

IND SAFETY REPORT: INITIAL WRITTEN REPORT

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

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1. IND NUMBER 61010 7921	2. AGENT NAME CCI-779 (temsirolimus, Torisel™) Bevacizumab (rhuMab VEGF)(704865)	3. DATE February 19, 2009
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4. SPONSOR
Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION L. Austin Doyle, MD-Senior Investigator for Investigational Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI	6. PHONE NUMBER 301-496-1196
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8. PROTOCOL NUMBER (AE #)
7190 (AE# 1360351)

9. PATIENT IDENTIFICATION 8669	10. AGE 67	11. SEX Female
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12. DESCRIPTION OF ADVERSE EVENT
The patient is a 67-year-old female with stage IV malignant melanoma who experienced a grade 2 posterior reversible encephalopathy syndrome (PRES) while on a phase 2 trial utilizing the investigational agent temsirolimus in combination with bevacizumab. She began the first course of the investigational therapy on December 15, 2008, and received her last dose of temsirolimus at a reduced dose of 20 mg and the last dose of bevacizumab on February 2, 2009 (Cycle 4, Day 8). The patient was doing well after the infusions and was about to leave for home when she had an acute midline supra umbilical pain described as sharp and constant with radiation to her back. She was admitted to the hospital for further evaluation of her abdominal pain and was started on IV pain management. The CT scan of the abdomen revealed mild thickening of the gallbladder wall with mild pericholecystic fluid collection and mild common bile duct dilation. A scheduled MRI of the brain with and without contrast revealed findings thought to be compatible with PRES. The patient did not have any significant neurological symptoms that are associated with the syndrome. Neurology recommended a follow-up MRI to re-evaluate the findings of this MRI in the future. On February 5, 2009, the patient was discharged in a stable condition. Additional information has been requested from the investigational site. There is a reasonable possibility that the experience may have been caused by the drugs.

13. DOSE, ROUTE, AND SCHEDULE
Cycle =14 Days (Max = 26 cycles)
Temsirolimus 25 mg IV over 30 minutes on Days 1 and 8; Bevacizumab 10 mg/kg IV over 90 minutes on Day 8

14. DATES OF TREATMENT
The patient began the investigational therapy on December 15, 2008, and received the last doses of temsirolimus and bevacizumab on February 2, 2009 (Cycle 4, Day 8).

15. ACCRUAL AND IND EXPERIENCE
Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1083 and using bevacizumab = 16753. There have been no other incidences of PRES, 4 other incidences of encephalopathy, and 1 other incidence of leukoencephalopathy reported to the NCI through AdEERS as serious adverse events for temsirolimus; and 11 other incidences of PRES/ reversible posterior leukoencephalopathy, and 20 other incidences of encephalopathy reported to the NCI through AdEERS as serious adverse events for bevacizumab.

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.