

**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  
**February 1, 2011**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, Investigational Drug Branch, CTEP, DCTD, NCI**6. PHONE NUMBER  
**301-496-1196**7. FAX NUMBER  
**301-402-0428**8a. PROTOCOL NUMBER (AE #)  
**GOG-0251 (AE# 1897814)**8b. AE GRADE: AE  
**Grade 2: Tinnitus**  
**Grade 2: Hearing: patients without baseline audiogram and not enrolled in a monitoring program**9. PATIENT IDENTIFICATION  
**078-0251-003**10. AGE  
**55 yrs**11. SEX  
**Female**

## 12. DESCRIPTION OF ADVERSE EVENT

The patient is a 55-year-old female with ovarian stromal cancer who experienced tinnitus and hearing impairment while on a phase 2 trial utilizing the investigational agent bevacizumab. She began the first course of the investigational therapy on December 21, 2009, and received the last dose of bevacizumab on December 30, 2010 (Cycle 18, Day 1). On July 15, 2010 (Cycle 10, Day 14), the patient reported the presence of constant bilateral tinnitus. She was seen in consultation on September 16, 2010, for evaluation of hearing sensitivity. The patient denied the presence of otalgia, aural fullness, otorrhea, dizziness and/or imbalance, or any significant history of noise exposure. Pure tone test results revealed a moderate high-frequency sensorineural hearing loss, as well as a moderately severe rising to moderate ultra high frequency hearing loss for the right ear, and a moderate to moderately severe high-frequency sensorineural hearing loss, as well as a moderately severe ultra high frequency hearing loss for the left ear, with essentially normal middle ear mobility bilaterally. Distortion product otoacoustic emissions test results were in essential agreement with the audiometric configuration. The patient was recommended to avoid noise exposure and use ear protection as appropriate. A follow-up audiological evaluation was performed on December 10, 2010, and revealed that both test results and patient's symptoms were overall not significantly different from the last evaluation. 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 = 21 Days**  
**Bevacizumab: 15 mg/kg IV over 30-90 minutes on Day 1**

## 14. DATES OF TREATMENT

**The patient began the investigational therapy on December 21, 2009, and received the last dose of bevacizumab on December 30, 2010 (Cycle 18, Day 1).**

## 15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using bevacizumab =31,358. There have been 3 other cases of tinnitus and 2 other cases of hearing impairment reported to the NCI as serious adverse events through AdEERS for bevacizumab.**16. COMMENTS **The prior therapies that the patient received include: surgery on January 5, 2007, 6 courses of Taxol® and carboplatin completed in May 2007, 4 courses of BEP treatment from July to September 2008, tumor reductive surgery on November 25, 2008, and pelvic radiation therapy of 50 Gy completed in January 2009.****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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