



NCCTG

NORTH CENTRAL CANCER TREATMENT GROUP

Date: November 9, 2007

To: NCCTG Primary Clinical Research Associates

From: Janis Wobschall
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_BE200710004138

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 Janis Wobschall at wobschall.janis@mayo.edu or 507-284-4852.

JW/dkf
enclosure

SUSPECT ADVERSE REACTION REPORT	

I. REACTION INFORMATION

1. PATIENT INITIALS (first, last) Unk	1a. COUNTRY BELGIUM	2. DATE OF BIRTH			2a. AGE 40 Years	3. SEX Female	3a. WEIGHT Unk	4-6 REACTION ONSET			8-12 CHECK ALL APPROPRIATE TO ADVERSE REACTION
		Day 20	Month JUN	Year 1967			Day 09	Month OCT	Year 2007		
7 + 13 DESCRIBE REACTION(S) (including relevant tests/lab data) Event Verbatim [PREFERRED TERM] (Related symptoms if any separated by commas) Thoracal pain [Chest pain] Haemptoe [Haemoptysis] Purulent sputae [Sputum purulent]										<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 trial case (H3E-BX-0014; Eudract number unknown) concerns a 40 year old female patient of unknown origin.											
The medical history of the patient was not provided with the initial report. (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 *CISPLATIN(*CISPLATIN)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 Unknown #2 131 mg, day 1 of cycle	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 Unknown #2 06-FEB-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 MEDROL (METHYLPREDNISOLONE) ; Unknown #2 DAFALGAN (PARACETAMOL) ; Unknown #3 CONTRAMAL (TRAMADOL HYDROCHLORIDE) ; Unknown		
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
	24b. MFR CONTROL NO. BE200710004138	
24c. DATE RECEIVED BY MANUFACTURER 16-OCT-2007	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 30-OCT-2007	25a. REPORT TYPE <input checked="" type="checkbox"/> INITIAL <input type="checkbox"/> FOLLOWUP.	

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

As concomitant medications, the patient was taking methylprednisolone for infection, paracetamol and tramadol hydrochloride for pain, ranitidine for prophylaxis, fluconazole for candida and budesonide/formoterol fumarate for a cough. It was not reported whether the patient was taking pemetrexed supplements folic acid, vitamin B12 and dexamethasone and this information has been requested in follow up with the investigator.

The patient was randomised to Arm A of the protocol, and received pemetrexed (Alimta)/cisplatin followed by pemetrexed and radiotherapy. The patient received the first doses of pemetrexed and cisplatin on 06-Feb-2007 (cycle one, day one; pemetrexed 872 mg and cisplatin 131 mg), for the treatment of non-small cell lung cancer. Following this, the patient received the following cycles of treatment with pemetrexed and cisplatin: cycle two, pemetrexed 855 mg and cisplatin 128 mg on 27-Feb-07 (day 1); cycle three pemetrexed 861 mg and cisplatin 129 mg on 20-Mar-07 (day 1), date of last dose of cisplatin prior to the event. The patient then began treatment with pemetrexed and radiotherapy: cycle four, pemetrexed 882 mg on 17-Apr-07 (day 1), radiotherapy 10 Gy (16-Apr-07 to 29-Apr-07), radiotherapy 08 Gy (30-Apr-07 to 06-May-07); cycle five, pemetrexed 865 mg on 08-May-07 (day 1, date of last dose of pemetrexed prior to the event), radiotherapy 10 Gy (07-May-07 to 13-May-07), radiotherapy 06 Gy (14-May-07 to 20-May-07), radiotherapy 10 Gy (21-May-07 to 27-May-07), radiotherapy 06 Gy (28-May-07 to 31-May-07). The frequency and route of administration of each study drug were not provided with the initial report. The date of the last dose of radiotherapy prior to the event was not provided. The patient became very ill, and in a few days had developed thoracic pain on the right side, haemoptysis (reported as haemoptoe) and purulent sputum. The patient was hospitalised for the events (to be confirmed), on 09-Oct-2007, approximately six and a half months after the last dose of cisplatin, five months after the last dose of pemetrexed and an unknown time period from the last dose of radiotherapy. An x-ray was taken on an unknown date and showed a large cavity in the right upper lobe, and a pneumectomy was performed. The results of the pathology tests will follow. As corrective treatments, the patient received unspecified pain killers and antibiotics. It was not reported whether the patient remained on the study as a result of the events, or whether the patient had discontinued the study drugs on the dates of the last doses given. At the time of the initial report, the patient had not recovered from any of the events. Further information has been requested.

In the opinion of the investigator, thoracic pain on the right side, haemoptysis and purulent sputum were all related to all study drugs and to protocol procedures.

Lilly Analysis Statement: 30-Oct-2007: This study case relates to certain expected events (chest pain/ haemoptysis) and an unexpected event of purulent sputum in this study patient on combined chemotherapy and radiation. The given information is limited (?temporal relation to study drugs/ clinical diagnosis/ lab results) and confounded by underlying malignancy. F/u is requested to analyse relatedness.

Update 30-Oct-2007: Lilly Analysis Statement added to the case.

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13. Lab Data

#	Date	Test / Assessment / Notes	Results	Normal High / Low
1		X-ray Abnormal showed large cavity in the right upper lobe		

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	Unknown; Unknown	non-small cell lung cancer(Non-small cell lung cancer)	Unknown; Unknown
#1 PEMETREXED (PEMETREXED UNKNOWN FORMULATION) Unknown; Regimen #2	855 mg, day 1 of cycle; Unknown		27-FEB-2007 00:00 / Unknown; Unknown
#1 PEMETREXED (PEMETREXED UNKNOWN FORMULATION) Unknown; Regimen #3	861 mg, day 1 of cycle; Unknown		20-MAR-2007 00:00 / Unknown; Unknown

ADDITIONAL INFORMATION

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 #4	882 mg, day 1 of cycle; Unknown		17-APR-2007 00:00 / Unknown; Unknown
#1 PEMETREXED (PEMETREXED UNKNOWN FORMULATION) Unknown; Regimen #5	865 mg, day 1 of cycle; Unknown		08-MAY-2007 00:00 / Unknown; Unknown
#2 *CISPLATIN (CISPLATIN) Unknown; Regimen #2	128 mg, day 1 of cycle; Unknown		27-FEB-2007 00:00 / Unknown; Unknown
#2 *CISPLATIN (CISPLATIN) Unknown; Regimen #3	129 mg, day 1 of cycle; Unknown		20-MAR-2007 00:00 / Unknown; Unknown
#3 *RADIATION (RADIATION) Unknown; Regimen #1	10 Gy; Unknown	non-small cell lung cancer(Non-small cell lung cancer)	16-APR-2007 00:00 / 29-APR-2007 00:00; 14 days
#3 *RADIATION (RADIATION) Unknown; Regimen #2	8 Gy; Unknown		30-APR-2007 00:00 / 06-MAY-2007 00:00; 7 days
#3 *RADIATION (RADIATION) Unknown; Regimen #3	10 Gy; Unknown		07-MAY-2007 00:00 / 13-MAY-2007 00:00; 7 days
#3 *RADIATION (RADIATION) Unknown; Regimen #4	6 Gy; Unknown		14-MAY-2007 00:00 / 20-MAY-2007 00:00; 7 days
#3 *RADIATION (RADIATION) Unknown; Regimen #5	10 Gy; Unknown		21-MAY-2007 00:00 / 27-MAY-2007 00:00; 7 days
#3 *RADIATION (RADIATION) Unknown; Regimen #6	6 Gy; Unknown		28-MAY-2007 00:00 / 31-MAY-2007 00:00; 4 days 0 hrs

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

#4 RANITIDINE (RANITIDINE) ; Unknown

#5 DIFLUCAN (FLUCONAZOLE) ; Unknown

#6 SYMBICORT (BUDESONIDE, FORMOTEROL FUMARATE) ; Unknown