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Cancer research news for clinicians

Breast Cancer:

Letrozole Cuts Risk Of Breast Cancer Recurrence Even After Tamoxifen Use

Treatment with the aromatase inhibitor letrozole (Femara) can reduce the risk of breast cancer recurrence even when initiated one to seven years after a course of tamoxifen therapy.

The results of a study involving women originally in the placebo arm of an international trial of letrozole will appear in the Journal of Clinical Oncology and are receiving early online release. Among those who chose to begin letrozole treatment after the initial trial was halted, the risk that their cancer would recur was cut in half compared with those who never received letrozole. In addition, the risk of metastasis was 60 percent lower

(Continued to page 2)

Ovarian Cancer:

Recurrent Low-Grade Serous Carcinoma Less Responsive To Chemotherapy

Recurrent low-grade serous carcinoma, a rare type of ovarian cancer, is less sensitive to chemotherapy and therefore more difficult to treat than more common high-grade ovarian cancers, according to researchers from the University of Texas M. D. Anderson Cancer Center.

The findings were reported at the Society of Gynecologic Oncologists annual meeting on women's cancers earlier this month.

The retrospective study is the first to analyze how women with low-grade tumors respond to chemotherapy in recurrent setting and confirms clinical impressions that the tumors are chemoresistant, said lead author David Gershenson, chairman of the Department of Gynecologic Oncology at M. D. Anderson. Previous studies have shown similar tumor resistance in newly diagnosed patients, and there is currently no standard of care for women facing the disease.

The results support a growing body of research that shows low-grade ovarian tumors behave differently than their high-grade counterparts, genetically and clinically. "In order to make meaningful advances in treatment, women with low-grade ovarian tumors must not be grouped together with those with more common ovarian tumors. They require unique consideration and more targeted treatment options for a better chance of survival," Gershenson said.

Gershenson and his colleagues identified all patients treated for recurrent low-grade serous carcinoma of the ovary seen at M. D. Anderson from 1990 through 2007 using databases from the Department of Gynecologic Oncology.

(Continued to page 4)

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Letrozole After Tamoxifen Reduced Risk Of Recurrence

(Continued from page 1)

with letrozole, and the chance that a new tumor would develop in the unaffected breast dropped more than 80 percent.

"It appears that estrogen-sensitive tumors remain hormone dependent and that patients' survival can be improved with careful use of aromatase inhibitors, even many years after completing tamoxifen treatment," said Paul Goss, director of Breast Cancer Research at Massachusetts General Hospital Cancer Center, who led both the current study and the earlier investigation, called the MA.17 trial. "These results can be put into practice right away to improve the outlook for women treated for receptor-positive breast cancer."

Letrozole is one of a class of drugs called aromatase inhibitors that suppress the production of estrogen, which stimulates the growth of breast tumors expressing the estrogen receptor. The most widely used estrogen-blocking drug is tamoxifen, but the benefits of tamoxifen treatment drop significantly after five years, while the drugs' side effects continue.

The original MA.17 trial, conducted through the National Cancer Institute of Canada, was designed to test whether letrozole could reduce tumor recurrence and increase survival in breast cancer patients who had completed five years of tamoxifen treatment. The study was halted in October 2003—a year earlier than planned—when interim data analysis showed that tumors of women taking letrozole were significantly less likely to recur. The final analysis of MA.17 data, published in the Sept. 7, 2005 Journal of the National Cancer Institute, confirmed that women taking letrozole had significantly better disease-free survival than those taking a placebo.

Since women who received letrozole in the MA.17 trial began taking the drug within a few months of stopping tamoxifen treatment, letrozole's current approval restricts the initiation of therapy to the first three months after tamoxifen discontinuation. However, participants in the placebo arm of the MA.17 trial were offered the opportunity to begin letrozole treatment when that trial was halted, which gave investigators the opportunity to determine whether those women could also benefit from the drug.

The current study analyzes data on more than 1,500 women from the placebo group who chose to take letrozole and about 800 who chose no further treatment. Almost three years after the MA.17 trial was halted and letrozole offered, those who began letrozole therapy had only a 2 percent risk of tumor recurrence, compared with almost 5 percent in those choosing no treatment. The risk of death from breast cancer during that period was cut in half in those receiving letrozole. Treatment also reduced the risk of metastasis by 61 percent and appeared to prevent development of a new tumor in the opposite breast by 82 percent.

The research team notes that this study is limited by the fact that participants choose whether to take the drug themselves and were not randomly assigned. While a randomized clinical trial would more conclusively determine the benefit of letrozole treatment for those who have been off tamoxifen for several months or years – or even those who never took the drug – the results of this study can help guide physicians and patients in deciding whether letrozole therapy would be appropriate.

"Every patient who has previously taken tamoxifen should discuss these new results with her oncologist," said Goss, a professor of Medicine at Harvard Medical School. "The risk that hormone-dependent breast cancer will recur continues indefinitely, and our results imply that aromatase inhibition is effective whenever initiated."

The study was supported by grants from the Canadian Cancer Society, the National Cancer Institute of Canada and the U.S. National Cancer Institute. Novartis Pharmaceuticals, which markets letrozole under the brand name Femara, also supported and provided study medications for the initial MA.17 trial.

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Exemestane Cuts Recurrence by More Than 50%

Another study in the same issue of JCO showed that taking another aromatase inhibitor, exemestane (Aromasin), soon after completing tamoxifen treatment reduces the risk of recurrence by 56 percent.

The National Surgical Adjuvant Breast and Bowel Project (NSABP) B-33 Trial was stopped early when the 2003 MA.17 letrozole results were reported, and women receiving a placebo were offered exemestane.

In the current study, led by Eleftherios Mamounas, associate professor of surgery at Northeastern Ohio University College of Medicine, 96 percent of the women who were originally designated to receive exemestane remained free of recurrence after four years, compared with 94 percent of those taking a placebo.

Exemestane was well tolerated by most of the women. It is currently approved for women who have completed two to three years of tamoxifen and switch to exemestane to complete the five-year course of hormonal therapy.

In an editorial accompanying these studies, Nancy Lin and Eric Winer, both of the Dana-Farber Cancer Institute, wrote: "The results of MA.17 and NSABP B-33, taken in context with the other adjuvant endocrine trials reported in the last five to seven years, strongly argue for a paradigm shift in the clinical research focus and management of patients with estrogen receptor-positive breast cancer...We need to identify predictors of late recurrence and treatment approaches that will change the low, but unrelenting, risk of recurrence seen in patients with estrogen receptor-positive breast cancer. Perhaps most importantly, we need to recognize the heterogeneity of both breast cancer and patients with breast cancer, in order to develop individualized treatment strategies that lead to the greatest benefit while minimizing risk."

BMI May Be Prognostic Tool For Types Of Breast Cancer

Body mass index, the measure of a person's fat based on their height and weight, may be an effective prognostic tool for specific types of breast cancer, according to research from University of Texas M. D. Anderson Cancer Center.

The study, published in the March 15 issue of Clinical Cancer Research, reports that women with locally advanced breast cancer (LABC) and inflammatory breast cancer (IBC) with high BMIs had worse prognosis than women with the disease whose BMIs were in the healthy range.

One's BMI is scored based on height and weight. A score less than 18.5 indicates that a person is underweight and a score of 18.5 -24.9 indicates that one is in a normal or healthy range. A person is overweight if their score is 25-29.9 and any score above 30 classifies that a person as obese.

LABC, or cancer that has spread to nearby tissue or lymph nodes, accounts for about five percent of newly diagnosed breast cancer cases each year in the U.S., according to Massimo Cristofanilli, the study's senior author. In underserved communities, LABC accounts for 50 percent of new cases.

"This is the first study to highlight the value of BMI at the time of diagnosis as a prognostic indicator in women with aggressive disease and at a high risk of recurrence and at the time of diagnosis in locally advanced disease, including it's most aggressive form, inflammatory breast cancer," said Cristofanilli, associate professor in M. D. Anderson's department of Breast Medical Oncology. "We embarked on this research because the vast majority of our newly-diagnosed inflammatory breast cancer patients were overweight or obese, and IBC is associated with a poor prognosis."

For the retrospective study, researchers reviewed 606 patients—495 (82 percent) with LABC and 111 (18 percent) with non-metastatic IBC. All were enrolled in clinical protocols at M. D. Anderson between 1974 and 2000. The median follow up was six years for all patients; for women still alive, the median follow-up was 9.9 years.

In calculating BMI, 208 (34 percent) of the patients were normal or underweight, 194 (32 percent) were overweight and 204 (34 percent) were obese. Obesity was more frequent in women with IBC, 45 percent vs. 31 percent in non-IBC cases.

For the entire group, the median overall survival was 8.6 years and recurrence-free survival was 5.8 years. Both statistics were significantly worse for overweight and obese patients compared to those who were of normal weight or underweight.

For overweight LABC patients, five-year survival was 58.3 percent and 10-year survival was 44.1 percent; 58.6 percent of obese LABC patients lived five years and 42.4 percent lived 10 years. In contrast, 69.3 percent of women with LABC who were normal or underweight lived five years and 57.3 percent lived 10 years.

In women with IBC who were overweight, five-year survival was 45.3 percent and 10-year survival was 29.1 percent; 49.3 percent of obese IBC patients lived five years and 43.7 percent lived 10 years. In comparison, 55.1 percent of women with IBC who were

normal or underweight lived five years and 50.9 percent lived 10 years.

All patients received similar anthracycline-based treatments and that doses were not adjusted based on a patient's weight, said Cristofanilli. "From a research standpoint, we really need to further look at the relationship between obesity and some endocrine factors that may explain why inflammatory breast cancer patients are more frequently obese," he said.

Cristofanilli acknowledged that dietary intervention might be difficult for women undergoing chemotherapy; however, some change of lifestyle habits for overweight and obese patients after diagnosis are vital.

Cristofanilli noted that before BMI is completely accepted as a prognostic tool for breast cancer, prospective trials and endocrinology studies must be conducted. However, to oncologists currently treating overweight and obese LABC and IBC patients, Cristofanilli recommends they be more aggressive in follow-up, including considering more frequent physical exams and imaging studies.

Ovarian Cancer:

Rare Ovarian Cancer Difficult To Treat, Less Responsive

(Continued from page 1)

Out of 52 patients with sufficient clinical information with which to assess response to one or more of 98 different chemotherapy regimens, the overall response rate was only 4 percent. Specifically, researchers found:

—Among 24 patients who received carboplatin for platinum-sensitive disease, there were two partial responses and one complete response.

—Of 11 patients who received a taxane/platinum combination for platinum-sensitive disease, no objective responses were observed.

—In the entire platinum-sensitive cohort, the overall response rate was only 6 percent.

—No response was observed in women with platinum-resistant disease to standard chemotherapy agents such as liposomal doxorubicin; topotecan; hexamethylmelamine; oral VP-16; xeloda and gemcitabine. One patient had a partial response to paclitaxel. The overall response rate in this subgroup was 2 percent.

—Sixty-one (62 percent) of the regimens stabilized the disease from 8 to 79 weeks, with a median of 22 weeks.

—In 18 instances of stable disease, CA125 levels decreased by 50 percent or more.

Gershenson said that these results compared unfavorably to findings from trials of more common ovarian cancers. "It is unclear whether the high rate of stable disease is more reflective of tumor biology of low-grade serous carcinoma of the ovary or of the therapy regimen administered," he said. "However, since these tumors do not respond to conventional types of chemotherapies, new agents to treat these tumors must be identified and tested."

One area to explore further is hormonal therapy, a treatment that has been shown to have some activity against low-grade serous carcinoma, he said. A detailed analysis of the M. D. Anderson experience with hormonal therapy is planned in the near future.

Low-grade serous carcinoma represents about 10 percent of all serous ovarian cancers. The disease is characterized by a young age at diagnosis—an average of 42 years old, versus more common ovarian cancers, which are generally diagnosed at about 60 years old. The median overall survival of women with low-grade serous carcinomas is much longer than that of patient with high-grade ovarian cancers: 82 or more months versus 50-67 months in various reported series.

Histologic grade has been shown to be one of the most important prognostic factors in ovarian serous carcinoma cases. However, no universal grading system exists. Over the last 15 years, researchers at M. D. Anderson have developed a two-tier grading system for serous carcinoma of the ovary (low and high), based on knowledge that this type of epithelial ovarian cancer comprises not one homogenous group of tumors but rather two distinct phenotypes.

Historically, a three-tier grading system to classify tumors has been used, but there has been no precise mechanism to define the thresholds between the grades, particularly grades two and three. Consequently, there were variations in designating how ovarian tumors should be classified and ultimately, treated.

The study of rare cancers, such as low-grade serous carcinoma of the ovary, brings inherent challenges, including the limited number of cases to examine, difficulty in obtaining tissue samples, low funding, and the small pool of investigators working on research, according to Gershenson.

Recognizing the need for more research, the Gynecologic Oncology Group, a National Cancer Institute-funded cooperative group, recently established a rare tumor committee that has initiated a separate series of clinical trials for recurrent low-grade serous carcinoma as well as for other rare ovarian cancers.

Gershenson said that changing the design of clinical trials to segregate patients is key. "In addition to providing direct benefits to patients and their families, the study of rare tumors can also uncover information about the etiology, biology, and treatment of more common cancers."

Gastric Cancer:

Postoperative Chemo Doesn't Improve Survival, Study Finds

The use of combination chemotherapy following surgery did not improve survival in patients with gastric cancer, according to a randomized clinical trial published online March 11 in the Journal of the National Cancer Institute.

The only potentially curative therapy currently available for non-metastatic gastric cancer is surgery. Recent studies have suggested that a combination of cisplatin, epirubicin, 5-fluorouracil and leucovorin (PELF) improves outcome in patients with metastatic gastric cancer.

To test the PELF combination in patients with localized disease, Francesco Di Costanzo, of the University Hospital Careggi in Florence, Italy, and colleagues in the Italian Oncology Group for Cancer Research conducted a randomized controlled trial in which 258 patients were treated with surgery or surgery followed by chemotherapy.

With a median follow-up of 72.8 months, there was no significant difference in disease-free survival or overall survival between the two trial arms. Specifically, 47.7 percent of the patients treated with chemotherapy had progressive disease compared with 51.6 percent of patients in the control arm. Overall survival was similar; at the end of the follow-up period, 47 percent of the patients in the chemotherapy were still alive compared with 45.3 percent in the surgery-only arm.

"Our study confirms that a dose-intense regimen like PELF, which showed very promising results in advanced gastric cancer, is not effective in an adjuvant setting," the authors write. Considering the negative results in this trial and other recent adjuvant chemotherapy trials in gastric cancer, the authors write, "Adjuvant chemotherapy alone remains a controversial approach in operable gastric cancer."

In an accompanying editorial, Aiwen Wu and Jiafu Ji, of the Beijing Cancer Hospital and Institute in China, discuss the conflicting results obtained from recent trials that tested the value of chemotherapy and radiation in localized gastric cancer.

Despite the inconsistency of the overall data, the editorialists conclude that chemotherapy, radiation, or a combination of the two should be used in patients with gastric cancer. "Surgery alone is no longer the standard treatment for patients with resectable gastric cancer, independent of the patient population or the practice location," they write.

Disease Prevention:

Risks Of Long-Term HRT Outweigh Benefits, WHI Finds

New results from the Women's Health Initiative confirm that the health risks of long-term use of combination (estrogen plus progestin) hormone therapy in healthy, postmenopausal women persist even a few years after stopping the drugs and clearly outweigh the benefits.

Researchers report that about three years after women stopped taking combination hormone therapy, many of the health effects of hormones such as increased risk of heart disease are diminished, but overall risks, including risks of stroke, blood clots, and cancer, remain high. The WHI is sponsored by the National Heart, Lung, and Blood Institute.

Results of the WHI three-year follow-up study of the estrogen plus progestin clinical trial were published in the March 5 issue of the Journal of the American Medical Association.

"The good news is that after women stop taking combination hormone therapy, their risk of heart disease appears to decrease," said NHLBI Director Elizabeth Nabel. "However, these findings also indicate that women who take estrogen plus progestin continue to be at increased risk of breast cancer, even years after stopping therapy. Today's report confirms the study's primary conclusion that combination hormone therapy should not be used to prevent disease in healthy, postmenopausal women."

The FDA recommends that hormone therapy never be used to prevent heart disease, and, when hormone therapy is used for menopausal symptoms, it should only be taken at the smallest dose and for the shortest time possible.

The new findings are from a follow-up study of 15,730 postmenopausal women with an intact uterus, ages 50 to 79 years (average age of 63) at enrollment, who participated in the WHI estrogen-plus-progestin clinical trial. Participants were randomly assigned to receive a combination of estrogen (0.625 milligrams of conjugated equine estrogens per day) plus progestin

(2.5 mg of medroxyprogesterone acetate) or placebo (inactive pill). The main estrogen-plus-progestin study was stopped in 2002 after an average of 5.6 years of treatment due to an increase in breast cancer. Women on combination hormone therapy were also at increased risk of stroke, blood clots, and heart disease, while their risk of colorectal cancer and hip fractures was lower, compared to women who did not take hormone therapy.

The follow-up study began in July 2002 after women in the study were instructed to stop taking combination hormone therapy, and continued through March 2005, with participants followed for an average of 2.4 years. All study participants were examined at least once a year by a WHI clinician and received an annual breast examination and mammogram, with biopsies performed as needed.

During the follow-up study, the numbers of heart attacks, strokes, and blood clots were not significantly different between the two groups (overall, 343 cardiovascular events among those who initially received hormone therapy versus 323 among those who did not). In addition, the number of deaths was not significantly different (233 women who had been in the hormone therapy group died, versus 196 women who had been in the placebo group).

"After being on combination hormone therapy for several years, the women's risk of cardiovascular disease was significantly higher—from a 29 percent increase in heart attacks to a 41 percent increase in strokes and nearly twice the risk of serious blood clots - compared to the women who did not take hormones," said Michael Lauer, director of the NHLBI Division of Prevention and Population Sciences. "While it is reassuring that heart attack risk decreased and that the risks for stroke and blood clots did not grow after the women stopped taking hormones, this study provides further evidence that five years of combination hormone therapy is harmful. All the accumulated risks do not simply disappear."

The study also found that other effects of combination hormones, such as decreased risk of colorectal cancer and hip fractures, also stopped when therapy ended.

"We continue to encourage women to use hormones only if needed for menopausal symptoms, and for the shortest time possible, and to adopt and maintain a healthy lifestyle, that is, engage in regular physical activity, maintain a healthy body weight, consume a diet low in saturated fat, and to not smoke, to reduce their risks of cardiovascular and other chronic diseases," said Marcia Stefanick, professor of medicine at Stanford University, Stanford, Calif., and a coauthor of the paper, as well as chairman of the WHI Steering Committee.

She added that women should know their cholesterol and blood pressure levels and other health risks and take preventative measures, as needed.

Breast Cancer Risk

In contrast to the other effects, the risk of breast cancer continued at a rate similar to that seen during treatment. Women who had stopped taking estrogen plus progestin were about 27 percent more likely to develop breast cancer than the women who didn't take hormones during the study, with 79 women in the post-treatment group developing breast cancer during the three-year follow-up study, compared to 60 women in the non-treatment group.

"The hormones' effects on breast cancer appear to linger," said Leslie Ford, associate director for clinical research in the NCI Division of Cancer Prevention. "These findings reinforce the importance of women getting regular breast exams and mammograms, even after they stop hormone therapy."

Researchers also report a 24 percent increased risk of developing any form of cancer among women who had been in the treatment group. Overall, there were 63 more diagnoses of cancer during the follow-up study, or three per 1,000 participants per year, among women who had taken combination hormone therapy compared to women who did not take hormones during the study (281 diagnoses compared to 218). A more detailed analysis on the cancer findings is underway.

"The continued increased risk of breast cancer clearly plays a role in the increased overall risk of cancer years after stopping long-term estrogen plus progestin therapy, and it is important that we continue to follow these women," added Stefanick, noting that the new results provide further evidence that the health risks of long-term combination hormone therapy outweigh the benefits.

The WHI is a major, 15-year research program designed to address the most frequent causes of death, disability, and poor quality of life in postmenopausal women: cardiovascular disease, cancer, and osteoporosis. The principal findings from the two WHI hormone therapy trials, which studied 27,347 postmenopausal women on estrogen plus progestin, estrogen-alone, or placebo, found that the overall risks of long-term use of hormone therapy outweigh the benefits. Both of these trials were stopped early because of increased health risks and failure to prevent heart disease, a key question of the studies.

Head & Neck, Colon Cancer:

Cause Of Allergic Reaction To Cetuximab Found

Clinicians have been perplexed by the fact that some patients given the drug cetuximab—an immune-based therapy commonly used to treat persons diagnosed with head and neck cancer, or colon cancer—have a severe and rapid adverse reaction to the drug. Sometimes the reaction includes anaphylaxis, a life-threatening condition characterized by a drop in blood pressure, fainting, difficulty breathing, and wheezing.

Now researchers funded by the National Institute of Allergy and Infectious Diseases, part of NIH, have discovered that specific pre-existing antibodies cause the severe reaction to the drug. This discovery in turn has enabled them to explain the unusual geographic pattern of this reaction seen among individuals in the United States. The unusual findings of this investigation appear in a report published in the March 13 edition of the New England Journal of Medicine.

"These intriguing research findings not only are potentially important to physicians treating certain cancer patients, but also may have broader implications for the use of immunotherapies for other diseases," said NIAID Director Anthony Fauci.

NIAID grantee Thomas Platts-Mills, who heads the Division of Allergy and Clinical Immunology at the University of Virginia, led a research study to investigate the cause of the clinical problem with cetuximab. Their newly reported findings are of immediate importance in the care of cancer patients, Platts-Mills said. "Because of the widespread use of cetuximab in cancer treatment, it may be useful to pre-screen patients for specific IgE antibodies to cetuximab to identify those who are at risk for serious adverse reactions, including anaphylaxis."

Cetuximab is a partially humanized mouse monoclonal antibody, which means it is produced by a single cell line and acts against a specific protein. The drug inhibits a growth factor receptor found on the cell surface, thereby controlling the growth of cancer cells.

Upon reviewing the scientific literature, the research team was intrigued by the unusual geographic distribution of patients with anaphylaxis. For example, 22 percent of patients treated with cetuximab in Tennessee and North Carolina had anaphylactic reactions, and even higher rates and clusters of cases were reported from regions of Arkansas, Missouri and Virginia. In contrast, less than 1 percent of patients receiving cetuximab in the Northeast U.S. suffered such reactions.

Anaphylactic reactions are typically triggered by immunoglobulin E (IgE) antibodies, which the immune system produces after being sensitized by prior exposure to an allergen, a normally harmless substance that in some people causes an abnormal immune response. But when Platts-Mills and his collaborators further reviewed the clinical data, they came across another unusual finding. Anaphylactic reactions in these individuals had occurred within minutes of their first exposure to cetuximab, suggesting that the patients had already been primed to respond to cetuximab.

The researchers then hypothesized that these patients had pre-existing IgE antibodies that cross-reacted with cetuximab and that these IgE antibodies were directed against a specific sugar molecule present on cetuximab. This hypothesis was derived, in part, from knowledge that all people develop natural antibodies to sugars found on foods, bacteria and viruses, although such antibodies are of a non-IgE class, called IgM.

To test their hypothesis, Platts-Mills and his colleagues analyzed the antibodies present in serum of 538 individuals. They developed a technique for measuring IgE antibodies to cetuximab and, in further experiments, proved that the IgE antibodies were directed against sugar molecules on cetuximab.

The 538 serum samples included pre-treatment samples taken from 76 cetuximab-treated cancer patients primarily from Tennessee, Arkansas and North Carolina. The remaining serum samples—from individuals in Nashville, Northern California and Boston—served as controls to investigate the geographical differences in hypersensitivity rates.

The researchers found that among the 76 cancer patients, 25 developed hypersensitivity reactions and 18 of these individuals showed a positive reaction for IgE antibodies to the drug. Among the 51 serum samples from patients who did not have a hypersensitivity reaction, only one had such antibodies. In control groups, IgE antibodies against cetuximab were found in 21 percent of the samples from Nashville, 6 percent of the samples from Northern California, and less than 1 percent of the samples from Boston.

Although severe anaphylactic reactions have been reported following treatment with several different monoclonal antibodies, this is the first time a clear mechanism underlying such a reaction has been defined.

"Dr. Platts-Mills and his colleagues have shown that the presence of pre-existing IgE antibodies to a specific sugar molecule on cetuximab is highly predictive of a hypersensitivity reaction to cetuximab,"

said Marshall Plaut, chief of the Allergic Mechanisms Section at NIAID. "Furthermore, their research answers an important question about how the local geographic prevalence of these antibodies leads to regional differences in anaphylactic reactions to cetuximab."

Now the researchers are looking for answers to yet another question: What causes a high proportion of the population in certain parts of the country to produce these particular IgE antibodies that react with cetuximab? Research is in progress to explore if the specific IgE antibodies are triggered by differences in regional exposures to ticks or other parasites or to infectious organisms.

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NCI Cooperative Group, Cancer Center Trials Listed

The National Cancer Institute's Cancer Therapy Program approved the following clinical research studies last month. For further information about a study, contact the principal investigator listed.

Phase II

Phase II Study of AZD0530 in Patients with Advanced, Recurrent Non-Small Cell Lung Cancer Who Have Previously Received Platinum-Based Combination Chemotherapy. University Health Network-Princess Margaret Hospital, protocol 7555, Laurie, Scott, phone 613-737-7700.

Phase II Study of AZD0530 in Recurrent or Metastatic Soft Tissue Sarcoma. University Health Network-Princess Margaret, protocol 7557, von Mehren, Margaret, phone 215-214-1663.

Phase II Study of GW 786034 (Pazopanib) in Advanced Thyroid Cancer. Mayo Clinic Rochester, protocol 7627, Bible, Keith, phone 507-284-2511.

Phase II Randomized Trial of Carboplatin and Topotecan; Flavopiridol, Mitoxantrone and Cytosine Arabinoside; and Sirolimus, Mitoxantrone, Etoposide and Cytosine Arabinoside for the Treatment of Adults with Primary Refractory or Initial Relapse of Acute Myelogenous Leukemia. Eastern Cooperative Oncology Group, protocol E1906, Litzow, Mark, phone 507-284-2511.

Phase III

Phase III Comparison of Thoracic Radiotherapy Regimens in Patients with Limited Small Cell Lung Cancer Also Receiving Cisplatin and Etoposide. Cancer and Leukemia Group B, protocol CALGB-30610, Jeffrey Alan, phone 315-464-5276.

Other

Carcinogen Metabolism, DNA Repair Parental Exposures and Retinoblastoma. Children's Oncology Group, protocol AEPI05N1, Bunin, Greta, phone 215-590-1445.

Breast Cancer Subtype (as Defined by HER2, Er, Ki67) as Predictive Factors for Sensitivity to Paclitaxel, and the Triple-Negative Subtype (Basal Versus Non-Basal) as Prognostic Factors in Intergroup Trial CALGB 9344. Cancer and Leukemia Group B, protocol CALGB-159905B-ICSC, Ellis, Matthew, phone 314-362-8866.

ER/HER2/Ki67 Breast Cancer Subtypes as Predictive Factors for Response to Adjuvant Dose-Dense Therapy, and Basal Subtypes of Triple-Negative Breast Subtypes of Triple-Negative Breast Intergroup Trial C9741. Cancer and Leukemia Group B, protocol CALGB-9741A-ICSC, Ellis, Matthew, phone 314-362-8866.

Evaluation of the LIAISONÆ S-100B Assay as a Means to Define Prognosis in Patients with Melanoma. Eastern Cooperative Oncology Group, protocol E1696T1, Kirkwood, John, phone 412-648-6570.

Pilot

Pilot Trial of Hu14.18-IL2 and Cilengitide in Subjects with Completely Resectable Recurrent Stage III or Stage IV Melanoma. University of Wisconsin Hospitals and Clinics, protocol 8071, Sondel, Paul, phone 608-263-9069.

The Role of VEGF-A Signaling in Maintenance of the Glomerular Filtration Barrier and Blood Pressure. University Health Network-Princess Margaret Hospital, protocol 8076, Moore, Malcolm, phone 416-964-2263.