YOUR GUIDE TO THE LATEST CANCER RESEARCH AND TREATMENTS

Highlights from the 2018 Annual Meeting of the American Society of Clinical Oncology

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How To Use This Booklet

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

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 advances in treatment that have come about are because of the many people who have taken part in such studies. If current drugs or other types of cancer treatment no longer benefit you, you may wish to explore joining a clinical trial. The members of your health care team will help you fully understand the possible risks and benefits involved.

On page 53 you will find a list of resources, including websites where you can search for a clinical trial. If your particular type of cancer is not discussed in this booklet and you wish to take part in a study, these websites can help.

About the Editors

The content of this booklet was taken from Cancer*Care's* two-part Connect Education Workshop 2018 ASCO Highlights series, during which the following leading experts presented:

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The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of patients as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in deciding whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

When considering participation in a clinical trial, it's important to consult with your primary care physician and your oncologist and make sure that all of your questions are answered.

This is a very exciting time in cancer research, and there are clinical trials underway to study newer treatment approaches, such as immunotherapy and targeted therapies. In immunotherapy, the immune system's ability to seek out and destroy cancer cells is enhanced. Targeted therapies are designed to target the specific cell mechanisms that are important for the growth and survival of tumor cells.

Brain Cancer

Researchers reported a number of important findings in brain cancer treatment at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **A first-in-human trial of a personalized peptide vaccine for people with newly diagnosed glioblastoma may lead to new treatment options** (page 10).
- **The combination of pembrolizumab and bevacizumab as treatment for recurrent glioblastoma was studied in a phase II trial** (page 11).
- **A peptide vaccine targeting the IDH1 R132H mutation in glioblastoma is being studied in a first-in-human trial** (page 12).
- **The combination of an antibody drug and chemotherapy was studied for the treatment of recurrent glioblastomas with EGFR mutations** (page 12).

Personalized peptide vaccines studied in treatment of newly diagnosed glioblastoma

As every glioblastoma tumor is molecularly unique, there is a need for personalization in treatment approaches, integrated with current standards of care (e.g. surgery, radiation and/or chemotherapy).

GAPVAC-101 is a multicenter, first-in-human phase I trial to investigate the safety and effectiveness of personalized peptide vaccines as a treatment approach in patients with newly diagnosed glioblastoma.

Peptides are compounds consisting of two or more amino acids linked in a chain. Cancer peptide vaccines use the body's immune system to produce a clinical benefit.

What Patients Need to Know

GAPVAC-101 found that treatment with personalized peptide vaccines resulted in promising biological activity (immune responses) and was generally well-tolerated. Further research will be conducted in larger trials.

Adding pembrolizumab to bevacizumab studied in phase II trial

Investigators in a phase II trial evaluated the effectiveness of pembrolizumab, given alone or with bevacizumab, for the treatment of recurrent glioblastoma.

Pembrolizumab works by targeting the proteins PD-1 and/or PD-L1 that can prevent the body's immune system from attacking tumors. Bevacizumab is an anti-angiogenic medicine, designed to block the growth of blood vessels that support tumor growth; it is approved by the Food and Drug Administration (FDA) for the treatment of recurrent glioblastoma.

This trial also tested the safety and tolerability of pembrolizumab when given alone or with bevacizumab.

What Patients Need to Know

The trial results showed that pembrolizumab was well tolerated but had limited benefit as a but had limited benefit as a monotherapy (therapy that uses one type of treatment) for recurrent glioblastoma. The anti-tumor activity of pembrolizumab combined with a standard dose of bevacizumab was comparable to the effectiveness of bevacizumab alone, based on historical data.

IDH1 R132H mutation targeted in first-in-human trial

The NOA-16 trial is a first-in-human trial evaluating the immune response to an IDH1 peptide vaccine in patients with IDH1 R132H-mutated, WHO grade III-IV glioblastoma. The study is also evaluating the peptide vaccine's safety and tolerability.

What Patients Need to Know

NOA-16 met its primary goals by demonstrating the vaccine's safety and immunogenicity (the ability to produce an immune response), and further study is warranted.

Combination of antibody drug and chemotherapy studied for EGFR-mutated glioblastoma

The phase II Intellance 2 trial evaluated the combination of an antibody therapy with chemotherapy as treatment for recurrent glioblastomas with a mutation of the epidermal growth factor receptor (EGFR) gene. About 50 percent of glioblastoma cases are characterized by the EGFR mutation.

What Patients Need to Know

Researchers reported that the one-year survival rate was 40 percent for those receiving the antibody drug depatuxizumab mafodotin combined with the chemotherapy temozolomide, compared to 28 percent for patients who received temozolomide or lomustine (another chemotherapy) alone.

Breast Cancer

Researchers reported a number of important findings in breast cancer treatment at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **A phase III trial showed that most women with hormone receptor-positive, HER2-negative early-stage breast cancer and a mid-range score on the Oncotype DX Breast Recurrence Score test do not need post-surgery chemotherapy** (page 14).
- **Long-term results of the combined TEXT and SOFT trials showed ovarian function suppression combined with tamoxifen reduced the risk of invasive recurrence compared with tamoxifen alone** (page 14).
- **In women with HER2-positive, early-stage breast cancer, a phase III randomized trial found that a shorter duration of treatment with trastuzumab can be as effective as the current standard, with fewer cardiac side effects** (page 15).
- **The FDA has granted a Priority Review of the investigational drug sacituzumab govitecan for the treatment of certain women with metastatic triple-negative breast cancer** (page 15).

Chemotherapy of no additional benefit for certain women with hormone receptor-positive, HER2-negative breast cancer

Results of the phase II TAILORx trial showed that post-surgery chemotherapy can be avoided for women with hormone receptor-positive, HER2-negative, axillary node-negative early-stage breast cancer and a mid-range score of 11-25 on a 21-tumor gene expression assay (the Oncotype DX Breast Recurrence Score). Gene expression assays (tests) analyze the gene activity of breast cancer tumors.

For this group of women, the trial found no improvement in disease-free survival when chemotherapy was added to hormone therapy.

What Patients Need to Know

Approximately 70 percent of hormone receptor-positive, HER2-negative, axillary node-negative breast cancers have a mid-range Oncotype DX Breast Recurrence Score. The TAILORx study shows that chemotherapy (and its side effects) can be avoided in treating this group of women.

Long-term results of TEXT and SOFT trials reported

Compared with tamoxifen and ovarian function suppression, long-term follow-up results of the combined TEXT and SOFT trials indicated that post-surgery treatment with an aromatase inhibitor, combined with ovarian function suppression, reduced the risk of recurrence among premenopausal women with hormone receptor-positive early-stage breast cancer.

The estrogen produced by the ovaries can fuel tumor growth. Ovarian function suppression stops the ovaries from producing estrogen. Aromatase inhibitors block the action of the aromatase enzyme, cutting off the remaining supply of estrogen that can stimulate tumor growth.

What Patients Need to Know

The combined study results also showed that in very young women (age 30 or younger) and women with a high enough risk to receive chemotherapy, ovarian function suppression combined with tamoxifen reduced the risk of invasive recurrence compared with tamoxifen alone.

Shortened duration of trastuzumab treatment shown to be effective

Results of the phase III Persephone trial showed that taking the targeted therapy trastuzumab for 6 months can be as effective as the current standard of 12 months in treating women with HER2-positive, early-stage breast cancer, with fewer cardiac side effects.

What Patients Need to Know

The four-year disease-free survival rate was 89.4 percent with 6 months of trastuzumab therapy and 89.8 percent with 12 months of therapy. Only 4 percent of the women in the 6-month group of the trial stopped treatment with trastuzumab early due to cardiac problems, compared with 8 percent in the 12-month group.

Priority Review granted to investigational drug for treatment of triple-negative breast cancer

A Priority Review designation means the FDA's goal is to take action on an application within 6 months. Based on data from a phase I/II

trial, the FDA has granted a Priority Review to the investigational drug sacituzumab govitecan for the treatment of women with metastatic triple-negative breast cancer who have received at least two prior therapies.

What Patients Need to Know

The FDA's Priority Review process applies to drugs that are considered a significant improvement over the available alternatives. If approved, sacituzumab govitecan would be the first antibody-drug conjugate (a targeted therapy designed to kill cancer cells while sparing healthy cells) approved for the treatment of metastatic triple-negative breast cancer.

Colorectal Cancer

Researchers reported a number of important findings in colorectal cancer treatment at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **A phase II trial showed that combination therapy with irinotecan, cetuximab and ramucirumab may help prolong progression-free survival when given as a second-line treatment for KRAS wild-type colorectal cancer** (page 17).
- **A combination of monoclonal antibodies may be more effective against HER2-positive colorectal cancer than standard chemotherapy treatment** (page 18).
- **The safety lead-in of a phase III trial showed a novel combination of drugs improved progression-free survival in patients with BRAF-mutant colorectal cancer** (page 19).
- **According to data from a phase III trial, heated chemotherapy delivered to the abdomen during surgery does not add benefit in patients with advanced colorectal cancer** (page 19).

Combination therapy studied in phase II trial as second-line treatment for KRAS wild-type colorectal cancer

In patients with KRAS wild-type colorectal cancer who received prior treatment with oxaliplatin and bevacizumab, results of a randomized phase II trial showed that progression-free survival may be extended by the combination of cetuximab (an anti-EGFR antibody), ramucirumab (an anti-VEGFR antibody) and the chemotherapy irinotecan.

What Patients Need to Know

Previous trials have shown both cetuximab and ramucirumab have benefit in the treatment of metastatic KRAS wild-type colorectal cancer. The results of this new trial support the fact that these antibodies can be combined for additional benefit in the appropriate patient population.

Monoclonal antibodies may be more effective than chemotherapy in treatment of certain HER2-positive colorectal cancers

Interim data from the randomized phase IIa MyPathway trial showed that the monoclonal antibodies trastuzumab and pertuzumab, given in combination, may work better than the chemotherapies cetuximab and irinotecan (the current standard of care) in treating patients with locally advanced or metastatic HER2-positive colorectal cancer that cannot be removed by surgery.

What Patients Need to Know

Monoclonal antibodies such as trastuzumab and pertuzumab are lab-generated molecules that target specific tumor antigens (substances that the immune system sees as being foreign or dangerous). While the MyPathway trial did not yield definitive results, monoclonal antibodies may become a treatment option in the future.

Safety lead-in of phase II trial showed combination of drugs improved progression-free survival in patients with BRAF-mutant colorectal cancer

Results from the safety lead-in of the phase III BEACON CRC trial showed an improvement in progression-free survival in certain patients with BRAF-mutant colorectal cancer when treated with a novel combination of encorafenib (a BRAF inhibitor), binimetinib (an MEK inhibitor) and cetuximab (an anti-EGFR antibody).

The 30 participants had BRAF-mutant metastatic colorectal cancer that had progressed after one or two prior therapy regimens.

What Patients Need to Know

In the safety lead-in, the three-drug combination was generally well-tolerated. Enrollment in the next phase of the BEACON CRC trial is ongoing.

No benefit added when hyperthermic intraperitoneal chemotherapy added to surgery in advanced colorectal cancer

A phase III trial showed no difference in survival between patients with advanced colorectal cancer who received heated chemotherapy delivered to the abdomen during surgery and those who received surgery alone. This was the first randomized trial evaluating the role of heated chemotherapy (also called hyperthermic intraperitoneal chemotherapy) in advanced colorectal cancer.

What Patients Need to Know

The results of the trial suggest that many patients with advanced colorectal cancer can be spared unnecessary chemotherapy and its associated side effects.

Leukemia

Researchers reported a number of important findings in leukemia treatment at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **A phase I trial showed the IDH1- inhibitor ivosidenib was effective and safe in the treatment of certain cases of acute myeloid leukemia** (page 21).
- **Data from a dose escalation trial demonstrated that venetoclax, combined with standard chemotherapy, led to durable responses in elderly patients with untreated acute myeloid leukemia** (page 21).
- **A phase III trial showed CPX-351 to be more effective than the standard "7+ 3" chemotherapy in the treatment of acute myeloid leukemia** (page 22).

Targeted therapy ivosidenib safe and effective in IDH1-mutated acute myeloid leukemia

A phase I trial showed the IDH1 inhibitor ivosidenib to be safe and effective in treating patients with advanced relapsed or refractory (not responding to treatment) acute myeloid leukemia (AML) that has a mutation in the IDH1 gene.

Ivosidenib, a targeted therapy, achieved durable (long-lasting) responses in some patients and reduced or eliminated patients' dependence on transfusions, whether or not those patients achieved a durable response.

What Patients Need to Know

Ivosidenib is the second IDH inhibitor to show promise in the treatment of AML. Some people with AML have a mutation in the IDH2 gene that stops cells from maturing in the way they should. Approved by the FDA in August 2017, the IDH inhibitor enasidenib works by helping leukemia cells mature into normal cells.

Venetoclax combined with chemotherapy studied for untreated acute myeloid leukemia in elderly patients

Data from a phase Ib dose-escalation trial showed that the targeted therapy venetoclax, given in combination with the chemotherapy azacitidine, led to durable responses with a tolerable safety profile in elderly patients with untreated AML.

What Patients Need to Know

Many people with AML have a mutation of the BCL2 gene that prevents the death of cancer cells and is associated with a resistance to chemotherapy. Venetoclax, a BCL2 inhibitor, is designed to correct this mutation.

Phase III trial shows CPX-351 to be more effective than standard chemotherapy in treatment of acute myeloid leukemia

A common chemotherapy regimen for AML is called "7 + 3"; it consists of the chemotherapy cytarabine given daily for 7 days, followed by an anthracycline given daily for 3 days. This treatment is administered intravenously (into a vein) and in an in-patient hospital setting.

A phase III trial showed CPX-351, a combination of cytarabine and the anthracycline daunorubicin, to be more effective than "7 + 3" chemotherapy in the treatment of AML.

What Patients Need to Know

In August 2017, the FDA approved CPX-351 (brand name Vyxeos) for the treatment of newly-diagnosed therapy-related AML (t-AML). It was also approved for the treatment of AML with myelodysplasia-related changes, which cause the body to stop making enough healthy red blood cells and platelets.

Lung Cancer

Researchers reported a number of important findings in lung cancer treatment at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **A phase III trial, KEYNOTE-042, evaluated pembrolizumab in the first-line treatment of non-small cell lung cancer** (page 23).
- **The international phase III trial KEYNOTE-407 evaluated the use of chemotherapy, with or without pembrolizumab, in treating advanced squamous cell non-small cell lung cancer** (page 24).
- **IMpower131, a phase III trial, evaluated the addition of the immunotherapy atezolizumab to chemotherapy in treating advanced squamous cell non-small cell lung cancer** (page 24).
- **Results of the phase III trial ARCHER 1050 showed patients with EGFR-mutated advanced non-small cell lung cancer gain benefit from first-line treatment with dacomitinib, compared with gefitinib** (page 25).

Immunotherapy pembrolizumab studied as first-line treatment for NSCLC

According to results from the phase III KEYNOTE-042 trial, certain patients with non-small cell lung cancer (NSCLC) respond better to pembrolizumab as a first-line treatment than to standard of care chemotherapy.

Depending on the level of PD-L1 expression shown in their tumors, patients with NSCLC treated with first-line pembrolizumab lived 4 to 8 months longer than those who received chemotherapy. PD-L1 is a protein that allows some cells to avoid an attack by the immune system.

What Patients Need to Know

The trial results indicate that pembrolizumab, an immunotherapy, could be a treatment option for patients with advanced NSCLC without EGFR or ALK mutations and whose tumors express PD-L1 at the level of ≥ 1 percent.

Chemotherapy with or without pembrolizumab studied in advanced squamous NSCLC

KEYNOTE-407, an international placebo-controlled phase III trial, evaluated the use of chemotherapy (carboplatin-paclitaxel/nab-paclitaxel) with or without the immunotherapy pembrolizumab in patients with advanced squamous cell NSCLC who were not previously treated with chemotherapy.

What Patients Need to Know

Patients who received chemotherapy plus pembrolizumab, compared with chemotherapy alone, had improved median overall survival and progression-free survival as well as improved response rates and duration of response. These results were seen in all PD-L1 subgroups and no new safety concerns were identified.

Addition of immunotherapy atezolizumab to chemotherapy studied for treatment of advanced squamous cell NSCLC

IMpower131 is an international, randomized phase III trial that evaluated adding the immunotherapy atezolizumab to the

chemotherapy combinations of carboplatin/paclitaxel and carboplatin/nab-paclitaxel in patients with advanced squamous cell NSCLC. The patients in the study had not previously been treated with chemotherapy.

What Patients Need to Know

Regardless of the level of PD-L1 expression, the median progression-free survival was improved with the addition of atezolizumab as compared with chemotherapy alone.

Phase III trial compares EGFR inhibitors in treatment of EGFR-mutated advanced NSCLC

The ARCHER 1050 trial showed that the EGFR inhibitor dacomitinib resulted in a significant benefit in overall survival in patients with advanced EGFR-mutated NSCLC compared to another EGFR inhibitor, gefitinib.

What Patients Need to Know

ARCHER 1050 represents the first randomized phase III trial that directly compares EGFR inhibitors to evaluate an overall survival benefit.

Lymphoma

Researchers reported a number of important findings in lymphoma treatment at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **The RELEVANCE trial compared rituximab/chemotherapy with rituximab/lenalidomide in patients with previously untreated follicular lymphoma** (page 26).
- **In Waldenstrom's Macroglobulinemia, the combination of ibrutinib and rituximab reduced the risk of disease progression by 80 percent, compared to rituximab alone** (page 27).
- **Follow-up data from the ZUMA-1 study showed CAR T-cell therapy had benefit in the treatment of relapsed or refractory large B-cell lymphoma** (page 27).

Chemo-free regimen not superior in previously untreated follicular lymphoma

For previously untreated follicular lymphoma, the RELEVANCE trial compared regimens that included the immunotherapy rituximab plus chemotherapy (the current standard of care) to a "chemo-free" regimen of rituximab and the immunotherapy lenalidomide.

In the rituximab/chemotherapy regimens, the types of chemotherapy administered included cyclophosphamide, doxorubicin and vincristine.

What Patients Need to Know

The results did not show better outcomes for the chemo-free regimen, as the response rate and two-year progression-free survival (a key prognostic factor in follicular lymphoma) were similar between the two groups.

Risk of disease progression in Waldenstrom's Macroglobulinemia greatly reduced by combination therapy

Results from the international phase III iNNOVATE trial showed that, in patients with Waldenstrom's Macroglobulinemia (WM), the risk of disease progression was reduced by 80 percent when treated with a combination of the immunotherapy rituximab and the targeted therapy ibrutinib, compared to rituximab alone.

Ibrutinib, a BTK inhibitor, works against a mutation that is present in approximately 90 percent of WM cases.

What Patients Need to Know

Ibrutinib is FDA-approved for the treatment of WM. Rituximab is also a standard treatment in both newly diagnosed patients and patients whose WM has recurred. Both ibrutinib and rituximab are often used alone (monotherapy) to treat WM.

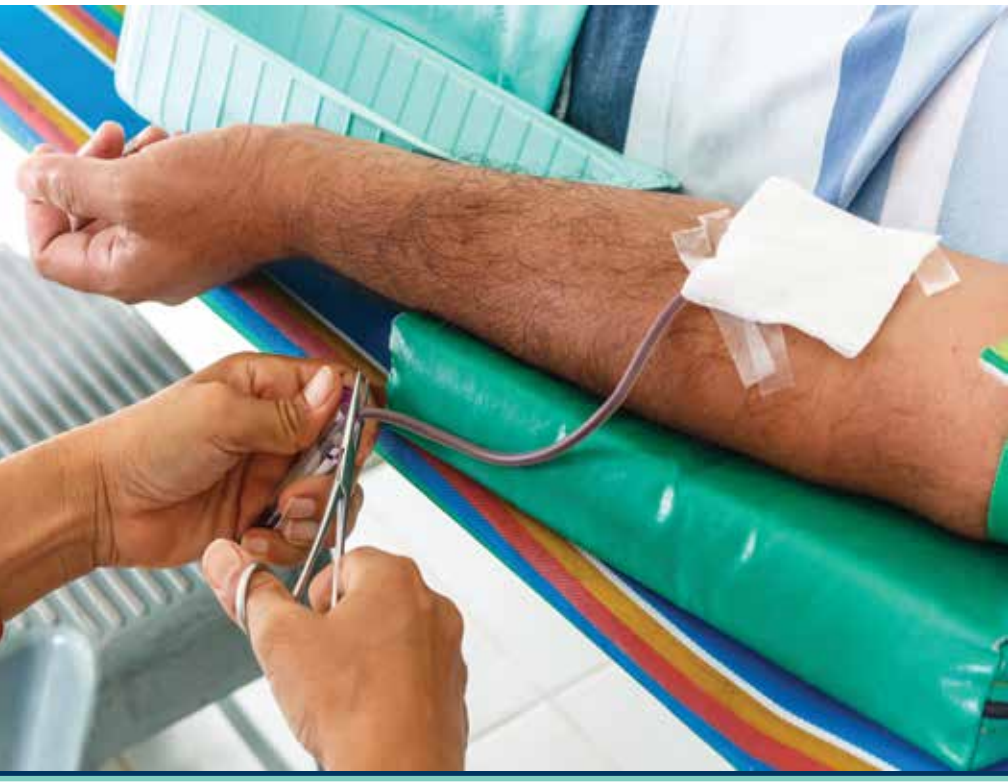
CAR T-cell therapy effective in treatment of relapsed or refractory large B-cell lymphoma

Axicabtagene ciloleucel, a chimeric antigen receptor T (CAR T) cell therapy, was approved by the FDA in October 2017 for the treatment of adult patients with relapsed or refractory large B-cell lymphoma who had previously received at least two other kinds of therapy.

Follow-up data from the ZUMA-1 study indicated that, after a single infusion, 42 percent of patients in this population continued to respond to therapy after more than one year, including 40 percent with a complete remission.

What Patients Need to Know

CAR T-cell therapy is a type of immunotherapy that follows certain steps, which include drawing blood, separating out and genetically modifying the T-cells, multiplying those cells in a laboratory and infusing them back into the patient, where they attack cancer cells.



Melanoma

Researchers reported a number of important findings in the treatment of melanoma at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **The results of two multicenter trials may change the practice of immediate CLND (complete lymph node dissection) after the detection of cancer in sentinel nodes** (page 29).
- **A phase III trial showed that, compared to vemurafenib, the combination of encorafenib and binimetinib improved progression-free survival in patients with BRAF V600-mutated advanced melanoma** (page 30).
- **The combination of nivolumab and ipilimumab is being studied as a neo-adjuvant (prior to surgery) treatment approach for melanoma** (page 30).

Studies evaluated benefit of complete lymph node dissection after cancer found in sentinel nodes

It is currently standard practice to perform a complete nymph node dissection (CLND) immediately after the detection of cancer in the sentinel nodes, with the thought that it helps prevent recurrence (cancer returning) and lowers the risk of the melanoma metastasizing (spreading).

Two multicenter randomized trials, DeCOG-SLT and MSLT-II, showed there was no improvement in melanoma-specific survival or overall survival in patients who underwent immediate CLND after a biopsy detected cancer in the sentinel nodes.

What Patients Need to Know

The results of these two studies showed that observation of the non-sentinel nodes, with a complete lymph node dissection only if cancer was detected, was as effective as immediate removal.

Combination of encorafenib and binimetinib shown to improve progression-free survival

The phase III COLUMBUS trial showed the combination of the BRAF inhibitor encorafenib with the MEK inhibitor binimetinib improved progression-free survival in patients with advanced BRAF V600-mutant melanoma, as compared to the BRAF inhibitor vemurafenib.

BRAF V600 mutations occur in 35 to 50 percent of people with melanoma.

What Patients Need to Know

In June 2018, the combination of encorafenib and binimetinib was approved by the FDA for the treatment of people with unresectable (cannot be completely removed though surgery) or advanced melanoma that has a BRAF V600E or V600K mutation.

Combination immunotherapy compared in neoadjuvant and adjuvant settings

The phase Ib OpACIN trial compared the combination of the immunotherapies nivolumab and ipilimumab as neoadjuvant (prior to surgery) therapy versus adjuvant (after surgery) therapy and found the neoadjuvant therapy was superior.

After a median follow-up of 24 months, none of the patients in the neoadjuvant group who had responded to the nivolumab and ipilimumab combination had experienced a return of their melanoma, compared to a 40 percent recurrence rate (the rate of which the cancer returns) for patients in the adjuvant group.

What Patients Need to Know

Adverse events were significant in both groups, and a phase II trial is being planned to identify dosing options to reduce adverse events and maximize benefits.

Myeloproliferative Neoplasms

Researchers reported a number of important findings in the treatment of myeloproliferative neoplasms (MPNs) at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **A retrospective study showed treating MPNs with a Janus kinase (JAK) inhibitor increased the risk of patients developing aggressive lymphomas** (page 32).
- **An experimental drug is being evaluated as a treatment option for anemia in patients with MPN-associated myelofibrosis** (page 33).
- **The impact of JAK1/2 inhibitor therapies in the context of stem cell transplantation is being studied in patients with myelofibrosis** (page 34).

Retrospective study showed increased risk of aggressive lymphomas when patients with MPNs treated with JAK inhibitors

A retrospective study showed that a small but significant proportion of patients with myeloproliferative neoplasms developed aggressive lymphomas during treatment with a Janus kinase (JAK) inhibitor. In a study of 929 patients, 9.7 percent of those treated with JAK1/2 inhibitors developed aggressive B-cell lymphomas compared to 0.54 percent of patients treated with other drugs.

What Patients Need to Know

Researchers determined that patients most at risk for developing an aggressive lymphoma had a pre-existing B-cell clone that underwent transformation during treatment with JAK inhibitors; they suggest that people with myelofibrosis be tested for this B-cell clone before undergoing treatment with JAK inhibitors.

Experimental drug being evaluated as treatment for anemia in MPN-associated myelofibrosis

Anemia is a significant complication of MPN-associated myelofibrosis, with few effective therapies other than red blood cell transfusions. A phase II multicenter global trial is evaluating the experimental drug luspatercept as a potential treatment option for anemia in these patients.

What Patients Need to Know

The trial will evaluate a number of endpoints, including the safety of luspatercept and the improvement in the anemia both short-term and long-term. A determination will also be made whether a randomized phase III trial should be conducted.

JAK1/2 inhibitors being studied in the context of stem cell transplantation for patients with myelofibrosis

Since its FDA approval in 2011, the JAK 1/2 inhibitor ruxolitinib has become a routine treatment for MPN-associated myelofibrosis. However, allogeneic hematopoietic stem cell transplant remains the only treatment with the potential to treat myelofibrosis. (In an allogeneic hematopoietic stem cell transplant, the person receives blood-forming stem cells from a genetically similar donor.)

Ongoing research is being conducted on the impact JAK 1/2 inhibitors could have on the timing of allogeneic hematopoietic stem cell transplant and their effect on post-transplantation outcomes.

What Patients Need to Know

Researchers say the identification of guidelines for the use of JAK1/2 inhibitors in the context of transplantation may lead to new treatment strategies for patients with myelofibrosis.

Oral, Head and Neck Cancers

Researchers reported a number of important findings in the treatment of oral, neck and head cancers at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **A phase I trial evaluated the safety of adding an immunotherapy drug to targeted therapy and radiotherapy in people with head and neck squamous cell carcinoma** (page 35).
- **The effectiveness and safety of chemoradiation followed by metronomic chemotherapy for the treatment of locally advanced nasopharyngeal cancer was studied in a phase II trial** (page 36).
- **A phase II trial evaluated the safety profile of pembrolizumab combined with cetuximab in patients with recurrent or metastatic head and neck squamous cell carcinoma** (page 36).
- **An investigational drug was shown to be effective in reducing the duration and severity of oral mucositis in patients with head and neck cancer** (page 37).

Combination therapy safe in treatment of HNSCC

A phase I trial evaluated the safety of giving the immunotherapy nivolumab at the same time as radiotherapy and the targeted therapy cetuximab in treating intermediate- and high-risk local and regionally advanced head and neck squamous cell carcinoma (HNSCC).

What Patients Need to Know

The results confirmed the safety of the combination, as there were no adverse reactions reported that interfered either with the treatment or with the subsequent nivolumab maintenance therapy.

Concurrent chemoradiation followed by metronomic chemotherapy promising approach for nasopharyngeal cancer

A phase II trial studied the effectiveness and safety of concurrent chemoradiation (CCRT) followed by capecitabine metronomic chemotherapy for the treatment of locally advanced nasopharyngeal cancer (NPC). "Metronomic" refers to the continuous use of low doses of conventional chemotherapeutics, without long drug-free intervals.

What Patients Need to Know

The study found that CCRT followed by the capecitabine metronomic chemotherapy was a promising treatment approach for locally advanced NPC, and concluded that further studies should be conducted.

Combination of pembrolizumab and cetuximab found to be safe

A phase II trial evaluated the safety of combining the immunotherapy pembrolizumab with the targeted therapy cetuximab in the treatment of recurrent or metastatic head and neck squamous cell carcinoma (HNSCC).

Both pembrolizumab and cetuximab are FDA-approved as second-line monotherapy in the treatment of recurrent or metastatic HNSCC. This is the first trial to combine pembrolizumab with cetuximab and evaluate its anti-tumor effectiveness. As the combination of these two drugs had not previously been tested, a safety analysis was first completed.

What Patients Need to Know

Pembrolizumab combined with cetuximab has a very tolerable safety profile, with no dose-limiting toxicities. The trial will now go on to analyze the clinical effectiveness of this combination.

Investigational drug studied for treatment of oral mucositis

Treating head and neck cancers with radiation often leads to oral mucositis (OM), a side effect that causes severe pain, inflammation, ulceration and bleeding of the mouth. There are currently no FDA-approved drugs to treat OM.

A phase IIb trial studied the effectiveness and safety of the investigational drug GC4419 in the treatment of severe oral mucositis (SOM).

What Patients Need to Know

In the study, GC4419 met its primary "endpoint," achieving a 92 percent reduction in the duration of SOM. The drug also demonstrated a reduction in SOM incidence and severity and was well tolerated. A phase III trial is being planned.

Ovarian Cancer

Researchers reported a number of important findings in ovarian cancer treatment at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **A phase I/II trial found a combination of niraparib and pembrolizumab to be significantly more effective than either drug alone in treating recurrent ovarian cancer** (page 38).
- **A triple combination of drugs showed promise in an ongoing phase Ib/II trial for the treatment of women with advanced recurrent ovarian cancer** (page 40).
- **The results of a phase II trial showed the administration of a dendritic cell vaccine, when given after chemotherapy, improved progression-free survival in women with epithelial ovarian cancer** (page 40).
- **A phase II trial found that the combination of cediranib and olaparib improved progression-free survival in women with platinum-sensitive recurrent ovarian cancer** (page 41).
- **The results of a phase II trial showed that anti-angiogenic therapy combined with chemotherapy could have benefit in the treatment of platinum-resistant ovarian cancer** (page 41).

Drug combination studied in treatment of advanced or recurrent ovarian cancer

The TOPACIO trial found that a combination of the drugs niraparib and pembrolizumab to be significantly more effective than either drug alone in treating advanced or recurrent ovarian cancer.

Niraparib is a PARP inhibitor, a type of drug designed to destroy cancer cells by preventing them from repairing their damaged DNA. Pembrolizumab is a type of immunotherapy called a PD-1 checkpoint inhibitor.

What Patients Need to Know

The combination of niraparib and pembrolizumab produced an "objective response" (a reduction in tumor size of a defined amount) in 25 percent of the trial participants and in 45 percent of those whose tumors had BRCA mutations. The objective response rate was less than 5 percent in women treated with niraparib or another PARP inhibitor alone and 11 percent in women treated with pembrolizumab alone.

The trial results also pertained to the treatment of advanced triple-negative breast cancer.

Triple combination of drugs showed promise in early stage trial

The phase Ib/II trial DeCidE is evaluating the effectiveness and safety of combining the investigational drug DPX-Survivac (a T-cell activating therapy) with low-dose cyclophosphamide (a chemotherapy) and an IDO1 enzyme inhibitor for the treatment women with advanced recurrent ovarian cancer. The IDO1 enzyme is activated in many human cancers, including ovarian cancer.

What Patients Need to Know

The triple combination of drugs showed promise in treating women with advanced recurrent ovarian cancer and will continue to be studied.

Dendritic cell vaccine shows promise as maintenance therapy

Dendritic cells help the immune system recognize and fight cancer cells. A phase II multicenter trial showed that administering a dendritic cell vaccine after surgery and chemotherapy improved progression-free survival (the length of time during and after treatment that the cancer did not get worse) in women with epithelial ovarian cancer.

What Patients Need to Know

Epithelial ovarian cancer often recurs after surgery and chemotherapy. Adding a dendritic cell vaccine to the treatment regimen shows promise as maintenance therapy to delay disease progression.

Combining olaparib with cediranib to treat platinum-sensitive ovarian cancer

A phase II trial compared the effectiveness of combining olaparib (which blocks DNA repair) with cediranib (a blood vessel inhibitor) versus olaparib alone in women with platinum-sensitive recurrent ovarian cancer. Both olaparib and cediranib are oral drugs.

What Patients Need to Know

The trial results showed that combining the two drugs nearly doubled progression-free survival compared to the use of olaparib alone. Combining olaparib and cediranib also improved overall response rates.

Investigational drug studied in treatment of platinum-resistant ovarian cancer

Apatinib is an investigational anti-angiogenic drug designed to block the growth of blood vessels that support tumor growth. A phase II trial tested the effectiveness and safety of combining apatinib with the oral chemotherapy etoposide in treating ovarian cancer that is platinum-resistant or refractory (not responding to other types of treatment).

What Patients Need to Know

The trial found that adding apatinib to etoposide could improve outcomes in the treatment of platinum-resistant or refractory ovarian cancer, with manageable side effects.

Pancreatic Cancer

Researchers reported a number of important findings in pancreatic cancer treatment at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **In patients with surgically removed pancreatic cancer, a phase III trial showed benefit from adjuvant FOLFIRINOX chemotherapy compared to standard gemcitabine chemotherapy** (page 43).
- **A phase III trial found that patients who received chemoradiotherapy before pancreatic cancer surgery had longer disease-free survival than those who started their treatment with surgery** (page 43).
- **The phase II PRODIGE 35-PANOPTIMOX trial evaluated the chemotherapy regimen LV5FU2 as a maintenance treatment approach for metastatic pancreatic cancer** (page 44).

Post-surgery FOLFIRINOX chemotherapy showed benefit over standard gemcitabine treatment

In a randomized phase III trial, patients who received a modified regimen of adjuvant (post-surgery) FOLFIRINOX lived a median of 20 months longer and were cancer-free 9 months longer than those who received gemcitabine, the current adjuvant standard of care.

The modified FOLFIRINOX regimen contained the chemotherapies oxaliplatin, leucovorin, irinotecan and fluorouracil.

What Patients Need to Know

The next step will be to explore the timing of chemotherapy, as patients may also benefit from neoadjuvant (before surgery) chemotherapy to destroy undetectable cancer cells that have spread to other parts of the body.

Phase III trial showed benefit from chemoradiotherapy before pancreatic cancer surgery

Results of the randomized phase III PREOPANC-1 trial showed that patients who received chemoradiotherapy before pancreatic cancer surgery had longer disease-free survival than those who started their treatment with surgery.

The median overall survival was 17.1 months with preoperative chemoradiotherapy compared to 13.7 months with surgery followed by chemoradiotherapy. Among patients whose tumor was successfully removed surgically, the difference in median survival was even greater: 42.1 months with preoperative treatment compared to 16.8 months with surgery followed by chemoradiotherapy.

What Patients Need to Know

In addition to a longer median overall survival, the chance of surviving longer than 2 years was higher with preoperative treatment than with surgery followed by chemoradiotherapy (42 percent versus 30 percent).

Chemotherapy regimen LV5FU2 shows benefit as maintenance therapy in metastatic pancreatic cancer

The randomized phase II trial PRODIGE35-PANOPTIMOX evaluated the effectiveness and safety of the chemotherapy regimen LV5FU2 (leucovorin plus bolus and infusional fluorouracil) as a maintenance treatment approach for patients with metastatic pancreatic cancer.

What Patients Need to Know

Maintenance with LV5FU2 appears to be feasible and effective in patients with metastatic pancreatic cancer that has been controlled after 4 months of FOLFIRINOX induction chemotherapy.

Prostate Cancer

Researchers reported a number of important findings in prostate cancer treatment at the 2018 Annual Meeting of the American Society of Clinical Oncology:

- **A retrospective review of patient data analyzed a novel imaging technique in detecting lesions in men with biochemical recurrence of prostate cancer** (page 45).
- **PARP inhibition is emerging as a treatment approach for prostate cancer** (page 46).
- **The PROPHECY trial investigated and confirmed the prognostic value of a test designed to identify men with mCRPC who will not benefit from androgen receptor-signaling inhibitor therapy** (page 46).

Non-conventional imaging technique studied

Conventional imaging techniques often do not detect the specific location of prostate cancer in men with biochemical recurrence (PSA ≥ 0.2 ng/m) following radical prostatectomy (the removal of the entire prostate gland and surrounding tissues).

A retrospective data review found that a novel imaging technique, Gallium-68 Prostate-Specific Membrane Antigen positron emission tomography (PSMA PET), detected lesions in a high proportion of men with biochemical recurrence following radical prostatectomy.

What Patients Need to Know

Many of the lesions PSMA PET detected were outside of the pelvis, areas typically not reached by post-surgery radiation. The detection of lesions, and their specific location in the body, may facilitate more precise targeting of treatment areas for men with biochemical recurrence of prostate cancer.

PARP inhibitor studied in treatment of metastatic disease

Drugs that inhibit a type of enzyme called PARP are designed to destroy cancer cells by preventing them from repairing their damaged DNA. PARP inhibition is not a standard therapy for prostate cancer.

In the phase II TOPARP trial, 50 men with metastatic castration-resistant prostate cancer (mCRPC) received the PARP inhibitor olaparib, with promising results in terms of treatment response.

What Patients Need to Know

With the reporting of the TOPARP results, interest in PARP inhibitors as a potential treatment approach for a subset of men with prostate cancer has increased. However, more research is needed to prove the effectiveness and safety of this treatment approach.

PROPHECY trial confirms prognostic value of AR-47 test

Androgen receptor-signaling inhibitor (ARSi) therapy is not effective in treating all cases of mCRPC. By detecting the presence of circulating tumor cells (CTCs) that are positive for the AR-V7 protein, the AR-V7 test is designed to identify men with mCRPC who will not benefit from ARSi therapy.

What Patients Need to Know

The multicenter PROPHECY trial investigated and confirmed the prognostic value of the AR-V7 test. PROPHECY concluded that most men with mCRPC whose AR-V7 test results showed the presence of AR-V7-positive CTCs received little or no clinical benefit from ARSi therapy (either enzalutamide or abiraterone).

Sarcoma

Researchers reported a number of important findings in sarcoma treatment at the 2018 Annual Meeting of the American Society of Clinical Oncology

- **The results of a phase III trial showed sorafenib resulted in significantly greater tumor shrinkage compared with placebo in patients with desmoid tumors** (page 48).
- **A phase II trial showed that the targeted therapy regorafenib was effective in treatment of metastatic osteosarcoma** (page 49).
- **The results of a phase I trial showed a combination of investigational drugs was effective against KIT mutations in gastrointestinal stromal tumors** (page 50).
- **The effectiveness and safety of apatinib in treating Ewing sarcoma was studied in a retrospective analysis** (page 50).

Sorafenib studied for treatment of desmoid tumors

Desmoid tumors (also called aggressive fibromatosis) are noncancerous growths that occur in the connective tissue, most often in the abdomen, arms and legs. If desmoid tumors grow, they can affect nearby tissues and organs, causing symptoms and complications.

A randomized phase III trial showed sorafenib significantly shrunk tumors, compared to placebo, in patients with desmoid tumors. Tumor shrinkage was also seen with placebo, as desmoid tumors can sometimes shrink without treatment.

What Patients Need to Know

Sorafenib, a tyrosine kinase inhibitor, is approved by the FDA approved for the treatment of certain cancers, including liver, kidney and thyroid. Sorafenib works by blocking the action of proteins that promote the growth of new blood vessels; these blood vessels carry oxygen, minerals, and other nutrients that tumors need to grow. Sorafenib also blocks some of the proteins on cancer cells that help them grow and multiply.

Regorafenib shows promise for treatment of metastatic osteosarcoma

The phase II trial REGOBONE evaluated the effectiveness and safety of the targeted therapy regorafenib for the treatment of metastatic osteosarcoma.

Regorafenib is a kinase inhibitor. Kinase proteins are substances near the surface of cells that send important signals to the cell's control center; by doing so, they can help tumor cells grow.

What Patients Need to Know

In the treatment of metastatic osteosarcoma after the failure of conventional chemotherapy, regorafenib demonstrated promising activity with acceptable toxicity, justifying further trials.

In another phase II trial, regorafenib failed to improve outcomes (compared to placebo) in the treatment of advanced or metastatic liposarcoma that is not responding to treatment (is refractory).

Investigational drugs studied in treatment of KIT mutations in gastrointestinal stromal tumors

An estimated 80 percent of gastrointestinal stromal tumors (GISTs) have a mutation of the KIT gene, resulting in an over-production of a protein which can cause cancer cells to grow.

The results of a phase I dose escalation trial suggested that the combination of the investigational drugs PLX9486 and pexidartinib showed some effectiveness against a range of KIT mutations in patients with GIST.

What Patients Need to Know

Both PLX9486 and pexidartinib are tyrosine kinase inhibitors (TKIs). The trial participants were people whose GIST had progressed after being treated with imatinib or other TKIs.

The trial found that the combination of PLX9486 and pexidartinib was generally well tolerated, with mild and reversible side effects.

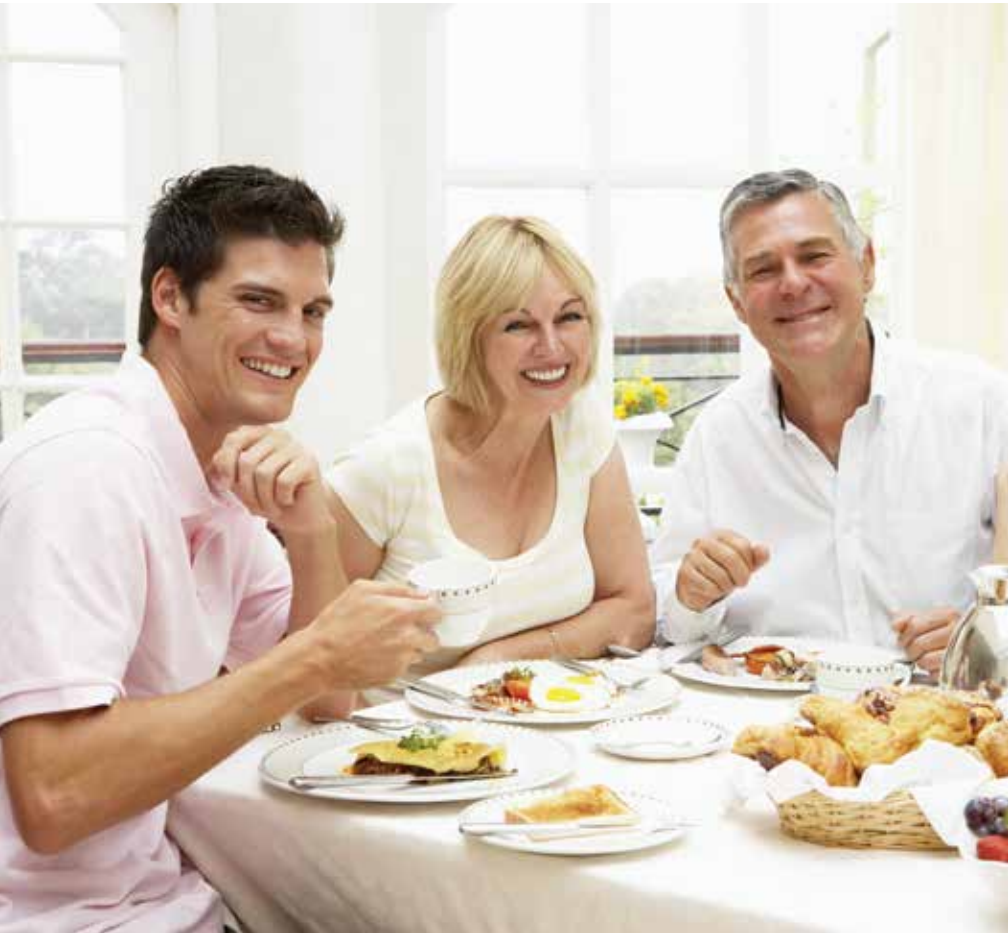
Study investigated use of apatinib for Ewing sarcoma

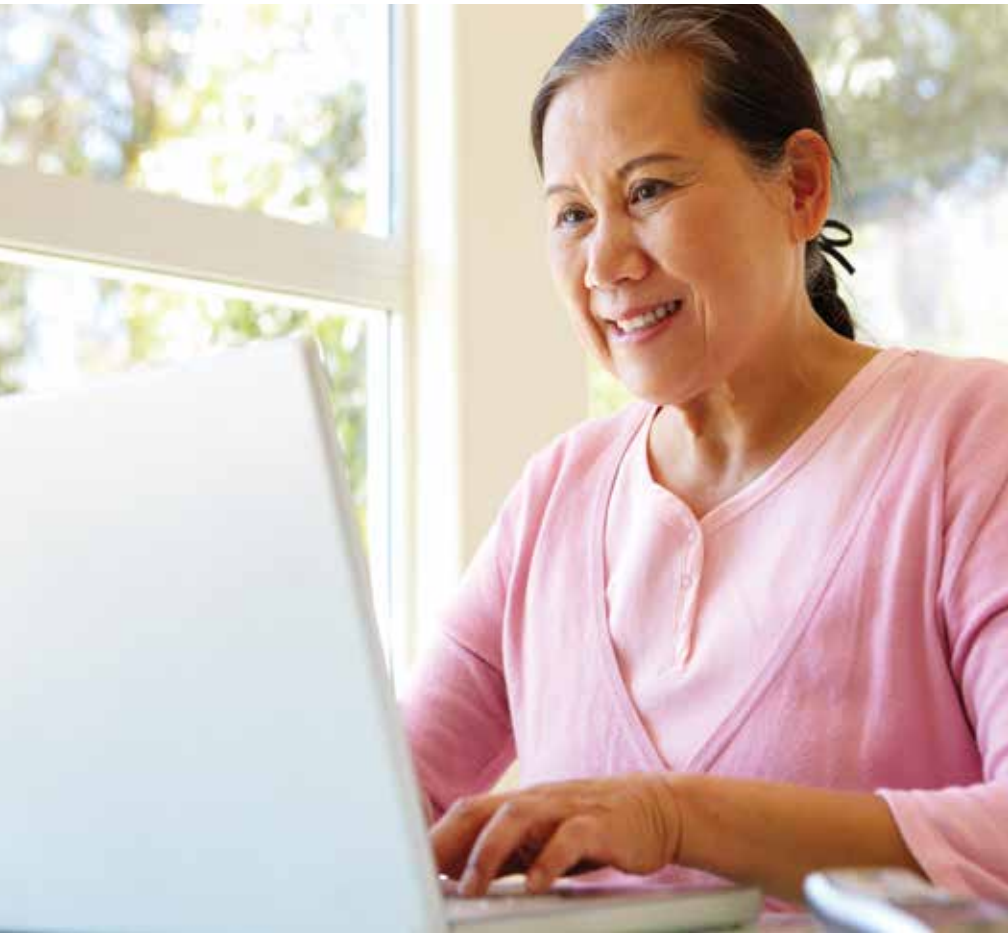
A retrospective analysis investigated the effectiveness and safety of apatinib, a VEGFR-2 inhibitor, in patients with advanced Ewing sarcoma (ES).

The results of the analysis suggested that apatinib may be effective as a second- or first-line treatment option for advanced ES patients, particularly in cases resistant to chemotherapy.

What Patients Need to Know

Further retrospective studies, which include more cases with longer follow-up times, are necessary to determine the clinical effectiveness of apatinib in treating Ewing sarcoma.





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