



# NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

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**Date:** February 20, 2009

**To:** NCCTG Primary Clinical Research Associates

**From:** Linda Long  
Protocol Development Coordinator

**Re:** N0543, A Phase II Trial of Pharmacogenetic-Based Dosing of Irinotecan, Oxaliplatin, and Capecitabine as First-Line Therapy for Advanced Small Bowel Adenocarcinoma

The purpose of this memorandum is to provide investigators with a recent report of an adverse event that has occurred in association with Oxaliplatin for a study where the Division of Cancer Treatment and Diagnosis (DCTD), National Cancer Institute (NCI) is distributing this agent. You may have also received this communication directly from DCTD.

**AE\_1118620**

Please note that all risks currently cited in the NCCTG consent form cannot be omitted; it is at the discretion of your local IRB as to whether they wish to add risks based on the enclosed information. (Do not use the following sentence if this involves a CTEP warning letter.) If a determination has been made by the NCCTG Research Base that a protocol amendment is necessary, you will receive the NCI-approved protocol addendum at a later date; for purposes of cross-reference, this communication will cite the adverse event noted above.

**Please submit this adverse event to your Institutional Review Board.**

If you have any questions concerning this communication, please contact Linda Long at [long.linda@mayo.edu](mailto:long.linda@mayo.edu) or 507-266-3853.

LL/kjm  
enclosure

**IND SAFETY REPORT: INITIAL WRITTEN REPORT #71****TO: Division of Biologic Oncology Products, Center for Drug Evaluation and Research, FDA****FAX: 301-796-9849**

1. IND NUMBER

**57004****7921**

2. AGENT NAME

**Oxaliplatin (Eloxatin®)****Bevacizumab (rhuMAb VEGF)**

3. DATE

**November 20, 2008**

4. SPONSOR

**Division of Cancer Treatment and Diagnosis, National Cancer Institute**

5. REPORTER'S NAME, TITLE, AND INSTITUTION

**S. Percy Ivy, MD-Associate Chief for Targeted Therapeutics 1, Investigational Drug Branch, CTEP, DCTD, NCI****Helen Chen, MD-Associate Chief for Targeted Therapeutics 3, Investigational Drug Branch, CTEP, DCTD, NCI**

6. PHONE NUMBER

**301-496-1196**

7. FAX NUMBER

**301-402-0428**

8. PROTOCOL NUMBER (AE #)

**E5204 (1118620)**

9. PATIENT IDENTIFICATION

**52255**

10. AGE

**61**

11. SEX

**Female**

12. DESCRIPTION OF ADVERSE EVENT

The patient is a 61-year-old female with rectal cancer who experienced grade 4 left ventricular systolic dysfunction (congestive heart failure) while on phase III trial using oxaliplatin in combination bevacizumab. The patient began the investigational therapy on September 09, 2008, and received the last doses of oxaliplatin and bevacizumab on September 23, 2008 (Cycle 2, Day 1). On September 26, 2008 (Cycle 2, Day 4), the patient called 911 complaining of dyspnea. She was admitted to the emergency room diagnosed as respiratory insufficiency of sudden onset. Upon admission her vital signs were remarkable for a blood pressure of 150/100 mmHg, echocardiogram showed 15% ejection fraction, chest X-rays showed pulmonary edema with prominent right pleural effusion, PRO-B-type natriuretic peptide (BNP) was 9089 pg/mL suggesting acute congestive heart failure. The patient was transferred to the Intensive Care Unit for closer monitoring. On October 7, 2008, the patient remained in the Intensive Care Unit in stable condition. The patient was removed from the research protocol. There is a reasonable possibility that the experience is related to the investigation therapy. Additional information has been requested from the investigative site.

13. DOSE, ROUTE, AND SCHEDULE (Cycle = 14 days)

**Oxaliplatin 85 mg/m<sup>2</sup> IV infusion over 2 hours on day 1****Bevacizumab 5 mg/kg IV over 30-90 minutes on day 1**

14. DATES OF TREATMENT

The patient started the investigational drug therapy on September 09, 2008, and received the last doses of oxaliplatin and the last dose of bevacizumab on September 23, 2008 (Cycle 2, Day 1).

15. ACCRUAL AND IND EXPERIENCE

Number of patients enrolled in NCI-sponsored clinical trials using Oxaliplatin = 18,989 and using bevacizumab = 18,130

There were 102 other incidences of left ventricular systolic dysfunction and 6 other incidences of congestive heart failure reported to the NCI through AdEERS as serious adverse events for bevacizumab and 18 other incidences of left ventricular systolic dysfunction and no other incidences of congestive heart failure reported to the NCI through AdEERS as serious adverse events for oxaliplatin.

16. COMMENTS

Also administered on this protocol: Leucovorin 400mg/m<sup>2</sup> IV infusion over 2 hours on day 1 followed by 5-FU 400 mg/m<sup>2</sup> IV bolus on day 1, and 5-FU 2.4 g/m<sup>2</sup> IV continues infusion over 46 hours immediately following bolus 5-FU on days 1 & 2

AT THIS TIME, NO OTHER INFORMATION IS AVAILABLE. IF UPON FURTHER INVESTIGATION RELEVANT INFORMATION BECOMES AVAILABLE, THEN A FOLLOWUP 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.**

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