



Mesothelioma Articles

Oncology Researchers Recognized As Heroes Of Chemistry

Three researchers who led the discovery and development of the first drug approved to treat malignant [pleural mesothelioma](#) (MPM), a cancer associated with exposure to asbestos, were named as Heroes of Chemistry by the American Chemical Society (ACS). Researchers Homer Pearce, Ph.D., Chuan (Joe) Shih, Ph.D., and Edward C. Taylor, Ph.D., led a long-standing collaboration between Eli Lilly and Company and Princeton University that resulted in the compound ALIMTA(R) (pemetrexed for injection), the first drug ever approved for the treatment of MPM. ALIMTA, in combination with cisplatin, is indicated for the treatment of patients with malignant pleural mesothelioma whose disease is unresectable or who are otherwise not candidates for curative surgery.

The scientists received the award on September 10 at the ACS national meeting in San Francisco.

"Heroes save lives and change them for the better," said ACS President E. Ann Nalley, Ph.D. "This year's Heroes of Chemistry have improved our lives through their inventions. We at ACS celebrate them and the corporate management that supports innovations that bring the benefits of chemistry to us all, every day."

The Heroes of Chemistry program, initiated by ACS in 1996, highlights the vital work of industrial chemical scientists and their companies in improving human welfare through successful commercial breakthroughs and products. This year's Heroes of Chemistry award honors scientists whose innovations have led to the benefit and progress of humanity in the past decade.

Although just approved for MPM in 2004, the rich history of the discovery of ALIMTA dates back to the 1940s, demonstrating the life-long commitment often needed in drug discovery. In the 1940s, researchers found that certain molecules that interfere with folic acid might delay the spread of cancer by disrupting the ability of tumors to process the folates that are necessary for cell survival. In December 1985, Princeton's Taylor began a long-term collaboration with scientists at Lilly to further evaluate the promise of these molecules that resulted in several potential drugs.

The Lilly team, led by Pearce and Shih, closely examined the biochemical properties of the molecule that would become ALIMTA. The team found that this exciting molecule could simultaneously target and block at least three key folate-requiring enzymes (thymidylate synthetase; dihydrofolate reductase; and glycinamide ribonucleotide formyltransferase) that cancer cells need for cell division and tumor growth. The Lilly-Princeton collaborators theorized that this multi-targeted action was the reason for the compound's potentially promising anti-tumor activity in mesothelioma. More than a decade after the partnership was formed, following additional development and pivotal clinical trials, ALIMTA received U.S. Food and Drug Administration (FDA) approval in 2004, bringing new hope to patients suffering from MPM.

ALIMTA is also paving the way for the medical breakthroughs of tomorrow. A new state-of-the-art chemistry building at Princeton University was financed by royalty payments from Lilly to Princeton based on the commercial success of ALIMTA. This guarantees that a new generation of innovative scientists will follow in the footsteps of Drs. Pearce, Shih and Taylor.

About the Researchers

Texas-born Homer Pearce, Ph.D., spent the last 27 years discovering and developing cancer therapies at Eli Lilly and Company in Indianapolis. Pearce received a Ph.D. in organic chemistry from Harvard University in 1979. In addition to his renowned leadership in clinical research, Pearce is recognized as an avid supporter of cancer education and patient advocacy, evidenced by his service as board member for the Little Red Door Cancer Agency, Indianapolis Hope Lodge and the American Cancer Society Foundation - Great Lakes Region. Pearce, now retired, is a former vice president of cancer research at Lilly.

Born in Taiwan, and the son of a physician, Chuan (Joe) Shih, Ph.D., is a distinguished research fellow at Lilly. Shih received a Ph.D. in organic chemistry from The Ohio State University in 1982. Shih attests to a fascination with the composition of life and the matters that surround us as his driving motivation to pursue a life-long career in chemistry and clinical research.

Perhaps one of the most renowned chemists today, Edward C. Taylor, Ph.D., is a professor emeritus with the Princeton University Department of Chemistry. Taylor received a Ph.D. in organic chemistry from Cornell University in 1949. Taylor is the author of over 450 scientific papers and 52 U.S. patents on heterocyclic chemistry, organothallium chemistry, natural product chemistry, medicinal chemistry and synthetic methodology.

About ALIMTA and Malignant Pleural Mesothelioma (MPM) ALIMTA is an antifolate that imultaneously blocks three separate enzyme targets important to the formation of basic building blocks by which cancer cells grow and divide.

In February 2004, ALIMTA, in combination with cisplatin, became the first and only chemotherapy drug approved by the FDA for the treatment of patients with malignant pleural mesothelioma (MPM) whose disease is unresectable or who are otherwise not candidates for curative surgery. The tumor in this particularly lethal cancer actually surrounds the lung, so as the tumor grows the dynamics of breathing are limited because the lungs are squeezed and the diaphragm is depressed. In many cases, the effects of MPM lead patients to die due to internal suffocation. Each year, there are 3,000 new cases in the US and 10,000-15,000 new cases globally. The incidence rate is expected to increase due to a latency period of 20-50 years.

ALIMTA Facts

- In the two years since its first approval, ALIMTA has been approved in 70 countries for MPM
- ALIMTA is a demonstration of modern-day chemotherapy as it is delivered via a 10-minute infusion

Important Safety Information

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

Patients must be instructed to take folic acid and vitamin B12 with ALIMTA as a prophylaxis to reduce treatment-related hematologic and GI toxicities. 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). 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 > 1500 cells/mm³ and the platelet count is > 100,000 cells/mm³. 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. 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. Concomitant administration of nephrotoxic drugs or substances that are tubularly secreted could result in delayed clearance of ALIMTA. 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.

Adverse Events

The most common adverse events (grades 3/4) with ALIMTA in combination with cisplatin for the treatment of patients with MPM were neutropenia (24%); leukopenia (16%); anemia (6%); thrombocytopenia (5%); infection without neutropenia (2%); fatigue (17%); thrombosis/embolism (6%); nausea (12%); vomiting (11%); dyspnea (11%); and chest pain (9%). The most common clinically relevant adverse events (all grades) were fatigue (80%); thrombosis/embolism (7%); nausea (84%); vomiting (58%); constipation (44%); anorexia (35%); stomatitis/pharyngitis (28%); diarrhea (26%); dyspnea (66%); chest pain (40%); and rash (22%). Copies of the package insert can be obtained via <http://www.ALIMTA.com> or calling 1-800-LILLY-RX (545-5979).

Lilly Oncology, a Division of Eli Lilly and Company

For more than four decades, Lilly Oncology has been collaborating with cancer researchers to deliver innovative treatment choices and valuable programs to patients and physicians. Inspired by courageous patients living with cancer, Lilly Oncology is providing treatments that are considered global standards of care and developing a broad portfolio of novel targeted therapies to accelerate the pace and progress of cancer care. To learn more about Lilly's commitment to cancer, please visit <http://www.LillyOncology.com>.

About Eli Lilly and Company

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