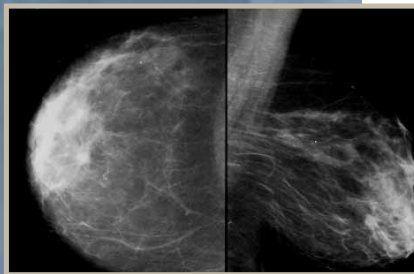


Roswellness for Doctors

Updates on Cancer Advances and Patient Care



*In the Business to Save Lives...
through Research, Prevention and Innovative Treatment*



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HRT AND BREAST CANCER RISK

Dr. Stephen Edge with patient.



Putting the Data in Perspective

by Stephen B. Edge, MD, FACS
Medical Director, Breast Center,
Roswell Park Cancer Institute

Is there a link between a decline in the use of hormone replacement therapy (HRT) in women and a recent significant drop in the number of new cases of breast cancer? Researchers at The University of Texas MD Anderson Cancer Center infer that there is, based on their analysis of national cancer incidence statistics for the period 1990-2003. The results of their study, presented in December 2006 at the 29th annual San Antonio Breast Cancer Symposium, conclude that a decrease in hormone therapy is directly responsible for the good news.

The researchers noted that millions of women on HRT stopped the therapy in late 2002, after a Women's Health Initiative (WHI) study determined that estrogen and progesterin, used in combination, somewhat increased a woman's chances of developing breast cancer. The WHI study, which enrolled 16,608 women between the ages of 50 and 79, also demonstrated that estrogen replacement therapy actually slightly increased the risk of heart disease and heart attack – a reversal of the

commonly held notion that it conferred a measure of protection against heart disease.

By the end of 2003, just a year after the WHI study was terminated on the basis of those concerns, the number of new cases of breast cancer – which had been on a steady 1% year-over-year annual decline between 1990 and 2002 – took a sharper turn downward, with a 7% decline. Of special note: the decline in estrogen receptor (ER)-positive breast cancer was nearly twice that of ER-negative breast cancer.

The MD Anderson researchers hypothesize that hormone therapy stimulated the growth of small, previously existing breast tumors, and that discontinuing HRT halted their growth. However, because it takes years for cancer to develop, only time will tell whether that is the case. It should be noted that the study examined population statistics alone and did not provide direct evidence of a connection between hormone therapy and incidence.

In the meantime, the study underscores the need for careful counseling of women who are candidates for estrogen replacement therapy. Short- or medium-term use of HRT remains a reasonable option for women who are experiencing severe symptoms of menopause, as it can dramatically improve their quality of life. They should be fully apprised of all benefits and possible deleterious effects before they make that decision.

If the hypothesis of the MD Anderson study is correct and can be substantiated, it provides compelling proof of the value of clinical trials, which are key to future advances in health care. The estrogen-progestin study is one of several conducted by the Women's Health Initiative, which collectively enrolled more than 160,000 subjects.

Jean Wactawski-Wende, PhD, and Maurizio Trevisan, MD, MS, of the University at Buffalo's Department of Social and Preventive Medicine, served as principal investigators for the WHI initiative in Buffalo, one of 40 across the nation. Some 4,000 women in Western New York participated in the WHI studies, contributing to a rich source of data with great potential for improving and extending the lives of women.

Author or co-author of more than 100 journal articles and book chapters, Dr. Edge focuses his research on breast cancer diagnosis, staging and treatment, with special emphasis on health services research. He is a member of the Board of Directors, the Outcomes Committee, the Breast Cancer Guideline Development Committee and the Guidelines Steering Committee of the National Comprehensive Cancer Network (NCCN), a group of leading cancer centers that sets the national standards in cancer care. To contact Dr. Edge, email him at Stephen.Edge@roswellpark.org.

Roswell Park Establishes Life Sciences Company in Buffalo

New Diagnostic Test Could Impact Cancer Care

Roswell Park Cancer Institute (RPCI) and Boston-based Venzyme Accelerator recently announced the formation of PersonaDX, a new life sciences company that will be based in Buffalo, NY. PersonaDX will commercialize a new clinical diagnostic test for cancer patients that is derived from basic research conducted in RPCI's Department of Cancer Genetics by Lionel Coignet, PhD.



When Roswell Park's governance was transitioned to a public benefit corporation in 1999, the Institute gained the ability to commercialize and locally manage its scientific discoveries under the control of its administration and Board of Directors. Formation of PersonaDX is the first in a series of new companies formed in collaboration with scientists at Roswell Park.

The new diagnostic test from Coignet's laboratory is based on the concept that the genetic make-up of the individual patient may determine whether a cancer will spread from its point of origin to sites in distant organs. A specific gene, called the SMRT gene, appears to naturally inhibit metastases. Clinical studies in patients with breast and prostate cancer indicate that those with "fragility" of the

SMRT gene are particularly prone to the development of metastases. Coignet and his colleagues believe that it is gene breakage at the "fragile site" that leads to metastatic spread and the blood test they have devised determines whether a fragile site is present on a patient's SMRT gene.

"The implications for improving treatment for the individual patient are potentially enormous," said Donald L. Trump, MD, RPCI's Associate Director and President-Elect. "The hope is that we may be able to prescribe the most intense treatment regimens only for patients with a positive test and avoid unnecessary drug treatment for those with a negative test – knowing that metastatic spread is unlikely and that surgery or radiation alone is likely to be curative."

Dr. Coignet will serve as PersonaDX's Chief Scientific Officer, and John Garrett, PhD, of Venzyme will serve as Interim President, directing corporate administrative and business activities.

For more information, visit RPCI's website at www.roswellpark.org, call 1-877-ASK-RPCI (1-877-275-7724) or email Dr. Richard Matner, Technology Transfer Officer, at Richard.Matner@roswellpark.org.

Pre-eminent Researcher to Join RPCI Faculty

Andrei V. Gudkov, PhD, has accepted the positions of Senior Vice President for Research Program Development and Chair of the Department of Cell Stress Biology at Roswell Park Cancer Institute. Dr. Gudkov comes to Roswell Park from the Cleveland Clinic Foundation, where he served as Chair of the Department of Molecular Genetics, Lerner Research Institute.

Dr. Gudkov also is Founder and Chief Scientific Officer for the biotechnology research and development company, Cleveland BioLabs, Inc., which will relocate its headquarters to the Buffalo Niagara Medical Campus in late spring.

More detailed information on this exciting development will be forthcoming.

HIGH-SPEED PRECISION IGRT: NEW TRILOGY SYSTEM IN PLACE AT ROSWELL PARK

Triology, the most advanced image-guided radiation therapy (IGRT) technology available, is now in place at Roswell Park Cancer Institute – the first facility in the Buffalo-Niagara region to offer the high-speed precision system. Trilogy delivers radiation over 60% faster than conventional systems, and can pinpoint areas as small as the tip of a pencil, thus sparing surrounding normal tissue from radiation damage.

“Trilogy enables us to provide the highest level of care for patients who need radiation therapy,” says Michael Kuettel, MD, MBA, PhD, Chair of Radiation Medicine. “Because the same system can deliver radiation in several ways, it gives us greater flexibility to design the best treatment plan for each patient.”

At some point in their cancer treatment, 60% to 70% of all patients receive radiation therapy. What distinguishes this system is the degree to which it can deliver higher doses of radiation to the target and the optimal number of beams to the tumor site with submillimeter accuracy.

Typically, most patients receive small doses of radiation every day over several weeks. “In cases where IGRT is an appropriate treatment,” explains Kuettel, “we can use it to deliver much higher doses over just a few days. In addition to shorter treatment times, patients experience greater comfort during the procedure, fewer side effects and the potential for better outcomes.”

In some cases, the new IGRT system may even eliminate the need for surgery or shrink

inoperable tumors sufficiently to make surgery possible. In other cases, it may have the potential to cure patients whose treatment would otherwise focus only on relieving pain and reducing other effects of a tumor.

Manufactured by Varian Medical Systems, Trilogy is equipped with imaging technology that makes it possible to track the exact location of a tumor immediately before treatment – making adjustments, for example, after the patient has moved about between treatment sessions or when the tumor has shrunk as a result of therapy. Its “gated” radiation therapy feature can synchronize delivery of the radiation beam with the patient’s breathing cycle, to compensate for tumor movement as the lungs expand and contract—an especially critical feature for

“In addition to shorter treatment times, patients experience greater comfort during the procedure, fewer side effects and the potential for better outcomes.”

Michael Kuettel, MD, MBA, PhD

patients who are being treated for lung tumors.

All forms of external-beam radiation therapy – including three-dimensional radiation therapy, intensity modulated radiation therapy, stereotactic body radiation therapy and stereotactic radiosurgery – can be delivered through this system. Its treatment application extends to a wide range of cancers including breast, head and neck, liver, lung, pancreatic and prostate cancer, and the system can target tumors that are close to critical structures such as the spinal cord.

For more information, call Roswell Park Cancer Institute at 1-877-ASK-RPCI (1-877-275-7724) or email Dr. Kuettel at Michael.Kuettel@roswellpark.org.

Improving Outcomes for Patients with Hematologic Malignancies

Roswell Park researchers present clinical study results at the 48th Annual Meeting & Exposition of the American Society of Hematology, December 9-12



NEW DRUGS PRODUCE COMPELLING RESPONSES IN RELAPSED, REFRACTORY CLL, MM PATIENTS

Chronic Lymphocytic Leukemia and Lenalidomide

Chronic lymphocytic leukemia (CLL) is the most common hematologic malignancy in the western hemisphere and it remains incurable. Although conventional therapeutic approaches, such as chemotherapy or chemoimmunotherapy (using monoclonal antibodies), has resulted in higher initial clinical responses, all patients eventually relapse and develop refractory disease,” according to Asher Chanan-Khan, MD, Department of Medicine. “There are limited therapeutic options for these patients with relapsed and refractory CLL.”

Lenalidomide – an immunomodulating cancer drug that is chemically similar to thalidomide – was recently approved for treatment of previously treated multiple myeloma and del 5q-myelodysplastic syndrome, but its clinical efficacy in CLL had not been investigated.

In this phase II study – the first to report clinical efficacy of lenalidomide in patients with CLL – 45 patients with relapsed or refractory B-CLL were treated with a daily dose of 25 mg of lenalidomide. Clinical responses were observed in 57% of the patients, with 13% achieving a complete response and toxicity predictable and manageable.

“Lenalidomide is clinically active in patients with relapsed or refractory B-CLL as a single agent,” noted Dr. Chanan-Khan. “We were excited to see that our seminal findings were confirmed by a subsequent clinical

trial done by colleagues at MD Anderson Cancer Center in Houston, Texas.”

Dr. Chanan-Khan and his colleague Swaminathan Padmanabhan, MD, Department of Medicine, presented the results of another phase II clinical trial of lenalidomide in patients with relapsed or refractory CLL. Analysis of pre- and post-treatment samples from these patients demonstrated that lenalidomide activated a type of immune cells known as natural killer (NK) cells, which offered significant antileukemic effects.

“This is the first clinical trial which provides strong clues of the mechanism of action of lenalidomide,” said Padmanabhan. He notes that the presence of NK cells is critical for the potent antileukemic effects of lenalidomide and may help explain “tumor flare,” a common side effect observed in the first week of treatment with this agent. “These strong correlative data are very encouraging and the trial will likely change the treatment paradigm for CLL,” he concluded.

Multiple Myeloma

Drs. Padmanabhan and Chanan-Khan also presented the final results of a phase II clinical study that demonstrated a sustained high response rate in patients with relapsed or refractory multiple myeloma (MM) treated with the combination of bortezomib (velcade), liposomal doxorubicin (doxil) and thalidomide (VDT).

“This is the first study to combine the three most active anticancer agents in this patient population. It produced remarkable responses, including 22% complete sustained responses and a median-free survival rate of 15.9 months,” said Padmanabhan.

For more information on the studies above, please email Dr. Chanan-Khan at Asher.Chanan-Khan@roswellpark.org or Dr. Padmanabhan at Swami.Padmanabhan@roswellpark.org.

GENETIC ANALYSIS IDENTIFIES PATIENTS APT TO DEVELOP POST-BMT TOXICITY

Theresa Hahn, PhD, in collaboration with Christine B. Ambrosone, PhD (Epidemiology/ Prevention), and Philip L. McCarthy, Jr., MD (Medicine), found that the genetic make-up of patients can predict who develops toxicity following the high doses of chemotherapy and/or radiation given prior to blood and marrow transplantation (BMT), and if their toxicity is likely to be moderate, severe or fatal. This finding has the potential to improve outcomes for BMT patients by allowing individualized conditioning regimens.

The research team performed a genotype analysis of blood and bone marrow samples from 268 BMT patients to determine whether the presence or absence of two glutathione-S-transferase isoenzymes could predict which patients would develop toxicity.

“These enzymes metabolize and detoxify many chemotherapeutic drugs and radiation,” explained Hahn. “Genotype analysis demonstrated that genetic variability affecting the activity of these enzymes in patients can predict which patients will develop toxicity.”

Hahn’s research was supported by a Mentored Research Scholar Grant in Applied and Clinical Research (MSRG-05-198-01-CCE) from the American Cancer Society.

For more information on this study, please email Dr. Hahn at Theresa.Hahn@roswellpark.org.



SIDE-EFFECTS EVALUATED IN INNOVATIVE TREATMENT FOR NHL

Treatment side-effects are moderate and consistent for patients treated with radioimmunotherapy (RIT) for relapsed or refractory non-Hodgkin’s lymphoma (NHL), according to the results of a large multi-institutional study which included Roswell Park.

RIT is an innovative therapy for patients with relapsed or refractory NHL. The treatment links radioactive atoms to monoclonal antibodies which deliver “internal” radiation therapy directly to the lymphoma by seeking out and latching onto proteins found on cancer cells. This study investigated the incidence of treatment-associated bone marrow damage (myelodysplastic syndrome or acute myelogenous leukemia) as a side-effect to RIT treatment.

“The medium-term effects of radiation on bone marrow were studied in patients after treatment with ibritumomab tiuxetan (ie, Zevalin) RIT and we found that incidence rates are consistent with those expected on the basis of the patient’s history of prior treatment for NHL,” said Myron C. Czuczman, MD, departments of Medicine and Immunology, and the Roswell Park PI on the study. “This study demonstrates that this novel therapy does not increase incidence of subsequent blood-related disorders and cancers at least for the period of three to five years following treatment.”

Cytogenetic data (chromosome studies) were available for 15 of the patients, and each had multiple cytogenetic aberrations, commonly on chromosomes 5 and 7, suggesting an association with previous exposure to chemotherapy. Czuczman and colleagues recommend cytogenetic testing before administration of RIT to identify existing chromosomal abnormalities in previously treated patients.

For more information on this study, please email Dr. Czuczman at Myron.Czuczman@roswellpark.org.

