LEUKEMIA

Newly Diagnosed Chronic Myeloid Leukemia

After showing promise against advanced chronic myeloid leukemia (CML), this study shows that the drug STI-571 (also called imatinib mesylate) is also effective for patients newly diagnosed with the disease.

STI-571 is already approved for CML patients who no longer respond to interferon (until now, the standard treatment) and for patients in accelerated phase or in myeloid blast crisis (the two most serious stages of CML), before now nearly impossible to treat.

This was a phase III study, involving 1,106 people from 16 countries newly diagnosed with CML. Patients were randomly assigned to one of two groups. One group received STI-571, and the other interferon-based therapy.

The study results showed that six months after treatment:

- CML continued to progress in eight patients taking STI-571, but in 57 patients taking the interferon-based therapy.
- Of the patients taking STI-571, 75% had a significant decrease in the number of cancer cells in their bone marrow.
- Cancer cells had completely disappeared in 54%. Of patients given the standard therapy, 15% had a significant reduction in the number of cancer cells, and 3% experienced a complete disappearance of cancer cells.
- Only six patients treated with STI-571 entered blast crisis, compared to 26 patients who received the interferon-based therapy.

Less than 1% of people taking STI-571 experienced severe side effects. Nineteen percent (19%) of people treated with interferon could not tolerate the therapy and were switched to STI-571.

(Abstract #1)

WHAT DOES THIS MEAN FOR PATIENTS?

This trial is the first large trial to evaluate STI-571 in people newly diagnosed with CML. It is also the first to compare STI-571 directly to the standard therapy.

With these results, there is a new standard of care for people newly diagnosed with CML. STI-571 has been used to treat people with more advanced stages of CML, and in rare stomach tumors called GIST. Now patients with CML can begin treatment with STI-571 right after diagnosis.

“Although the long-term results of STI-571 remain unknown, it should now be considered as standard therapy for newly diagnosed CML patients,” said Brian Druker, MD, of the Oregon Health & Science University, on behalf of the International Gleevec Study Group.

Less than 1% of people taking STI-571 experienced severe side effects. Nineteen percent (19%) of people treated with interferon could not tolerate the therapy and were switched to STI-571.

(Abstract #1)

This newsletter is designed to provide you with cancer research news from the 38th Annual Meeting of the American Society of Clinical Oncology, held May 18-21, 2002 in Orlando, Florida.

These articles feature some of the most important research presented at the meeting. Some treatments are not yet available to patients outside of a clinical trial, so you may want to talk to your doctor about clinical trials that offer these or other treatments.

At each ASCO meeting, research advances bring us closer to our goal: the eradication of cancer. We hope you find this newsletter helpful.

Abstract numbers are provided at the end of each article. Original scientific abstracts are available on ASCO’s website at www.asco.org.

Information in ASCO’s patient information materials is not intended as medical advice or as a substitute for the treating physician’s own professional judgment; nor does it imply ASCO endorsement of any product or company.
New Drug for Pleural Mesothelioma

In this study, people with pleural mesothelioma (cancer of the lining of the lung) lived longer and had less pain and shortness of breath if they received the new chemotherapy drug pemetrexed.

The phase III randomized study is the largest mesothelioma trial ever conducted, involving 456 patients. Patients were chosen at random to receive pemetrexed plus cisplatin (a common chemotherapy drug) or cisplatin alone.

Mesothelioma patients treated with pemetrexed plus cisplatin lived about a year after their diagnosis, nearly three months longer than patients who received only cisplatin.

The two-drug combination caused the cancer to shrink in 41% of patients, compared to 17% of patients who received only cisplatin.

The drug combination was also more effective at reducing pain and shortness of breath, symptoms commonly experienced by mesothelioma patients.

Shortly after the study began, many patients began having low levels of folic acid and vitamin B12. These patients who received pemetrexed were more likely to experience severe side effects (very low white blood cell counts, severe diarrhea, and severe mouth ulcers) than patients who received only cisplatin.

Following the observation, all patients in the study began receiving folic acid and vitamin B12. This reduced the side effects associated with pemetrexed, and more patients benefited from the drug.

Mesothelioma is most commonly caused by exposure to asbestos. Pemetrexed is a cousin of an early chemotherapy drug, methotrexate, used to treat other types of cancer. Methotrexate blocks one enzyme necessary for cell division and tumor growth, and pemetrexed blocks three such enzymes.

WHAT DOES THIS MEAN FOR PATIENTS?

Pemetrexed is the first drug shown to prolong the lives of people with mesothelioma. “The results are very encouraging and significant because mesothelioma patients and their families now have proof that this new chemotherapy drug offers real and tangible benefits,” said Nicholas J. Vogelzang, MD. Dr. Vogelzang is the Fred C. Buffett Professor and Director of the University of Chicago Cancer Research Center.

PROSTATE CANCER

PSA Test

This study suggested that annual PSA screening tests for prostate cancer might not be necessary for many men. Men whose initial tests show very low PSA levels may safely choose less frequent screening, once every five years in some cases.

Some organizations currently recommend that a PSA test be offered annually to men age 50 and older. The test detects blood levels of prostate-specific antigen. Higher than normal levels may indicate prostate cancer.

This study is part of the National Cancer Institute’s nationwide PLCO (prostate, lung, colorectal, ovarian) cancer screening trial. The PLCO trial is still ongoing. In this particular analysis, researchers followed 27,863 men ages 55-74 for five years. Of those men, 90% had initial PSA levels that were considered normal (less than 4 ng/ml). Based on the results, they predicted how many men would have PSA levels rising above normal in five years.

The researchers found that most men (98.8%) with extremely low initial PSA levels (under 1 ng/ml) would continue to have normal PSA tests over the next four years. Most men (98.8%) with PSA levels of 1-2 ng/ml would also have a normal PSA test the following year.

One question of the PLCO trial is if PSA screening improves survival in men with prostate cancer, and that question has not been answered yet. These are interim results and do not yet indicate if PSA screening itself improves survival.

WHAT DOES THIS MEAN FOR PATIENTS?

The researchers estimate that if men with a PSA below 1 ng/ml are screened once every five years and those with PSA levels of 1-2 ng/ml are screened every two years, only 2.6% of men would miss an earlier potentially positive test.

The researchers recommend that men with PSA levels of 2-4 ng/ml, should be followed more closely. They predict that 24% of this group’s PSA levels will become elevated within one year, and 83% rise within four years.

“We found that the vast majority of men whose initial PSA levels are very low do not need to worry that they would skyrocket within one year,” said E. David Crawford, MD, Senior Associate Director at the University of Colorado’s Health Sciences Center.
Surgery to Prevent Breast and Ovarian Cancer

Researchers have shown for the first time that women with mutations in BRCA1 and BRCA2 genes can reduce their risk of breast and ovarian cancers if they have surgery to remove their ovaries and fallopian tubes.

The study involved 173 women whose genetic tests showed mutations in the BRCA1 and BRCA2 genes. These mutations place women at higher risk for developing breast and ovarian cancer. The women received genetic counseling regarding their options, and chose a course of action. Of the group, 101 chose surgery to remove their ovaries and fallopian tubes (a procedure called salpingo-oophorectomy). The other 72 chose intensive screening: transvaginal ultrasound and a CA-125 blood test twice a year.

Compared to screening, surgery to remove the ovaries and fallopian tubes reduced the risk of breast and ovarian cancers by 75%.

After two years, three breast cancers and one peritoneal cancer were diagnosed in women who had preventive surgery. In the group of women who chose intensive screening, there were eight breast cancers, four ovarian cancers, and one peritoneal cancer.

Among the women who chose preventive surgery, doctors detected three unsuspected early-stage ovarian tumors during the operation. “This highlights the limitations of current screening tests for ovarian cancer,” said Richard Barakat, MD, Chief of Gynecologic Oncology at MSKCC, and a co-author of the study.

Removing the ovaries may also reduce breast cancer risk by decreasing estrogen and halting or slowing breast cancers that depend on estrogen to grow.

The researchers will continue to follow the women in the study to evaluate the long-term effects of preventive surgery on cancer rates, on other health risks, and on overall survival. (Abstract #3)

WHAT DOES THIS MEAN FOR PATIENTS?

Every woman with BRCA1 and BRCA2 mutations makes a highly individual decision with help from family, her doctors, and genetic counselors. These results are short-term, but suggest that women with these mutations may now have another option when making decisions.

“We now have prospective evidence to present to patients so that they can make informed decisions about their care,” said lead investigator Kenneth Offit, MD, Chief of the Clinical Genetics Service at Memorial Sloan-Kettering Cancer Center.

Women at high risk for breast and ovarian cancer should talk with their doctor.

LUNG CANCER

Combination Chemotherapy for Lung Cancer

Combination chemotherapy (more than one chemotherapy drug) is standard treatment for patients with advanced non-small cell lung cancer. But previous studies have not shown that it prolongs life compared to treatment with a single agent. This study shows that for some patients, combination chemotherapy offers a modest increase in survival compared to one chemotherapy drug.

In this phase III study, 584 patients were randomly assigned to two groups. People in one group received carboplatin plus paclitaxel, and the other received paclitaxel alone.

Patients who received carboplatin plus paclitaxel had a median survival of 8.5 months, compared to 6.5 months for paclitaxel alone. The one-year survival rates (36% for combination chemotherapy versus 31% for paclitaxel) were not statistically significant. There was no difference between the two treatments in their effects on patients’ quality of life.

Patients who could perform their daily activities with ease (higher performance status) were more likely to benefit from combination therapy. Patients over age 70 had similar outcomes in both groups. Patients with overall poor health (lower performance status) did not appear to benefit from either treatment.

More patients responded to the combination therapy (30%) than paclitaxel alone (16%). Patients who received the combination therapy were more likely to experience serious side effects such as anemia, low white blood cell counts, and low platelet counts. (Abstract #2)

WHAT DOES THIS MEAN FOR PATIENTS?

“Patients with non-small cell lung cancer who are otherwise in good health should be treated with combination chemotherapy,” said lead investigator Rogerio Lilenbaum, MD, Director, Thoracic Oncology Program, The Mount Sinai Comprehensive Cancer Center in Miami Beach.

Treatment for advanced non-small cell lung cancer should be decided individually, based on each patient’s age and overall health.
Advanced Colorectal Cancer

The new chemotherapy drug oxaliplatin delays tumor progression and extends the lives of patients with advanced colorectal cancer, according to this study.

Because the new drug (in combination with two other drugs) was significantly more effective than the standard therapy, the results of the trial were released earlier than planned.

Oxaliplatin is an experimental chemotherapy drug under review by the U.S. Food and Drug Administration. It is a platinum-based chemotherapy like the drugs cisplatin and carboplatin. It works by preventing DNA duplication, the process where genetic material is passed on to new cells. Earlier studies have shown that oxaliplatin can kill colon cancer cells that are resistant to other platinum-based drugs.

The study involved 795 patients from the U.S. and Canada. Patients were randomly assigned to one of three groups: one group received FOLFOX (oxaliplatin, 5-fluorouracil (5-FU) and leucovorin); one group received oxaliplatin plus irinotecan; and one received the standard therapy (irinotecan (CPT-11), 5-FU, and leucovorin).

The results:

1. More patients responded to FOLFOX (38%) than the standard therapy (29%).
2. Patients who received FOLFOX on average had no signs of tumor progression for nine months, compared to seven months for those on standard therapy.
3. People who received FOLFOX had fewer severe side effects, such as infections associated with low blood cell counts, diarrhea, hair loss, and vomiting.
4. People who received FOLFOX lived for a median of 18 months after beginning therapy, compared to 14 months for those who received the standard chemotherapy.
5. One year after beginning treatment, 70% of patients who received FOLFOX were still living, compared to 57% who received standard therapy. (Abstract #511)

WHAT DOES THIS MEAN FOR PATIENTS?

These results support adding the FOLFOX regimen as an option for advanced colorectal cancer patients. People interested in learning more about oxaliplatin should speak with their doctors.

“These results are an important step forward for patients with advanced colorectal cancer,” said lead investigator Richard M. Goldberg, MD. Dr. Goldberg is Professor of Oncology at the Mayo Clinic in Rochester, MN, and Coordinator of the North Central Cancer Treatment Group’s Gastrointestinal Cancer Program.

HEAD AND NECK CANCER

Radiation Therapy for Head and Neck Cancer

After surgery, people with head and neck cancer who receive a combination of radiation and chemotherapy do not have lower rates of local cancer recurrence or better survival, compared to patients who receive radiation alone, this study indicates.

The study involved 459 patients who had surgery to completely remove head and neck cancer and who were at high risk for cancer recurrence. They were randomly assigned to two groups: one received radiation alone, and the other received radiation plus the chemotherapy drug cisplatin.

Two years after treatment, the researchers found no significant difference in local cancer recurrence between the two groups. Cancer did not recur in 74% of patients who received radiation alone after surgery and in 79% who received a combination of chemotherapy and radiation. Patients who received the combination therapy experienced more nausea, vomiting, mouth soreness, and lower blood counts, all common side effects of chemotherapy.

The combination therapy did improve disease-free survival, but the difference between the two groups was not significant. Fifty-four percent (54%) of surviving patients treated with combination therapy remained free of disease after two years, compared to 43% who received radiation only. (Abstract #903)

WHAT DOES THIS MEAN FOR PATIENTS?

At this time, there is not a change in the standard of care for head and neck cancer patients after surgery. Radiation therapy alone is still the best known treatment for preventing recurrence after surgery.

“While further patient follow-up is needed and additional studies are warranted, we continue to recommend that patients receive the current standard of care – surgery followed by radiation alone,” said study investigator Arlene Forastiere, MD, Professor of Oncology at the Johns Hopkins Sidney Kimmel Cancer Center in Baltimore.
A treatment for acute myeloid leukemia (AML) that combines a monoclonal antibody with chemotherapy helps to improve patients’ response to therapy compared to chemotherapy alone, this study shows.

Patients in this phase III study had limited stage cancer (confined to one lung and nearby lymph nodes). They were treated with chemotherapy and radiation to the chest at the same time.

Smoking status was recorded for 186 patients in the study. Of this group, 79 smoked during treatment and 107 had quit smoking before treatment. Based on factors such as age, sex, and overall health, there were no significant differences between the two groups to account for the difference in outcomes.

Two years after therapy:
- Twenty-eight percent (28%) of non-smokers were still living, compared with 16% of smokers. At five years, nearly 9% of non-smokers were still alive, compared with 4% of smokers.
- Thirty-two percent (32%) of non-smokers and 18% of smokers remained free of disease. At five years, 18% of non-smokers were disease free, compared with 7% of smokers.

Smokers were just as likely as non-smokers to stop treatment because of side effects. But smokers who had to stop treatment to recover from side effects had poorer overall survival compared to other patients. (Abstract #1176)

**WHAT DOES THIS MEAN FOR PATIENTS?**

Though quitting smoking is difficult, this study shows that quitting smoking can have benefits at any stage of lung cancer.

“The evidence shows that smokers tolerated the treatment as well as non-smokers did,” said study leader Greg Videtic, MD, of the Dana-Farber Cancer Institute in Boston. “Even so, the lower survival rates of smokers suggest that smoking itself may reduce the effectiveness of the therapy.”

“I tell my patients to stop smoking so they can gain all the possible benefits of treatment,” said Dr. Videtic.

**NOVEL TARGETS**

**Monoclonal Antibody Treatment for Acute Myeloid Leukemia (AML)**

A treatment for acute myeloid leukemia (AML) that combines a monoclonal antibody with chemotherapy helps to improve patients’ response to therapy compared to chemotherapy alone, this study shows.

Patients in this phase III study had AML that either did not respond to initial treatment or returned after treatment. They were randomly assigned to two groups: one group received chemotherapy alone, and the other received chemotherapy in combination with the monoclonal antibody HuM195.

Monoclonal antibodies are genetically engineered proteins designed to target specific antigens on the surface of tumor cells. In this case, HuM195 seeks out and binds to the antigen CD33, found on myeloid leukemia cells. This interaction causes the cancer cells to rupture.

The combination therapy could be safely given and did not increase the occurrence of chemotherapy-related side effects.

Of the 94 patients who received combination therapy, 27 experienced complete remission, and 13 had partial remission, an overall response rate of 43%. In the 97 patients who received only chemotherapy, the overall response rate was 26% (20 patients had complete remission and five had partial remission). Patients with partial remission met all the criteria for complete remission but had a lower platelet count.

Mortality rates in both groups were similar: 15% for combination therapy vs. 13% for chemotherapy alone. Some patients who received HuM195 experienced mild to moderate flu-like symptoms such as fever and chills. (Abstract #1142)

**WHAT DOES THIS MEAN FOR PATIENTS?**

“Our results suggest that HuM195 plus chemotherapy should become the standard treatment for patients with AML if their cancer returns or if they don’t respond to initial treatment,” said Eric J. Feldman, MD, of the Weill Medical College of Cornell University in New York City.

The study’s results are especially important because about 25% of the patients had a blood disorder, such as myelodysplastic syndrome, before developing AML. Because this disease is usually resistant to chemotherapy, patients are often excluded from clinical trials, said Dr. Feldman.
Targeted Treatment for Head and Neck Cancer

The new targeted drug C225 shows no benefit over standard treatment in people with advanced head and neck cancer, according to this study.

The study was a phase III trial involving 123 patients with head and neck cancer that had spread or recurred following initial treatment. Half received the drug C225 plus the standard chemotherapy drug cisplatin; the other half received cisplatin plus a placebo.

Patients treated with C225 and cisplatin had a slightly higher response rate than patients who received cisplatin and placebo, but the difference was not statistically significant. There were no significant differences between the two groups in progression-free survival or overall survival.

Further follow-up is required to evaluate the small improvement in one- and two-year survival rates experienced by some patients who received C225.

Patients treated with C225 had some side effects from the drug, such as a skin rash, chills, and allergic reactions. C225 did not seem to significantly increase the side effects of cisplatin. C225 is a monoclonal antibody that is targeted against epidermal growth factor receptor (EGFR) on the surface of cancer cells. C225 blocks that receptor, making it harder for tumor cells to divide. Researchers suspect that C225 works by making cancer cells more vulnerable to other chemotherapy drugs and radiation. The drug has shown effectiveness against other tumors, most notably colorectal cancer. About 90% of patients with head and neck cancer have high levels of EGFR, and these patients are more likely to have a poor prognosis and a poor response to therapy.

C225 is not yet recommended as a treatment for head and neck cancers.

“While cisplatin-based chemotherapy remains the standard of care for patients with advanced head and neck cancer, our results suggest that further evaluation of C225 is warranted in these patients,” said Barbara Burtness, MD, of Yale University, the study’s lead investigator.

Breast Cancer

Early-Stage Breast Cancer

The chemotherapy drug docetaxel, used to treat metastatic breast cancer, significantly reduces the risk of recurrence and improves survival in women with early-stage breast cancer, according to interim results of a large, international phase III study.

The study involved 1,500 women whose breast cancer had spread to their lymph nodes but no further. Fifty-four percent (54%) were under age 50, and 56% were premenopausal. They were randomly selected to receive either docetaxel plus doxorubicin and cyclophosphamide (called TAC) or the standard chemotherapy (5-fluorouracil plus doxorubicin and cyclophosphamide, called FAC). All women received chemotherapy after surgery to remove their primary breast tumor.

TAC showed the most benefit in women whose breast cancer had spread to one to three lymph nodes. For these women, TAC reduced the mortality rate by 54% and the risk of recurrence by 50%. The improvements seen in women whose cancer had spread to four or more lymph nodes were not statistically significant.

Overall, the women who received TAC had a 24% reduction in mortality, an important difference but not yet statistically significant.

Nearly three years after treatment, TAC reduced the risk of breast cancer recurrence by 32%, compared to a standard chemotherapy.

Women who received TAC more often experienced lower white blood cell counts, fever, and diarrhea. Women treated with FAC reported more nausea and vomiting. All side effects could be treated.

“These are the interim results from this study, and are promising but not final. Women should talk with their doctors about this new chemotherapy regimen. While further follow up is necessary, these initial results merit consideration in choosing therapy for many women diagnosed with early breast cancer. They indicate a significant improvement over one of the best standard treatments available today,” said Jean-Marc Nabholz, MD, chairman of the Breast Cancer International Research Group, which conducted the study. Dr. Nabholz is also Professor of Medicine at the University of California at Los Angeles, and Director, Cancer Therapy Development Program, Jonsson Comprehensive Cancer Center.
**LUNG CANCER**

**Advanced Lung Cancer**

For the first time, an oral drug that blocks growth signals in cancer cells can shrink tumors in people with advanced lung cancer, new research shows.

This phase II study involved 216 patients from 30 U.S. hospitals, all with advanced lung cancer. All patients had received at least two different chemotherapy regimens that included the standard drugs docetaxel and either cisplatin or carboplatin. Patients received either 250 mg or 500 mg of ZD1839 (a new targeted cancer treatment) daily.

Ten percent (10%) of patients who took ZD1839 had their lung tumors shrink by 50% or more. Thirty-six percent (36%) had improvement in symptoms such as shortness of breath, poor appetite, cough, and weight loss. For a majority of these patients, symptoms improved within 10 days of taking the drug. In general, the more tumors shrank the more cancer-related symptoms improved.

Tumor shrinkage was about the same with both dosages, but more side effects occurred at the higher dose. These included a mild acne-like rash, dry skin, and loose bowel movements. Very few patients had to take a lower dosage of ZD1839 or stop taking the drug because of side effects.

ZD1839 works by blocking a key enzyme, tyrosine kinase, which turns on epidermal growth factor receptor, a protein that signals cancer cells to grow and divide. (Abstract #1166)

**WHAT DOES THIS MEAN FOR PATIENTS?**

ZD1839 is the first targeted treatment for lung cancer to shrink tumors, and may lead to other promising treatments for lung cancer.

“These results are as good as or better than other medicines that have been tested in a comparable group of patients,” said the study’s lead investigator Mark Kris, MD, Chief of the Thoracic Oncology Service at Memorial Sloan-Kettering Cancer Center. “Most importantly, ZD1839 gives us a whole new way to fight lung cancer and raises our hopes that this disease can be attacked even more effectively by blocking other cellular growth signals.”

**BREAST CANCER**

**Tamoxifen After Chemotherapy**

Previous studies have shown that women with hormone-receptor positive, early-stage breast cancer can significantly reduce their risk of cancer recurrence by taking a combination of tamoxifen and chemotherapy after surgery. This study shows that these women gain the most benefit if they start taking tamoxifen after they have finished chemotherapy, not at the same time.

In this study, 1,477 women were randomly selected to receive one of three therapies: tamoxifen after chemotherapy, tamoxifen and chemotherapy at the same time, and tamoxifen only. All women in the study were postmenopausal, had breast cancer that had spread to the lymph nodes but no further, and had tumors that contained estrogen or progesterone receptors.

The women in the study were followed for eight years. After eight years, 67% of women who received tamoxifen after chemotherapy remained breast cancer-free, compared with 62% who received the two therapies together and 55% who received tamoxifen only.

After the researchers accounted for other factors that predict breast cancer recurrence (such as tumor size, degree of lymph node involvement, progesterone receptor status, and race) they found an 18% advantage to completing chemotherapy before starting tamoxifen versus simultaneous administration. (Abstract #143)

**WHAT DOES THIS MEAN FOR PATIENTS?**

Women with early breast cancer that is hormone-receptor positive should now begin tamoxifen after chemotherapy is finished instead of at the same time. Before this study, it was unclear if taking tamoxifen along with chemotherapy had any effect on the risk of recurrence.

“Many women in the United States receive tamoxifen and chemotherapy together after surgery,” said Kathy S. Albain, MD, the study’s lead investigator. “Our results show that it is best to wait until chemotherapy is finished before starting tamoxifen to obtain optimal benefit from the chemotherapy.” Dr. Albain is Director, Breast Cancer Research and Co-Director, Breast Care Center at Loyola University Cardinal Bernardin Cancer Center in Chicago.
Aromatase inhibitors are a class of hormone treatments designed to reduce the amount of estrogen in a woman’s body and slow or stop the growth of breast cancers that are estrogen “receptor-positive” (tumors that grow faster on estrogen). Aromatase inhibitors are newer treatments, and show some promise in preventing recurrence in women with early stage breast cancer.

Tamoxifen is another hormone treatment for breast cancer. It blocks the effects of estrogen on tumor growth, and has proven to prevent recurrence in women with early stage breast cancer. It has been studied for 30 years and the benefits and side effects are well known.

To see if aromatase inhibitors are more effective than tamoxifen, researchers have started a five-year clinical trial called the ATAC trial (Arimidex (anastrozole), Tamoxifen Alone or in Combination). In 2001, researchers released some early results of the trial, which show that anastrozole is effective in reducing risk for recurrence, maybe more than tamoxifen.

After the results were released, ASCO formed a panel of breast cancer experts to assess aromatase inhibitors. This is the first independent assessment of aromatase inhibitors for the prevention of breast cancer recurrence following surgery. The panel finds that the early results are promising but does not support routine use outside of clinical trials.

ASCO examined the ATAC trial, published medical literature, and unpublished data from drug companies on planned and ongoing studies. Their report is one of ASCO’s Technology Assessments, designed to recommend if new procedures, tests, or devices are appropriate for broad use.

**ATAC TRIAL FINDINGS**
The ATAC study is designed to compare anastrozole and tamoxifen for five years. It includes over 9,000 women with early stage breast cancer. All women in the study had received primary surgery and were candidates to receive adjuvant (added) hormonal therapy.

After a median of 33 months, 317 of the 3,125 women taking anastrozole had a relapse of breast cancer or died, compared to 379 of the 3,116 women on tamoxifen. This is a 17% reduction in the risk of recurrence with anastrozole compared to tamoxifen.

The impact of anastrozole on patient survival has not yet been formally studied.

**FINDINGS OF ASCO’S EXPERT PANEL**
The reduction in breast cancer recurrence seen in the ATAC trial is promising. However, the panel found that it is premature to recommend anastrozole for routine use. Because tamoxifen provides its greatest benefit when taken for five years, the two drugs cannot be properly compared until anastrozole has been tested for five years also.

While there were few serious side effects in the ATAC trial for both anastrozole and tamoxifen, the long-term side effects of anastrozole are still unknown. Since there is extensive, long-term data on tamoxifen and a clearer understanding of its risks, the panel recommends that tamoxifen remain the standard of care.

The expert panel found no evidence to suggest that women who have started a standard course of tamoxifen should switch to anastrozole or other aromatase inhibitors.

For women who cannot take tamoxifen for specific reasons or severe side effects, anastrozole may be an option. Healthcare providers and women should make decisions with careful consideration of all the available data.

**ASCO ASSESSMENT OF TAMOXIFEN AND RALOXIFENE**
ASCO has also updated its recommendations on the use of hormonal therapies for reducing breast cancer risk in pre-menopausal women at elevated
NOVEL TARGETS

Classification of Adult Sarcomas

Scientists have demonstrated that genetic “fingerprinting” can help classify subtypes of soft-tissue sarcomas that otherwise look virtually identical.

Soft-tissue sarcomas begin in tissues such as fat, muscles, nerves, tendons, and blood vessels. There are more than 50 known subtypes of soft-tissue sarcomas. For decades, many pathologists have lumped difficult-to-diagnose sarcomas into a “catch-all” category called malignant fibrous histiocytomas (MFH). With current treatments, about 50% of patients with MFH sarcoma survive long-term.

Doctors have long debated whether MFH is one distinct subtype of sarcoma. In this study, researchers used a gene technology called oligonucleotide array analysis to analyze the pattern of activity of 12,500 genes from 52 subtypes of adult soft-tissue sarcoma on a single slide, or “chip.” This provides a genetic fingerprint unique to each subtype of sarcoma.

The analysis could easily distinguish between sarcomas with specific genetic alterations. But the technology also differentiated between certain MFH sarcomas and found that some of them formed a distinct subtype. Genetic fingerprinting technology may also help scientists evaluate how genes in cancer cells are turned on or off in response to therapy. That will help to determine if a particular sarcoma subtype will eventually become resistant to a given treatment, said Dr. Maki.

WHAT DOES THIS MEAN FOR PATIENTS?

This discovery opens the door to better diagnosis of sarcoma, and may lead to new, more targeted treatments that attack sarcomas based on their genetic differences.

“Genetic fingerprinting of adult sarcomas will likely be useful when pathologists disagree about a diagnosis or when the appearance of tumor cells does not conclusively link them to a particular subtype,” said lead investigator Robert Maki, MD, a medical oncologist at Memorial Sloan-Kettering Cancer Center.

Women interested in a clinical trial of anastrozole should talk with their doctor.
Lung Cancer Prevention

Quitting smoking significantly reduces lung cancer risk, but former smokers remain at high risk years after they quit. A chemical cousin of vitamin A can reverse some precancerous changes in the lungs of former smokers, according to this study.

The researchers studied the preventive effects of two forms of vitamin A: 9-cis retinoic acid and 13-cis retinoic acid. Retinoic acid helps maintain normal growth and differentiation of epithelial cells (cells that line the lung) by activating retinoic acid receptor-beta (RAR-β). Heavy smoking leads to precancerous changes that reduce levels of this receptor.

The study involved 226 people who had smoked for years but had quit at least one year before. They were randomly selected to receive for three months a daily dose of one of three agents: 9-cis retinoic acid; 13-cis retinoic acid plus alpha-Tocopherol, a synthetic form of vitamin E; or a placebo.

The investigators took lung biopsies before treatment began and after treatment ended. In the biopsies taken before treatment, 30% did not express RAR-β. Precancerous cells were present in 7% of the biopsies.

After three months of treatment, expression of RAR-β had increased significantly in people who received 9-cis retinoic acid, but not in those who took 13-cis retinoic acid or a placebo. Neither retinoic acid significantly reduced the presence of precancerous cells. Side effects such as headache, skin rashes, and fatigue were more common in the 9-cis retinoic acid group. (Abstract #1177)

STI-571 for Gastrointestinal Stromal Tumors (GIST)

More than half of patients with advanced gastrointestinal stromal tumors (GIST) who receive the drug STI-571 have a lasting response and experience significant tumor shrinkage, this study shows.

This phase II study included 147 patients with GIST that was either inoperable or had metastasized (spread). Participants received STI-571 (either a 400 or 600 mg dose) daily in pill form. The response rate did not differ substantially between the two dosages.

One year after beginning treatment with STI-571 (also known as imatinib mesylate), over 60% of patients had tumors that shrunk by at least half (called a partial response), and another 20% had tumors that shrunk by one-quarter to one-half (stabilized).

Some patients experienced side effects that included nausea, diarrhea, muscle cramps, and skin rash. About 20% of patients had severe side effects that included low white blood cell counts, tumor hemorrhage, and abdominal pain.

During treatment, 14% of patients experienced progression of their cancer. Studies are already underway to learn why some tumors have become resistant to the drug.

STI-571 is a type of drug called a signal transduction inhibitor. It blocks a defective version of a protein found in nearly all GISTs. This disrupts a signal that encourages the growth of these tumors, and leaves normal cells unharmed. It is already approved to treat patients with chronic myeloid leukemia (CML). (Abstract #1608)

WHAT DOES THIS MEAN FOR PATIENTS?

This is a promising early study that identifies an agent that may help to prevent lung cancer in former smokers. In the future, larger studies may provide more information.

“"This study shows that 9-cis retinoic acid is biologically active in the lung,” said Jonathan Kurie, MD, of the M.D. Anderson Cancer Center in Houston. “These encouraging results now deserve further study in a larger group of patients.”

WHAT DOES THIS MEAN FOR PATIENTS?

This study is ongoing, and continues to show that STI-571 is safe and effective for treatment of advanced GISTs. “These responses are lasting and are in marked contrast to standard chemotherapy, which has a response rate of 5%,” said Margaret von Mehren, MD, Associate Member of the Fox Chase Cancer Center in Philadelphia.

People interested in this drug should talk with their doctor about clinical trials evaluating STI-571.
Monoclonal Antibody Treatment for Advanced Kidney Cancer

In people with metastatic kidney cancer, a monoclonal antibody called bevacizumab delayed tumor progression when given in high doses, a new study shows.

The phase II, double-blind study involved 110 patients randomly selected to one of three groups: either high or low doses of the anti-VEGF antibody, or a placebo. The antibody significantly prolonged the time before cancer progressed by 2.5 times in people who received it in high doses (10 mg/kg every two weeks), compared to patients who received a placebo. Patients who received bevacizumab in lower doses (3 mg/kg every two weeks) also experienced a significant but shorter delay in tumor progression. The antibody caused tumors to shrink in only a few patients, all of whom had received the higher dose.

The antibody caused few side effects, although some patients experienced hypertension or had protein in their urine that caused no symptoms.

The antibody is designed to neutralize vascular endothelial growth factor (VEGF, pronounced vegend-eff). VEGF promotes the growth of blood vessels (a process called angiogenesis), and it is over-produced in tumor cells. In laboratory animals, VEGF helps to stop the growth of cancer by blocking the effects of VEGF. In other preliminary studies, the anti-VEGF antibody has shown activity in combination with chemotherapy for lung and colon cancer.

WHAT DOES THIS MEAN FOR PATIENTS?

“We are encouraged by the results of the anti-VEGF antibody in these difficult-to-treat patients,” said the study’s lead investigator James C. Yang, MD, of the National Cancer Institute. “This is a convincing demonstration that anti-angiogenic agents can inhibit tumor growth in patients.”

People interested in learning more about clinical trials for advanced kidney cancer should talk with their doctors.

QUICK FACTS

Clinical trials are designed to evaluate whether a new development is safe, effective, and better than the current standard of care. In the case of cancer, clinical trials have led to scientific advances that have increased doctors’ understanding of how and why tumors develop and grow.

Clinical trials are carried out in steps called phases. Each of the three phases is designed to find out different information.

PHASE I trials gather data on dosage, timing, and safety — but not efficacy — of an investigational therapy. Phase I trials generally last several months to a year and usually involve a very small number of patients, usually no more than 10 to 20. Once there is a hint of response by a patient to a therapy, disease specific research can begin with a phase II trial.

PHASE II trials are designed to provide more detailed information about the safety of the treatment, as well as to evaluate the efficacy of the drug. They take approximately two years to complete and usually involve a small number of patients, typically 20 to 40. The response rate in this phase needs to be equal or higher than normal in order to proceed to phase III trials.

PHASE III trials compare a promising new treatment with the current standard of care. The number of patients enrolled in a phase III trial can range in the hundreds to thousands. These trials may take many years to complete. Once a drug has been proven successful in a phase III trial, an application for U.S. Food and Drug Administration (FDA) approval can be submitted.

SOME CLINICAL TRIALS TERMS DEFINED:

Significance: The evaluation of the results of a trial or survey. Statistical significance occurs if there is less than a 5% chance that the same results would occur by chance.

Randomization: Assigning by chance. Researchers use randomization to assign people to different treatment groups in a clinical trial.

Standard of care: The best known therapy for a particular cancer accepted by the medical community. It is used as a benchmark for comparison against new treatments.

FOR MORE INFORMATION

For more information about cancer, visit People Living With Cancer at www.plwc.org. People Living With Cancer is ASCO’s comprehensive website for patients, families, and the public. Find detailed information on different types of cancer, clinical trials, cancer news, coping, and connect with others with cancer.

Also on People Living With Cancer, you can find:

Patient Guides Adapted from the recommendations in ASCO’s Clinical Practice Guidelines, these guides offer easy to understand information and helpful resources. View the following guides:

Follow-Up Care for Breast Cancer, Advanced Lung Cancer Treatment, Follow-Up Care for Colorectal Cancer, Preventing and Treating Nausea and Vomiting Caused by Cancer Treatment, and Understanding Tumor Markers for Breast and Colorectal Cancers.

JCO News Digest Provides summaries of important cancer research published in ASCO’s semi-monthly peer-reviewed scientific publication, Journal of Clinical Oncology.

Cancer Advances This series provides summaries of important research presented at ASCO’s Annual Meeting and Meet the Experts Sessions, and published in the Journal of Clinical Oncology.
For more information about cancer or the research presented at ASCO’s 2002 Annual Meeting, please call 703-299-0150.

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