

**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  
**57004**2. AGENT NAME  
**Oxaliplatin (Eloxatin)**3. DATE  
**September 23, 2010**4. SPONSOR  
**Division of Cancer Treatment and Diagnosis, National Cancer Institute**5. REPORTER'S NAME, TITLE, AND INSTITUTION  
**S. Percy Ivy, MD - Associate Branch Chief for Investigational Therapeutics I, Investigational Drug Branch, CTEP, DCTD, NCI**6. PHONE NUMBER  
**301-496-1196**7. FAX NUMBER  
**301-402-0428**8a. PROTOCOL NUMBER (AE #)  
**E5204 (AE# 1060315)**8b. AE GRADE: AE  
**Grade 4: Secondary malignancy-possibly related to cancer treatment: Leukemia**9. PATIENT IDENTIFICATION  
**52009**10. AGE  
**62 years**11. SEX  
**Male**

## 12. DESCRIPTION OF ADVERSE EVENT

**The patient is 62 year-old male with colon cancer and rectal cancer who developed grade 4 acute myelogenous leukemia (AML) while on a phase 3 trial utilizing the investigational agent oxaliplatin. He began the investigational therapy on August 2, 2006, and received the last dose of oxaliplatin on December 6, 2006 (Cycle 9, Day 1), the last dose of leucovorin on January 17, 2007 (Cycle 12, Day 1), and the last dose of 5-FU on January 19, 2007 (Cycle 12, Day 3). On July 24, 2010 (Cycle 12, Day 1285), the patient presented to the emergency room with 3 weeks of progressive dyspnea. His complete blood count was abnormal: WBC  $17.3 \times 10^9/L$  (reference range:  $5-10 \times 10^9/L$ ), hemoglobin 7.6 g/dL (reference range: 14-18 g/dL), 54% blasts (reference value: 0%), 2% myelocytes (reference value: 0%), and 5 nucleated red blood cells. The patient was admitted for further evaluation. Bone marrow biopsy on July 25, 2010, revealed: 50% blasts in the peripheral smear, most exhibiting myeloid characteristics, but some showing monocytoid differentiation; increased cellularity in the marrow smear with about 70% blast cells (reference range: <5%), exhibiting myelomonocytic features consistent with FAB-M-4; and 90% cellularity in the marrow biopsy with the majority of cells exhibiting blast features, all leading to a diagnosis of AML with monocytic differentiation (myelomonocytic leukemia, FAB-M-4). Cytogenetics testing showed that one copy of chromosome 3 had a paracentric inversion of the long arm and one copy of chromosome 7 was missing, which suggested adverse prognosis in a myeloid disorder. The patient was discharged on July 31, 2010 and transferred to University of Chicago for chemotherapy. 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 = 2 weeks for a total of 12 cycles  
Oxaliplatin: 85 mg/m<sup>2</sup> IV infusion over 2 hours on Day 1**

## 14. DATES OF TREATMENT

**The patient began the investigational therapy on August 2, 2006, and received the last dose of oxaliplatin on December 6, 2006 (Cycle 9, Day 1).**

## 15. ACCRUAL AND IND EXPERIENCE

**Number of patients enrolled in NCI-sponsored clinical trials using oxaliplatin =22,348. There have been 2 other cases of secondary malignancy possibly related to cancer treatment reported to the NCI through AdEERS as serious adverse events for oxaliplatin.**

## 16. COMMENTS: Also administered on this protocol:

**Leucovorin: 400 mg/m<sup>2</sup> IV infusion over 2 hours on Day 1  
5-FU: 400 mg/m<sup>2</sup> IV bolus on Day 1 and 2.4 g/m<sup>2</sup> IV continuous infusion over 46 hours immediately following bolus 5-FU on Days 1 and 2**

**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.**

0002