



## **Lilly Presents New Data in Head and Neck Cancer - a Difficult-To-Treat Cancer With Poor Survival Rates**

INDIANAPOLIS, Oct 11, 2010 /PRNewswire via COMTEX News Network/ -- Eli Lilly and Company (NYSE: LLY) announced today that its global Phase III trial evaluating ALIMTA(R) (pemetrexed for injection) in combination with cisplatin in patients with recurrent or metastatic squamous cell cancer of the head and neck (SCCHN) did not meet its primary endpoint for overall survival. Data were presented for the first time today at the 35th Annual Meeting of the European Society for Medical Oncology (ESMO).

The Phase III study, the largest trial conducted in SCCHN to date, evaluated ALIMTA in combination with cisplatin compared with placebo plus cisplatin given every three weeks in a total of 795 patients. The primary objective of the study was to determine overall survival. Patient quality of life was also assessed, in addition to several pre-planned sub-group analyses.

The ALIMTA/cisplatin regimen showed a median overall survival of 7.3 months compared with 6.3 months with cisplatin alone, a result not considered a statistically significant improvement ( $p=0.082$ ). There was no significant difference in the quality of life scores for patients treated with either ALIMTA/cisplatin or cisplatin alone ( $p=0.200$ ).

As a result, Lilly will not be submitting marketing authorization applications for ALIMTA in SCCHN with either the U.S. Food and Drug Administration (FDA) or the European Medicine Agency (EMA).

"The fact that combination treatment with pemetrexed and cisplatin did not improve overall survival in this study is disappointing, although perhaps not surprising given how difficult it can be to effectively treat metastatic or locally advanced head and neck cancer," said the study's principal investigator, Professor Susan Urba, M.D., Division of Hematology/Oncology, University of Michigan Comprehensive Cancer Center, USA. "We did, however, gain valuable information in this large study, which we hope will help us plan even better future trials for head and neck cancer."

Out of the nine pre-planned subgroup analyses, two showed survival advantage, which may be of clinical interest.

First, in the analysis of 690 patients with ECOG performance status of 0 or 1(1), those treated with the ALIMTA/cisplatin had a longer overall survival than those treated with cisplatin alone (8.4 vs. 6.7 months,  $p=0.026$ ). These patients represented 87 percent of the total population.

However, for those patients with an ECOG performance status of 2, there was no survival benefit for those treated with the ALIMTA/cisplatin regimen versus those treated with cisplatin alone (3.5 months vs. 3.3 months,  $p=0.243$ ).

In another pre-planned analysis evaluating the primary site of disease, the group of 192 patients with oropharyngeal cancer showed improved overall survival when treated with ALIMTA/cisplatin versus cisplatin alone (9.9 vs. 6.1 months,  $p=0.002$ ). No survival advantage was seen in patients whose primary site of disease included the oral cavity, hypopharynx, larynx and "other."

Safety results showed that although the number of deaths on study therapy or within 30 days of treatment discontinuation were similar for ALIMTA/cisplatin and cisplatin alone (23.5% vs. 24.9%), there were 13 (3.3%) ALIMTA/cisplatin and one (0.03%) cisplatin-alone related deaths. Drug related serious adverse events were seen more frequently with ALIMTA/cisplatin than cisplatin alone (febrile neutropenia: 3.1% vs. 0.0%; pneumonia: 1.8% vs. 0.3%; neutropenia: 2.8% vs. 0.3%)

"Trying to improve patient outcomes in difficult-to-treat cancers continues to be a significant challenge. We will, though, continue with Lilly Oncology's commitment toward finding innovative solutions in this area," said Richard Gaynor, M.D., vice president of oncology product development and medical affairs at Lilly.

### **Important Safety Information for ALIMTA**

#### ***What is the most important information that I should know about ALIMTA?***

ALIMTA can suppress bone marrow function, which may cause low blood cell counts.

ALIMTA may not be appropriate for some patients.

If you are allergic to ALIMTA, tell your doctor because you should not receive it.

If you have liver or kidney problems, be sure to tell your doctor. Your dose of ALIMTA may have to be changed, or ALIMTA may not be right for you.

Your doctor will prescribe a medicine called a "corticosteroid" to take for 3 days during each treatment with ALIMTA. Corticosteroids lower your chances for getting skin reactions with ALIMTA.

It is very important to take folic acid and vitamin B12 prior to and during your treatment with ALIMTA to lower your chances of harmful side effects.

- You must take folic acid every day for at least 5 days out of the 7 days before your first dose of ALIMTA. You must keep taking folic acid every day during the time you are getting treatment with ALIMTA, and for 21 days after your last treatment.
- Your doctor will give you vitamin B12 injections while you are getting treatment with ALIMTA. You will get your first vitamin B12 injection during the week before your first dose of ALIMTA, and then about every 9 weeks during treatment.

You will have regular blood tests before and during your treatment with ALIMTA. Your doctor may adjust your dose of ALIMTA or delay your treatment based on the results of your blood test and on your general condition.

### ***What should I tell my doctor before receiving ALIMTA?***

If you think you are pregnant, are planning to become pregnant, or are nursing, please tell your healthcare team. ALIMTA may harm your unborn or nursing baby. Your physician may advise you to use effective contraception (birth control) to prevent pregnancy while you are being treated with ALIMTA.

Tell your doctor if you are taking other medicines, including prescription and nonprescription medicines, vitamins, and herbal supplements. ALIMTA and other medicines may affect each other, causing serious side effects. Especially, tell your doctor if you are taking medicines called "nonsteroidal anti-inflammatory drugs" (NSAIDs) for pain or swelling.

### ***What are the possible side effects of ALIMTA?***

Most patients taking ALIMTA will have side effects. Sometimes it is not always possible to tell whether ALIMTA, another medicine, or the cancer itself is causing these side effects.

**Call your doctor right away if you have a fever, chills, diarrhea, or mouth sores.** These symptoms could mean you have an infection, which may be severe and could lead to death.

The most common side effects of ALIMTA when given alone or in combination with cisplatin are:

- **Stomach upset, including nausea, vomiting, diarrhea, or constipation.** You can obtain medicines to help control some of these symptoms. Call your doctor if you get any of these symptoms.
- **Low blood cell counts:**
  - **Low red blood cells.** Low red blood cells may make you feel tired, get tired easily, appear pale, and become short of breath.
  - **Low white blood cells.** Low white blood cells may give you a greater chance for infection. If you have a fever (temperature above 100.4°F) or other signs of infection, call your doctor right away.
  - **Low platelets.** Low platelets give you a greater chance for bleeding. Your doctor will do blood tests to check your blood counts before and during treatment with ALIMTA.
- **Tiredness.** You may feel tired or weak for a few days after your ALIMTA treatments. If you have severe weakness or tiredness, call your doctor.
- **Mouth, throat, or lip sores** (stomatitis, pharyngitis). You may get redness or sores in your mouth, throat, or on your lips. These symptoms may happen a few days after ALIMTA treatment. Talk with your doctor about proper mouth and throat care.
- **Loss of appetite.** You may lose your appetite and lose weight during your treatment. Talk to your doctor if this is a problem for you.

- **Rash.** You may get a rash or itching during treatment. These usually appear between treatments with ALIMTA and usually go away before the next treatment. Rarely, these reactions may be severe (can lead to Stevens-Johnson syndrome or toxic epidermal necrolysis) and could lead to death. Call your doctor if you get a severe rash, itching, or blistering.

Talk with your doctor, nurse, or pharmacist about any side effect that bothers you or that doesn't go away.

These are not all the side effects of ALIMTA. For more information, ask your doctor, nurse, or pharmacist.

### ***How is ALIMTA given?***

ALIMTA is slowly infused (injected) into a vein. The injection or infusion will last about 10 minutes. You will usually receive ALIMTA once every 21 days (3 weeks).

**For more information about all of the side effects of ALIMTA, please talk with your healthcare team, see Patient Prescribing Information and full Prescribing Information, visit [www.ALIMTA.com](http://www.ALIMTA.com), or call 1-800-545-5979.**

**You are encouraged to report negative side effects of prescription drugs to the FDA. Visit [www.fda.gov/](http://www.fda.gov/)**

### **Notes to the Editor:**

#### **About Head and Neck Squamous Cell Carcinoma (SCCHN)**

Although ranked the sixth most common cancer worldwide,(2) advanced SCCHN remains difficult to treat with poor survival rates.(3) Globally, head and neck cancer is the sixth most common cancer(2) and approximately 650,000 new head and neck cancers are diagnosed each year.(4)

Head and neck cancer includes epithelial malignancies of the upper aerodigestive tract, including the paranasal sinuses, nasal cavity, oral cavity, pharynx, and larynx.(2) There is a greater incidence of head and neck cancer observed in men compared to women,(4) and diagnosis is usually made in men aged over 50.(5)

Advanced (stage IV) head and neck cancer has traditionally carried a poor prognosis.(6) Chemotherapy and radiotherapy in combination have been increasingly used for advanced-stage SCCHN, both for primary and adjuvant treatment. As patients often do not start treatment until the disease is advanced, the overall survival rate remains low, despite the use of combination therapy.(5)

#### **About ALIMTA**

For more information about ALIMTA, please see the full prescribing information (<http://pi.lilly.com/us/alimta-pi.pdf>) and patient prescribing information (<http://pi.lilly.com/us/alimta-ppi.pdf>). You may also learn more about ALIMTA at [www.ALIMTA.com](http://www.ALIMTA.com).

#### **About Lilly Oncology**

For more than four decades, Lilly Oncology, a division of Eli Lilly and Company, 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. To learn more about Lilly's commitment to cancer, please visit [www.LillyOncology.com](http://www.LillyOncology.com).

#### **About Lilly**

Lilly, a leading innovation-driven corporation, is developing a growing portfolio of 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. Additional information about Lilly is available at [lilly.com](http://lilly.com).

#### **P-LLY**

*This press release contains forward-looking statements about the potential of ALIMTA and platinum chemotherapy for the treatment of head and neck cancer and reflects Lilly's current beliefs. However, as with any pharmaceutical product, there are substantial risks and uncertainties in the process of development and commercialization. There is 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.

(1) Eastern Cooperative Oncology Group ECOG Performance Status ([http://ecog.dfci.harvard.edu/general/perf\\_stat.html](http://ecog.dfci.harvard.edu/general/perf_stat.html)), accessed September 16, 2010.

(2) Cognetti DM, Weber RS, Lai SY. Head and Neck Cancer: An Evolving Treatment Paradigm. *Cancer* 2008;113 (7 Suppl):1911-1932.

(3) Specenier PM, Vermorken JB. Review. Recurrent head and neck cancer: current treatment and future prospects. *Expert Review of Anticancer Therapy* 2008;8: 375-391.

(4) Parkin DM, Bray F, Ferlay J et al. Global cancer statistics, 2002. *CA: A Cancer Journal for Clinicians* 2005;55:74-108.

(5) *Atlas of Genetics and Cytogenetics in Oncology and Haematology*: Head and Neck Squamous Cell Carcinoma (<http://atlasgeneticsoncology.org/Tumors/HeadNeckSquamID5090.html>) accessed September 16, 2010.

(6) Brockstein B, Haraf DJ, Rademaker AW et al. Patterns of failure, prognostic factors and survival in locoregionally advanced head and neck cancer treated with concomitant chemoradiotherapy: a 9-year, 337-patient, multi-institutional experience. *Annals of Oncology* 2004 Aug;15(8):1179-86.

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