caused by the drug.

13. DOSE, ROUTE, AND SCHEDULE

Cycle: 28 Days; Bevacizumab: 10 mg/kg IV over 30-90 minutes on Days 1 and 15

14. DATES OF TREATMENT

The patient started the investigational therapy on September 21, 2009, and received the last dose of bevacizumab on July 1, 2010 (Cycle 10, Day 15).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab = 28,650. Infections are known events for bevacizumab. There have been 15 other cases of ARDS reported to the NCI through AdEERS as serious adverse events for bevacizumab.

16. COMMENTS Also administered on this protocol:

Nab-paclitaxel: 150 mg/m² IV over 30 minutes on Days 1, 8 and 15

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.

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