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NEW EXPERIMENTAL DRUG SHOWN TO SLOW THE GROWTH OF PROSTATE CANCER TUMORS IN MICE

Los Angeles, CA (**Embargoed until November 1, 2001 at 12:30 p.m., Eastern**) - A new experimental drug has been found to slow the growth of prostate cancer tumors in laboratory studies conducted at Cedars-Sinai Medical Center. The findings, presented at the AACR-NCI-EORTC International Conference in Miami Beach, Florida, may lead to a new way to treat prostate cancer, a disease that strikes about 198,000 men each year.

The drug, called 2C4, is a monoclonal antibody, or protein that enlists the body's immune system to attack foreign invaders, such as viruses or bacteria. Produced by Genentech, Inc., 2C4 targets HER-2/*neu*, a protein from the HER kinase family, that controls cell growth. When the HER-2/*neu* protein is expressed on cancer cells, it can stimulate tumor growth and spread.

"Our lab studies show that 2C4 significantly inhibited tumor growth in both hormone dependent prostate cancer, and in that which had become resistant to hormone blocking drugs," said David Agus, M.D., Research Director at the Cedars-Sinai Prostate Cancer Center and senior author of the study. "These laboratory findings have led us to launch the first clinical trial to test the safety and effectiveness of 2C4 in patients with prostate cancer and other forms of the disease."

In the laboratory study, the investigators evaluated the effectiveness of 2C4 both in cell-lines established in culture and in human tumors grown in mice. In both evaluations, the prostate cancer cells were either dependent on the male hormone, testosterone, to grow (androgen-dependent), or were the type that had become resistant to hormone blocking drugs and grew independently of testosterone (androgen-independent). The prostate cancer cells were then subdivided within the androgen-dependent and independent groups as either slow growing or as the more aggressive form of the disease. The investigators found that 2C4 blocked HER kinase activity, resulting in a significant decrease in tumor growth.

"Although testosterone-blocking drugs initially work by causing tumors to shrink, the tumors inevitably return and resist further treatment. Now, we may have found a therapy to treat patients with recurrent prostate cancer or, even better, at the outset of their disease," commented Dr. Agus.

To determine whether 2C4 would block HER-2/*neu* activity, the investigators added the drug to prostate cancer cell lines in culture and subsequently stimulated cell growth by adding Heregulin, a stimulant from the HER kinase family of proteins. They found over a 90 percent decrease in HER kinase activity.

Simultaneously, the researchers injected the mice with both androgen-dependent and independent tumors with 2C4 twice weekly for approximately five weeks. In the androgen-dependent group, the investigators found that tumor growth was inhibited by 96 percent in the aggressive prostate cancer cells and by 75 percent in those that were slower-growing. In the androgen-independent groups, tumor growth was inhibited by 66 percent in the aggressive form of the disease, while there was a 77 percent decrease in the slower growing cancer cells.

“These results are exciting because they show that 2C4 effectively decreased the activity of not only HER-2/*neu*, but of the entire HER kinase family,” commented Dr. Agus.

Building on earlier clinical research that had established an increased survival rate for breast cancer patients receiving the monoclonal antibody trastuzumab (Herceptin®) in conjunction with chemotherapy, the investigators added the chemotherapy drug, Paclitaxel, to treatment with 2C4 in the mice with androgen-dependent and independent human prostate cancer tumors. They found that androgen-dependent tumor growth was 99 percent inhibited in the aggressive form of the disease, while the slower-growing cell lines had to be excluded because the growth was too slow to determine significance. In the androgen-independent group, tumor growth was arrested by 91 percent in the aggressive cancer cells, and 97 percent in the slow-growing tumor cells. PSA levels went down significantly as the tumors responded.

“Our results indicate that 2C4 is even more effective when added to treatment with chemotherapy, which may mean that treatment with the combination of both drugs may lead to a new way to treat this disease,” said Dr. Agus.

A Phase I clinical trial started in October at Cedars-Sinai Medical Center to evaluate the safety and tolerability of 2C4 in patients with advanced cancers of the prostate, breast, ovary, lung and colon. Although Phase I trials are not designed to test the efficacy of a drug for the treatment of a disease, results of the phase I study should tell investigators whether to proceed further with subsequent clinical trials.

Cedars-Sinai Medical Center is one of the largest non-profit academic medical centers in the Western United States. For the fifth straight two-year period, Cedars-Sinai has been named Southern California’s gold standard in health care in an independent survey. Cedars-Sinai is internationally renowned for its diagnostic and treatment capabilities and its broad spectrum of programs and services, as well as breakthrough biomedical research and superlative medical education. Named among the 100 “Most Wired” hospitals in health care in 2001, the Medical Center ranks among the top seven non-university hospitals in the nation for its research activities.

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