

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

103846**63383**

2. AGENT NAME

GDC-0449**OSI-774 (erlotinib, Tarceva®)**

3. DATE

February 3, 2011

4. SPONSOR

Division of Cancer Treatment and Diagnosis, National Cancer Institute

5. REPORTER'S NAME, TITLE, AND INSTITUTION

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6. PHONE NUMBER

301-496-1196

7. FAX NUMBER

301-402-0428

8a. PROTOCOL NUMBER (AE #)

8231 (AE# 1392174)

8b. AE GRADE: AE

Grade 4: Platelet count decreased

9. PATIENT IDENTIFICATION

EX150875

10. AGE

60 years

11. SEX

Female

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 60-year-old female with metastatic papillary serocystic adenocarcinoma of the ovaries who experienced grade 4 thrombocytopenia while on a phase 1 study utilizing the investigational agents GDC-0449 and OSI-774 in combination with gemcitabine. She began her first course of the investigational treatment on January 3, 2011, and received the last doses of GDC-0449 and OSI-774 on January 17, 2011 (Cycle 1, Day 15), and the last dose of gemcitabine on January 10, 2011 (Cycle 1, Day 8). On January 17, 2011 (Cycle 1, Day 15), the patient presented to the clinic for treatment and had a platelet count of $25 \times 10^9/L$ (reference range: $150-450 \times 10^9/L$), from a baseline value of $165 \times 10^9/L$ on January 3, 2011. The patient was removed from the study per protocol guidelines and she was advised on bleeding precautions. On January 19, 2011, a repeat laboratory report showed a platelet count of $24 \times 10^9/L$. On January 25, 2011, the patient returned for a follow-up visit and her platelet count had recovered to $202 \times 10^9/L$. 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 1 = 56 Days and Cycle 2 + = 28 Days**GDC-0449: 150 mg PO daily; and OSI-774: 75 mg PO daily**

14. DATES OF TREATMENT

The patient began the investigational therapy on January 3, 2011, and received the last doses of GDC-0449 and OSI-774 on January 17, 2011 (Cycle 1, Day 15).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using GDC-0449 = 265 and using OSI-774 = 3,398. There have been 6 other cases of thrombocytopenia reported to the NCI through AdEERS as serious adverse events for GDC-0449; and 44 other cases of thrombocytopenia reported to the NCI through AdEERS as serious adverse events for OSI-774.

16. COMMENTS **Also administered on this protocol:****Cycle 1 = 56 Days: Gemcitabine: 750 mg/m² IV over 30 minutes on Days 1, 8, 15, 22, 29, 36, and 43.****Cycle 2 + = 28 Days: Gemcitabine: 750 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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