



ASCO Study Confirms Importance of Histology in Treatment of Non-Small Cell Lung Cancer With ALIMTA (pemetrexed for injection)

INDIANAPOLIS, May 15, 2008 /PRNewswire-FirstCall via COMTEX News Network/ -- Lung cancer patients whose histology is factored into treatment decisions may fare better as a result, according to data from a pivotal non-small cell lung cancer (NSCLC) clinical trial. Data from the trial, which involved Eli Lilly and Company's ALIMTA(R) (pemetrexed for injection), will be presented at the 44th Annual Meeting of the American Society of Clinical Oncology (ASCO) in Chicago, Ill., May 30 -- June 3, 2008.

"The data presented at ASCO confirms that histology matters when treating non-small cell lung cancer," said Richard Gaynor, M.D., vice president, cancer research and global oncology platform leader for Lilly. "We are seeing continued affirmation that when physicians factor in a patient's histology, pemetrexed becomes an even more valuable treatment option in non-small cell lung cancer."

Results from a multicenter, double-blind Phase III trial will be presented on June 2, 2008, at ASCO (Abstract # 8011). The study also was one of those featured during ASCO's live online presscast, a virtual press event that marked the first time researchers were invited to present key abstracts to the media prior to the annual meeting.

The trial compared the efficacy and safety of pemetrexed versus a placebo in 663 patients with stage IIIB/IV NSCLC whose disease had not progressed after four cycles of platinum-based induction chemotherapy. According to the results, patients treated with pemetrexed demonstrated increased efficacy with respect to progression-free survival compared to those treated by placebo (4.3 months vs. 2.6 months), and pemetrexed patients also achieved better tumor response ($p < 0.001$).

However, when data was broken down by histology, it was comparable to previous pemetrexed trials evaluating histology -- patients with a non-squamous histology fared better than those with a squamous histology. Patients with non-squamous histology who were treated with pemetrexed achieved 4.5 months of median progression-free survival compared to 2.8 months for patients with squamous histology.

"The efficacy findings of this data show that pemetrexed performed better in patients with non-squamous histology for the treatment of non-small cell lung cancer," said the trial's lead investigator, Tudor Ciuleanu, M.D. of the Institutul Oncologic I Chiricuta in Cluj, Romania.

Patients in the trial were treated with pemetrexed (500 mg/m²) plus best supportive care or placebo plus best supportive care. All patients were supplemented with vitamin B12, folic acid and dexamethasone.

No significant toxicity differences were identified between the two trial arms with the exception of grade 3/4 anemia (pemetrexed 4.5%, placebo 1.4%) and total serious adverse events due to the treatment (pemetrexed 4.3%, placebo 0%).

The data presented at ASCO reaffirmed findings from previous studies, most notably a Phase III study of pemetrexed plus cisplatin versus gemcitabine plus cisplatin in chemo-naïve patients with locally advanced or metastatic NSCLC. That study showed NSCLC patients with a non-squamous histology (those with adenocarcinoma or large cell carcinoma) demonstrated increased benefits when treated with pemetrexed(1).

Notes to Editor

About Non-Small Cell Lung Cancer (NSCLC)

NSCLC is the most common type of lung cancer and represents 85 to 90 percent of all lung cancers(2). NSCLC has five-tier staging, starting at 0 and rising to the severity of stage IV(3). NSCLC can spread through the lymphatic system, penetrating the chest lining, ribs and the nerves and blood vessels that lead to the arm. The liver, bones and brain are potential targets if the cancerous cells enter the bloodstream.

According to the World Health Organization (WHO) Cancer Report, lung cancer is the world's most common cancer and the leading cause of cancer death for both men and women. More than 1 million people die from lung cancer each year(4).

NSCLC is defined as a group of histologies, that is, tumor types differentiated by cellular structure. The most common NSCLC histology types are squamous (or epidermoid) carcinoma, adenocarcinoma, and large cell carcinoma. These histologies are often classified together because to date, approaches to diagnosis, staging, prognosis and treatment have been similar(5).

About Lilly Oncology, a Division of Eli Lilly and Company

For more than four decades, Lilly Oncology has been dedicated to delivering innovative solutions that improve the care of people living with cancer. Because no two cancer patients are alike, Lilly Oncology is committed to developing novel treatment approaches. Our quest is to develop a broad portfolio of tailored therapies that accelerate the pace and progress of cancer care.

About Eli Lilly and Company

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of first-in-class and best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers -- through medicines and information -- for some of the world's most urgent medical needs.

ALIMTA(R) (pemetrexed for injection), Lilly

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This press release contains forward-looking statements about the potential of ALIMTA for the treatment of non-small cell lung cancer and reflects Lilly's current beliefs. However, as with any pharmaceutical product under development, there are substantial risks and uncertainties in the process of development, commercialization, and regulatory review. There is no guarantee that the product will receive additional regulatory approvals. There is also no guarantee that the product will continue to be commercially successful. For further discussion of these and other risks and uncertainties, see Lilly's filings with the United States Securities and Exchange Commission. Lilly undertakes no duty to update forward-looking statements.

Important Safety Information for ALIMTA

Myelosuppression is usually the dose-limiting toxicity with ALIMTA therapy.

Contraindication

ALIMTA is contraindicated in patients who have a history of severe hypersensitivity reaction to pemetrexed or to any other ingredient used in the formulation.

Warnings

ALIMTA should not be administered to patients with a creatinine clearance < 45 mL/min. One patient with severe renal impairment (creatinine clearance 19 mL/min) who did not receive folic acid and vitamin B12 died of drug-related toxicity following administration of ALIMTA alone.

ALIMTA can suppress bone marrow function, as manifested by neutropenia, thrombocytopenia, and anemia (or pancytopenia).

Patients must be instructed to take folic acid and vitamin B12 with ALIMTA as a prophylaxis to reduce treatment-related hematologic and GI toxicities.

Pregnancy Category D-ALIMTA may cause fetal harm when administered to a pregnant woman.

Precautions

Complete blood cell counts, including platelet counts and periodic chemistry tests, should be performed on all patients receiving ALIMTA.

Patients should not begin a new cycle of treatment unless the ANC is greater than or equal to 1500 cells/mm³ and the platelet count is greater than or equal to 100,000 cells/mm³ and creatinine clearance is greater than or equal to 45 mL/min.

Pretreatment with dexamethasone or its equivalent has been reported to reduce the incidence and severity of skin rash.

The effect of third space fluid, such as pleural effusion and ascites, on ALIMTA is unknown.

In patients with clinically significant third space fluid, consideration should be given to draining the effusion prior to ALIMTA administration.

Concomitant administration of nephrotoxic drugs or substances that are tubularly secreted could result in delayed clearance of ALIMTA.

Caution should be used when administering ibuprofen concurrently with ALIMTA to patients with mild to moderate renal insufficiency (creatinine clearance from 45 to 79 mL/min). Patients with mild to moderate renal insufficiency should avoid taking NSAIDs with short elimination half-lives for a period of 2 days before, the day of, and 2 days following administration of ALIMTA. In the absence of data regarding potential interaction between ALIMTA and NSAIDs with longer half-lives, all patients taking these NSAIDs should interrupt dosing for at least 5 days before, the day of, and 2 days following ALIMTA administration. If concomitant administration of an NSAID is necessary, patients should be monitored closely for toxicity, especially myelosuppression, renal and gastrointestinal toxicities.

It is recommended that nursing be discontinued if the mother is being treated with ALIMTA.

ALIMTA should be administered under the supervision of a qualified physician experienced in the use of antineoplastic agents.

Dose adjustments may be necessary in patients with hepatic insufficiency.

Dosing and Modification Guidelines

Dose adjustments at the start of a subsequent cycle should be based on nadir hematologic counts or maximum nonhematologic toxicity from the preceding cycle of therapy. Modify or suspend therapy according to the Dosage Reduction Guidelines in the full Prescribing Information.

Abbreviated Adverse Events (% incidence)

The most common adverse events (grades 3/4) with ALIMTA versus docetaxel, respectively, for the treatment of patients with NSCLC were anemia (8 vs 7); leukopenia (5 vs 28); neutropenia (5 vs 40); thrombocytopenia (2 vs 1); ALT elevation (3 vs 1); febrile neutropenia (2 vs 13); infection without neutropenia (6 vs 4); infection/febrile neutropenia -- other (2 vs 1); fatigue (16 vs 17); thrombosis/embolism (3 vs 3); cardiac ischemia (3 vs 1); anorexia (5 vs 8); dyspnea (18 vs 26); and chest pain (7 vs 8). The most common clinically relevant adverse events (all grades) with ALIMTA versus docetaxel, respectively, were fatigue (87 vs 81); anorexia (62 vs 58); nausea (39 vs 25); constipation (30 vs 23); vomiting (25 vs 19); diarrhea (21 vs 34); stomatitis/pharyngitis (20 vs 23); edema (19 vs 24); dyspnea (72 vs 74); chest pain (38 vs 32); neuropathy/sensory (29 vs 32); infection without neutropenia (23 vs 17); anemia (33 vs 33); fever (26 vs 19); and rash (17 vs 9).

The most common adverse events (grades 3/4) with ALIMTA in combination with cisplatin versus cisplatin alone, respectively, for the treatment of patients with MPM were neutropenia (24 vs 4); leukopenia (16 vs 1); anemia (6 vs 0); thrombocytopenia (5 vs 0); infection without neutropenia (2 vs 0); infection with grade 3/4 neutropenia (1 vs 0); infection/febrile neutropenia -- other (1 vs 0); febrile neutropenia (1 vs 0); fatigue (17 vs 13); thrombosis/embolism (6 vs 4); nausea (12 vs 6); vomiting (11 vs 5); dyspnea (11 vs 7); and chest pain (9 vs 6). The most common clinically relevant adverse events (all grades) with ALIMTA in combination with cisplatin versus cisplatin alone, respectively, were neutropenia (58 vs 16); leukopenia (55 vs 20); anemia (33 vs 14); thrombocytopenia (27 vs 10); fatigue (80 vs 74); thrombosis/embolism (7 vs 4); nausea (84 vs 79); vomiting (58 vs 52); constipation (44 vs 39); anorexia (35 vs 25); stomatitis/pharyngitis (28 vs 9); diarrhea (26 vs 16); dyspnea (66 vs 62); chest pain (40 vs 30); and rash (22 vs 9).

See complete Warnings, Precautions, Adverse Reactions, and Dosage and Administration sections in the full Prescribing Information for safety and dosing guidelines.

(1) Scagliotti G, Purvish P, et al. Phase III study of pemetrexed plus cisplatin versus gemcitabine plus cisplatin in chemonaive patients with locally advanced or metastatic non-small cell lung cancer (NSCLC). Abstract PRS-3, 12th World Conference on Lung Cancer (WCLC) 2007. Journal of Thoracic Oncology, Vol 2 No 8, Supplement 4, Page S306, August 2007.

(2) American Cancer Society, "What Is Non-Small Cell Lung Cancer?," October 15, 2007, American Cancer Society, http://www.cancer.org/docroot/CRI/content/CRI_2_4_1x_What_Is_Non-Small_Cell_Lung_Cancer.asp?nav=cri, (February 21, 2008).

(3) American Cancer Society, "How Is Non-Small Cell Lung Cancer Staged?" October 15, 2007, American Cancer Society, www.cancer.org/docroot/CRI/content/CRI_2_4_3x_How_Is_Non-Small_Cell_Lung_Cancer_Staged.asp?nav=cri, (February 21, 2008).

(4) World Health Organization, Gender in Lung Cancer and Smoking Research, Department of Gender, Women and Health, 2003, <http://www.who.int/gender/documents/en/lungcancerlow.pdf> .

(5) National Cancer Institute, "Non-Small Cell Lung Cancer Treatment (PDQ(R)) Health Professional Version," December 14, 2007, National Cancer Institute, www.cancer.gov/cancertopics/pdq/treatment/non-small-cell-lung/HealthProfessional/page2 , (February 14, 2008).

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