THE CLINICAL CANCER LETTER

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Cancer research news for clinicians

American Association for Cancer Research:

New Drugs And Older Ones In New Uses Show Progress Against Several Cancers

New drug compounds, and old ones put to new use, show progress against brain, rectal, and pancreatic cancers and lymphoma, according to studies presented at the annual meeting of the American Association for Cancer Research earlier this month.

Phase II Study of AZD2171 In Recurrent Glioblastoma

The investigational drug AZD2171 (cediranib) may help shrink tumors and prolong survival of patients with a relatively common, aggressive type of brain cancer, according to results from a clinical trial conducted by Boston researchers.

In a phase II study of 31 patients with recurrent glioblastoma, researchers observed that daily treatment with cediranib decreased tumor volume by more

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Lung Cancer:

High-Dose Chemo Doesn't Improve Survival In Small Cell Lung Cancer

Small cell lung cancer patients treated with high-dose chemotherapy did not have better survival rates than those treated with standard doses, according to a randomized controlled trial published online April 8 in the Journal of the National Cancer Institute.

Although many patients with SCLC initially respond to chemotherapy, most suffer disease recurrence relatively quickly. Laboratory data suggest that increasing the dose of chemotherapy agents kills SCLC cells that were resistant to standard doses, and thus might improve patient survival.

To test this possibility, Serge Leyvraz, of the University Hospital in Lausanne, Switzerland, and colleagues enrolled 140 patients with SCLC in a randomized trial that compared high-dose and standard-dose chemotherapy. Both groups were treated with the same chemotherapy agents, ifosfamide, carboplatin, and etoposide.

The three-year survival rates in the two arms were similar, with 18 percent of patients in the high-dose arm and 19 percent of patients in the standard-dose arm still alive. Also, a similar fraction of patients in both arms showed tumor shrinkage in response to therapy—78 percent in the high-dose arm and 68 percent in the standard-dose arm, which was not a statistically significant difference.

"The approach explored in the present trial succeeded in raising the peak dose, total dose, and dose intensity of ICE by threefold but has clearly been

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AACR Annual Meeting: New Drug Compounds Tested

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than half in 56 percent of patients.

Nearly 26 percent of patients were alive and their cancer had not progressed six months into treatment. On average, patients experienced a progression-free survival of 117 days and overall survival of 221 days. In addition, cediranib was found to alleviate brain swelling—a major cause of morbidity among these patients.

Cediranib is a selective signaling inhibitor for vascular endothelial growth factor (VEGF), which promotes formation of new blood vessels that tumors need for nourishment and growth. The drug targets all three receptors for VEGF, one of which is expressed on the endothelial cells in glioblastoma.

"These are promising, early results but are from a single study of 31 patients, so ongoing larger studies will be critical to determine if the findings are corroborated," said lead author Tracy Batchelor, executive director of the Stephen E. and Catherine Pappas Center for Neuro-Oncology at the Massachusetts General Hospital Cancer Center. "One important question is whether a combination of cediranib and chemotherapy will be more effective than cediranib alone. We have designed a randomized trial in patients with recurrent glioblastoma that will open at multiple sites in Europe, the U.S., Canada and Australia this summer that will address this and other questions."

Two of the 31 patients were removed from the current study because of toxicity (fatigue). However, dose reductions or short breaks from the drug were required for most patients, usually due to hypertension, diarrhea and fatigue.

By analyzing blood samples from patients, the researchers found that the biomarkers FGF (fibroblast growth factor) and Tie-2 were associated with tumor progression and could be used to predict treatment failure in this study population, Batchelor says. FGF is a protein tied to new blood vessel growth; Tie-2 is a receptor that binds to and is activated by the angiopoietins—protein growth factors required for the formation of blood vessels.

Phase I/II Study of Bevacizumab In Rectal Cancer

Adding bevacizumab to standard chemotherapy and radiation in patients with rectal cancer fully prevented tumor spread and "normalized" tumor blood vessels enough to enable effective therapy, researchers report.

"I know of no other therapy in this patient population where we can even get close to 100 percent tumor control. Although this needs to be confirmed in a randomized trial against a placebo group, these are very impressive numbers," said Rakesh Jain, the Andrew Werk Professor of Tumor Biology at Harvard Medical School.

Bevacizumab is currently approved for colorectal cancer, and works by destroying the blood vessels that tumors need to grow.

"This mechanism of action was a conundrum for scientists because in order for radiation and chemotherapy to work, you need blood vessels," Jain said. "However, the current study adds evidence to a concept called normalization whereby restoring order to blood vessels inside a tumor opens up a window of opportunity for treatment."

Blood vessel normalization allows the vessels that remain to perform more efficiently. "With a drug like bevacizumab, some of the tumor vasculature is pruned away immediately, but the vessels that remain become less abnormal," Jain said. "These normalized vessels make the surviving cancer cells more vulnerable to the treatments that can now be delivered more efficiently. Cancer therapies in this environment should be maximally effective."

In the current study, researchers enrolled 24 patients with late-stage rectal cancer. All patients completed four cycles of therapy including bevacizumab, additional standard chemotherapy, radiation and surgery.

At four years, local control, or the absence of

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cancer spread beyond the original tumor site, was observed in 100 percent of patients and disease-free survival in 88 percent.

Of the 24 patients treated, five had no residual cancer. Of the 19 patients with residual disease, 12 displayed severe disease. Downstaging of the tumor was observed in 12 out of 22 observable tumors.

"We had shown in previous mouse studies that normalizing blood vessels would decrease tumor activity, but the question with mouse studies is whether it will work in humans," Jain said. "This is the first study to confirm the idea of the effect of normalization in patients."

Phase I Study of AME-133v In Lymphoma

A second generation, highly targeted monoclonal antibody appears to provide benefit for some patients with follicular lymphoma for whom other treatments have failed, according to results of a phase I clinical trial.

In the 16 patients evaluated so far, four have achieved either a partial or complete response with use of the novel agent AME-133v, said the study's lead investigator, Andres Forero, associate scientist at the University of Alabama, Birmingham, Comprehensive Cancer Center.

"These first results suggest that AME-133v provides a mechanism of action that may be more potent and ultimately more effective than the treatments we have on hand for a subset of patients with this cancer," Forero said. "Given these encouraging results, patients are currently being enrolled in a phase II study."

The majority of patients in this study either did not initially respond or relapsed after use of rituximab, the first monoclonal antibody therapy approved for use in lymphoma treatment. AME-133v is a second-generation therapy that is believed to be a more specific treatment for follicular lymphoma in general, compared to rituximab, but is also thought to offer particular benefits for those patients who have a variant in the immune cells needed to attack the cancer, Forero says.

Follicular lymphoma is a particularly difficult to treat subtype of non-Hodgkin lymphoma, which is a cancer that arises from white blood immune cells known as lymphocytes. Rituximab binds to CD20, a cell surface antigen expressed on almost all B-cell lymphomas as well as on normal B cells, and works to kill the cancer cell via a mechanism that is not yet understood.

Of the 22 patients treated with AME-133v in this study, 20 had been treated with rituximab and 18 also had chemotherapy. All were Fc?RIIIa 158-F carriers. This was a dose escalation study, and researchers report that the agent was well tolerated at all doses – 90 percent of patients experienced only grade I adverse events.

"AME-133v appears to be capable of binding with high specificity to cell-surface antigens, resulting in targeted killing of malignant cells, relative sparing of normal tissues, and low toxicity," Forero said.

Paclitaxel Plus Gemcitabine In Pancreatic Cancer

A novel combination of nanoparticle albumin-bound (nab) paclitaxel and gemcitabine showed a significant clinical benefit in more than 70 percent of pancreatic cancer patients, according to researchers.

"Unfortunately most patients with pancreatic cancer have a very poor survival" said Daniel Von Hoff, physician in chief of the Translational Genomic Research Institute and chief medical officer for the Scottsdale Clinical Research Institute at Scottsdale Healthcare in Arizona.

SPARC (Secreted Protein Acidic and Rich in Cysteine) was noted to be commonly found in pancreatic cancer specimens in an ongoing Target Now Research Program being performed by Caris-MPI. This finding, also described by other investigators, was the basis for this phase I clinical trial that Von Hoff presented here.

"Chemotherapy often means combining more than one drug, and we do not want to just take the next thing off the shelf. We want to know as much about a tumor as possible going in," Von Hoff said.

In this trial, patients received escalating doses of nab- paclitaxel (which binds to a potential target SPARC in pancreatic cancer specimens) from 100 mg/m2 to 150 mg/m2 combined with 1000 mg/m2 of gemcitabine. Researchers from TGen/SHC, Johns Hopkins, University of Alabama, and South Texas Hematology/ Oncology reported on the first 20 patients who received nab-paclitaxel 100 mg/m2 of what will eventually be a 42-patient trial. Investigators assessed tumor response by measuring levels of the cancer marker CA 19-9 and by PET and/or CAT scan. A drop in CA 19-9 levels had been previously linked in other research with improved survival.

Of the original 20 patients enrolled at the nab-paclitaxel 100 mg/m2 dose, 17 had levels of CA 19-9 that could be evaluated. CA 19-9 levels dropped more than 20 percent in 82 percent of patients, researchers report. Reductions in CA 19-9 of more than 70 percent were observed in 64 percent of patients. Utilizing CAT scan criteria, 9 of the 16 patients (56 percent) who had serial scans had responses. Twelve of the 16 (75 percent) had responses or stable disease for more than

four months.

"This was a phase I trial, and phase I trials are usually designed to test safety and hoping for efficacy. The fact that we saw this kind of activity in a phase I trial is impressive," Von Hoff said.

Side effects were considered tolerable. The most common side effect was low blood counts, followed by fatigue and occasional peripheral neuropathy.

Celecoxib Effective To Prevent Colon Adenomas, Study Finds

Colon adenoma prevention with celecoxib, a non-steroidal anti-inflammatory drug, is effective and can be safe for patients without underlying cardiovascular risk factors, according to five-year data of a randomized phase III trial presented at the American Association for Cancer Research annual meeting earlier this month.

The Adenoma Prevention with Celecoxib (APC) trial enrolled 2,035 patients and randomly assigned them to 200 mg twice-daily (400 mg) of celecoxib, 400 mg twice-daily (800 mg) of celecoxib or a placebo group.

At three years, patients taking celecoxib at 400 mg had a 29 percent reduction in adenomas, a precursor to colon cancer, while those taking 800 mg had a 38 percent reduction. Advanced adenomas, which are lesions with a high-risk for cancer development, were reduced by 55 percent with 400 mg and 63 percent with 800 mg.

After three years, patients stopped taking celecoxib and were followed for another two years to assess safety and effectiveness. After two years off medication, the five-year rate of advanced adenoma was reduced by 41 percent among patients taking the lower dose and 26 percent among patients taking the higher dose.

Cardiovascular events were more common in patients taking celecoxib, with a rate of 3.8 percent among those patients taking placebo to 6 percent among the low dose group and 7.5 percent among the high dose group. However, when researchers looked at factors that might predict cardiovascular complications, they found a much different story.

For patients with no cardiovascular risk factors before using celecoxib, the rate of cardiovascular adverse events was 0.9 percent in the placebo group, 3.9 percent in the 400 mg group and 1.9 percent in the high dose group. Cardiovascular risk factors included smoking, high cholesterol, high blood pressure, diabetes, presence of atherosclerosis and age over 65.

If a patient had one risk factor, the risk was 2.2 percent in the placebo group, 3.7 percent in the 400 mg dose group and 4.9 percent in the high dose group.

The greater cardiovascular risk was observed among patients who had at least two cardiovascular risk factors at the time they entered the study, where the placebo group had a 5.9 percent risk, the 400 mg group had an 8.2 percent risk and the 800 mg group had an 11.2 percent risk.

"This new data allows us to carefully select patients who can benefit from this drug," said Monica Bertagnolli, associate professor of surgery at the Brigham and Women's Hospital and the lead researcher on the study. "Although it should be used with caution, those patients with a high risk for colon cancer and a low risk for cardiovascular disease are going to receive significant benefit."

Low Dose DFMO Reduces Colon Adenoma Recurrence

A combination of the targeted agent difluoromethylornithine (DFMO) at a low dose and sulindac, a non-steroidal anti-inflammatory drug, reduces the risk of recurrent colorectal adenomas, an early sign of colon cancer, by up to 95 percent with less toxicity than with chemotherapy, researchers reported at the American Association for Cancer Research annual meeting earlier this month.

"There is a great hope that we will be able to prevent colon cancer effectively using this method," said Frank Meyskens, director of the Cancer Center at the University of California, Irvine. "We had not been able to do this before due to the high toxicity of available therapies. Difluoromethylornithine is a targeted agent that represents a new treatment paradigm."

In earlier studies, Meyskens's team had established a safe and well-tolerated dose of DFMO that was 1/50th of what would typically be used to treat advanced cancers. By combining this reduced dose of DFMO with sulindac researchers believed they could achieve a significant clinical effect with reduced toxicity.

For the current study, researchers enrolled 375 patients who had a history of at least one colorectal polyp within the previous five years. Patients were randomly assigned to either a combination of 500 mg of daily DFMO and 150 mg of the NSAID sulindac, or placebo. Patients were followed for three years to measure adenoma recurrence.

Overall, the combination treatment reduced the risk of a recurrent adenoma from 41.1 percent in the placebo group to 12.3 percent with treatment, a 70 percent reduction.

When researchers measured advanced adenomas

only, the rate was 8.5 percent in the placebo group compared with 0.7 percent in the treatment group, a 92 percent reduction.

For adenomas larger than one centimeter, the rate was 7 percent in the placebo group compared with 0.7 percent in the treatment group, a 90 percent reduction. Among patients who had previously had more than one adenoma, the rate of subsequent adenomas was 13.2 percent in the placebo group compared with 0.7 percent in the treatment group, a 95 percent reduction.

The rate of reduction was so pronounced that the trial's independent data and safety monitoring board stopped the trial early.

An analysis of side effects and toxicity found no difference between the treatment and placebo groups. There was no difference in side effects requiring an overnight hospitalization, gastrointestinal side effects, cardiovascular side effects, or hearing loss between the two groups.

"These are important findings, but they are not ready for prime time yet. What we have shown here is that there is value in testing these agents at lower doses and in combination to determine if we can achieve the same effect without the damaging side effects," Meyskens said.

Plant-Based Diet Associated With Improved Survival

A plant-based diet high in cancer-fighting lignans may be associated with improved survival among postmenopausal women with breast cancer, according to a study presented by Susan McCann, of the Division of Cancer Prevention and Population Sciences, Roswell Park Cancer Institute, at the annual meeting of the American Association for Cancer Research.

Lignans are plant compounds found in seeds, whole grains, vegetables and fruits. In laboratory studies, lignans have been shown to impact hormone levels and tumor growth. Researchers from Roswell Park and the University at Buffalo evaluated the dietary lignan intakes of 1,122 women diagnosed with breast cancer who participated in the Western New York Exposures and Breast Cancer Study between 1996 and 2001. Lignan intake was calculated based on responses to a questionnaire that charted intake of over 100 foods.

The study found that dietary lignan intake had no relevance among premenopausal women with breast cancer. However, in postmenopausal women, those with a high lignan intake were 70% less likely to die from breast cancer.

"This study suggests that certain fruits and vegetables may offer more protection than others," said McCann. "Postmenopausal women diagnosed with breast cancer who reported high intakes of lignans, which in this study were supplied mostly by dark bread, peaches, broccoli, oranges, winter squash, strawberries, coffee and tea, had a statistically significant reduction in death rates."

Lung Cancer:

SCLC Requires Further Research, Editorial Says

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ineffective and highly toxic," the authors wrote. "As a result, this strategy should be abandoned."

In an accompanying editorial, Paul Bunn Jr., director of the University of Colorado Cancer Center, agrees with that assessment and emphasizes that other avenues of therapy should now be explored. "The declining incidence of SCLC and the lack of progress seem to have dampened the enthusiasm of funding agencies and industry for exploring novel therapies. This is indeed unfortunate because SCLC remains a common cancer in both the developed and developing world," Bunn wrote.

FOLFOX4 Improved PFS In Colorectal Cancer

Results of the randomized phase III EORTC 40983 Intergroup study published in the March 22 issue of The Lancet showed that in eligible patients Eloxatin (oxaliplatin injection) in combination with 5-fluorouracil/leucovorin (5-FU/LV), a chemotherapy regimen called FOLFOX4, significantly improved three-year progression-free survival compared to surgery alone when given perioperatively (before and after surgery) to colorectal cancer patients with initially resectable liver metastases.

PFS is the time from randomization until disease progression/recurrence or death. The EORTC 40983 Intergroup study is also referred to as the EPOC (Eloxatin for Peri-Operative Use) trial.

Among the 342 eligible patients treated in the EPOC study, perioperative FOLFOX4 chemotherapy and surgery significantly improved PFS by 8.1% (from 28.1% to 36.2%) versus surgery alone (Hazard Ratio (HR) of 0.77; Confidence Interval (CI): 0.60-1.00; p=0.041). Among patients who were also able to undergo resection of the liver metastases, post-entry (n=303),

perioperative FOLFOX4 significantly improved PFS by 9.2% (from 33.2% to 42.4%) compared with surgery alone (HR=0.73 (CI: 0.55-0.97, p=0.025)).

"Seventy-five percent of patients relapse after liver metastases have been surgically removed. We found that the investigational use of perioperative FOLFOX4 reduces the risk of relapse by one fourth over surgery alone," said principal investigator Bernard Nordlinger, past chairman of the EORTC GI group, chair of the Department of Surgery and Oncology, Hospital Ambroise Pare, Assistance Publique-Hôpitaux de Paris, Boulogne, France. "EPOC is the first randomized phase III clinical trial to demonstrate three-year PFS of perioperative FOLFOX4 in eligible metastatic colorectal patients with initially resectable liver metastases. Perioperative chemotherapy was found compatible with major liver surgery with operative mortality of less than one percent in both treatment arms."

The most common adverse events seen with pre-operative FOLFOX4 include: neutropenia (Grade 3/4: 18.1%), diarrhea (Grade 3: 8.2%), stomatitis/pharingitis (Grade 3: 6.4%), leucopenia (Grade 3⁄4: 5.9%), other neurological toxicity (Grade 3: 5.8%), and nausea (Grade 3: 3.5%). The most common adverse events seen with post-operative chemotherapy include: neutropenia (Grade 3/4: 34.8%), leucopenia (Grade 3: 12.2%), other neurological toxicity (Grade 3: 12.2%), sensory neuropathy (Grade 3: 9.6%), thrombocytopenia (Grade 3: 7.0%), infection (Grade 3: 6.0%), hepatic (Grade 3: 5.2%), diarrhea (Grade 3: 5.2%), allergy (Grade 3⁄4: 4.4%), nausea (Grade 3: 4.3%), dysesthesia (Grade 3: 4.3%), and febrile neutropenia (Grade 3: 3.5%). In both patient groups, operative mortality remained very low (<1%): two deaths occurred after surgery in the standard arm and one in the experimental arm. Reversible complications of surgery were more frequent among patients who had received chemotherapy before surgery.

The EPOC Study is a randomized multicenter phase III Intergroup study sponsored and conducted by the EORTC (European Organization for Research and Treatment of Cancer), in collaboration with AGITG (Australasian Gastro-Intestinal Trials Group), EORTC GITCG (EORTC Gastrointestinal Tract Cancer Group), ALM-CAO (Arbeitsgruppe Lebermetastasen und –tumoren in der Chirurgischen Arbeitsgemeinschaft Onkologie), CRUK (Cancer Research UK) and FFCD (Fédération de Cancérologie Digestive). The EPOC study was supported by sanofi-aventis.

The primary objective of the trial was to detect a 40% increase in median PFS or equivalently an increase of 3-year PFS from 21% to 32.8% in all patients randomized to perioperative chemotherapy, with 80% power and two-sided significance level of 5%, resulting in HR=0.71.

SGO Annual Meeting

BRCA Status Can Guide Ovarian Cancer Treatment

Two abstracts underscoring the importance of testing for BRCA1/2 mutations in women with ovarian cancer were presented at this week's Society of Gynecologic Oncologists 39th Annual Meeting on Women's Cancers, by researchers from The University of Texas M. D. Anderson Cancer Center.

In the first study, a multicenter research team led by M. D. Anderson found advanced- stage ovarian cancer patients with non-Ashkenazi Jewish BRCA (non-AJ BRCA) mutations experience longer progression-free and overall survival rates compared to those with sporadic ovarian cancer. The data confirms previous research which reported that among ovarian cancer patients of Ashkenazi-Jewish heritage, BRCA1/2 mutations (AJ BRCA) are associated improved long-term survival.

For this study, researchers examined 85 advanced-stage ovarian cancer patients with non-AJ BRCA mutations and 116 patients who did not express any type of BRCA mutation. Compared to patients without BRCA mutations, non-AJ BRCA carriers had longer progression-free survival of 19.0 vs. 27.8 months and improved overall survival of 65.6 vs. 101.4 months. Non-AJ BRCA patients had a 2.15 times greater odds of complete response to initial chemotherapy response over sporadic, non-carrier patients.

Karen Lu, associate professor in the Department of Gynecologic Oncology at M. D. Anderson and senior author on the study said the difference in survival rates indicate that individuals with BRCA mutations might respond better to standard chemotherapy for ovarian cancer. "Thus, it becomes increasingly valuable to know a patient's BRCA status to guide and personalize treatment decisions," Lu said.

A second study conducted at M. D. Anderson concluded that, despite being available for more than 10 years, a majority of women with ovarian cancer were unaware genetic counseling and testing for BRCA1/2 mutations was an option. Of the 225 ovarian cancer patients surveyed, 56 percent had not heard of BRCA testing. This lack of awareness was more profound in minorities—69 percent of Hispanic and 88 percent of African American respondents were unaware of BRCA

testing compared to 52 percent of white women.

"Both of these studies illustrate that it is equally important for the cancer patient to get information from their doctors about genetic testing, because it not only has implications for their family, but their own treatment and prognosis," Lu said.

She said that more than 85 percent of ovarian cancer patients surveyed would be willing to undergo BRCA testing if it would affect their care, but the cost of testing may be a barrier. "Currently, oncologists are inconsistent in their testing for BRCA mutations. Based on the treatment implications of our findings and the surprisingly low knowledge that such testing is available, we recommend developing ways to systematically evaluate every ovarian cancer patient for BRCA," Lu said.

A family history of breast and/or ovarian cancer is reported in approximately five percent to 15 percent of ovarian cancer cases, with BRCA1/2 mutations expressed in a significant proportion of these cases.

Cancer Disparities:
Not All Women Benefitting From Less Invasive Staging

A study from the American Cancer Society finds racial, economic, and age disparities in the use of a less invasive technique to help determine if breast cancer has spread.

The study, published online March 25 in the Journal of the National Cancer Institute, finds women who are non-white, older, come from lower income areas, are uninsured, or have less education are less likely to receive sentinel lymph node biopsy compared to women who are white, younger, or from a more affluent areas.

Determining whether breast cancer has spread into neighboring lymph nodes is a key prognostic indicator for the disease. In 1998, clinical care guidelines were broadened to include the use of SLNB, which is associated with easier recovery and fewer long-term problems that the previously used method, called axillary lymph node dissection.

Using the National Cancer Database, ACS researchers led by Amy Chen looked at the use of the tests among 490,899 women who underwent breast cancer surgery with early stage disease, for which SLNB would be appropriate, between 1998 and 2005.

The researchers found the proportion of patients who underwent SLNB more than doubled over the time period, from about one in four (26.8 percent) in 1998 to two in three (65.5 percent) in 2005. But while the use of SLNB increased overall, gaps associated with sociodemographic characteristics, like age, race, median income, and insurance status, actually increased during the time period.

"[E]ven though the rate of SLNB increased substantially over the study period, our results indicate that the disparities in receipt of SLNB, including among racial/ethnic minority groups and those with lower socioeconomic status (i.e., type of insurance) appear to have increased over time," the authors wrote.

Although use of SLNB increased over time in all types of hospitals, current clinical guidelines recommend that SLNB should be performed in facilities where there are experienced teams. Data were not available to assess whether disparities in SLNB use were related to clustering of women of ethnic minority and lower SES to hospitals with lack of SLNB experience.

Cancer Statistics

In a related development, a separate ACS study found that while breast cancer death rates are decreasing for white women in every state, for African American women, death rates are either flat or rising in at least half the states.

The study, published online in the journal Cancer Causes and Control, finds breast cancer death rates among African American women are decreasing in only 11 of 37 states with sufficient numbers for analysis and in the District of Columbia. In the rest, death rates are either flat (24 states) or increasing (two states: Arkansas and Mississippi).

ACS researchers led by Carol DeSantis analyzed mortality data from the National Center for Health Statistics for 1975 through 2004 by state and race. At the national level, death rates began to decline in 1990 for white women and in 1991 for African American women. But they decreased far slower in African American women. As a result, the gap in death rates from breast cancer between African American and white women has increased substantially. In 1991, death rates among African American women were 18 percent higher compared to white women; by 2004, they were 36 percent higher.

Although breast cancer death rates have decreased in both African American and white women in the U.S. as a whole, the study found death rates have increased or remained level for African American women in 26 states. Access to and utilization of screening as well as regional variations in the quality and timeliness of treatment likely play important roles in the disparity, write the authors, and states should focus their cancer

control efforts to increase health awareness within underserved communities and to ensure that all women have access to high-quality early detection and treatment services.

"We've known for some time that these disparities exist," said Otis Brawley, ACS chief medical officer. "This new study helps us drill down to identify pockets of need. We need to ensure that we level the playing field for all women regardless of race, income level, or where they live."

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 I

Phase I Study of Bortezomib and Cetuximab without or with Cisplatin in Patients with Advanced Head and Neck Cancer. Radiation Oncology Branch, NCI, protocol 7893, Van Waes, Carter, phone 301-402-4216.

Phase I/II

Phase I/II Trial of PTC299 in Patients with HIV-Related Kaposi's Sarcoma. AIDS-Associated Malignancies Clinical Trials Consortium, protocol AMC-059, Krown, Susan, phone 212-639-7426.

Phase II

Phase II Trial of Intravenous Administration of Reovirus Serotype 3 - Dearing Strain (ReolysinÆ) in Patients with Metastatic Melanoma. Mayo Clinic Rochester, protocol 7848, Galanis, Evanthia, phone 507-284-2511.

Phase II Study of IMC-A12 in Hepatocellular Carcinoma. Sloan-kettering Cancer Center, protocol 8124, Abou-Alfa, Ghassan, phone 212-639-3112.

Phase II Pilot Study of Bortezomib(PS-341, Velcade) Combined with Reinduction Chemotherapy in Children and Young Adults with Recurrent, Refractory or Secondary Acute Myeloid Leukemia. COG Phase I Consortium, protocol AAML07P1, Moscow, Jeffrey, phone 859-323-1436.

Group-Wide Double-Blind Randomized Placebo-Controlled Trial of Palifermin to Prevent Chemotherapy and/or Radiotherapy Induced Oral Mucositis in Children Undergoing Autologous or Allogeneic Hematopoietic Stem Cell Transplantation. Children's Oncology Group, protocol COG-ACCL0521, Sung, Lillian, phone 416-813-5287.

Phase II Trial of Azacitidine Plus Gemtuzumab Ozogamicin as Induction and Post-Remission Therapy in Patients of Age 60 and Older with Previously Untreated Non-M3 Acute Myeloid Leukemia. Southwest Oncology Group, protocol SO703, Nand, Sucha, phone 708-327-3182.

Phase III

Phase III Randomized, Double-Blind Study of Induction(Daunorubicin/Cytarabine) and Consolidation (High-Dose Cytarabine) Chemotherapy + Midostaurin (PKC412) or Placebo in Newly Diagnosed Patients < 60 Years of Age with FLT3 Mutated Acute Myeloid Leukemia. Cancer and Leukemia Group B, protocol CALGB-10603, Stone, Richard, phone 617-632-2214.

Study of the Effect of Vitamin E and/or Selenium on Adenomatous Colorectal Polyps in Participants Enrolled in Select. Southwest Oncology Group, protocol SOOOOD, Coltman, Charles, phone 210-677-8808.

Other

Molecular Mechanisms of OSCC Tumor. American College of Surgeons Oncology Trials Group, protocol Other ACOSOG-Z3081, Ziober, Barry, phone 610-329-7963.

Angiogenesis Pathway Gene Polymorphisms Associated with Clinical Outcome in Patients Enrolled in ECOG 4599. Eastern Cooperative Oncology Group, protocol E4599T1, Lenz, Heinz-Josef, phone 323-865-3967.

Development of a Serum Proteomic Classifier for the Prediction of Benefit from Bevacizumab in Combination with Carboplatin and Paclitaxel. Eastern Cooperative Oncology Group, protocol E4599T2, Carbone, David, phone 615-936-3321.

Phase II/III Study Comparing Acupuncture-like Transcutaneous Electrical Nerve Stimulation Versus Pilocarpine in Treating Early Radiation-Induced Xerostomia. Radiation Therapy Oncology Group, protocol RTOG 0537, Curran, Walter, phone 215-955-6700.

Pilot

Companion Protocol to Evaluate Anogenital Human Papillomavirus Infection and Anogenital Squamous Intraepithelial Lesions in Subjects Participating in AMC Clinical Trials. AIDS-Associated Malignancies Clinical Trials Consortium, protocol AMC-058, Berry, J., phone 415-353-7443.