



iuscc research news

November 2008

Gleevec holds potential as first drug to successfully treat neurofibromatosis, IU scientists report

IU School of Medicine researchers report that the anti-cancer drug imatinib (Gleevec) holds out promise to become the first effective treatment for neurofibromatosis, a genetic disease that has resisted treatments until now.

The research team -- which includes members of the IU Simon Cancer Center and the Herman B Wells Center for Pediatric Research -- is conducting clinical tests of the drug following successful laboratory tests and a "compassionate use" of the drug that showed dramatic results in a three-year-old girl at Riley Hospital for Children.

Neurofibromatosis results from mutations in a gene called NF1, which causes tumors to form in the cells that make up the protective sheaths around nerves. In humans, NF1 mutations resulting in neurofibromatosis occur in one in 3,500 births, equally affecting both sexes and all races and ethnicities. It is the most common genetic disease in humans that results in a predisposition to cancer.

IU researchers have begun a phase 2 clinical test of imatinib, treating neurofibromatosis patients with plexiform neurofibromas, which affect about 40 percent of people with neurofibromatosis. Such tumors often have a severe impact on patients' quality of life and can be fatal. They do not respond to chemotherapy drugs and are difficult or impossible to remove surgically.

"We are very hopeful about the potential of this drug and related therapies. There are no other therapies for these tumors. These patients often suffer for years; they sometimes die from these tumors. These are very slow growing tumors that impair people's everyday lives," D. Wade Clapp, MD, said.

The researchers reported in the Oct. 31 issue of the journal *Cell* that the mutated nervous system cells, while still in a pre-tumor state, use molecular signals to recruit inflammatory system cells from the bone marrow to the vicinity of the nerve cells. Those inflammatory system cells -- called mast cells -- then are put to work helping create the cellular "scaffolding" and blood vessels necessary for the cancerous tumors to form.

The tumorigenic cells use a signaling system protein called c-kit to recruit the mast cells, making imatinib an attractive treatment candidate because it acts on the c-kit molecule, said the researchers, who include Feng-Chun Yang, MD, PhD; David Ingram Jr., MD; and Luis Parada, PhD, of the University of Texas Southwestern Medical Center.

The researchers discovered that while both copies of the NF1 gene in the nervous system cells must be mutated in order for tumors to form, those mutations alone are not sufficient. Tumor growth is enabled by additional NF1 mutations in nearby cells -- most likely the mast cells. However, unlike the nerve cells, where both NF1 genes are mutated, only one of the mast cell NF1 genes needs to be mutated for tumor growth to begin.

While the research was being conducted in animal models, a critically ill three-year-old patient presented at Riley hospital with a plexiform neurofibroma that was compressing her airway. With imatinib administered under a compassionate use protocol, the patient's tumor was reduced by about 80 percent, Clapp said. The patient was subsequently removed from treatment and is being followed, he said.

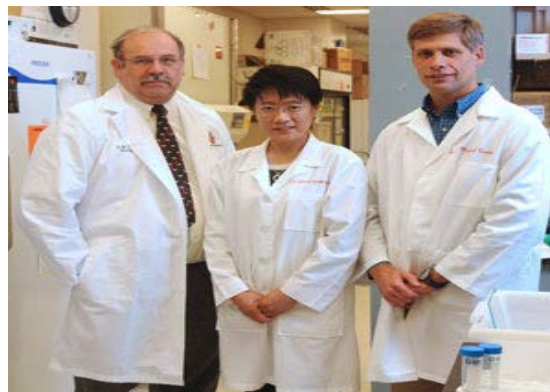
Because imatinib is already an FDA- approved drug used to treat chronic myeloid leukemia and several other types of cancer, the human testing for NF1 will not need to begin with safety testing.

"Patients taking Gleevec for chronic myeloid leukemia have often been taking it for 10 to 15 years without major consequences, and live a normal life. It's a very good, very well tolerated drug," Clapp said.

Researchers expect to enroll about 40 patients, ranging from age three to adults, in the clinical trial.

The research was funded by the National Institute of Neurological Disorders and Stroke and the National Cancer Institute -- both institutes of the National Institutes of Health -- the Department of Defense, and the Riley Children's Foundation.

--Eric Schoch & Cindy Fox Aisen



Clapp, Yang, and Ingram.

Rocky Rothrock photo



November 2008

Annual report finds declines in cancer incidence and death rates

A new report from the nation's leading cancer organizations shows that, for the first time since the report was first issued in 1998, both incidence and death rates for all cancers combined are decreasing for both men and women, driven largely by declines in some of the most common types of cancer.

The report notes that, although the decreases in overall cancer incidence and death rates are encouraging, large state and regional differences in lung cancer trends among women underscore the need to strengthen many state tobacco control programs.

The findings come from the "Annual Report to the Nation on the Status of Cancer, 1975-2005, Featuring Trends in Lung Cancer, Tobacco Use and Tobacco Control" published online Nov. 25 and appearing in the Dec. 2 *Journal of the National Cancer Institute*.

Although cancer death rates have been dropping since the first report 10 years ago, the latest edition marks the first time the report has documented a simultaneous decline in cancer incidence, the rate at which new cancers are diagnosed, for both men and women.

Based on the long-term incidence trend, rates for all cancers combined decreased 0.8 percent per year from 1999 through 2005 for both sexes combined; rates decreased 1.8 percent per year from 2001 through 2005 for men and 0.6 percent per year from 1998 through 2005 for women.

The decline in both incidence and death rates for all cancers combined is due in large part to declines in the three most common cancers among men (lung, colon/rectum, and prostate) and the two most common cancers among women (breast and colon/rectum), combined with a leveling off of lung cancer death rates among women.

The special feature section of the report highlights wide variations in tobacco smoking patterns across the United States, which, coupled with differences in smoking behaviors in younger versus older populations, helps explain the delay in an expected decrease in lung cancer

deaths among women and a slowing of the decrease in lung cancer deaths among men.

The study was conducted by scientists at the ACS, CDC, NCI, which is part of the National Institutes of Health, and the NAACCR.

[Read](#) the full report.

--NCI Office of Media Relations



November 2008

News Briefs

CCCG: 2 IU Simon Cancer Center researchers' breast cancer trials offer greatest potential to improve treatment, survival

Two breast clinical trials led by IU Simon Cancer Center researchers are among 13 considered to have the greatest potential to improve treatment and survival.

A panel of breast cancer experts convened by the Coalition of Cancer Cooperative Groups (CCCG) recently identified clinical trials led by Kathy Miller, MD, and Victoria Champion, RN, DNS, FAAN, among 13 phase III breast cancer research studies from more than 515 currently underway.

The IU Simon Cancer Center and M.D. Anderson Cancer Center were the only cancer centers in the nation to have two studies among the 13.

Miller is the PI for "A Double-Blind Phase III Trial of Doxorubicin and Cyclophosphamide Followed by Paclitaxel with Bevacizumab or Placebo in Patients with Lymph Node Positive and High Risk Lymph Node Negative Breast Cancer" and Champion leads "Quality of Life in Younger Breast Cancer Survivors."

The Coalition of Cancer Cooperative Groups' Scientific Leadership Council (SLC) in Breast Cancer outlined its consensus -- Research Priorities in Breast Cancer: Recommendations of the Scientific Leadership Council in Breast Cancer of the Coalition of Cancer Cooperative Groups -- at a meeting of physicians, researchers, patient advocates, government, and industry representatives in Dallas Sept. 12-13, and urged physicians to enroll as many of their eligible patients into the trials as possible.

IUSCC receives Keep Indianapolis Beautiful award

The new patient care building of the Indiana University Melvin and Bren Simon Cancer Center took home the coveted Monumental Award, presented by Keep Indianapolis Beautiful Inc., as the most significant project of the year in Marion County during an awards ceremony Nov. 13.

"The Indiana University Mel and Bren Simon Cancer Center is a remarkable place, built and designed sensitively to be a supportive environment for cancer patients and families who will come from around the world," David Forsell, president of Keep Indianapolis Beautiful, said.

The Monumental Award is the highest award of distinction and is chosen from the honor award winners in each category of the Monumental Affair event. The awards were selected by an impartial jury of community and professional leaders.

Three companies also earned honor awards for their role in the new IU Simon Cancer Center building: Turner Construction Co. of Indiana, LLC, construction; Maregatti Interiors, interior design; and 2nd Globe Studios, public art.

The 31st annual Monumental Affair Awards ceremony recognized 37 projects that represent the most significant visual and physical enhancements in Marion County.

IUSM-SB breaks ground for expanded medical, cancer research

A groundbreaking ceremony for Harper Hall, the new home of expanded medical and cancer research initiatives at the Indiana University School of Medicine-South Bend (IUSM-SB) and the University of Notre Dame, was Nov. 21.

Charles M. "Mike" Harper, the retired chair and chief executive officer of ConAgra Foods and RJR Nabisco, made a \$10 million gift to Notre Dame to support the construction. The gift was matched with \$10 million appropriated by the state to IU for the project.

Harper's gift is in memory of his late wife, Josie, who died of cancer.

The new facility will be of similar design as Raclin-Carmichael Hall, which houses IUSM-SB and Notre Dame's Keck Center for Transgene Research. It will include laboratories and offices for IUSM-SB and Notre Dame cancer research activities under the auspices of a new Mike and Josie Harper Cancer Research Institute.

Scientists from Notre Dame and Indiana University will collaborate on research in cancer biology, with an emphasis on such areas as genomics and proteomics, and breast, prostate, and colon cancers.

IUSCC sponsors December cancer/oncology summit

The IU Simon Cancer Center is the headline sponsor of the Indiana Health Industry Forum's "Emerging Trends and New Developments in Cancer Discovery, Diagnosis and Treatment" cancer/oncology summit.



The summit is Dec. 1-2 at University Place Conference Center on the IUPUI campus.

"The event will provide a unique combination of presentations, panel discussions, and networking opportunities for scientists, clinicians, and supporting institutions and private corporations," conference co-chair Mark Kelley, PhD, said. "And we hope the format of the meeting will stimulate new interactions, connections, and collaborations among all of us in Indiana working in oncology," he said.

Keynote speakers are Eric K. Rowinsky, MD, chief medical officer and executive vice president of ImClone Systems Inc., and Douglas W. Blayney, MD, medical director, University of Michigan Comprehensive Cancer Center, and president-elect of the American Society of Clinical Oncology.

For more information, visit www.IHIF.org.

IUSCC members in the news

G. Marie Swanson, PhD, MPH, has been named chair of the IU Department of Public Health by IUSM Dean Craig

Brater. A professor of public health, Dr. Swanson has served as an associate chair of the department since she joined the IUSM faculty in August 2007. She also is an associate director for population sciences at the IU Simon Cancer Center. She succeeds former Indiana State Department of Health Commissioner Gregory Wilson, MD, who has served as interim chair for two years since the founding chair Stephen Jay, MD, stepped down as chair.



Swanson

Harikrishna Nakshatri, BVSc, PhD, has been named the first Marian J. Morrison Professor of Breast Cancer Research. He will retain his current titles of professor of surgery and of biochemistry and molecular biology. The named professorship was established in 2004 by Marian J. Morrison, a patient at the IU Simon Cancer Center, in appreciation of the care she received from Drs. Robert Goulet and Kathy Miller.

Nasser Hanna, MD, presented "Carboplatin/paclitaxel With/without Sorafenib in Chemonaive Patients with Stage

IIIB-IV Non-small Cell Lung Cancer (NSCLC): Interim Analysis (IA) Results from a Randomized Phase III Trial: ESCAPE" at the 2008 Chicago Multidisciplinary Symposium in Thoracic Oncology.



Hanna

Patrick Loehrer, MD, earned the Dr. Harold Burdette Award during a ceremony Nov. 20 for continuing to foster the ideals, beliefs, and values of Burdette. Burdette played a leading role in the support of behavioral oncology through

the Walther Cancer Institute.

ACS Institutional Research Grant is available

The IU Simon Cancer Center is pleased to announce the availability of funds for new pilot projects to assist new investigators who hold the rank of assistant professor, research assistant professor, or assistant scientist.

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