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THE
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Cancer research news for clinicians

American Society of Clinical Oncology:

Large, Conclusive Trials Provide Answers To Treatment Questions For GI Cancers

The findings from several large clinical trials of new treatment regimens for gastrointestinal cancers were released at the American Society of Clinical Oncology annual meeting in Orlando earlier this month.

"The studies presented today answer many important questions about the best care for people with gastrointestinal cancers," said Nicholas Petrelli, medical director of the Helen F. Graham Cancer Center in Wilmington, Del. "These large, conclusive trials tell us what works, and importantly, tell us

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Lung Cancer:

Large Studies Show Promising Results For Targeted Therapies Alimta, Tarceva

The findings from several large studies on lung cancer were released at the American Society of Clinical Oncology annual meeting.

"Lung cancer is one of the most challenging cancers to treat, but the studies presented today highlight promising new targeted therapies and milder treatment regimens that improve survival," said Bruce Johnson, director of the Dana-Farber Harvard Medical Center Lung Cancer Program. "Researchers also report that hormone therapy among menopausal women with lung cancer is associated with a higher risk of death. These findings add to growing concerns about the safety of hormone therapy."

Studies highlighted include:

Pemetrexed Improves Overall Survival

An international, multi-institutional study finds that use of pemetrexed (Alimta) as maintenance therapy following standard treatment improves overall survival for patients with advanced non-small cell lung cancer; the study also further confirms that this benefit is primarily limited to those with the nonsquamous subtype.

The efficacy, tolerability and ease of administration provided a strong rationale for evaluating pemetrexed as maintenance therapy in patients with advanced non-small cell lung cancer whose cancer had not progressed following four cycles of platinum-based chemotherapy. The drug was given on an ongoing basis until patients' disease progressed.

"This study will change the overall standard of care," said Chandra Belani, deputy director of the Penn State Cancer Institute and the study's lead

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Avastin Didn't Improve DFS In Randomized Phase III Trial

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what doesn't work. Some settle long-time debates in the field, others demonstrate that the current standard of care is actually superior to experimental treatments, and others will allow patients to avoid unnecessary side effects or surgery."

Studies highlighted include:

Bevacizumab Doesn't Improve DFS

The results of a randomized, phase III trial have found that adding bevacizumab (Avastin) to standard adjuvant chemotherapy did not improve disease-free survival (the time that patients are free of tumor recurrence) in early-stage colon cancer.

This was the first study to report results on the use of bevacizumab as an adjuvant treatment. The antibody, which targets the vascular endothelial growth factor (VEGF) receptor, is currently approved for metastatic colorectal, breast, and lung cancers, and other trials are ongoing to evaluate it as an adjuvant treatment for a variety of solid tumors.

The current study enrolled 2,710 patients who were randomized to receive six months of standard adjuvant chemotherapy or six months of adjuvant chemotherapy combined with bevacizumab plus an additional six months of bevacizumab after the chemotherapy had ended. All patients in the study had stage II or stage III disease and first had surgery to remove their tumors. After a median follow-up of three years, the investigators found that 77.4 percent of patients in the experimental group (bevacizumab) were alive and free of disease, compared with 75.5 percent of patients in the control group, a difference that was not statistically significant. There were no unexpected side effects in either arm and the toxicities from bevacizumab were well tolerated.

"One interesting effect was that during the year that patients were receiving bevacizumab we saw a benefit in disease-free survival that subsequently diminished when follow-up was completed," said Norman Wolmark, chairman of the Department of Human Oncology at Allegheny General Hospital and the study's lead author. "Our overall conclusion is that bevacizumab was not effective as an adjuvant treatment for early-stage colon cancer, but the transient benefit we saw in patients who received bevacizumab illustrates that we have more to learn about how this reagent works, and we need to design more clinical trials to determine how it can be used most effectively."

The trial was conducted by the National Surgical Adjuvant Breast and Bowel Project, chaired by Wolmark, and was funded by the National Cancer Institute.

Surgery Unnecessary For Some Patients

New research shows that patients who are newly diagnosed with metastatic, surgically incurable colorectal cancer do not need immediate surgery to remove their primary tumor unless the tumor is causing complications.

Surgical removal of the primary tumor at the time of diagnosis was once standard practice and is still common in patients with metastatic colorectal cancer. Because cancer has already spread to other parts of the body by this stage, the purpose of this surgery is not to extend survival, but to prevent future complications, such as intestinal blockage, perforation of the bowel, and severe bleeding. However, over the past decade several new effective chemotherapy drugs for colorectal cancer have been introduced and until now there has been little data to assess whether this pre-emptive surgery is still warranted.

"In this era of modern chemotherapy, routine surgery to remove the primary tumor in patients with unresectable metastases is no longer supported by the data," said Philip Paty, an attending surgeon and vice chairman of clinical research at Memorial Sloan-Kettering Cancer Center and the study's senior author. "In addition to being an unnecessary procedure that carries its own risks of morbidity and mortality, surgery

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delays the start of chemotherapy for several weeks, and in some cases may make the patient less fit for and less tolerant of chemotherapy. Unless there is an immediate need for surgery, patients should begin chemotherapy first."

This retrospective study identified 233 consecutive patients who presented with metastatic colorectal cancer between 2000 and 2006, and were treated with chemotherapy at MSKCC, but had no serious symptoms to prompt immediate surgery. The patients received one of three triple-drug chemotherapy combinations as their initial treatment (the regimens known as FOLFOX, IFL, and FOLFIRI). Some were also treated with the targeted therapy bevacizumab (Avastin).

Investigators determined that 93 percent of patients never developed complications that required removal of their tumor. For the 7 percent who did eventually need surgery, the vast majority (14/16) had successful operations. In addition, the mortality attributable to surgery was very low (0.8 percent), suggesting that this approach, by avoiding unnecessary surgery, improves the overall safety of treatment.

No Survival Difference In Pancreatic Cancer

The results of an international, multicenter study reports no difference in survival between the adjuvant chemotherapy regimens gemcitabine (Gemzar) and 5-fluorouracil/folinic acid (5-FU/FA) when given after surgery for pancreatic cancer, though gemcitabine was associated with fewer side effects.

5-FU/FA is the current standard adjuvant treatment for pancreatic cancer in parts of Europe, whereas gemcitabine alone or in combination with radiation therapy is more commonly used in the United States. It has not been clear until now whether one was superior. Gemcitabine is also considered the standard treatment in patients with metastatic and locally advanced, inoperable pancreatic cancer. This is the first study to directly compare the two treatments in the adjuvant setting.

In this phase III trial, 1,088 patients were randomized to receive one of the two treatments after surgery. All patients had histologically confirmed disease, 72 percent with metastases to lymph nodes and 35 percent with microscopically involved resected tumor margins. After a median follow up of 34 months, the investigators found that the median overall survival of patients treated with 5-FU/FA was 23 months, compared with 23.6 months in patients treated with gemcitabine. However, patients who received 5-FU/FA reported more toxicities, compared to those treated with gemcitabine, including: grade 3/4 toxicity stomatitis, or inflammation in the mouth (10 percent in the 5-FU/FA group; none in the gemcitabine group); diarrhea (13 percent and 2 percent of patients, respectively); and treatment-related hospitalizations (10 percent and 3.5 percent, respectively).

"This study is important because it shows no difference between these treatments in prolonging survival," said John Neoptolemos, head of the Division of Surgery and Oncology at the University of Liverpool and the lead author of the study, known as ESPAC-3. "On the basis of the safety profile, however, this trial shows that gemcitabine is likely to be the preferred adjuvant therapy. We are now also looking at combining the two treatments to see if we get a better response, because the drugs have different mechanisms of action."

Anal Cancer Standard of Care

Findings from the largest trial ever conducted for anal cancer have shown that the current standard of care, using a novel, continuous radiation therapy delivery program combined with 5-fluorouracil (5-FU) and mitomycin-C chemotherapy, results in the best outcomes so far reported for patients with anal cancer, and that cisplatin chemotherapy is not superior to mitomycin-C. The study also showed no evidence of a benefit of adding maintenance chemotherapy to the standard of care.

Anal cancer is rare, with about 5,000 patients diagnosed in the United States each year. Unlike colorectal cancer, the majority of patients with anal cancer do not need surgery, largely because the tumors are the squamous cell type, which are very responsive to chemotherapy and radiation. Cisplatin is commonly used for other squamous cell cancers, but it is less convenient to deliver and is known to have different toxicities from mitomycin-C, such as neurological and renal side effects and hearing loss.

The current study, called ACT II, conducted by the National Cancer Research Institute in the United Kingdom, and funded by Cancer Research UK, randomized 940 patients to receive radiation therapy given at the same time as 5FU with either mitomycin-C or cisplatin. Patients were also randomized to receive follow-up maintenance therapy with cisplatin and 5-FU after chemoradiation or no maintenance therapy.

After a median follow-up of three years, the investigators found no significant difference in outcome in the two randomized comparisons:

The complete response rate at 6 months (the number of patients who had all signs of their cancer disappear) was 94 percent in the mitomycin-C group

compared with 95 percent in the cisplatin group.

Recurrence-free survival at 3 years (the number of patients whose tumors did not return) was 75 percent both in patients who got maintenance therapy and in those who did not.

Overall survival at 3 years was 85 percent in patients who received maintenance therapy and 84 percent in those who did not.

"These findings are good news in spite of the lack of evidence for an improvement in giving either cisplatin or maintenance therapy, since the standard chemoradiation schedule given in this trial was highly effective," said Roger James, a radiation oncologist from Maidstone Hospital, Kent, and the study's lead author. "Although this trial did not show an improvement from adding maintenance therapy, some form of additional treatment will be the subject of future studies, to determine whether some subset of patients might benefit from it."

Oxaliplatin Doesn't Improve Local Response

A large, multicenter Italian study has found that adding oxaliplatin (Eloxatin) to standard preoperative radiochemotherapy in patients with locally advanced rectal cancer does not improve tumor shrinkage. However, preliminary and exploratory data suggest that it may reduce the number of distant metastases.

Chemotherapy and radiation are often administered before surgery for rectal cancer to shrink the tumor and make it easier to remove. Previous results from this study showed that although adding oxaliplatin to standard chemotherapy increased some side effects, especially diarrhea, it did not affect the ability to deliver the full course of radiation therapy or to perform surgery. Oxaliplatin has been found effective and is commonly used in patients with more advanced colon and rectal cancer.

In this phase III trial, 747 patients with locally advanced rectal cancer were randomized to receive standard preoperative chemoradiotherapy or the standard plus oxaliplatin. Researchers found no significant difference between the two groups in terms of tumor reduction: 16 percent of patients in both groups had no tumor present at the time of surgery, and 29 percent in the oxaliplatin group had mildly invasive tumors (T1 or T2) without nodal involvement, compared with 30 percent in the control group. There was also no significant difference in the number of patients who had cancer in the lymph nodes (27 percent in the oxaliplatin group versus 25 percent in the control group). Consistently, the proportions of patients who could have conservative surgery were similar between the two arms.

In an unplanned analysis, when looking at intra-abdominal disease spread at the time of surgical removal of the primary tumor, only 0.5 percent of patients in the oxaliplatin group (2 patients) had distant metastases, versus 3 percent in the control group (11 patients), a difference that was statistically significant.

"Although adding oxaliplatin to the current standard of care did not improve tumor response rates, we found this course of treatment was associated with a reduced number of early distant metastases in the abdomen in a very small number of patients," said Carlo Aschele, attending physician and lead clinician in Colorectal/Gastrointestinal Cancer in the Department of Medical Oncology and Cancer Prevention at E.O. Ospedali Galliera in Genoa, Italy, and the study's first author. "Although the numbers are very small and the analysis of distant metastases was unplanned and exploratory, the difference is significant and indicates that the lack of an effect on local tumor shrinkage does not necessarily imply a lack of effect on micrometastases at distant sites. Longer follow-up is necessary to assess whether treatment with oxaliplatin will have an effect on recurrence rates or survival."

Lung Cancer:
Maintenance With Alimta Offers Survival Advantage

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author. "Maintenance therapy with pemetrexed offers a new paradigm for patients who have advanced lung cancer, because it has a low toxicity and can be given on an ongoing basis over a prolonged period of time to extend patients' lives."

Pemetrexed is currently approved as a first-line treatment for advanced nonsquamous non-small cell lung cancer in combination with the chemotherapy agent cisplatin and as a single agent in patients with recurrent disease. Preliminary results of the current study presented at the 2008 ASCO annual meeting had demonstrated that maintenance therapy with pemetrexed delayed disease progression, but this is the first time a significant improvement in overall survival has been shown in this setting.

In this randomized, double-blind, phase III study, patients were given either pemetrexed (441 patients) or placebo (222 patients), along with the best supportive care. All patients had advanced or metastatic (stage 3B or 4) NSCLC (both squamous and nonsquamous subtypes) that had not progressed after four cycles of

platinum-based chemotherapy.

Patients who received pemetrexed had an overall survival of 13.4 months, versus 10.6 months for patients in the placebo group. For the nonsquamous subgroup (482 patients), overall survival was 15.5 months for patients on pemetrexed, versus 10.3 months for patients on placebo. Patients with the squamous subtype do not seem to benefit with pemetrexed, confirming what has been shown in other studies. Researchers suspect the possible mechanism for this difference in effectiveness may be related to the expression of biomarkers such as thymidylate synthetase, which has been shown to correlate with sensitivity to pemetrexed.

Severe (grade 3 or 4) side effects were low but more common in the pemetrexed group, specifically fatigue (five percent in the pemetrexed group, versus 0.5 percent in the placebo group) and low white blood cell counts (2.9 percent versus 0 percent). Side effects did not increase for patients who received pemetrexed for a longer period of time, and there were no drug-related deaths.

Erlotinib Improves Outcomes

An international team of researchers has shown that adding erlotinib (Tarceva) to bevacizumab (Avastin) maintenance therapy after initial treatment with chemotherapy and bevacizumab in patients with advanced non-small cell lung cancer delays disease progression better than bevacizumab alone.

"There is ongoing interest among medical oncologists about the potential role of maintenance therapy for patients with advanced non-small cell lung cancer," said Vincent Miller, associate attending physician on the Thoracic Oncology Service at Memorial Sloan-Kettering Cancer Center and lead author of the study, known as ATLAS. "Bevacizumab is a core component of the treatment of advanced non-small cell lung cancer, and we've shown here we can delay progression with the addition of a targeted agent, erlotinib. Critical future work will try to determine which patients will get the greatest benefit from this combination, based in large part on the identification of genetic biomarkers."

Maintenance therapy, a relatively new concept in NSCLC, refers to the continuation of one or more agents of a chemotherapy regimen but not the whole regimen to delay progression of disease and potentially improve survival after patients have received several months of stronger standard chemotherapy, which can carry significant side effects. This is the first study to show that adding erlotinib to maintenance therapy with bevacizumab delays disease progression in patients who have already received bevacizumab as part of their initial chemotherapy. Both bevacizumab and erlotinib have fewer side effects than traditional cytotoxic chemotherapy.

Previous research has shown that bevacizumab along with chemotherapy improved progression-free and overall survival among patients with advanced, metastatic, or recurrent non-squamous NSCLC when compared to chemotherapy alone. In that study, bevacizumab was continued after chemotherapy until disease progression. The purpose of the current study was to determine if progression could be further delayed by the addition of erlotinib.

In this randomized, double-blind, phase III trial, 768 patients were randomized to receive bevacizumab plus erlotinib or bevacizumab plus placebo. All patients had already received four cycles of chemotherapy and bevacizumab as first-line therapy. Patients who had not progressed then continued bevacizumab and were blinded and randomized to receive placebo or erlotinib.

This study reports the results of the trial's second planned interim analysis of the data, which identified a statistically significant improvement in efficacy, favoring the erlotinib group; the trial was stopped early based on these findings. Patients in the erlotinib group experienced a 29 percent reduced risk of disease progression. Median progression-free survival (the time it took for the cancer to get worse) was 4.8 months for patients in the erlotinib plus bevacizumab group, compared with 3.7 months for patients in the bevacizumab-placebo group. There were no unexpected side effects in either arm.

HRT Linked to Increased Death from NSCLC

Researchers have shown that use of hormone therapy with estrogen plus progestin increases the risk of dying from non-small cell lung cancer in women with the disease. Lung cancer is the leading cause of cancer death in U.S. women.

These findings are based on secondary analyses from the Women's Health Initiative, a randomized, placebo-controlled clinical trial evaluating the health effects of conjugated equine estrogen (CEE) plus medroxyprogesterone acetate (MPA) in 16,608 mostly healthy postmenopausal women.

Previous research suggested that hormones play a role in non-small cell lung cancer because women tend to have higher survival rates than men and respond better to certain therapies. However, this is the first study to

examine a specific correlation in a randomized clinical trial setting.

"Many women entering menopause have symptoms that make them consider hormone therapy," said Rowan Chlebowski, a medical oncologist at the Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center and the study's lead author. "We already know that combined hormone therapy has more risks than benefits, including a higher risk of stroke and breast cancer, the most common cancer in U.S. women. The link we describe between hormone therapy with CEE plus MPA and death from non-small cell lung cancer should influence discussions between physicians and women considering hormone therapy use, especially for those with a smoking history."

This study looked at non-small cell lung cancer incidence and mortality during 5.6 years of intervention with hormone therapy or placebo and 2.4 years of additional follow-up. While there was no significant difference in NSCLC incidence between the two randomized groups, mortality after a NSCLC diagnosis was significantly higher in the combined hormone therapy group: women in the hormone therapy group were 61 percent more likely to die from non-small cell lung cancer than women in the placebo group (67 versus 39 deaths, respectively).

The researchers said the magnitude of the mortality risk of CEE plus MPA use in current smokers raises particular concerns. One in 100 current smokers in the trial using combined hormone therapy experienced an avoidable death from non-cell lung cancer during the eight years of this study. The mortality rate was 3.4 percent among smokers in the hormone therapy group, versus 2.3 percent among smokers in the placebo group over the 7.9 year study period.

Researchers noted that study strengths include the randomized, double-blind study design and the large, ethnically diverse population; limitations include the secondary nature of the analyses as these findings were not a primary objective of the trial. The researchers suspect their finding will prompt reconsideration of the risk-to-benefit balance of combined hormone therapy use for menopause symptoms and prompt further studies, both preclinical and clinical, on hormonal effects in NSCLC.

Vandetanib Improves PFS in NSCLC

The results of an international trial have shown that adding the experimental targeted therapy vandetanib (Zactima) to docetaxel improves progression-free survival in patients with advanced non-small cell lung cancer whose disease has progressed after first-line treatment. This is the first phase III study to show that adding a targeted therapy to second-line chemotherapy with docetaxel results in a clinical benefit for patients with advanced NSCLC. It is also the first phase III trial of vandetanib for NSCLC, which is being evaluated for certain types of thyroid cancer as well.

Vandetanib is a pill that targets two receptors already known to play a role in NSCLC—epidermal growth factor receptor (EGFR) and vascular endothelial growth factor (VEGF). These receptors are targeted separately by other drugs, but vandetanib is the first drug to target both.

In this study, 1,391 patients who had previously been treated with chemotherapy were randomized to receive the docetaxel and vandetanib, or docetaxel and placebo. After a median follow-up of 12.8 months, patients in the vandetanib group had a 21 percent reduction in the risk of disease progression compared with patients in the placebo group. The median progression-free survival time was 17.3 weeks in the vandetanib arm versus 14 weeks in the control arm.

While there was no statistical difference in overall survival, a significant improvement in objective response rate was observed. Vandetanib treatment was also associated with an improvement in symptoms related to the underlying cancer and a 22 percent reduction in the risk that symptoms would worsen. For example, it took longer for patients in the vandetanib group to report that their disease symptoms, such as cough, weight loss, and difficulty breathing, had worsened.

Some side effects were more common in the vandetanib arm, including diarrhea (42 percent versus 33 percent in the placebo group), rash (42 percent versus 24 percent), and low white blood cell counts (32 percent versus 27 percent). Other side effects (nausea, vomiting, and anemia) were more common in the control group. About 22 percent of patients in the study discontinued vandetanib due to side effects, which is relatively low for a second-line therapy in advanced lung cancer.

"Clearly in a disease as heterogeneous as lung cancer the need to target multiple pathways has become clear—hence, this agent targeting two key pathways critical for NSCLC growth and metastasis is novel and could play a key role," said Roy Herbst, chief of thoracic medical oncology at the University of Texas M. D. Anderson Cancer Center and the study's lead author. "The fact that more patients had an improvement in the symptoms from their lung cancer suggests that the drug could be important for the future management of this disease."

Quality of Life:

Combination Skin Treatments Reduce Rash From Vectibix

Studies examining new approaches to improving the quality of life of people with cancer and cancer survivors were released at the ASCO annual meeting.

Treatments Reduce Severe Skin Rash

A randomized study has shown that giving patients a combination regimen consisting of moisturizers, sunscreen, topical corticosteroids and oral antibiotics before they receive panitumumab (Vectibix) reduces the incidence of a severe skin rash by more than half and has a significant impact on patients' quality of life, and decreases delays in receiving therapy, which could potentially impact cancer outcomes. Panitumumab belongs to a class of drugs known as epidermal growth factor receptor (EGFR) inhibitors.

About 90 percent of patients receiving panitumumab and up to 75 percent of those who take cetuximab (Erbitux) develop a significant acne-like rash that can lead to serious skin infections causing delays in treatment. The rash develops because these drugs target the epidermal growth factor receptor, which is found in very high amounts in the skin.

In this study, presented by Edith Mitchell, clinical professor of medicine and medical oncology at Thomas Jefferson University, skin toxicity was compared between 48 patients with metastatic colorectal cancer who were randomly assigned to receive prophylactic skin treatment (moisturizers, sunscreen, topical steroids and the antibiotic doxycycline) for six weeks starting 24 hours before panitumumab-based therapy and 47 patients whose skin was not treated until after the rash developed.

Twenty-nine percent of those in the prophylactic group experienced skin toxicity versus 62 percent of those in the delayed treatment group. Patients who received the prophylactic skin treatment also reported better quality of life because they felt better about their appearance and were more physically comfortable.

Cancer Surveillance Tests

A new report from the Childhood Cancer Survivors Study has found that too few survivors of childhood cancer are undergoing recommended screening for cancers of the breast, colon and skin, even though the treatments they received (particularly radiation therapy) may have elevated their risk of these cancers.

"We were surprised to find that many survivors of childhood cancer are not following surveillance guidelines that may detect new cancers during their earlier, more curable stages," said Paul Nathan, staff oncologist at the Hospital for Sick Children in Toronto and the study's lead author. "Many of these survivors are seen by their family physicians, who may not have full knowledge of the recommended surveillance for childhood cancer survivors."

The Childhood Cancer Survivor Study is a long-term follow-up study funded by the National Cancer Institute. In this analysis, investigators surveyed cancer screening behaviors among 8,318 survivors who were originally diagnosed between 1970 and 1986, 2,661 of their siblings, and 8,318 controls from the 2003 National Health Interview Survey.

Many survivors of childhood cancer are at increased risk for a second cancer because of their treatment and should follow Children's Oncology Group guidelines (which vary significantly by treatment exposure, but include recommendations for increased surveillance for breast, colon, and skin cancers based on risk). Among survivors at increased risk for a second cancer who should have been following these surveillance guidelines, only 11.5 percent of those for whom a colonoscopy was recommended had one within the last five years, 46.3 percent had a mammogram within the last two years, and 26.7 percent had ever had a complete skin exam (for skin cancer, the most common radiation-associated second cancer in survivors). High-risk patients were more likely to seek mammography or a skin exam if they were receiving their routine medical care at a cancer center.

Fertility Preservation Guidelines Not Followed

A national survey of oncologists has found that while most report discussing fertility preservation with patients of childbearing age, only a quarter of them are referring patients to reproductive specialists or distributing educational materials, and most were unaware of current guidelines regarding fertility preservation for people with cancer.

"Discussing fertility preservation should be something else that we do early in a patient's care, rather than waiting until infertility occurs," said lead author Gwendolyn Quinn, associate member at the H. Lee Moffitt Cancer Center and Research Institute.

In 2006, ASCO issued guidelines recommending that oncologists address the risks of infertility with patients treated during their reproductive years and be prepared to discuss fertility preservation options (such as sperm and embryo cryopreservation) or refer appropriate

and interested patients to reproductive specialists.

The survey was distributed to 1,979 oncologists and 613 completed it (a 33 percent response rate). Among oncologists completing the survey, 79 percent reported that they address fertility issues with their patients of childbearing age—though Quinn said such discussions vary widely. Gynecological or medical/hematological oncologists were 2.1 times more likely than other specialists to report feeling comfortable discussing fertility preservation with their patients.

Less than 25 percent of physicians reported referring a patient to a fertility specialist or distributing educational materials. Many physicians said they did not discuss fertility preservation because they believed that the patient had a poor prognosis. Only 38 percent said they were aware of ASCO's guidelines.

Partial Breast Irradiation for Early-Stage Cancer

A meta-analysis of data from three clinical trials shows that partial breast irradiation may offer the same benefits in terms of overall survival and reduction of metastases as conventional whole-breast radiation therapy for early-stage breast cancer. Investigators noted that several additional randomized studies are underway and no recommendations about this approach can be made until they are complete.

"Although more research is necessary, this study suggests that partial breast irradiation may be safe and feasible for women with early-stage breast cancer because it does not jeopardize patient survival or increase the risk of metastasis," said lead author Antonis Valachis, associate breast cancer researcher at the Panhellenic Association for Continual Medical Research in Greece. "Partial breast irradiation reduces treatment time and radiation exposure to normal tissue, may improve cosmetic results, and is likely to enhance patients' ability to comply with therapy."

Valachis evaluated data on 1,140 women in three clinical trials comparing partial breast irradiation and traditional whole-breast radiation therapy. There were no significant differences in overall survival or the development of metastases between the two groups. Women who received partial breast irradiation were twice as likely to have a recurrence in the same breast as the primary tumor and three times more likely to develop cancer in the underarm lymph nodes. These recurrences had no affect on overall survival, however.

The researchers cautioned that partial breast irradiation will continue to be considered investigational until the results of additional, ongoing clinical trials can be analyzed.

NCI Cooperative Group Clinical Trials Approved

The National Cancer Institute Cancer Therapy Evaluation Program approved the following clinical research studies last month. For further information, contact the principal investigator listed.

Phase I/II

8297 A Phase 1/2 Study of Vorinostat (ZolinzaÆ) in Combination with Gemtuzumab Ozogamicin and Azacitidine in Patients 50 Years of Age and Older with Relapsed/Refractory non-APL Acute Myeloid Leukemia. Fred Hutchinson Cancer Research Center, Walter, Roland Bruno (206) 667-3599.

8169 A Phase II Study of Suberoylanilide Hydroxamic Acid and Bortezomib in Advanced Soft Tissue Sarcomas. Mayo Clinic Rochester, Bailey, Howard H. (608)263-8624.

Phase II

8281 Phase II Clinical Trial of the MEK 1/2 Inhibitor AZD6244 in Cancers with BRAF Mutations Identified by Prospective Genotypic Analysis. Massachusetts General Hospital Cancer Center, Lawrence, Donald P. (617) 643-3614.

8300 A Broad Multi-Histology Phase II Study of Kinase Inhibitor R935788 (Fostamatinib Disodium) in Advanced Colorectal, Non-Small Cell Lung, Head and Neck, Hepatocellular and Renal Cell Carcinomas and Pheochromocytoma and Thyroid Tumors. National Cancer Institute Medicine Branch, Kummar, Shivaani (301) 435-5402.

GOG-0170N A Phase II Evaluation of a Urokinase-Derived Peptide (A6) (IND #64,298) in the Treatment of Persistent or Recurrent Epithelial Ovarian, Fallopian Tube, or Primary Peritoneal Carcinoma. Gynecologic Oncology Group, Gold, Michael Alan (615) 322-0093.

N0871 A Phase II Study of Carboplatin, Paclitaxel, and Everolimus in Previously Untreated Patients with Measurable Disease with Cancer of Unknown Primary. North Central Cancer Treatment Group, Goetz, Matthew P. (507) 284-2511.

Phase III

NSABP-B-45.1 Biobehavioral Mechanisms of Fatigue in Patients Treated on NSABP B-45: A Phase III Clinical Trial Comparing Adjuvant Sunitinib Malate to Placebo in Women with Residual Invasive Breast Cancer Following Neoadjuvant Chemotherapy. National Surgical Adjuvant Breast and Bowel Project, Wolmark, Norman (412) 330-4600.

Other

S8516, S8736, S9125, S9240, S9349A Pharmacogenomics of Oxidative Stress-Related Genes in Lymphoma. Southwest Oncology Group, Briehl, Margaret (520) 626-6827.