



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: January 18, 2008

To: NCCTG Primary Clinical Research Associates

From: Alicia Elsing
Protocol Development Coordinator

Re: N0626, Phase II Randomized Study Pemetrexed With Sorafenib versus Pemetrexed Alone as Second-line Therapy in Patients With Advanced Non-Small Cell Lung Cancer

The purpose of this memorandum is to provide investigators with a recent industry report of an adverse event that has occurred in association with ALIMTA at a non-NCCTG institution. You may have also received this communication directly from the drug manufacturer.

AE_US200801000066

Please note that all risks currently cited in the NCCTG consent form can not be omitted; it is at the discretion of your local IRB as to whether they wish to add risks based on the enclosed information. 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 Alicia Elsing at elsing.alicia@mayo.edu or 507-538-3893.

AE/dkf
enclosure

SUSPECT ADVERSE REACTION REPORT

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last)	1a. COUNTRY UNITED STATES	2. DATE OF BIRTH			2a. AGE	3. SEX	3a. WEIGHT	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day 02	Month OCT	Year 1945	62 Years	Female	46.26 kg	Day 24	Month DEC	Year 2007	
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data) Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas) TRANSESOPHAGEAL FISTULA, GRADE 3 [Oesophageal fistula] difficulty swallowing grade 3 [Dysphagia]											<input type="checkbox"/> PATIENT DIED <input checked="" type="checkbox"/> INVOLVED OR PROLONGED INPATIENT HOSPITALISATION <input type="checkbox"/> INVOLVED PERSISTENT OR SIGNIFICANT DISABILITY OR INCAPACITY <input type="checkbox"/> LIFE THREATENING
Case Description: This investigator-initiated clinical trial case (IIT) concerns a 62-year-old female of unspecified origin.											
The patient's medical history and concomitant medications were not reported.											
The patient first received pemetrexed disodium (Alimta) 300 mg/m ² (477 mg) intravenously (IV), carboplatin IV AUC 4 (370 mg), bevacizumab IV 15 mg/kg (continue)											

II. SUSPECT DRUG(S) INFORMATION

(Continued on Additional Information Page)

14. SUSPECT DRUG(S) (include generic name) #1 PEMETREXED (PEMETREXED UNKNOWN FORMUL (continue)) #2 *CARBOPLATIN(*CARBOPLATIN)Unknown		20. DID REACTION ABATE AFTER STOPPING DRUG? <input type="checkbox"/> YES <input type="checkbox"/> NO <input checked="" type="checkbox"/> NA
15. DAILY DOSE(S) #1 300 mg/m ² . UNK #2 4 AUC, other	16. ROUTE(S) OF ADMINISTRATION #1 Unknown #2 Unknown	21. DID REACTION REAPPEAR AFTER REINTRODUCTION? <input type="checkbox"/> YES <input type="checkbox"/> NO <input checked="" type="checkbox"/> NA
17. INDICATION(S) FOR USE #1 non-small cell lung cancer(Non-small cell lung cancer) #2 non-small cell lung cancer(Non-small cell lung cancer)	19. THERAPY DURATION #1 161 days #2 161 days	
18. THERAPY DATES(from/to) #1 01-MAR-2007 00:00 / 08-AUG-2007 00:00 #2 01-MAR-2007 00:00 / 08-AUG-2007 00:00		

III. CONCOMITANT DRUG(S) AND HISTORY

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction)		
23. OTHER RELEVANT HISTORY (e.g. diagnostics, allergies, pregnancy with last month of period, etc.)		
From/To Dates	Type of History / Notes	Description
14-FEB-2007 to Unknown	Medical Condition	Non-small cell lung cancer
NOV-2007 to Unknown	Procedure	Oesophageal dilation procedure

IV. MANUFACTURER INFORMATION

24a. NAME AND ADDRESS OF MANUFACTURER Eli Lilly & Company Lilly Corporate Center, Global Product Safety, Indianapolis, IN 46285 UNITED STATES		26. REMARKS
	24b. MFR CONTROL NO US200801000066	25b. NAME AND ADDRESS OF REPORTER
24c. DATE RECEIVED BY MANUFACTURER 31-DEC-2007	24d. REPORT SOURCE <input checked="" type="checkbox"/> STUDY <input type="checkbox"/> LITERATURE <input checked="" type="checkbox"/> HEALTH PROFESSIONAL <input type="checkbox"/> OTHER	
DATE OF THIS REPORT 14-JAN-2008	25a. REPORT TYPE <input checked="" type="checkbox"/> INITIAL <input type="checkbox"/> FOLLOWUP	

ADDITIONAL INFORMATION**7+13. DESCRIBE REACTION(S) continued**

(870 mg) (weeks 1 and 4), beginning on 01Mar07 for the treatment of non-small cell lung cancer. Pemetrexed and carboplatin therapy were completed with the last doses received on 08Aug07 and bevacizumab on 19Dec07. On 24Dec07, the patient was hospitalized due to difficulty swallowing grade three (possibly due to recurrent esophageal stricture) and transesophageal fistula grade three, which was confirmed. No laboratory data was provided. It was noted that the patient was to have a percutaneous endoscopic gastrostomy tube placed on an unspecified date. Corrective treatment was unknown. At the time of the report (28Dec07) the patient was recovering from the events.

In the opinion of the investigator, the events were considered possibly related to the study drugs. An opinion of relatedness was not provided for protocol procedures.

Edit 08Jan08: Case edited, listedness changed from listed to unlisted for the event transesophageal fistula grade 3.

Lilly Analysis Statement: Patient developed grade 3 dysphagia and transesophageal fistula a few days after completing therapy with bevacizumab and about eighteen weeks after completing therapy with pemetrexed and carboplatin, for lung cancer. Dysphagia is a listed event for pemetrexed, while the two events are unlisted for carboplatin and bevacizumab. However, the events have been reported to be associated with bevacizumab. The earlier co-administration of the chemotherapeutic agents with bevacizumab may have been a contributory factor to the subsequent development of the events in this case.

14-19. SUSPECT DRUG(S) continued

14. SUSPECT DRUG(S) (include generic name)	15. DAILY DOSE(S) 16. ROUTE(S) OF ADMIN	17. INDICATION(S) FOR USE	18. THERAPY DATES (from/to): 19. THERAPY DURATION
#1 PEMETREXED (PEMETREXED UNKNOWN FORMULATION) Unknown; Regimen #1	300 mg/m ² , UNK; Unknown	non-small cell lung cancer(Non-small cell lung cancer)	01-MAR-2007 00:00 / 08-AUG-2007 00:00; 161 days
#3 *BEVACIZUMAB (BEVACIZUMAB) Unknown; Regimen #1	15 mg/kg, UNK; Unknown	non-small cell lung cancer(Non-small cell lung cancer)	01-MAR-2007 00:00 / Unknown; Unknown