

IND SAFETY REPORT: INITIAL WRITTEN REPORT

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

FAX: 301-796-9845

1. IND NUMBER 63383 61010	2. AGENT NAME OSI-774 (erlotinib; Tarveva) CCI-779 (temsirolimus, Torisel™)	3. DATE March 4, 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 Targeted Therapeutics 2, Investigational Drug Branch, CTEP, DCTD, NCI	6. PHONE NUMBER 301-496-1196
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8. PROTOCOL NUMBER (AE #)
NABTC-04-02 (AE# 1192065)

9. PATIENT IDENTIFICATION 64	10. AGE 31	11. SEX Female
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12. DESCRIPTION OF ADVERSE EVENT
The patient was a 31-year-old female with glioblastoma multiforme who experienced a grade 3 cerebrospinal fluid leak, a grade 4 wound complication, and death NOS, while on a phase 1/2 trial utilizing the investigational agents erlotinib and temsirolimus. She began the investigational therapy on March 29, 2008, and received her last dose of erlotinib on May 25, 2008 (Cycle 2, Day 28), and the last dose of temsirolimus on May 19, 2008 (Cycle 2, Day 22). On April 3, 2008 (Cycle 1, Day 6), the patient underwent a craniotomy with resection. On May 26, 2008 (Cycle 3, Day 1), patient presented to the emergency room complaining of fluid leakage from the craniotomy incision site. The patient was afebrile and alert. A wound culture of the craniotomy site was positive for leukocytes and gram-positive bacilli. A CT scan of the head revealed subgaleal fluid collection and air under the bone flap with possible infection of the glioma. The patient was admitted to the hospital on May 26, 2008, antibiotics were started, and she was removed from the study. On June 13, 2008, an MRI of the head showed an increase in the subgaleal fluid collection, subdural hematoma, and post-surgical changes of the left temporal region. A fluid culture was repeated on June 10, 2008, which showed no growth. The patient was discharged to home on June 10, 2008, and passed away on June 25, 2008. 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. Erlotinib 150 mg PO QD
 Temsirolimus 15 mg IV weekly**

14. DATES OF TREATMENT
The patient began the investigational therapy on March 29, 2008, and received the last dose of erlotinib on May 25, 2008 (Cycle 2, Day 28), and temsirolimus on May 19, 2008 (Cycle 2, Day 22).

15. ACCRUAL AND IND EXPERIENCE
Number of patients enrolled in NCI-sponsored clinical trials using temsirolimus = 1501 and using erlotinib = 2749. There have been 18 death NOS, 8 infectious wound, and no cerebrospinal fluid leak incidences reported to the NCI through AdEERS as a serious adverse event for temsirolimus; and 27 death NOS, 3 infectious wound, and 1 cerebrospinal fluid leak incidences reported to the NCI through AdEERS as serious adverse events for erlotinib, excluding this report.

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.