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Your Guide to the Latest Cancer Research and Treatments

Highlights from the 2013 Annual Meeting of the American Society of Clinical Oncology

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This special edition of the Cancer*Care* Connect Booklet Series highlights cutting-edge research presented at the 2013 Annual Meeting of the American Society of Clinical Oncology, which took place May 31 to June 4 in Chicago, Illinois.

Some of the treatments discussed in this booklet are still in the very early stages of research and may not be available to the general public outside of a clinical trial.

The information contained in this booklet is intended for discussion with your doctor. He or she can tell you whether these advances in the treatment of cancer affect your treatment plan and whether a clinical trial is right for you.

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About the Editors

Each year, Cancer*Care*® publishes a special edition of the Cancer*Care* Connect Booklet Series that presents research highlights from the Annual Meeting of the American Society of Clinical Oncology. For this 2013 report, we are indebted to the following medical experts, who ensured the accuracy of the information discussed in this publication.

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Brain Cancer

At the 2013 Annual Meeting of the American Society of Clinical Oncology, researchers reported important progress in brain tumor treatment:

Combining bevacizumab with irinotecan shows some promise for people with an aggressive brain tumor called MGMT-unmethylated glioblastoma. The tumors either stopped growing or took longer to grow in those who received these medications *(page 6)*.

Donepezil may offer some improvement in memory and movement for people with brain cancer. This Alzheimer's drug benefited certain patients who have received radiation for a brain tumor *(page 8)*.

Bevacizumab for Treating Newly Diagnosed Brain Cancer

Two recent studies showed that adding bevacizumab (Avastin) to standard treatment (radiation and then temozolomide [Temodar and others]) does not appear to help people with newly diagnosed brain cancer live longer. However, according to another clinical trial, the combination of bevacizumab and irinotecan (Camptosar and others) may be a promising treatment option for those who have a more aggressive type of brain cancer called MGMT-unmethylated glioblastoma.

The two clinical trials—known as the RTOG 0825 and AVAglio studies—included nearly 1,400 people with newly diagnosed brain cancer. Half of the patients received standard treatment plus bevacizumab, while the others received standard treatment alone. In both studies, there was no real survival difference between the groups treated with bevacizumab

and those that were not. In RTOG 0825, the patients in both groups survived between about 15 and 16 months. In the AVAglio study, the patients in both groups survived about 17 months. However, in the AVAglio study, researchers reported that it did take longer for the tumor to grow in those who received bevacizumab than in those who did not (10.6 months versus 6.2 months).

The third study (the German GLARIUS trial) included more than 180 people with MGMT-unmethylated brain cancer. All of these patients received radiation. In addition, half of them received bevacizumab and irinotecan, and the others received temozolomide. The combination of bevacizumab and irinotecan seemed to be better than temozolomide in delaying the growth of cancer. The cancer did not continue to grow in about

80 percent of the patients on bevacizumab and irinotecan, compared with about 40 percent of those on temozolomide.

Bevacizumab is a targeted treatment that helps block the development of blood vessels in brain tumors. (Targeted treatments are designed to spare healthy tissues and tend to cause less severe side effects than chemotherapy.) This is an important part of treating brain tumors because they develop strong networks of blood vessels that feed their growth.

What Patients Need to Know

Bevacizumab has been approved by the U.S. Food and Drug Administration to treat people with brain tumors that continue growing after standard treatment. Researchers wanted to find out whether bevacizumab might also be an effective way to treat newly diagnosed brain tumors. It seems that the standard treatment of radiation and temozolomide is still the most effective way to treat people with these tumors.

However, there may be a place for bevacizumab in the treatment of the more aggressive MGMT-unmethylated brain cancer. This type of tumor usually does not respond well to standard treatment with temozolomide. Further studies are needed to confirm these early results with bevacizumab and irinotecan for this group of people. Then, doctors should have a better idea of how best to use bevacizumab in combination treatment to help people with brain cancer.

Donepezil to Improve Memory Function for People With Brain Cancer

Donepezil (Aricept and others) may offer some improvement in memory and motor function (the ability to move muscles precisely). This medication has been used to treat the symptoms of Alzheimer's disease, such as memory loss and

mental confusion. According to a recent study, donepezil benefited certain people who have received radiation for brain cancer. However, the improvement in memory was seen only in those who had more mental symptoms than other patients before the start of the study.

Nearly 200 people who had received radiation for brain cancer took part in this clinical trial. Half of them were given donepezil daily, and the others were given a placebo (a look-alike pill with no active ingredient). Six months later, those who took donepezil and had more mental symptoms at the start of treatment experienced improvement in verbal memory. In this smaller group of people who received donepezil, motor function also seemed to be better. However, for the rest of the patients in the study, there were no major differences in mental or motor function between those who received donepezil and those who did not.

What Patients Need to Know

Studies have shown that more than half of people who receive radiation for brain tumors may experience some difficulty with memory and paying attention. According to the results of this recent study, donepezil may offer small benefits to certain people with brain cancer who have had radiation. Researchers may study donepezil further in a larger group of people with brain cancer to see whether it can improve some of the side effects associated with radiation treatment.

Breast Cancer

Researchers reported a number of major findings in breast cancer at the 2013 Annual Meeting of the American Society of Clinical Oncology:

For women with early-stage breast cancer, taking a lower weekly dose of paclitaxel is effective. Low-dose paclitaxel taken weekly is just as effective as taking a higher dose every two weeks—with fewer side effects *(page 11).*

Taking tamoxifen for 10 years instead of five years appears to be beneficial. Studies show that the longer course of treatment helped women with early-stage breast cancer live longer without their cancer returning *(page 12).*

Radiating the underarm may be just as effective as surgery to remove cancerous lymph nodes in women with early-stage breast cancer. Many women with early-stage breast cancer can be spared the side effects of surgery such as lymphedema (painful swelling). Researchers believe this finding could change the way women with early-stage breast cancer are treated (page *14).*

A new genetic screening test may prove to be especially important for African-American women. African-American women are disproportionately affected by early-onset and triple-negative breast cancers. By looking for mutations (changes) in 18 different breast cancer genes, a new test helps doctors identify genetic mutations in women at high risk of developing breast cancer *(page 15).*

Comparing Paclitaxel Treatment Schedules

Weekly treatment with the anti-cancer drug paclitaxel seems to be equally effective as paclitaxel given every two weeks in preventing breast cancer from returning. In addition, there were fewer side effects with weekly paclitaxel. These were the findings from a recent clinical trial that was the first to compare these two common chemotherapy schedules.

More than 3,000 women with early-stage breast cancer took part in this clinical trial. Some of the patients were given a lower dose of paclitaxel weekly for 12 cycles, and the others were given a higher dose of paclitaxel every two weeks for six cycles. Those in the every-two-week treatment group also had to have an injection of growth factors, which was given to protect the white blood cells. (White blood cells are part of the body's immune system. They help fight infection and other diseases such as cancer.)

More than four years after treatment, about 80 percent of women in both treatment groups were free of cancer. The women who received weekly paclitaxel treatment experienced less pain in the muscles and bones and less peripheral neuropathy (nerve pain that causes numbness and tingling in the hands and the feet) than those who received higher doses every two weeks. Allergic reactions were also fewer in those who received weekly treatment.

What Patients Need to Know

Women faced with making decisions about chemotherapy for their breast cancer can be reassured that low-dose paclitaxel taken weekly does not decrease their chances of survival. Taking paclitaxel weekly seems to be just as effective as taking it every two weeks—with fewer side effects and no need for added treatment with growth factors.

Extending Tamoxifen Treatment in Early-Stage Breast Cancer

Women with early-stage breast cancer who have already received five years of tamoxifen treatment may live longer without their cancer returning if they continue taking tamoxifen for another five years. The benefits of additional treatment were seen in a major clinical trial called the aTTom study, conducted in the United Kingdom.

Nearly 7,000 women with early-stage estrogen receptor-positive breast cancer took part in this study. All of these women received five years of tamoxifen treatment. Approximately half of them stopped taking tamoxifen after five years; the others continued to take tamoxifen for another five years. When the women were evaluated 10 years after their treatment began, the cancer returned in fewer women who were given the extended tamoxifen treatment than in

those who stopped treatment at five years. As time went on, researchers found that more women who continued treatment with tamoxifen had survived compared with those who stopped treatment at five years.

What Patients Need to Know

With many years of data, the aTTom clinical trial was one of the most important to be presented at the 2013 ASCO meeting. These findings support results from another recent major study called the ATLAS trial. This is very good news for women with estrogen receptor-positive breast cancer, especially younger women already taking tamoxifen. (For women with breast cancer who are postmenopausal, another class of drugs called aromatase inhibitors has become the most commonly used additional hormone treatment. At this time, there are no study results on taking these medications for more than five years.)

There are some side effects associated with the use of tamoxifen, such as a higher risk of blood clots, hot flashes, night sweats and insomnia (sleeplessness). In some women, the drug may also increase the chance of developing uterine cancer. As with all medical treatments, the benefits and risks of extended treatment with tamoxifen must be weighed for each woman and discussed with her doctor to be sure it is the right choice for her. Many researchers believe that extended tamoxifen treatment may be considered a better option for women at high risk of their cancer returning than for women at low risk.

Radiating the Underarm for Node-Positive Breast Cancer

Radiating axillary (underarm) lymph nodes appears to be as effective as surgery to treat women with breast cancer that has spread to the lymph nodes, according to the results of a recent clinical trial. (Lymph nodes are small "filtering stations" that rid the body of waste and fluids and help fight infections.) Women treated with radiation to the armpit were less likely to experience lymphedema (swelling in the armpit and arm) than those treated with surgery to remove the lymph nodes. Many researchers believe that, in the future, axillary radiation may replace surgery as the standard of care for women with node-positive breast cancer.

In the AMAROS clinical trial, more than 1,400 women with early-stage breast cancer had a positive sentinel lymph node. This lymph node, found in the armpit, is the first one to which cancer cells are likely to spread from the main tumor. About half of these women had surgery to remove more lymph nodes to prevent cancer from returning to the area. The other women in the study had radiation to the underarm lymph nodes.

Six years after treatment, researchers found that both treatments were equally effective in reducing the chance of

cancer returning to the remaining lymph nodes. However, one year after treatment, more women who had surgery experienced lymphedema than those who had radiation (40 percent versus 22 percent). Five years after treatment, although the symptoms of lymphedema had improved for many of the women in both groups, 28 percent of those who had surgery still had lymphedema compared with 14 percent of those who had radiation.

What Patients Need to Know

The results of the AMAROS study show that axillary radiation may prove to be as effective as surgery to prevent cancer from returning to the remaining lymph nodes in women with early-stage breast cancer. This means that many women with early-stage breast cancer can be spared the side effects of surgery such as lymphedema. Many doctors believe that using radiation instead of surgery in the armpit may change the way women with early-stage breast cancer are treated in the future.

Genetic Counseling for African-American Women at High Risk of Breast Cancer

Genetic screening with the BROCA test may help doctors identify genetic mutations (changes) in women who may be at high risk of developing breast cancer. This new test looks for mutations in 18 different breast cancer genes (including the BRCA1 and BRCA2 genes). Known as next-generation sequencing, this type of genetic screening is a sophisticated way to look at a person's DNA, the blueprint for the body's functions found in all cells of the body.

A clinical trial of the BROCA test focused on African-American women, who are disproportionately affected by early-onset and triple-negative breast cancers. Nearly 250 African-American women with breast cancer took part. Researchers

found that of these women, nearly one-fourth had at least one inherited genetic mutation. Most of them were in the BRCA1 or BRCA2 gene, but other, less well known gene mutations also were identified. In addition, a hereditary breast cancer gene mutation was found in about 30 percent of those whose breast cancer was diagnosed before age 45, those who had a close relative with breast or ovarian cancer and those who developed triple-negative breast cancer.

What Patients Need to Know

Next-generation sequencing is making it possible for doctors to identify genetic mutations that may increase a woman's chance of developing breast cancer. The results of this clinical trial suggest that an inherited genetic mutation may be found in 20 percent to 30 percent of African-American women who develop breast cancer. Comprehensive genetic screening in high-risk groups may become routine in the future, as researchers learn more about how best to use the BROCA test in women at high risk of developing breast cancer.

Colorectal Cancer

Important treatment advances in metastatic colorectal cancer (mCRC) were reported at the 2013 Annual Meeting of the American Society of Clinical Oncology:

FOLFIRI plus cetuximab may be as effective at shrinking metastatic colorectal tumors as the standard treatment of FOLFIRI plus bevacizumab. But for now, doctors will not change the way they treat people with this type of advanced cancer *(page 17).*

Chemotherapy alone was more effective at delaying tumor regrowth than chemotherapy plus cetuximab. For patients with mCRC who have had surgery to remove tumors, taking chemotherapy alone is more beneficial *(page 19).*

The combination of FOLFOXIRI and bevacizumab may be slightly more effective than FOLFIRI and bevacizumab as a first-time treatment of people with mCRC. In patients who have the BRAF gene mutation (change), FOLFOXIRI seems to offer the greatest benefit *(page 20).*

Continuing capecitabine and bevacizumab as maintenance therapy after standard treatment may help some people with mCRC survive longer without their cancer growing. Researchers will continue to study this maintenance therapy to confirm the benefits *(page 22).*

Cetuximab and FOLFIRI for mCRC

According to the results of a recent clinical trial, FOLFIRI plus cetuximab (Erbitux) may be as effective at shrinking tumors in these patients as FOLFIRI plus bevacizumab (Avastin). FOLFIRI, made up of 5-fluorouracil, leucovorin and irinotecan (Camptosar and others), is the standard treatment of mCRC.

Nearly 600 people with newly diagnosed mCRC and the normal, unmutated (unchanged) KRAS gene took part in the FIRE-3 clinical trial. Half of them were given FOLFIRI plus cetuximab, and the other half were given FOLFIRI plus bevacizumab. Both cetuximab and bevacizumab, which target certain proteins that control the growth of tumors, have been approved by the U.S. Food and Drug Administration for treating different types of advanced cancer.

The tumors shrank in 57 percent to 62 percent of patients in both treatment groups, suggesting that both FOLFIRI combinations may be equally effective.

What Patients Need to Know

Studies have shown that mCRC in people who have the normal KRAS gene may respond to cetuximab. To destroy

cancer cells, targeted treatments such as cetuximab and bevacizumab focus on specific cell mechanisms thought to be important for the growth and survival of tumor cells. Although the combination of FOLFIRI and cetuximab may prove to be an effective way to shrink colorectal tumors, researchers do not believe that this study is likely to change the way people with mCRC are treated in the near future. However, this drug combination will be studied further.

Cetuximab and Chemotherapy for Colorectal Cancer That Has Spread to the Liver

For certain patients with mCRC that has spread to the liver, surgical removal of the tumors in the liver is one treatment option. Often, chemotherapy is used before and after surgery to improve the outcome of surgery. A clinical trial known as the EPOC study looked at whether chemotherapy could improve patients' chances of having successful surgery to remove these liver tumors.

In the EPOC study, nearly 300 people had the normal KRAS gene and mCRC that had spread to the liver. Some study participants received chemotherapy plus cetuximab for 12 weeks before and 12 weeks after surgery. The others received chemotherapy alone. Three different chemotherapy combinations were used: FOLFOX (5-fluorouracil, leucovorin and oxaliplatin [Eloxatin and others]), CAPEOX (capecitabine [Xeloda and others] and oxaliplatin) and FOLFIRI.

Researchers found that adding cetuximab to chemotherapy did not benefit these patients. In fact, overall, chemotherapy alone was more effective at delaying tumor regrowth than chemotherapy plus cetuximab.

What Patients Need to Know

Over the years, researchers have learned that giving chemotherapy to people with mCRC before surgery to remove liver tumors may improve their outcomes. They had hoped that adding cetuximab to this chemotherapy might benefit these patients even more, but that was not the case. However, researchers did learn that people who received the FOLFIRI combination plus cetuximab benefited more than those who received either of the other two chemotherapy combinations plus cetuximab.

FOLFOXIRI and Bevacizumab for First-Time Treatment of mCRC

The combination of FOLFOXIRI and bevacizumab may prove to be more effective than FOLFIRI and bevacizumab for first-time treatment of people with mCRC, according to the results of a recent clinical trial in Italy. FOLFOXIRI contains all of the standard drugs used to treat mCRC: 5-fluorouracil, leucovorin, oxaliplatin, irinotecan and bevacizumab.

More than 500 people with newly diagnosed mCRC took part in the TRIBE study. Approximately half of the patients were given FOLFOXIRI and bevacizumab, and the others were given FOLFIRI and bevacizumab. More than two years after treatment, the tumors shrank in 64 percent of the patients in the FOLFOXIRI group, compared with 53 percent of those in the FOLFIRI group. The combination of FOLFOXIRI and bevacizumab did not increase the chances of needing surgery to remove the tumors. But more side effects were reported among people who received FOLFOXIRI than among those who received FOLFIRI.

What Patients Need to Know

Combining FOLFOXIRI and bevacizumab offers some advantage over standard chemotherapy for people with mCRC. However, as with most new combination treatments, doctors will have to evaluate the benefits of FOLFOXIRI plus bevacizumab and weigh them against the higher risk of side effects in individual patients. FOLFOXIRI plus bevacizumab seems to be more beneficial in those whose colorectal tumors have the BRAF gene mutation. This mutation, which can increase the growth and spread of cancer cells, has become an important target for treatment.

Maintenance Therapy With Capecitabine Plus Bevacizumab for mCRC

Continuing capecitabine and bevacizumab as maintenance therapy after standard treatment may help some people with mCRC survive longer without their cancer growing. Sometimes given for a long time, maintenance therapy is used to help prevent the return of cancer after it is first treated.

Approximately 550 people with mCRC took part in a clinical trial called CAIRO3. All of these patients were first given the standard treatment known as CAPEOX-B (capecitabine, oxaliplatin and bevacizumab). Some of the patients went on to receive maintenance therapy of additional capecitabine and bevacizumab, while the others did not. It took longer for the tumor to continue growing in those on maintenance therapy than in patients who were not on it. Eventually, most people in the clinical trial received treatment again and then were evaluated. This makes it more challenging to interpret the results.

What Patients Need to Know

Maintenance therapy with capecitabine and bevacizumab may benefit people with mCRC. In the United States it is standard practice to continue chemotherapy, whereas in Europe it is more common to treat for several months and then take a break from treatment. The CAIRO3 study supports the continuation of chemotherapy. Researchers will study this maintenance therapy further to confirm the benefits in controlling the growth of mCRC. Single-drug maintenance therapy also may be an effective option.

Head and Neck Cancer

Important developments in head and neck cancer treatment were reported at the 2013 Annual Meeting of the American Society of Clinical Oncology:

Researchers are gaining a better understanding of squamous cell carcinoma (SCC) and how best to treat people with this common type of head and neck cancer. Through the Cancer Genome Atlas, they have learned that people with certain types of SCC may have better outcomes than others, depending on the genetic makeup of their tumors. This important research could lead to more effective treatments in the future *(page 24).*

For the first time, researchers have showed that two biomarkers, or indicators, may be able to help guide doctors to the best SCC treatment choices. Tumors of the head and neck that are linked to the human papillomavirus (HPV) or a p16 gene mutation (change) appear to respond better to treatment. People with these types of tumors may survive longer as a result. The presence of a protein called ERCC1 may also improve survival for these patients *(page 25).*

For people with HPV-positive SCC of the head and neck, treatment that includes a lower dose of radiation and cetuximab appears to be beneficial. The new combination shrank the tumors in a large majority of treated patients, with fewer side effects than the standard treatment of chemotherapy and a higher dose of radiation *(page 26).*

Cetuximab plus radiation may be as effective as chemotherapy and radiation for people with locally advanced head and neck cancer. Cetuximab tends to cause less severe side effects than chemotherapy, so it offers an advantage for patients *(page 28).*

Genetic Information and SCC of the Head and Neck

Researchers are gaining a better understanding of SCC and how best to treat people with this common type of head and neck cancer. They are studying the cancer's genetic mutations through the Cancer Genome Atlas. This project uses sophisticated techniques to catalog the genetic mutations responsible for cancer. Through the Cancer Genome Atlas, researchers have learned that people with certain types of SCC of the head and neck may have better outcomes than others, depending on the genetic makeup of their tumors.

Of the many gene mutations identified in the head and neck tumors of more than 275 patients studied, HPV was found in up to 25 percent. Along with the use of tobacco, HPV

infection is a risk factor for head and neck cancer and may affect patients' treatment outcomes.

Researchers working on the Cancer Genome Atlas also learned more about SCC that does not affect the middle part of the throat (including the base of the tongue and the tonsils). They focused on the p16 gene, which is commonly changed in people with this type of SCC and HPV. The patients who had a p16 gene mutation seemed to have better treatment outcomes than those who did not have the mutation.

What Patients Need to Know

One of the most exciting topics presented in the 2013 ASCO meeting was the Cancer Genome Atlas. Researchers learned a lot about gene mutations in head and neck cancer, which they hope will lead to the development of new treatments for patients in the future. It appears that the presence of the p16 gene mutation may suggest a favorable outcome for people who have SCC of the head and neck that does not affect the middle part of the throat. However, it is important to remember that genetic testing for head and neck cancers is currently being used mostly in research studies and is not yet the standard of care for people with this type of cancer.

Genetic Markers as Predictors in Resistant or Metastatic Head and Neck Cancer

HPV-associated head and neck tumors that have the p16 gene mutation appear to respond better and patients may survive longer after treatment than those who do not have HPV or the mutation. The presence of a protein called ERCC1 may also improve survival for people with resistant or metastatic head and neck cancer. (Cancer that is metastatic has spread from its original location to another part of the body.)

Researchers studied tumor samples from patients who were treated for advanced head and neck cancer. Of the 65 tumors tested for HPV, 11 had the virus (were positive). Of the 66 tumors tested for the p16 gene mutation, 12 were positive for the mutation. In the mutation-positive group, 60 percent to 70 percent of the tumors responded to chemotherapy. About 22 percent of tumors that were negative for HPV or the p16 gene mutation responded to treatment. Many of the people who had low levels of the ERCC1 protein responded better to treatment—and so may survive longer—than some of the patients who had high levels of the ERCC1 protein.

What Patients Need to Know

With each new study, researchers are learning more about the different types of head and neck tumors and the genetic markers that may guide doctors to the best treatment decisions. This is the first study to show that head and neck tumors that are linked to HPV, have the p16 gene mutation and are metastatic may respond better to treatment, enabling patients to survive longer. Further studies are needed on how ERCC1 levels may affect tumor response to chemotherapy for advanced head and neck cancers.

Lower Radiation Dose and Cetuximab for Head and Neck Cancer

For people with HPV-positive SCC of the head and neck, treatment that includes a lower dose of radiation and cetuximab (Erbitux) appears to be beneficial. The new combination shrank the tumors in a large majority of treated patients, with fewer side effects than the standard treatment of chemotherapy and a higher dose of radiation.

Ninety people with HPV-positive SCC of the head and neck took part in the ECOG 1308 clinical trial. First, the patients were given chemotherapy. Those people whose cancer completely responded to chemotherapy with no evidence of remaining cancer went on to receive low-dose radiation and cetuximab. Of the 80 people evaluated so far, the tumor shrank in 86 percent of them. Very few severe side effects were reported.

What Patients Need to Know

Chemotherapy and radiation has been the standard treatment for HPV-positive SCC of the head and neck. However, this treatment often doubles the rate of both short- and long-term side effects. But lowering the dose of radiation and using the targeted treatment cetuximab instead of chemotherapy may prove to be an effective way to treat people with this type of cancer and may cause fewer side effects. (To destroy cancer

cells, targeted treatments focus on specific cell mechanisms thought to be important for the growth and survival of tumor cells. Unlike chemotherapy, targeted treatments are designed to spare healthy tissues and tend to cause less severe side effects.)

Early results suggest that cetuximab and lower-dose radiation may be as good as chemotherapy and higher-dose radiation in stopping the cancer from spreading beyond the head and neck. Further studies and longer follow-up are needed to confirm these early results.

Cetuximab and Radiation for Locally Advanced Head and Neck Cancer

Another study that looked at combination treatment with cetuximab and radiation showed that it may be as effective as chemotherapy and radiation for people with locally advanced head and neck cancer. (Locally advanced cancer has spread from where it started to nearby tissues or lymph nodes.) People who have locally advanced head and neck tumors may need more than one treatment.

More than 400 people took part in a clinical trial comparing cetuximab and radiation with chemotherapy and radiation. Some of these patients were given initial chemotherapy with docetaxel (Docefrez, Taxotere and others), cisplatin and 5-fluorouracil, and some were not. Then, nearly two-thirds of all of the patients were given chemotherapy and radiation, and the others received cetuximab and radiation. The tumor shrank in more than 80 percent of patients in both groups. There did not seem to be a difference between the two treatments in how long it took the tumor to continue growing or in how long people survived after treatment.

What Patients Need to Know

Researchers are always looking for better ways to treat cancer, but sometimes they find out that several treatments are equally effective. That appears to be the case with this study comparing chemotherapy plus radiation and cetuximab plus radiation for people with locally advanced head and neck cancer. Because the targeted treatment cetuximab tends to cause less severe side effects than standard chemotherapy, using cetuximab rather than chemotherapy with radiation may prove to be more beneficial. Further studies will shed more light on the effectiveness of this new combination and how best to use it to treat people with locally advanced head and neck tumors.

Leukemia

Important treatment advances in two types of leukemia were among the reports at the 2013 Annual Meeting of the American Society of Clinical Oncology:

Nilotinib is proving to be more effective than imatinib in treating some people with chronic myelogenous leukemia (CML). Patients who switched from imatinib to nilotinib continued to benefit two years after treatment *(page 30).*

A newly approved medication called obinutuzumab plus a standard drug called chlorambucil is a promising combination treatment for people with chronic lymphocytic leukemia (CLL). This new combination seems to be more effective than chlorambucil alone in stopping the growth of leukemia cells *(page 31).*

Combination treatment with idelalisib and rituximab may prove to be an effective way to treat older people with CLL. So far, none of the patients studied has had the cancer return *(page 33).*

Switching From Imatinib to Nilotinib for CML

Nilotinib (Tasigna) continues to prove to be more effective than imatinib (Gleevec and others) in treating some people with CML, according to the follow-up results of a recent clinical trial. Researchers know that the benefits of nilotinib reported last year now extend to two years after treatment.

More than 200 people with CML took part in a large clinical trial known as the ENESTnd study. All of the study participants shared a similar treatment history: their cancer had originally responded to treatment with imatinib, but they still had a few signs of cancer after two years. Half of them continued on

imatinib, and the other half switched to nilotinib. After another two years of treatment, the cancer disappeared in more than twice as many patients who switched to nilotinib compared with those who did not (22 percent versus 9 percent).

What Patients Need to Know

Nilotinib has already been approved by the U.S. Food and Drug Administration (FDA) as a first-time treatment for people with CML. Now it seems that nilotinib, a second-generation drug with many of the same features as imatinib, may be even better than imatinib in treating resistant cancers. In the future, people with CML may receive nilotinib earlier in their course of treatment, with imatinib saved for later. However, further studies are needed for doctors to understand how best to use nilotinib to effectively treat people with CML.

Obinutuzumab for CLL

A drug newly approved by the FDA called obinutuzumab (Gazyva) plus a standard drug called chlorambucil (Leukeran)

is a promising combination treatment for people with CLL, a common, slow-growing type of blood cancer. This new combination treatment seems to be more effective than chlorambucil alone in stopping the growth of leukemia cells.

Obinutuzumab is the first in a new class of anti-cancer treatments called chemoimmunotherapy. This type of treatment works in two ways: it destroys cancer cells directly and also boosts the body's immune system so that it can more effectively destroy cancer cells.

Nearly 600 people who had not already received treatment for their CLL took part in a clinical trial called CLL11. They received one of three different treatments: obinutuzumab plus chlorambucil, rituximab plus chlorambucil and chlorambucil alone.

Researchers found that those who were given the combination of obinutuzumab and chlorambucil survived longer without their cancer growing than those who were given either of the other two treatments (23 months versus 16 months for rituximab and chlorambucil and 11 months for chlorambucil alone). The cancers responded in three-quarters of the patients who received obinutuzumab and in about two-thirds of those who received rituximab. About one-third of cancers treated with chlorambucil alone responded to treatment.

What Patients Need to Know

The approval of obinutuzumab is an important new addition to the treatments available for people with CLL. Additional clinical trials in more people with CLL and other types of leukemia should help doctors further their understanding of how best to use newer drugs like obinutuzumab in the future.

Idelalisib and Rituximab for Older People With CLL

Combination treatment with idelalisib and rituximab may prove to be an effective way to treat older people with CLL, according to the early results of a recent clinical trial. Idelalisib belongs to a new class of treatments called PI3K inhibitors. These drugs target the PI3K pathway, which plays an important role in the growth of many different types of leukemia and lymphoma cells.

Nearly 65 people with CLL received treatment with idelalisib plus rituximab. All of them were at least 65 years old and had not already received treatment for their cancer. Of the 50 patients evaluated so far, cancers in 48 of them responded to the combination treatment. Some of these responses were seen within two months or less. In addition, 65 percent of patients who had symptoms before receiving idelalisib plus rituximab had no symptoms eight weeks into treatment.

What Patients Need to Know

Many people with CLL are older than age 70, so these are encouraging results. So far, no patients on this treatment have had a relapse of their cancer. (Relapse is a return of cancer after treatment and the absence of cancer symptoms.) The combination of idelalisib and rituximab may offer older people with CLL an alternative to chemotherapy and its side effects. Researchers are predicting that the use of drugs such as idelalisib will change the way people with CLL are treated in the near future. However, it is important to remember that these results are from an early stage of research. Additional clinical trials will be needed to find out whether idelalisib plus rituximab can help people with CLL survive longer.

Lung Cancer

Many exciting developments in lung cancer treatment were reported at the 2013 Annual Meeting of the American Society of Clinical Oncology:

Testing lung tumors for the gene mutations (changes) that define tumor subtypes and tailoring treatment accordingly is becoming a part of the standard of care for people with lung cancer. That's important because it allows doctors to choose the right treatment for each patient, helping many people with lung cancer survive longer *(page 35).*

Two new targeted treatments—cabozantinib and vandetanib—are being studied in people whose lung cancer has the RET fusion gene mutation. The results are promising enough to warrant further study *(page 38).*

A new targeted treatment called dabrafenib appears to be an effective way to treat people with lung cancer who have the BRAF V600E gene mutation. This is the first study to show success in targeting this particular lung cancer gene mutation *(page 40).*

The targeted treatment crizotinib appears to be an effective way to treat people who have advanced lung cancer with the ROS1 gene mutation. This mutation occurs in about 1 percent to 2 percent of those with non-small cell lung cancer *(page 41).*

The combination of a new targeted drug called AUY922 and erlotinib may be an effective way to treat people who have the EGFR gene mutation and whose lung cancer no longer responds to other drugs. AUY922 acts by targeting a substance in lung tumors that they need to grow and survive *(page 42).*

Identifying Driver Genetic Mutations in Lung Cancer

Three different studies show how doctors on both sides of the Atlantic are embracing the need to do genetic testing in people with lung cancer to choose the right treatment with the best chance of success for each person. Such testing can identify "driver mutations," the type of changes in tumor cells that cause the cancer to grow. Newer targeted treatments are designed to block these drivers and destroy cancer cells. (Targeted treatments spare healthy cells and tend to cause less severe side effects than chemotherapy.)

The first study was conducted by the Lung Cancer Mutation Consortium, made up of 14 different lung cancer centers across the United States. Researchers evaluated tumor

samples from more than 1,000 people with lung cancer to identify any of 10 different types of gene mutations. They found a genetic driver in two-thirds of the mutations. These results were then used to help doctors select the right targeted treatment for the tumors with that particular gene mutation. More than 260 people with a driver mutation received targeted treatment, and a little over 300 people with a driver mutation did not receive targeted treatment. The patients given the targeted treatment survived about a year longer than those who were not.

The second study, known as Biomarkers France, is the largest ever to evaluate gene mutations in people with non-small cell lung cancer (NSCLC), the most common type of lung cancer. A total of 10,000 tumor samples were studied to identify any of six known gene mutations. Researchers found that nearly 30 percent of the samples had the KRAS gene mutation, almost 10 percent had the EGFR gene mutation and less than 5 percent had either the BRAF or EML4-ALK gene mutation. More than half of the patients evaluated so far have received treatment targeted to their specific type of gene mutation, which has the best chance of success.

In the third study, a commercial company called Foundation Medicine tested more than 2,200 tumor samples (20 percent of which were from lung cancers) to identify cancer-related genes. About 75 percent of all the samples had at least one gene mutation that could be used to select the right targeted treatment. Not only did these researchers identify the eight known gene mutations for which targeted treatments are now available, they also found 13 other gene changes that may be possible treatment targets in the future.

What Patients Need to Know

Identifying driver mutations is revolutionizing the way in which people with lung cancer are being treated. Testing lung tumors for the gene mutations that define the tumor subtypes and tailoring treatment accordingly is becoming the standard of care for people with lung cancer, helping many of them survive longer. Researchers advise doctors to test their patients for such gene mutations at the time lung cancer is diagnosed. The information learned from such testing can guide doctors in making the best treatment recommendations for people with lung cancer.

New Targeted Treatments for Lung Cancer

As mentioned, there are eight different gene targets in lung cancer for which treatments are now available. More are being studied every day. Five newer drugs that target

certain gene mutations are discussed here. These promising treatments may prove to be effective in treating lung tumors that have genetic mutations such as the RET fusion gene, BRAF V600E, ROS1 and EGFR.

Cabozantinib and Vandetanib for Lung Tumors With the RET Fusion Gene

Two new targeted treatments—cabozantinib (Cometriq) and vandetanib (Caprelsa)—are being studied in people whose lung cancer has the RET fusion gene mutation. This type of gene alteration, which has already been seen in thyroid cancer, may be found in about 1 percent to 2 percent of NSCLC tumors.

In a clinical trial, 60 people with metastatic lung cancer received cabozantinib every day for 12 weeks. (Metastatic lung cancer has spread from the lungs to other organs in the body.) All of the patients had already received treatment with the targeted drug erlotinib (Tarceva). Researchers found that the tumor shrank in more than 60 percent of the people treated. Seven of those whose cancer responded to treatment were known to have either the KRAS or EGFR driver mutation. The most common side effect with cabozantinib appeared to be fatigue, which was reported in about 13 percent of patients.

More than 4,000 people with NSCLC took part in four different clinical trials with vandetanib. Genetic testing was done on more than 2,500 tumor samples from these patients. Of the nearly 1,000 tumor samples evaluated so far, seven of them had the RET fusion gene mutation. However, none of the tumors in three patients treated with vandetanib had a major response, although the tumor in two of the patients did appear in X-rays to shrink.

What Patients Need to Know

According to these two recent studies, the results are somewhat mixed with treatments that target the RET fusion gene mutation in lung cancer, although this is very early clinical research on this rare mutation. Cabozantinib, which the U.S. Food and Drug Administration (FDA) has approved for treating metastatic cancer of the thyroid (a hormone gland), may prove to be an effective way to treat metastatic NSCLC as well. As for vandetanib, there were too few patients with the RET fusion gene mutation in this study who were treated with the new drug, so it may be too early to be sure about its effectiveness in treating lung tumors. However, because vandetanib also is approved by the FDA for treatment of thyroid tumors, it will be studied further to see whether it may offer any benefit to people with lung cancer who have the RET fusion gene mutation.

Dabrafenib for Lung Cancer With the BRAF V600E Gene Mutation

The new targeted treatment dabrafenib (Tafinlar) appears to be an effective way to treat people with lung cancer who have the BRAF V600E gene mutation, according to the recent results of a small clinical trial. This gene change, which has been found in people with the skin cancer melanoma, may be present in less than 2 percent of those with NSCLC.

Seventeen people whose advanced lung cancer had the BRAF V600E mutation were treated with dabrafenib. All of their tumors no longer responded to chemotherapy. Of the 13 patients evaluated so far, the tumor shrank in seven of them and stopped growing in one. In one patient, it took nearly a year before the cancer continued to grow. The most common side effects reported with dabrafenib were decreased appetite, fatigue, shortness of breath and nausea. Most of these reactions to the drug were mild.

What Patients Need to Know

Dabrafenib has been approved to treat skin cancers with the BRAF V600E mutation. It also is a promising way to treat lung tumors that have the same gene mutation. This is the first study to show success in targeting the BRAF V600E gene mutation in lung cancer. Although it's a small study at an early stage of research, dabrafenib will be the focus of larger clinical trials with more people taking part. Then, doctors should have a better idea of whether patients with lung cancer who have this gene mutation will benefit from dabrafenib.

Crizotinib for Lung Cancer With the ROS1 Gene Mutation

The targeted treatment crizotinib appears to be an effective way to treat people who have advanced lung cancer with the ROS1 gene mutation. This mutation, which occurs in about 1 percent to 2 percent of those with NSCLC, may be more common in younger people and in those who have never smoked or are light smokers. Researchers also think that the ROS1 gene mutation promotes the growth of lung tumors and may play a part in their spread to other organs.

In a small clinical trial, 33 people with advanced NSCLC with the ROS1 gene mutation were treated with crizotinib. Seventy-nine percent had never smoked. At the time of the report, the tumor shrank in 59 percent of patients. The study is ongoing.

What Patients Need to Know

This is the first study to show that using a drug that targets the ROS1 gene mutation may be beneficial. (Crizotinib already is approved by the FDA for treating lung cancer with the ALK gene mutation.) This is another example of the importance of testing for different gene mutations in people with lung cancer. However, larger clinical trials with more people taking part are needed to confirm these promising results with crizotinib in advanced lung cancer with the ROS1 gene mutation.

AUY922 and Erlotinib for Resistant Lung Cancer With the EGFR Gene Mutation

The combination of a new targeted treatment called AUY922 and a standard one, erlotinib, may be an effective way of treating people whose lung cancer has the EGFR gene mutation. AUY922 acts by targeting a substance in lung tumors that they need to grow and survive.

Sixteen people with lung cancer and the EGFR gene mutation took part in this early stage of research. All of their tumors had developed resistance and no longer responded to treatments they had already received that targeted this gene mutation. In two of these patients, the tumor shrank, and in four others, the tumor stopped growing for at least eight weeks after they received AUY922 plus erlotinib. The most common side effects reported with this combination treatment were diarrhea, fatigue, muscle pain and nausea.

What Patients Need to Know

People whose lung cancer has an EGFR gene mutation are often treated with a medication that targets this gene mutation. However, after a while, the tumor often finds a way to come back, and it usually does so by developing a second gene mutation. The new targeted drug AUY922 seems to work in some patients, even in those whose tumors have double gene mutations. Although this is a very small study, the combination of AUY922 and erlotinib may prove to benefit patients with this resistant type of lung cancer. Larger studies should show whether this combination treatment could help these patients survive longer.

Lymphoma

These were among the most important progress reports on lymphoma treatment presented at the 2013 Annual Meeting of the American Society of Clinical Oncology:

Two new medications—idelalisib and IPI-145—have shown promising results in the treatment of people with resistant non-Hodgkin lymphoma (NHL). These drugs may change the way this blood cancer is treated in the future *(page 44).*

A new drug called belinostat may benefit people with peripheral T-cell lymphoma (PTCL), a fast-growing type of NHL. Belinostat belongs to a class of drugs that target and block enzymes that spur the growth of lymphoma cells *(page 45).*

The combination of ibrutinib and chemotherapy seems to be safe and effective in treating people with fast-growing lymphomas such as B-cell NHL. This is important because, for most patients with these diagnoses, the cancer eventually stops responding to the current standard treatment of chemotherapy alone *(page 46).*

ABT-199 may prove to be an effective treatment for people who have resistant NHLs, especially mantle cell lymphoma (MCL). This new drug belongs to a class of treatments that block proteins that play an important role in the growth of certain types of lymphomas *(page 47).*

Lenalidomide—an FDA-approved treatment of the blood cancer multiple myeloma—also may prove to benefit people who have MCL that no longer responds to treatment with bortezomib. Lenalidomide helps the body's immune system destroy lymphoma cells *(page 49).*

The current standard of post-treatment care for people with diffuse large B-cell lymphoma (DLBCL) includes routine imaging every six months for two years after treatment. But a recent study shows that imaging identifies a return of the cancer in only a small number of patients without symptoms *(page 49).*

Idelalisib and IPI-145 for Resistant NHL

Two new medications—idelalisib and IPI-145—have shown promising results in the treatment of people with resistant NHL. These drugs may change the way this blood cancer is treated in the future. Both drugs belong to a new class of treatments called PI3K inhibitors. They target the PI3K pathway, which often plays an important role in the growth of many different types of lymphoma cells. (A pathway is a series of actions among molecules in cells, including cancer cells, that can lead to cell growth and reproduction, for example.)

In a recent study, idelalisib and standard treatment were given to 78 people with resistant indolent (slow-growing) NHL. (Before the clinical trial, all of these patients had already received an average of three other treatments for their lymphoma.) Thirty study participants received idelalisib plus rituximab (Rituxan), 34 received idelalisib plus bendamustine (Treanda) and 14 received idelalisib plus both rituximab and bendamustine. The lymphomas in nearly 80 percent of people in all three groups responded to treatment with idelalisib. Slightly better results were achieved with idelalisib plus bendamustine. After 20 months of treatment, the tumor had not continued to grow in nearly three-quarters of those whose cancer responded.

In another study, the medication IPI-145 was given to 55 people with resistant T-cell lymphomas as well as fast- and slow-growing B-cell lymphomas. In the 27 patients who have

been evaluated so far, the tumor shrank or did not continue to grow in 19 of them. Ninety-two percent of these responses were seen within three months of treatment with IPI-145.

What Patients Need to Know

Idelalisib, in combination with approved treatments, and IPI-145 appear to be promising ways to improve outcomes for people with some resistant types of NHL. The results are from an early stage of research, but both of these drugs seem to be beneficial. Further studies in more patients with lymphoma (both resistant and newly diagnosed) are ongoing to confirm these results and help doctors learn how best to use these drugs in the future.

Belinostat for Treatment of PTCL

A new drug called belinostat may benefit people with PTCL, a fast-growing type of NHL. Belinostat belongs to a class of

drugs known as HDAC inhibitors. These medications target and block enzymes that spur the growth of lymphoma cells.

Nearly 130 people with resistant PTCL that no longer responded to at least one previous treatment received belinostat as part of the BELIEF clinical trial. Researchers found that with belinostat, the tumor shrank in about 26 percent of these patients. The benefits of belinostat were seen even in people with low platelet counts and in those who had already received a stem cell transplant. (Platelets are blood cells that help the blood clot to stop bleeding. Stem cell transplant is a treatment of lymphoma in which blood-forming cells that have been destroyed by cancer are removed and replaced with stem cells, which make healthy blood cells.)

What Patients Need to Know

These early results on belinostat are encouraging, especially now that some treated patients have benefited for more than a year. Belinostat works similarly to another HDAC inhibitor called vorinostat (Zolinza), which the U.S. Food and Drug Administration (FDA) has approved for treatment of a type of lymphoma that affects the skin. Researchers plan to study belinostat further in combination with traditional treatments to see whether they can improve outcomes for people with PTCL.

Combination Treatment With Ibrutinib for B-cell NHL

The combination of the new drug ibrutinib (Imbruvica) with standard chemotherapy may be an effective treatment for people with B-cell NHL. Ibrutinib belongs to a new class of drugs called Bruton's tyrosine kinase (BTK) inhibitors. These medications block the effects of BTK, an important enzyme found in blood cells (including B cells) in the BCR pathway.

This pathway appears to be involved in the growth and survival of many types of B-cell tumors.

In a recent clinical trial, 17 patients with B-cell NHL were treated with ibrutinib and R-CHOP chemotherapy. (R-CHOP chemotherapy includes rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone.) None of these people had received prior treatment for their cancer. Of the 15 patients evaluated so far, the tumor shrank in 100 percent of them, regardless of the dose of ibrutinib used.

What Patients Need to Know

R-CHOP remains the standard treatment for people with common B-cell lymphomas. However, for most patients with these diagnoses, the cancer eventually stops responding to this treatment. So it's encouraging to learn that the combination of ibrutinib and chemotherapy seems to be safe and effective. Adding ibrutinib to R-CHOP did not appear to cause additional side effects. This new combination treatment will be studied further in patients with other types of newly diagnosed B-cell lymphomas to help doctors learn how best to use it in the future.

ABT-199 for Resistant NHLs and MCL

A medication known as ABT-199 may prove to be an effective treatment for people who have resistant NHLs, especially MCL, according to the results of a recent clinical trial. This new drug belongs to a class of treatments known as BCL-2 inhibitors. ABT-199 blocks the function of BCL-2 proteins, which play an important role in the growth of certain types of NHL.

Thirty-one people with resistant NHL, including people with MCL, took part in this study. All of the patients had already received an average of three other treatments for their cancer.

Of the 29 people evaluated so far, the cancer responded to treatment with ABT-199 in more than 50 percent of them. The tumor shrank in all eight patients with MCL.

What Patients Need to Know

ABT-199 is related to another drug that was developed to target the BCL-2 gene, but that medication caused a decrease in platelet counts, which can lead to increased bruising, bleeding or both. This redesigned version of the drug appears to be effective without causing a drop in platelet counts. The promising results with ABT-199 are from an early-stage clinical trial. Researchers are now studying this drug further, using it alone and in combination with chemotherapies such as rituximab and bendamustine to see how best to treat those with NHL. ABT-199 also may be effective in treating people

with chronic lymphocytic leukemia, so it is being studied in people with this type of blood cancer as well.

Lenalidomide in Resistant MCL

Lenalidomide (Revlimid)—an FDA-approved treatment of the blood cancer multiple myeloma—also may prove to benefit people who have MCL that no longer responds to bortezomib (Velcade). Lenalidomide helps the body's immune system destroy lymphoma cells.

As part of a larger clinical trial, researchers analyzed the results of lenalidomide used to treat 134 people with MCL that no longer responded to standard chemotherapy. These people had already received an average of four treatments for their cancer. Of the patients evaluated, nearly 30 percent responded to treatment with lenalidomide. The benefits of lenalidomide appeared to last for almost 18 months. In fact, researchers found that treatment with lenalidomide offered some benefit even in many patients with risk factors usually linked to less successful outcomes.

What Patients Need to Know

In 2006, lenalidomide in combination with the steroid medication dexamethasone was approved by the FDA for treating people with multiple myeloma that no longer responded to other treatments. Now, based on the results of this study, lenalidomide plus dexamethasone is an approved treatment for people with MCL whose cancer no longer responds to bortezomib or other treatments.

Imaging for Relapse of DLBCL

Routine imaging appears to offer little benefit when it comes to identifying which people with DLBCL—the most common

form of NHL—are likely to have a relapse. (Relapse is a return of cancer after treatment and a period when symptoms of cancer were not seen.)

In a large clinical trial of people with newly diagnosed DLBCL, 644 patients had no sign of cancer after treatment. Of these people, about 20 percent relapsed. In this smaller group, nearly 70 percent had symptoms. About 40 percent had a change in their physical exam, and 55 percent had a change in their blood test results. Imaging with computed tomography (CT) identified relapse in only eight patients, or 1.5 percent, who had no symptoms. (CT records images of the body's organs by scanning them with X-rays.)

What Patients Need to Know

The current standard of post-treatment care for people with DLBCL includes routine imaging every six months for two years after treatment. However, according to the results of this recent study, imaging only seems to identify a relapse in a small number of patients without symptoms. Because doctors do not want to expose patients unnecessarily to the small amount of radiation from imaging tests such as CT, more studies are needed to better understand whether these tests are still a useful tool after treatment for DLBCL.

For now, patients should discuss the use of routine X-ray imaging to detect relapse with their doctor to decide whether it is right for them. Research indicates that most relapses are found because of symptoms or changes seen during a physical exam or blood test. So, people who have been treated for DLBCL should continue to have regular blood tests and physical exams.

Melanoma

Exciting advances in melanoma treatment were reported at the 2013 Annual Meeting of the American Society of Clinical Oncology:

The combination of dabrafenib and trametinib may prove to be particularly effective for people who have not already received treatment targeting the BRAF V600E gene mutation (change). Researchers continue to explore the benefits of blocking BRAF V600E and other mutations at the same time *(page 52).*

Selumetinib appears to be a promising treatment for people who have metastatic melanoma of the eye. This is the first time that a drug has been shown to improve outcomes for people with this type of cancer *(page 54).*

Nivolumab alone and in combination with ipilimumab shrank tumors in many patients and may prove to be an effective way to extend survival. To confirm the benefits of this and other treatments, it's important to conduct additional clinical trials with more people taking part *(page 55).*

The new immunotherapy lambrolizumab may be a promising way to treat people with metastatic melanoma—whether or not they have already taken ipilimumab. Early-stage clinical trials show that lambrolizumab is safe and warrants further study *(page 56).*

A new drug known as MPDL3280A, which targets PD-L1, may prove to be an effective treatment for people with metastatic melanoma. As with other medications in its class, this drug is designed to help the body's immune system so it is better able to destroy cancer cells *(page 57).*

Dabrafenib and Trametinib for Metastatic Melanoma

The combination of two targeted treatments—dabrafenib (Tafinlar) and trametinib (Mekinist)—appears to be an effective way to treat people whose metastatic melanoma has the BRAF V600E gene mutation. (Cancer that is metastatic—also called advanced—has spread to other parts of the body from its original site.) According to the results of a recent clinical trial, this combination treatment may prove to be most beneficial to those who have never received treatment targeting this gene mutation. To destroy cancer cells, targeted treatments focus on specific cell mechanisms thought to be important for the growth and survival of tumor cells. Unlike chemotherapy, targeted treatments are designed to spare healthy tissues and tend to cause less severe side effects.

Last year, researchers reported results from a clinical trial that showed more than half of the 77 people with melanoma taking part responded to treatment with the combination of dabrafenib and trametinib. This year, the same researchers discovered that it took much longer for the tumor to grow in patients who had never before received treatment targeting the BRAF V600E gene mutation, compared with those who had received such targeted treatment (10.8 months versus 3.6 months).

More of the patients receiving dabrafenib plus trametinib for the first time benefited than those who had received treatment before the clinical trial. In the group treated for the first time, 63 percent of the cancers responded; in the group that had already received other treatments, 15 percent of the cancers responded.

What Patients Need to Know

When the U.S. Food and Drug Administration (FDA) approved vemurafenib (Zelboraf), it changed the way people with metastatic melanoma are treated. This medication was the first treatment to target the BRAF V600E gene mutation. Now, dabrafenib (also targeting BRAF V600E) and trametinib (targeting another gene mutation known as MEK) have been shown to be effective treatments. And, according to these promising results, the combination of dabrafenib and trametinib may prove to be particularly effective for people who have not already received treatment targeting the BRAF V600E gene mutation. Researchers believe that blocking both the BRAF and MEK mechanisms at the same time may be even better than blocking just one of them. They will continue to study this promising treatment in people with different types of cancer.

Selumetinib for Metastatic Melanoma of the Eye

Selumetinib appears to be a promising treatment for people who have metastatic melanoma of the eye. (Also known as uveal melanoma, this rare type of melanoma affects the colored part of the eye.) Early results show that selumetinib shrank these eye tumors in half of those who received it.

At 16 cancer centers, 98 people with metastatic uveal melanoma took part in this clinical trial. Approximately half of them were given selumetinib, and the others were given chemotherapy with temozolomide (Temodar and others). Of the 92 patients evaluated so far, the tumor shrank in 50 percent of those who received selumetinib, compared with 11 percent of those who received temozolomide. In addition, it took longer for the tumor to continue growing with selumetinib than with temozolomide (nearly 16 weeks versus seven weeks).

What Patients Need to Know

It is very challenging to treat uveal melanoma. That is why researchers are calling these early results with selumetinib "remarkable." This is the first time that a drug has been shown to improve outcomes in people with this type of advanced melanoma of the eye. Like trametinib, selumetinib targets the MEK protein, which plays an important part in the growth of cancer cells in many of these eye tumors. Further studies in more patients will show whether this new drug (either alone or in combination with other treatments) can help to extend survival.

Immunotherapy for Melanoma

One of the most exciting new developments in treating melanoma is immunotherapy that targets the PD-1 pathway. Immunotherapy is treatment that helps the body's immune system fight cancer. The PD-1 pathway, which includes the two proteins PD-1 and PD-L1, is involved in the growth of tumor cells and their ability to resist treatment. Recent studies with nivolumab and lambrolizumab (drugs that target PD-1) as well as MPDL3280A (a drug that targets PD-L1) have shown possible benefits for people with melanoma.

Nivolumab Alone and in Combination for Metastatic Melanoma

Two recent clinical trials have shown encouraging results with nivolumab in treating people with advanced melanoma. The use of nivolumab alone and in combination with ipilimumab (Yervoy) shrank tumors in many patients and may prove to be an effective way to extend survival.

In the first study, more than 100 people with metastatic melanoma were given nivolumab. (One-quarter of the patients had already received at least three other treatments for their cancer.) Several different doses of nivolumab were studied. Researchers found that tumors shrank in about 30 percent of all of the patients taking nivolumab. The benefits of treatment lasted for more than one year in nearly half of those whose cancer responded. In addition, more than 60 percent of the patients were surviving one year after treatment, and nearly 45 percent were surviving two years after treatment.

In the second study, about 70 patients with metastatic melanoma were given the combination of nivolumab plus

ipilimumab. Twelve weeks after treatment, the tumor shrank by at least 80 percent in 30 percent of the 37 patients evaluated so far. Researchers found that these results with the two-drug combination may prove to be better than using nivolumab alone. Ipilimumab, which blocks another pathway called CTLA-4, was the first immunotherapy to be approved for treating people with melanoma.

What Patients Need to Know

The use of immunotherapies such as ipilimumab and nivolumab is an exciting new chapter in the treatment of melanoma. Researchers are encouraged by the benefits seen so far with nivolumab—both alone and in combination with ipilimumab. They believe that combining these treatments to target different pathways may prove to be the best way to improve outcomes for people with metastatic melanoma. However, it's important to remember that these results are from an early stage of research in a small number of people. Additional clinical trials in which more people take part are needed to confirm these benefits and to help doctors know how best to use these and other new medications for people with melanoma.

Lambrolizumab for Metastatic Melanoma

In an early-stage clinical trial, lambrolizumab has shown encouraging results in treating people with advanced melanoma. Approximately 300 people took part in an ongoing international study. More than two-thirds of them had not already received ipilimumab. Of the 85 patients evaluated so far, the tumor shrank in nearly 50 percent of them. The tumor completely shrank in about 10 percent of those who received lambrolizumab.

What Patients Need to Know

The new immunotherapy lambrolizumab may be a promising way to treat people with metastatic melanoma, whether or not they have already taken ipilimumab. With these early results showing its safety, lambrolizumab will now be compared with chemotherapy to see whether it may benefit those whose melanoma no longer responds to ipilimumab.

MPDL3280A for Metastatic Melanoma

Two recent clinical trials have shown that a new drug known as MPDL3280A, which targets PD-L1, may prove to be an effective treatment for people with metastatic melanoma. This medication is designed to help the body's immune system destroy cancer cells.

The first study included approximately 170 people with different types of cancer, including melanoma. All of them

received injections of MPDL3280A. Of the 122 patients evaluated so far, cancer in about 21 percent responded to treatment. In several patients, the tumors shrank within days of receiving MPDL3280A. Six months after treatment, the tumor had not continued to grow in nearly 45 percent of patients. As expected, this treatment seemed to work better in people whose tumors tested positive for the presence of PD-L1. However, researchers found that it also worked in some people who did not have the PD-L1 protein.

In the second study, 45 people with metastatic melanoma received treatment with MPDL3280A. More than 90 percent of them had surgery for their skin cancer, and two-thirds had already received other treatments as well. Of the 35 patients evaluated so far, the tumor shrank in about one-quarter of them. And, as in the first study, for some people the tumor shrank within days of receiving treatment. Six months after treatment, the tumor had not continued to grow in 35 percent of patients.

What Patients Need to Know

Targeting PD-L1 with immunotherapies such as MPDL3280A appears to be an effective strategy for helping the body's immune system find and destroy cancer cells. Researchers plan to continue studying this new treatment—alone and in combination with the approved targeted treatment vemurafenib—in more people with metastatic melanoma. MPDL3280A is also being studied in people with other types of cancer, such as kidney, colon, breast and lung, to see whether it may be benefit them as well.

Ovarian Cancer

Some important developments in ovarian cancer treatment were reported at the 2013 Annual Meeting of the American Society of Clinical Oncology:

The combination of paclitaxel and carboplatin remains the most effective way to treat women with advanced ovarian cancer. But taking the drugs weekly instead of every three weeks, which is the standard schedule, causes fewer side effects and may be more effective *(page 60).*

Pazopanib may help prevent cancer from recurring (coming back) in women who have already finished taking chemotherapy for advanced ovarian cancer. This is a study to show that a targeted treatment may be beneficial for women with ovarian cancer, following standard treatment *(page 61).*

The new targeted treatments volasertib and olaparib may improve outcomes for women with resistant ovarian cancer. Volasertib appears to be effective in stopping the growth of cancer in some women with ovarian cancer. Women with ovarian cancer that has the BRCA gene mutation (change) may benefit most from olaparib *(page 62).*

Paclitaxel and Carboplatin for Advanced Ovarian Cancer

The combination of paclitaxel (Taxol and others) and carboplatin remains the most effective way to treat women with advanced ovarian cancer, according to the results of one recent clinical trial. In another study, researchers found that taking these medications weekly instead of every three weeks, which is the standard schedule of treatment, may be just as effective and may cause fewer side effects.

In the first study, known as the OV16 trial, more than 800 women with newly diagnosed advanced ovarian cancer were treated with chemotherapy. Half of them were given standard treatment with paclitaxel and carboplatin. The others received cisplatin and topotecan (Hycamtin and others) first and then paclitaxel plus carboplatin. More than eight years after treatment, women in both groups survived for about 44 months.

In the second study, known as the Italian MITO-7 trial, more than 800 women with advanced ovarian cancer who had not already received chemotherapy took part.

Some of these patients received paclitaxel and carboplatin in the standard way—every three weeks for six cycles. The others were given paclitaxel and carboplatin weekly for 18 consecutive treatments. Nearly 20 months after treatment, it took about the same time for the tumor to continue growing in both groups of patients.

However, the women who received the weekly treatment had less hair loss, nerve damage and vomiting than those who received the standard schedule of treatment every three weeks. In addition, the weekly treatment caused less severe neutropenia (a low white blood cell count that can increase the risk of infection).

What Patients Need to Know

Paclitaxel and carboplatin remain the standard treatment for women with advanced ovarian cancer. Although the search continues for better ways to treat women with advanced ovarian cancer, studies such as the OV16 trial should reassure doctors and their patients that this treatment is still the most effective available. As for how best to give this combination treatment, weekly treatment may improve the quality of life for these women, compared with treatment every three weeks. The MITO-7 trial showed that weekly paclitaxel plus carboplatin was no better than standard treatment in stopping ovarian tumors from growing. However, a Japanese study presented in 2012 showed that weekly treatment may stop the tumor from growing and may even help these women survive longer. Further studies are needed to confirm the best way to give these drugs in the future.

Pazopanib for Advanced Ovarian Cancer

Pazopanib (Votrient) may help prevent cancer from coming back in women who have already finished taking chemotherapy for advanced ovarian cancer, according to a recent clinical trial. Pazopanib is a targeted treatment approved by the U.S. Food and Drug Administration for the treatment of advanced kidney cancer and soft-tissue sarcoma (a type of cancer) found in muscle or fat, for example.

More than 900 women with advanced ovarian cancer took part in the AGO-OVAR16 international study. All of them had already successfully completed chemotherapy. Some of the patients then were given pazopanib daily for two years, and the others were given a placebo (a look-alike pill that has no active ingredient). Researchers found that it took longer for the tumor to continue growing in those who were treated with pazopanib than in those who were not (17.9 months versus 12.3 months). The most common side effects of pazopanib were high blood pressure, diarrhea and fatigue.

Targeted treatments such as pazopanib block certain cell activities thought to be important for the growth of cancer cells. They work differently from traditional chemotherapy in that they target cancer cells while sparing healthy tissues and tend to cause less severe side effects.

What Patients Need to Know

These are very promising results with pazopanib maintenance therapy in women with advanced ovarian cancer. (Maintenance therapy helps prevent cancer from returning after the initial treatment has been completed.) Researchers hope that further studies will show that pazopanib also helps these women survive longer. In addition, doctors want to find out whether it's better to use pazopanib as part of the first treatment for ovarian cancer or as a later treatment. Future clinical trials should help answer this question.

Volasertib and Olaparib for Resistant Ovarian Cancer

Volasertib and olaparib are new targeted treatments that may improve the outcomes for women with resistant ovarian cancer, according to the results of two recent clinical trials.

More than 100 women with ovarian cancer that no longer responded to standard chemotherapy took part in the first study. Half of them received volasertib, and the others received chemotherapy. The chemotherapy treatments included doxorubicin, topotecan, paclitaxel or gemcitabine (Gemzar and others). About six months after treatment, the tumor shrank or stopped growing in about 30 percent of the women on volasertib and in 43 percent of those on chemotherapy. However, no patients taking volasertib stopped treatment because of side effects, compared with eight patients taking chemotherapy who did stop their treatment.

More than 250 women with ovarian cancer that no longer responded to standard chemotherapy took part in the second clinical trial evaluating olaparib. Researchers were particularly interested in a subgroup of women who had the BRCA gene mutation, which has been linked to an increased risk of breast and ovarian cancers. In this group of women, it took longer

for the cancer to continue growing in those who received olaparib than in those who did not (11.2 months versus 4.1 months). In addition, all of the women treated with olaparib had an improved quality of life compared with those who did not receive olaparib.

What Patients Need to Know

Both volasertib and olaparib may prove to be beneficial for women with ovarian cancer. Although better results were achieved with standard chemotherapy than with volasertib, this new drug appears to be effective in stopping the growth of cancer in some women with ovarian cancer. The next step will be to find out which women with ovarian cancer would benefit most from volasertib.

Researchers now know that women with ovarian cancer that has the BRCA gene mutation may benefit most from olaparib. All ovarian cancers are not the same, and a treatment that may work for some tumors may not work for others. Targeted treatments such as olaparib, which focus on certain genetic mutations in a certain type of ovarian cancer, are a promising way to improve the outcomes for women with ovarian cancer. Additional studies in larger groups of women with ovarian cancer are needed to help doctors learn whether olaparib can help patients survive longer.

Pancreatic Cancer

Important developments in pancreatic cancer treatment were reported at the 2013 Annual Meeting of the American Society of Clinical Oncology:

Taking nab-paclitaxel plus gemcitabine is more effective than gemcitabine alone for the treatment of metastatic pancreatic cancer. Researchers believe this drug combination will be a standard treatment option for patients *(page 66).*

A new drug known as S-1 may be at least as good as—and perhaps even better than—the standard drug gemcitabine for treating people with pancreatic cancer after surgery. Studied in Japan, S-1 may become a new standard treatment in Asia to prevent the return of pancreatic cancer after surgery, but further studies are needed to show its benefit in non-Asian people in other parts of the world *(page 67).*

Chemotherapy alone appears to be more effective than chemotherapy plus radiation in treating people with locally advanced pancreatic cancer. Routinely adding radiation after a course of chemotherapy, as doctors have done, may not improve patients' outcomes *(page 68).*

Adding a type of vaccine to the chemotherapy drugs gemcitabine and capecitabine does not appear, overall, to improve outcomes in people with locally advanced or metastatic pancreatic cancer. Studies are underway to find out whether a subset of patients may benefit *(page 69).*

Nab-Paclitaxel and Gemcitabine for Metastatic Pancreatic Cancer

The combination of nab-paclitaxel (Abraxane) and gemcitabine (Gemzar and others) is more effective than gemcitabine alone in the treatment of people with newly diagnosed, untreated metastatic pancreatic cancer, according to the results of a recent clinical trial. Researchers are so encouraged by this new drug combination, they believe it may become a new standard treatment option for people with metastatic pancreatic cancer. (Cancer that is metastatic has spread from its original location—in this case, the pancreas—to other parts of the body.)

More than 860 people with metastatic pancreatic cancer took part in the IMPACT study. Half of the patients received nab-paclitaxel plus gemcitabine, and the others received gemcitabine alone. The tumor shrank in more patients who were given the combination treatment than those who were not given it (23 percent versus seven percent). It also took longer for the cancer to grow in patients on nab-paclitaxel plus gemcitabine than in those on gemcitabine alone (5.5 months versus 3.7 months). Patients taking the combination treatment survived several months longer than those on the single-drug treatment.

What Patients Need to Know

The results of this clinical trial have led the U.S. Food and Drug Administration to approve nab-paclitaxel plus gemcitabine for the first-time treatment of metastatic cancer of the pancreas. This treatment option represents a new standard of care. It also may become the backbone for many future pancreatic cancer treatments.

Chemotherapy With S-1 for Pancreatic Cancer After Surgery

A new anti-cancer drug known as S-1 may be at least as good as—and perhaps even better than—the standard drug gemcitabine for preventing a return of pancreatic cancer after surgery. Although S-1 may become a new standard of treatment in Asia to prevent the return of pancreatic cancer after surgery, further studies are needed to show its benefit in non-Asian people in other parts of the world.

About 380 people who had surgery to remove their pancreatic cancer took part in the Japanese trial known as JASPAC 01. Half of these patients received standard treatment with gemcitabine after surgery, and the others received S-1. Two years later, the cancer had not returned in more people treated with S-1 than in those who had received gemcitabine (49 percent versus 29 percent). Seventy percent of patients on S-1 continued to survive two years after treatment, compared with 53 percent of those on gemcitabine.

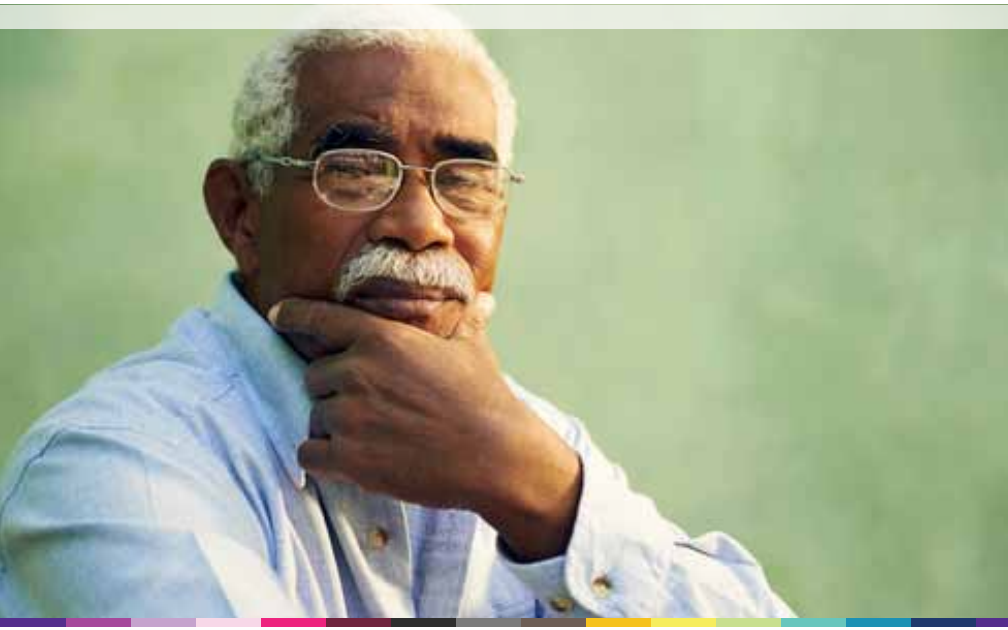
S-1 is an oral version of the commonly used chemotherapy drug 5-fluorouracil. It is currently an approved treatment for different types of cancer, including colorectal, lung and pancreatic, in several Asian countries and most of Europe but not yet in the United States.

What Patients Need to Know

Most people with pancreatic cancer are diagnosed at an advanced stage, and surgery is not possible. S-1 may become a new standard treatment option and possibly change how people with pancreatic cancer are treated in Japan after surgery. This drug will be tested further in people from North America and Europe to see whether it is as effective in them as in people from Asia.

Chemotherapy for Locally Advanced Pancreatic Cancer

Chemotherapy alone appears to be as effective as chemotherapy plus radiation in treating people with locally advanced pancreatic cancer. Recent results from the LAP 07 clinical trial show that chemotherapy alone remains a standard treatment option for these patients. (Cancer that is locally advanced has spread from where it started to nearby tissue or lymph nodes.)



Nearly 450 people with locally advanced pancreatic cancer took part in the LAP 07 study. All of these patients were first treated with gemcitabine alone or gemcitabine and erlotinib (Tarceva) for four months. Then, the 269 patients whose cancer did not continue to grow were given additional treatment. Half of those whose cancer responded to initial chemotherapy were given an extra two months of chemotherapy. The other half whose cancer responded to initial chemotherapy also were given an extra two months of chemotherapy plus radiation. The clinical trial showed that additional chemotherapy was as effective as additional chemotherapy followed by radiation.

What Patients Need to Know

Doctors often consider adding radiation to the treatment of people with pancreatic cancer after their tumors respond to initial chemotherapy. But, according to the results of the LAP 07 trial, routinely adding radiation to chemotherapy may not improve their outcomes. Further study is needed to find out whether there is a subset of patients who may benefit from adding radiation to their treatment plan. In the LAP 07 clinical trial, researchers also learned that adding erlotinib to gemcitabine did not seem to offer any real benefit over gemcitabine alone. For now, gemcitabine alone remains a treatment option to control the growth of locally advanced pancreatic cancer.

Vaccine and Chemotherapy for Locally Advanced or Metastatic Pancreatic Cancer

Adding a vaccine to the chemotherapy drugs gemcitabine and capecitabine (Xeloda and others) does not appear to improve outcomes in people with locally advanced or metastatic pancreatic cancer. Such combination treatment is

known as chemoimmunotherapy. It helps the body's immune system in destroying cancer cells.

More than 1,000 people with locally advanced or metastatic pancreatic cancer from more than 50 centers in the United Kingdom were given one of three treatments:

1. Gemcitabine plus capecitabine;
2. Gemcitabine plus capecitabine *with* the vaccine (given at the same time as chemotherapy, or chemoimmunotherapy);
3. Gemcitabine plus capecitabine, *followed by* the vaccine (given later, after chemotherapy).

The tumor shrank in about 18 percent of those in the first group of patients who received gemcitabine plus capecitabine but not the vaccine. In the second group of people, who received chemoimmunotherapy, the tumor shrank in about 16 percent. The least effective treatment seemed to be the third one, in which patients received gemcitabine plus capecitabine followed by the vaccine. Researchers noted that survival did not improve for patients in either group that received the vaccine, compared with the group that did not receive the vaccine.

What Patients Need to Know

This is the first large-scale study of a vaccine for the treatment of pancreatic cancer. The combination of gemcitabine, capecitabine and the vaccine has been used in Europe to treat pancreatic cancer that cannot be removed by surgery. In this study, giving the vaccine with or after chemotherapy was not more effective than chemotherapy alone in extending survival for patients with locally advanced or metastatic pancreatic cancer. However, because some patients did respond to the vaccine, it will be studied further to find out who might benefit.

Prostate Cancer

Important developments in prostate cancer treatment were reported at the 2013 Annual Meeting of the American Society of Clinical Oncology:

A new genetic test may help doctors decide whether treatment is needed for men with prostate cancer. This test allows doctors to predict which men are more likely to develop fast-growing tumors that should be treated and which men are more likely to develop slow-growing tumors that may never need treatment *(page 72).*

The targeted treatment enzalutamide may prove to be an effective first-time treatment for men with prostate cancer. The drug appears to benefit patients who have never received hormone therapy *(page 73).*

Combining the drug abiraterone and the steroid prednisone appears to be a safe and effective way to treat men with metastatic prostate cancer. The combination of these two drugs also may delay the growth of new tumors *(page 74).*

Researchers have confirmed that the standard of care for men with metastatic prostate cancer remains the combination of docetaxel and prednisone. They had hoped that adding the targeted treatment ziv-aflibercept would extend survival for these men, but it did not *(page 77).*

A new drug, now called DSTP3086S, appears to be a promising treatment for men with metastatic prostate cancer, according to the early results of a small clinical trial. DSTP3086S targets STEAP1, a substance found in many prostate tumors as well as in colon, ovarian and bladder cancers *(page 78).*

New Genetic Test for Guiding Prostate Cancer Treatment

A new genetic test called Prolaris may help doctors decide whether treatment is needed for men with prostate cancer. This test allows doctors to look at certain genes in prostate tumors. They can then predict which men are more likely to develop fast-growing tumors and which ones are more likely to develop slow-growing tumors. With slow-growing tumors, it may be better to adopt the "watchful-waiting" approach when treatment is not needed now and may never be needed.

Recently, researchers studied Prolaris in more than 1,600 men who had already received treatment for prostate cancer. The treatments included surgery and radiation. Prolaris looked at about 46 genes, and then a score was calculated for each patient. The score was used to predict which patients' tumors were most likely to return and which ones were not.

What Patients Need to Know

Not every man with prostate cancer requires treatment. It can be challenging for doctors to predict how prostate cancer will develop in different patients, which tumors may need further treatment and which ones may not. Now, with the early results with the Prolaris genetic test, doctors may be better able to select the right treatment for the right person based on whether that person has a fast-growing type of tumor or not. Prolaris is similar to the Onco*type* DX test, which has helped doctors choose the most appropriate treatment for women with metastatic breast cancer. (Metastatic cancer is cancer that has spread beyond its original site to other parts of the body.) However, additional studies are needed to help doctors understand how best to use Prolaris to improve future treatment outcomes for men with prostate cancer.

Enzalutamide as a First Drug Treatment for Prostate Cancer

The targeted treatment enzalutamide (Xtandi) may prove to be an effective treatment for men with prostate cancer who have not received hormone therapy, according to a recent clinical trial. (Targeted treatments are designed to target cancer cells while sparing healthy cells and tend to cause less severe side effects than chemotherapy.) Enzalutamide has already been approved by the U.S. Food and Drug Administration (FDA) for treatment of metastatic prostate cancer, after docetaxel (Taxotere and others) is given.

Nearly 70 men with prostate cancer received enzalutamide for 25 weeks in a clinical trial. About one-third of these men had already had surgery for their cancer, and nearly one-fourth had already received radiation. None of these men had ever taken hormone therapy.

More than 90 percent of the men responded to treatment with enzalutamide, with a drop in their prostate-specific antigen (PSA) levels. Rising PSA levels often signal the return of prostate cancer. In 16 patients evaluated so far, the tumor shrank partly or disappeared in 50 percent.

Another study known as the AFFIRM trial showed similar benefits with enzalutamide in men with metastatic prostate cancer that no longer responded to other treatment—regardless of their age. Researchers focused on the outcomes for nearly 300 older patients in this larger study of 800 men. Enzalutamide helped these men live longer without their cancer growing and extended their survival as well. Fatigue and nausea were the most common side effects of enzalutamide, but they occurred in about the same number of older and younger patients treated.

What Patients Need to Know

The AFFIRM trial offered new hope to men whose prostate cancer stopped responding to other treatments. In the summer of 2012, the FDA approved enzalutamide for men with metastatic prostate cancer who had already received docetaxel. These more recent results indicate that enzalutamide may also be an effective first-time treatment for men with prostate cancer. However, further studies are needed to confirm the benefits of this treatment earlier in the course of prostate cancer.

Abiraterone and Prednisone for Metastatic Prostate Cancer

Combining the drug abiraterone (Zytiga) and the steroid prednisone appears to be a safe and effective way to treat men with metastatic prostate cancer, according to the results

of a large clinical trial. More than 1,000 men took part in this study, which compared abiraterone plus prednisone with a placebo (a look-alike pill with no active ingredient) plus prednisone. None of these men had ever received chemotherapy for their advanced prostate cancer.

Abiraterone delayed the time it took before patients needed to start chemotherapy and also seemed to help them survive longer. After 24 months of treatment, there were few severe side effects in the men who received abiraterone.

Researchers also have learned that the combination of abiraterone and prednisone may delay the occurrence of severe pain in men with metastatic prostate cancer. Of nearly 800 such patients, half of them received abiraterone plus prednisone, and the others received prednisone alone. After

about 20 months of treatment, more men taking abiraterone plus prednisone experienced pain relief than those on prednisone alone (45 percent versus 29 percent). Also, pain relief occurred more quickly with abiraterone and prednisone than with prednisone alone (within about 5.5 months versus 13.5 months).

What Patients Need to Know

Combining abiraterone and prednisone is an effective treatment for metastatic prostate cancer that no longer responds to chemotherapy. This combination also seems to be an effective treatment for men who have not already received chemotherapy for their metastatic prostate cancer. In addition, there are benefits of abiraterone and prednisone in terms of pain relief for men who are on treatment for more than two years. Abiraterone works by helping prevent the

body from making testosterone, which, in turn, can prevent the cancer from spreading. Researchers plan to study this promising combination further to better understand how best to extend survival in men with advanced prostate cancer.

Docetaxel and Prednisone for Metastatic Prostate Cancer

Adding the targeted treatment ziv-aflibercept (Zaltrap) to the combination of docetaxel and prednisone does not seem to extend survival for men with metastatic prostate cancer, according to the results of a recent study. Therefore, the standard of care for such patients remains docetaxel and prednisone.

More than 1,200 men with metastatic prostate cancer took part in a study known as the VENICE trial. None of these patients had ever received chemotherapy for their advanced cancer. Half of the men were given ziv-aflibercept along with the standard combination treatment, and the others received a placebo plus the standard combination treatment.

Researchers found that ziv-aflibercept did not help these men survive longer than those who did not take the targeted drug. In fact, those on ziv-aflibercept experienced more side effects than those who were not taking it. Many more men stopped taking ziv-aflibercept because of side effects than stopped taking the combination treatment with placebo (44 percent versus 21 percent).

What Patients Need to Know

Ziv-aflibercept plus the chemotherapy combination called FOLFIRI has been approved by the FDA to treat people with metastatic colorectal cancer that no longer responds to

other treatments. Researchers had hoped that adding this new drug to the standard treatment for metastatic prostate cancer might be beneficial as well. However, the results of the VENICE study show that, for now, docetaxel plus prednisone remains the most effective way to treat men with metastatic prostate cancer who have not already received chemotherapy.

On the Horizon in Metastatic Prostate Cancer

A new type of drug called DSTP3086S appears to be a promising treatment for men with metastatic prostate cancer, according to the early results of a small clinical trial. DSTP3086S targets a substance called STEAP1, which has been found in many prostate tumors as well as in colon, ovarian and bladder cancers.

Nearly 30 men took part in this study; seven of them had already received several treatments for their prostate cancer. All of these patients were given an average of three injections of DSTP3086S. In some of the men evaluated so far, PSA levels decreased by more than 50 percent. In several men, the number of circulating tumor cells (CTCs) was reduced, according to blood test results. Researchers believe that lower blood levels of CTCs may be a good sign that treatment is working.

What Patients Need to Know

These findings on DSTP3086S are encouraging for people with metastatic prostate cancer. This new drug also is being studied in the treatment of people with advanced lymphoma (a type of blood cancer) and metastatic breast cancer. However, it is important to remember that these results are from very early stages of research. Additional studies in larger groups of people are needed to confirm these promising results.

Sarcoma

At the 2013 Annual Meeting of the American Society of Clinical Oncology, researchers reported important information on sarcoma treatment:

In the largest study yet of people with osteosarcoma, researchers confirmed that combination chemotherapy before and after surgery is still the best standard of care. Adding peginterferon alfa-2b, which can cause additional side effects, did not improve the outcome compared with standard treatment *(page 79).*

For people with a gastrointestinal stromal tumor (GIST), taking imatinib for two years after surgery may stop the cancer from coming back. If a patient stops taking imatinib after surgery and the tumor returns, he or she can still benefit from taking the drug at that time *(page 81).*

Scientists have found a new and easier way to study the genetic makeup of GIST. That's important because in the future, it will help doctors match specific treatments to specific types of tumors *(page 82).*

Combination Chemotherapy for Osteosarcoma

Combination chemotherapy given before and after surgery is more effective than the same treatment given with peginterferon alfa-2b (Sylatron) for people who have osteosarcoma, a fast-growing bone tumor. According to a large international clinical trial, the chemotherapy combination called MAP (methotrexate, doxorubicin and cisplatin) remains the standard of care for patients whose osteosarcoma responds well to treatment before surgery.

More than 2,200 people with osteosarcoma that had not spread to other parts of the body took part in the EURAMOS-1 clinical trial. Researchers focused on 715 patients whose cancer responded well to MAP chemotherapy before surgery (also known as upfront chemotherapy). In this smaller group, more than 90 percent of the tumor was destroyed by upfront chemotherapy. Then, half of these "good responders" received more MAP alone, and the others received more MAP with peginterferon alfa-2b (a medication that helps the immune system fight cancer). About three years after treatment, researchers found that adding peginterferon, which can cause additional side effects, was no better than MAP alone.

What Patients Need to Know

The EURAMOS-1 clinical trial is the largest study yet of people with this rare type of bone cancer. These early results show that MAP chemotherapy given before and after surgery remains the standard of care for those whose osteosarcoma responded well to upfront chemotherapy. Researchers are also looking at different types of chemotherapy in the treatment

of patients whose cancer does not respond as well to upfront chemotherapy. Scientists want to learn whether they can improve the outcome for these people.

Imatinib in GIST

Taking imatinib (Gleevec) for two years after surgery may stop the cancer from coming back in people with a GIST, a type of cancer that affects the tissues in the digestive system. According to a recent Italian study, people whose tumors were more likely to recur (come back) seemed to benefit most from imatinib, compared with those who were less likely to have a recurrence.

More than 900 people with GIST that had not spread to other parts of the body took part in this clinical trial. All of them were considered to be at either high or intermediate risk of their tumor coming back. Half of the patients were given imatinib for two years after surgery, and the others were not. During the first three years after treatment, researchers found there were fewer recurrences in those at high risk who took imatinib than in those who did not take the drug. However, those who took imatinib and were at intermediate risk of recurrence did not benefit as much. Researchers also learned that using imatinib after surgery did not seem to affect a person's chances of benefiting from its later use, if the tumor did come back.

What Patients Need to Know

Over the past 10 years, researchers have learned a lot about GIST. They now know that targeted treatments such as imatinib can be used effectively to stop the cancer from returning after surgery to remove the tumor. (Targeted treatments are designed to spare healthy tissues and tend to cause less severe side effects than chemotherapy.) These early

results support the current practice of using imatinib after surgery in those who are at high risk of recurrence. Those who are at intermediate risk of recurrence should discuss the benefits and risks of imatinib with their doctor to find out whether it is right for them.

Identifying Genetic Mutations in GIST

Researchers have found a new and easier way to study the genetic makeup of GIST. BEAMing, or "liquid biopsy," is a technique in which genetic mutations (changes) can be identified simply by taking a blood sample. Unlike the standard biopsy, BEAMing does not require tissue from the tumor to be removed and then examined.

These promising results are from a clinical trial called the GRID study. It focused on the benefits of a new drug called regorafenib (Stivarga). This treatment for GIST was approved by the U.S. Food and Drug Administration in the spring of 2013. In this clinical trial, mutations in the KIT gene, which are found in GIST, were more commonly identified using BEAMing rather than standard biopsy.

What Patients Need to Know

Researchers believe that new technologies such as BEAMing can help them learn more about GIST, which will help doctors match promising treatments to those most likely to benefit. Not all people with GIST have the same KIT mutation; some of these genetic mutations tend to respond better to certain treatments than others. The GRID study results are from a very early stage of research, and BEAMing is not yet available for patients outside of a clinical trial. As more information is gathered about BEAMing and other similar technologies, doctors will have a better idea of how best to use them to improve GIST treatment.

Supportive Care and Quality-of-Life Issues

Reducing the symptoms of cancer treatment side effects was an important focus of the 2013 Annual Meeting of the American Society of Clinical Oncology:

Two different clinical trials have shown that a type of acupuncture may relieve joint pain in women who have been treated for breast cancer. That's important because joint pain can reduce quality of life and interrupt treatment for some women *(page 84).*

Women with breast cancer who took fluoxetine for depression were more likely to complete their cancer treatment and survive longer. This antidepressant medication appeared to improve depressive symptoms and quality of life *(page 85).*

People taking the bone-healing drug denosumab for cancer that has spread to the bone should also take calcium and vitamin D. Those who do appear to be less likely to develop a condition called hypocalcemia (a decrease in the level of calcium in the blood), which is a known risk with the use of denosumab *(page 86).*

Modafinil seems to be no better than placebo (a look-alike pill with no active ingredient) in improving cancer-related fatigue for people with advanced lung cancer. However, another recently published study suggests that the herb ginseng may prove to be a more promising treatment *(page 88).*

Electroacupuncture for Joint Pain in Breast Cancer Survivors

The results of two small clinical trials suggest that electroacupuncture may relieve joint pain in women who have been treated for breast cancer. Acupuncture is the use of small, thin needles that penetrate the skin (not too deeply) to stimulate certain points on the body. With electroacupuncture, the needles carry a mild electric current.

The first study included nearly 70 breast cancer survivors from the United States. All of these women had received treatment with an aromatase inhibitor, a type of drug used to reduce estrogen levels. Researchers found that electroacupuncture seemed to provide relief from the patients' joint aches and pain.

A second study, which is ongoing, recruited 67 women from Australia who have been taking an aromatase inhibitor for

at least six months for early-stage breast cancer. Some of these women received electroacupuncture twice a week for six weeks, and the others did not. The women who received acupuncture reported decreased joint pain.

What Patients Need to Know

Joint pain is a common side effect of treatment with aromatase inhibitors such as anastrozole (Arimidex and others), exemestane (Aromasin and others) and letrozole (Femara and others). In fact, it may occur in up to 50 percent of women who receive these drugs to treat breast cancer. About 15 percent of women taking these medications experience severe joint pain. In some cases, joint pain may cause women to stop their treatment, which might increase the risk of their breast cancer coming back after surgery. So these early results showing electroacupuncture can relieve joint pain are very encouraging. Another large study is ongoing to more clearly understand the benefits and possible side effects of acupuncture.

Antidepressants for Women With Newly Diagnosed Breast Cancer

Before women receive chemotherapy or hormone therapy for early-stage breast cancer, doctors should consider prescribing an antidepressant for those who have symptoms of depression, according to a recent clinical trial. Women in the study whose depressive symptoms and quality of life were improved with an antidepressant were more likely to complete their treatment and survive longer than those who did not receive help for their depression.

Based on a screening questionnaire of more than 350 women with newly diagnosed, early-stage breast cancer, approximately 200 (nearly 60 percent) were found to have

some depressive symptoms. The women with depressive symptoms were given the antidepressant fluoxetine (Prozac, Sarafem and others) or a placebo for six months, along with treatment for their breast cancer. More women given fluoxetine had an improvement in both their depressive symptoms and their quality of life than those who did not receive the drug. Patients on the antidepressant had a better chance of completing their chemotherapy—and surviving longer—than those on the placebo.

What Patients Need to Know

It's very important for women with early-stage breast cancer to complete their treatment—whether it is chemotherapy, hormone therapy or a combination of the two. When diagnosed with breast cancer, women may be at high risk of developing depression. If women are depressed or develop depressive symptoms before or during treatment, they may be less likely to complete their treatment and benefit from it. So these results with the antidepressant fluoxetine are promising. Ideally, this study's results should be confirmed in a larger clinical trial.

Calcium and Vitamin D With Denosumab for Metastatic Cancer in the Bone

People taking the bone-healing drug denosumab (Xgeva) for cancer that has spread to the bone should also take calcium and vitamin D. Those who do are less likely to develop a condition called hypocalcemia (a decrease in the level of calcium in the blood), which is a known risk with the use of denosumab. (Cancer that is metastatic has spread from its original location to another part of the body—in this case, the bone.)

Researchers studied patients with metastatic bone tumors from three different large clinical trials. More than 2,800

of these patients had received treatment with denosumab. About 10 percent of these patients developed hypocalcemia. This side effect was most common within six months of starting treatment with denosumab. It was less common in those who reported using calcium and vitamin D than in those who did not (9 percent versus 16 percent).

What Patients Need to Know

Many people whose cancer has spread to the bone may benefit from the use of denosumab, including those with breast cancer. Hypocalcemia is a possible side effect of treatment with this bone-strengthening drug. Researchers now know that it is very important for people who are receiving denosumab to take both calcium and vitamin D to reduce the risk of developing hypocalcemia. Doctors should be correcting the decreased calcium levels in patients before starting treatment with denosumab. Also, patients should have their calcium levels checked closely during treatment.

Modafinil for the Treatment of Cancer-Related Fatigue

Modafinil (Provigil and others) seems to be no better than placebo in improving cancer-related fatigue for people with advanced lung cancer, according to a recent clinical trial. Based on these results, doctors may have to use different approaches to treat this side effect.

Approximately 200 people with locally advanced or metastatic lung cancer and fatigue took part in a study in the United Kingdom. (Cancer that is locally advanced has spread from where it started to nearby tissue or lymph nodes. Lymph nodes are small "filtering stations" that rid the body of waste and fluids and help fight infections.) Altogether, 160 patients completed questionnaires on fatigue; half of them then received modafinil, while the others received a placebo. Although there was some improvement in fatigue in both treatment groups, modafinil offered no real benefit over placebo. In fact, nearly 50 percent of people taking modafinil reported that treatment was not helpful, compared with less than 25 percent of those on placebo.

What Patients Need to Know

Fatigue is a very common side effect reported by many people being treated for lung cancer. Stimulants such as modafinil had been thought to improve the symptoms of fatigue in people with cancer. But researchers now believe that modafinil is no more effective than a placebo in managing treatment-related fatigue. However, a recent study suggests that the herb ginseng appears to mildly improve fatigue in patients with breast cancer.

Resources

Cancer*Care*®
800-813-HOPE (4673)
www.cancercare.org

American Cancer Society
800-227-2345
www.cancer.org

Cancer.Net
Patient information from the American Society of Clinical Oncology
888-651-3038
www.cancer.net

National Cancer Institute
800-422-6237
www.cancer.gov

National Comprehensive Cancer Network
215-690-0300
www.nccn.com

National Library of Medicine (MedlinePlus)
www.medlineplus.gov

To find out about clinical trials:

Coalition of Cancer Cooperative Groups
877-227-8451
www.CancerTrialsHelp.org

EmergingMed
877-601-8601
www.emergingmed.com

National Cancer Institute
800-422-6237
www.cancer.gov/clinicaltrials

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