



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: February 29, 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_DE200802002043

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) RD	1a. COUNTRY GERMANY	2. DATE OF BIRTH Day: 06 Month: DEC Year: 1941	2a. AGE 66 Years	3. SEX Male	3a. WEIGHT 74.00 kg	4-6 REACTION ONSET Day: 07 Month: FEB Year: 2008	8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data) Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas) suspicion of pulmonary cavity of the right upper lobe [Pulmonary cavitation] Case Description: This post-marketing study case (H3E-SB-S109, EudraCT unknown) concerns a 66 year old Caucasian male. The patient's medical history included non-small cell lung cancer since Nov-2007. Concomitant medication included cyanocobalamin, folic acid and dexamethasone as prophylaxis, bisoprolol, digoxin and phenprocoumon for atrial fibrillation, all ongoing. (continue)							<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

II. SUSPECT DRUG(S) INFORMATION

14 SUSPECT DRUG(S) (include generic name) #1 PEMETREXED (PEMETREXED) Vial #2 *CARBOPLATIN(*CARBOPLATIN)Unknown	20. DID REACTION ABATE AFTER STOPPING DRUG? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> NA Unknown
15. DAILY DOSE(S) #1 950 D/F, unknown #2 700 D/F, unknown	16. ROUTE(S) OF ADMINISTRATION #1 Unknown #2 Unknown
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)	21. DID REACTION REAPPEAR AFTER REINTRODUCTION? <input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> NA Unknown
18. THERAPY DATES(from/to) #1 13-NOV-2007 00:00 / Unknown #2 13-NOV-2007 00:00 / Unknown	19. THERAPY DURATION #1 Unknown #2 Unknown

III. CONCOMITANT DRUG(S) AND HISTORY (Continued on Additional Information Page)

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION (exclude those used to treat reaction) #1 VITAMIN B12 (CYANOCOBALAMIN) ; 06-NOV-2007 00:00 / Ongoing #2 FOLIC ACID (FOLIC ACID) ; 06-NOV-2007 00:00 / Ongoing #3 DEXAMETHASONE (DEXAMETHASONE) ; 06-NOV-2007 00:00 / Ongoing	
23. OTHER RELEVANT HISTORY. (e.g. diagnostics, allergies, pregnancy with last month of period, etc.) From/To Dates Type of History / Notes Description Unknown	

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
24c. DATE RECEIVED BY MANUFACTURER 08-FEB-2008	24b. MFR CONTROL NO. DE200802002043
24d. REPORT SOURCE <input checked="" type="checkbox"/> STUDY <input type="checkbox"/> LITERATURE <input checked="" type="checkbox"/> HEALTH PROFESSIONAL <input type="checkbox"/> OTHER	25b. NAME AND ADDRESS OF REPORTER NAME AND ADDRESS WITHHELD.
DATE OF THIS REPORT 19-FEB-2008	

ADDITIONAL INFORMATION

7+13. DESCRIBE REACTION(S) continued

This patient was enrolled in a randomized phase II study of pemetrexed (Alimta) in combination with cisplatin or carboplatin in the first line therapy of advanced non-small cell lung cancer (NSCLC). On 13-Nov-2007, the patient first received study pemetrexed (950 unit unspecified, route and frequency unspecified) and carboplatin (700 units unspecified, route and frequency unspecified) for the treatment of NSCLC. The last dose of both pemetrexed and carboplatin was received on 18-Jan-2008. On 07-Feb-2008, 21 days after the last dose of pemetrexed and Acarboplatin, the patient was hospitalized for the fifth cycle scan as planned. A computerized tomography (CT) on 07-Feb-2008 as planned, showed a new cavitation in the right upper lobe that was suspect for a aspergilloma (reported as suspicion of pulmonary cavity of the right upper lobe (pulmonary cavitation)), serious for prolonging hospitalization (to be confirmed). The CT also revealed the primary pulmonal tumor on the right side showing back formation and a new alteration on the left sided lower area of the lung. A bronchoscopy was planned to confirm diagnosis (results have been requested). Laboratory data on 07-Feb-2008 included c-reactive protein: 6.0 mg/l (normal range: 0.0-10.0), HST (to be confirmed): 62 mg/dl (normal range:0-50), creatine urine (CREA-S): 0.98 mg/dl (normal range: 0.00-1.25), blood sodium: 140 mmol/l (normal range: 135-145), blood potassium: 3.8 mmol/l (normal range:3.5-5.1), blood calcium: 2.00 mmol/l (normal range: 2.10-2.60), blood lactate dehydrogenase (LDH): 622 U/l (normal range: 0-225), aspartate aminotransferase (GOT): 31 U/l (normal range: 0-50), alanine aminotransferase (GPT): 87 U/l (normal range: 0-50), gamma-glutamyltransferase (GGT): 46 U/l (normal range:0-66), blood alkaline phosphatase: 82 U/l (normal range: 0-129), bilirubin: 0.4 mg/dl (normal range: 0.0-1.3), protein-S: 5.8 g/dl (normal range:5.5-8.0), glucose urine: 109 mg/dl (normal range 75-115) and the following flagged results with no normal ranges provided, white blood cells:8.23 x10E9/uL, neutrophils: 4.81 x10E9/uL (58.5%), lymphocyte: 2.16 x10E9/uL (26.2%), monocytes:1.12 x10E9/uL (13.6%), basophils: 0.12 x10E9/uL (1.5%) and platelet count: 119 x10E8/uL (flagged as thrombocytopenia). Corrective treatment medication was not reported. The outcome of the event was unknown. Planned chemotherapy was delayed until an unspecified date. It was unknown if the event resulted in permanent discontinuation of the study drug.

In the opinion of the study investigator, the pulmonary cavitation was related to pemetrexed and carboplatin but not to protocol procedures.

Initial and follow-up (email from investigator on 11-Feb-2008) processed at the same time.

13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1	07-FEB-2008	Computerised tomogram Result:Aspergilloma Revealed primary tumor pulmonal on the right side shows back formation, new focus on the upper lobe of lung, new alteration on the left sided lower area of lung.		
2	07-FEB-2008	C-reactive protein Within Normal Limits	<6.0 mg/l	10.0 0.0
3	07-FEB-2008	Creatine urine Within Normal Limits CREA-S (spot test)	0.98 mg/dl	1.25 0.0
4	07-FEB-2008	Blood sodium Within Normal Limits	140 mmol/l	145 135
5	07-FEB-2008	Blood potassium Within Normal Limits	3.8 mmol/l	5.1 3.5
6	07-FEB-2008	Blood calcium Low	2.00 mmol/l	2.60 2.10
7	07-FEB-2008	Blood lactate dehydrogenase High	622 U/l	225 0
8	07-FEB-2008	Aspartate aminotransferase Within Normal Limits	31 U/l	50 0
9	07-FEB-2008	Alanine aminotransferase High	87 U/l	50 0
10	07-FEB-2008	Gamma-glutamyltransferase Within Normal Limits	46 U/l	66 0
11	07-FEB-2008	Blood alkaline phosphatase Within Normal Limits	82 U/l	129 0
12	07-FEB-2008	Blood bilirubin Within Normal Limits	0.4 mg/dl	1.3 0.0
13	07-FEB-2008	Protein S	5.8 g/dl	8.0

ADDITIONAL INFORMATION**13. Lab Data**

#	Date	Test / Assessment / Notes	Results	Normal High / Low
		Within Normal Limits		5.5
14	07-FEB-2008	Glucose urine Within Normal Limits	109 mg/dl	115 75
15	07-FEB-2008	White blood cell count	8.23 x10E9/ul	
16	07-FEB-2008	Neutrophil count 58.5 %	4.81 x10E9/ul	
17	07-FEB-2008	Lymphocyte count 26.2%	2.16 x10E9/ul	
18	07-FEB-2008	Monocyte count 13.6%	1.12 x10E9/ul	
19	07-FEB-2008	Basophil count 1.5%	0.12 x10E9/ul	
20	07-FEB-2008	Platelet count	119 x10E8/ul	

22. CONCOMITANT DRUG(S) AND DATES OF ADMINISTRATION continued

#4 BISOPROLOL (BISOPROLOL) ; 05-DEC-2007 00:00 / Ongoing

#5 DIGOXIN (DIGOXIN) ; 05-DEC-2007 00:00 / Ongoing

#6 PHENPROCOUMON (PHENPROCOUMON) ; 05-DEC-2007 00:00 / Ongoing