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UCLA Department of Urology, the National Cancer Institute Division of Cancer Prevention, Genentech/OSI Pharmaceuticals, and Tokyo Food Techno Announce First of Its Kind Adjuvant Clinical Trial to Prevent the Recurrence and Progression of Bladder Cancer

$7 Million National Cancer Institute Grant To Fund Large Clinical Trial Testing Green Tea Extract and Tarceva as Cancer Prevention Agents

Bladder cancer is now the fifth most common cancer in the United States, with nearly 55,000 new cases diagnosed each year. As many as half of all bladder tumors are believed to be attributable to cigarette smoking. In the absence of a reliable, non-invasive way to diagnose the disease, bladder cancer can be difficult to detect in the early, most treatable stages. When not found early, these tumors are typically very aggressive, with more than half of advanced bladder cancer patients experiencing recurrences many of whom develop worsening of bladder cancer requiring major surgery and/or chemotherapy. And at best, aggressive chemotherapy treatment only slows tumor progression in patients whose cancer has moved outside the bladder.

Scientists and physicians at UCLA’s Jonsson Comprehensive Cancer Center and the David Geffen School of Medicine Departments of Urology, Medicine, Pathology, and School of Public Health today (May 13) are launching a first-of-its-kind, comprehensive program to prevent the recurrence and progression of smoking-related bladder cancer. As part of the program, researchers will develop biomarker tests to help predict who will get bladder cancer, discover the molecular profile of the disease to identify those most at risk, and conduct a clinical trial testing green tea extract and the experimental drug Tarceva as cancer prevention agents and create a tumor bank to aid in scientific research.

The five-year effort is funded through a $7 million cancer prevention grant from the National Cancer Institute (NCI) with a supplement from the National Center for Complementary and Alternative Medicine (NCCAM) to the Department of Urology, division of urologic oncology, headed by Dr. Arie Belldegrun, a cancer researcher, chief of the division of urologic oncology, a professor of urology and principal investigator for the project. This is the largest prevention study in the United States to focus on bladder cancer in former smokers, UCLA researchers said, and the first study approved by the Food and Drug Administration (FDA) to use a new class of experimental drug in the prevention of any type of cancer. Unlike chemotherapy, which kills normal cells as well as tumor cells, Tarceva is among a new generation of cancer medications that are designed to target only defects in cancer cells. Tarceva, which belongs to a novel class of drug called an Epidermal Growth Factor Receptor (EGFR) Tyrosine Kinase Inhibitor, blocks a protein in cancer cells thought to cause them to grow aggressively. Tarceva has
recently been the focus of significant attention when it was announced that it "significantly" improved survival for certain lung cancer patients, who failed to respond to standard chemotherapy. The drug is the first of its kind to show in a major study that the approach can extend survival in patients in non-small cell lung cancer. A body of evidence suggests that EFGR is highly expressed in the bladder and as such is important in the development and progression of bladder tumors. Although this drug was initially developed for the treatment of advanced cancers, the UCLA study will use it in an earlier setting as adjuvant therapy.

"There are no oral agents currently approved to prevent superficial bladder cancer or its recurrence," notes Ronald Lieberman, MD, program director for NCI’s Division of Cancer Prevention. "From a clinical point of view, this is an important niche that needs to be addressed." "We will study innovative approaches to reduce the risk of bladder cancer," Beldegrun said. "And while we’ll study how to prevent cancer recurrence and progression in smokers who have already had bladder cancer, our goal is to develop effective prevention strategies for people who may be at risk but who do not yet have bladder cancer."

This year, doctors will diagnose 56,500 cases of bladder cancer, most in men. In all, more than 12,600 people will die from bladder cancer. Most bladder cancer cases are smoking related, said Dr. Robert Figlin, a Jonsson Cancer Center researcher, a professor of hematology/oncology and urology and co-principal investigator for the study. "What we’re doing is looking for specific biologic signals that tell us why some people get this disease and others don’t," Figlin said. "We want to decrease bladder cancer occurrence and develop molecular profiles that tell us who is most at risk." The clinical trial will bring together physicians and scientists from different disciplines, including medicine, urology, epidemiology, biomathematics, biostatistics, pathology and surgery.

The program includes:

· A clinical trial, "Parallel, Randomized, Double-Blind, Placebo Controlled, Phase II Adjuvant Study of Erlotinib and Polyphenon E to Prevent the Recurrence and Progression of Tobacco-Related, High-Grade Superficial Bladder Cancer," for 330 former smokers who have already had bladder cancer will be enrolled in this study from all participating sites, which include UCLA, Mayo Clinic in Rochester, MN, and Mayo Clinic in Scottsdale, AZ. The study, led by Drs. Arie Beldegrun, Robert Figlin, and Allan Pantuck, an assistant professor of urology, will investigate the effectiveness of two compounds in preventing or delaying recurrence of the cancer and will divide volunteers into three arms. One group will receive green tea extract, which has been shown in UCLA laboratories to reduce the growth of bladder cancer tumors both in animal models and in humans. The second group will receive Tarceva. The third group will receive a placebo. The oral administration of the study drugs as noted below will last for nine months. Participants will continue follow-up visits for the duration of the five-year study.
As standard of care for patients with this type of bladder cancer, participants will receive cystoscopies every 3 months for 2 years. Participants will need to stop taking study drugs if their bladder cancer returns or if they experience side effects or if new scientific developments occur that indicate that this study drug is not in their best interest. Over the course of approximately 15 visits in five years, other tests and monitoring will continue to be provided.

Development of a set of biomarkers for bladder cancer that can be used to predict who is likely to develop the disease. Such tests, to be developed by Drs. Zuo-Feng Zhang, Jian Yu Rao, and David Heber could work similarly to the PSA test for prostate cancer.

With Dr. David Seligson of the UCLA Department of Pathology and Laboratory Medicine, discover a molecular profile of bladder cancer that will help determine susceptibility to the disease. Researchers will seek to uncover what specific genetic mutations and other abnormalities may put people at risk for bladder cancer, such as the BRCA1 and 2 genes do for breast cancer.

Create a bladder cancer tumor bank for use by UCLA scientists from various medical and research disciplines for development of better prevention, detection and treatment methods for bladder cancer.

No one yet knows all of the causes of bladder cancer. Risk factors besides tobacco smoking include age, being a man (men are two to three times more likely to get bladder cancer than women), family history and race (Caucasians are two to three times more likely to get bladder cancer than African Americans, Latinos or Asians). There’s a 20-year latency period for smoking-related bladder cancer, UCLA researchers said, meaning it takes about 20 years for the cancer to develop in smokers and former smokers.

Symptoms of bladder cancer include blood in the urine, pain during urination and frequent urination or the need to urinate without results.

For more information on the UCLA bladder cancer prevention study, or to volunteer for the clinical trial, please call the Clinical Trial Coordinator, Nazy Zomorodian, at (310) 794-7704.