YOUR GUIDE TO THE LATEST CANCER RESEARCH AND TREATMENTS

Highlights from the 2019 Annual Meeting of the American Society of Clinical Oncology

CANCER*CARE* CONNECT® BOOKLET SERIES

CANCER*care*®

WWW.CANCERCARE.ORG

The Cancer*Care* Connect® Booklet Series offers up-to-date, easy-to-read information on the latest treatments, managing side effects and coping with cancer.

Founded in 1944, Cancer*Care* is the leading national organization providing free, professional support services and information to help people manage the emotional, practical and financial challenges of cancer. Our comprehensive services include counseling and support groups over the phone, online and in person, educational workshops, publications and financial and co-payment assistance. All Cancer*Care* services are provided by master's-prepared oncology social workers.

Cancer*Care* relies on the generosity of supporters to provide our services completely free of charge to anyone facing a cancer diagnosis. If you have found this resource helpful and wish to donate, please do so online at www.cancercare.org/donate. You may also mail a check, payable to Cancer*Care*, to Cancer*Care*, Attn: Donations, 275 Seventh Avenue, New York, NY 10001.

Thank you.

Cancer*Care*®
National Office
275 Seventh Avenue
New York, NY 10001

Toll-free 800-813-HOPE (4673)
Fax 212-712-8495
Email info@cancercare.org
Web www.cancercare.org

Highlights from the 2019 Annual Meeting of the American Society of Clinical Oncology

TABLE OF CONTENTS

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 47 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 CancerCare's two-part Connect Education Workshop 2019 ASCO Highlights series, during which the following leading experts presented:

Al B. Benson, III, MD, FACP, FASCO
Colorectal Cancer
Professor of Medicine, Associate Director for Cooperative Groups, Robert H. Lurie Comprehensive Cancer Center, Northwestern University

Gregory A. Daniels, MD, PhD
Melanoma
Clinical Professor of Medicine, Moores UCSD Cancer Center, VA San Diego Healthcare System

Julie R. Gralow, MD
Breast Cancer
Professor and Director, Breast Medical Oncology, Jill Bennett Endowed Professorship in Breast Cancer, University of Washington School of Medicine, Director, Breast Medical Oncology, Seattle Cancer Care Alliance

Fabio Iwamoto, MD
Brain Cancer
Assistant Professor of Neurology, Deputy Director, Division of Neuro-Oncology, Department of Neurology, Columbia University Irving Medical Center

Mark G. Kris, MD
Lung Cancer
Attending Physician, Thoracic Oncology Service, Department of Medicine, Memorial Sloan Kettering Cancer Center, Professor of Medicine, Weill Cornell Medical College

Peter Martin, MD
Lymphoma
Chief, Lymphoma Program, Associate Professor of Medicine, Weill Cornell Medicine, Associate Attending Physician, New York-Presbyterian Hospital

Michael J. Mauro, MD
Leukemia
Leader, Myeloproliferative Neoplasms Program, Member, Memorial Sloan Kettering Cancer Center, Professor of Medicine, Weill Cornell Medical College

Priscilla Merriam, MD
Sarcoma
Physician, Medical Oncology, Sarcoma and Bone Cancer Treatment Center, Dana-Farber Cancer Institute, Instructor in Medicine, Harvard Medical School

Ruben A. Mesa, MD, FACP
Myeloproliferative Neoplasms
Director, Mays Cancer Center at UT Health San Antonio MD Anderson, Mays Family Foundation Distinguished University Presidential Chair, Professor of Medicine

Krzysztof Misiukiewicz, MD, MSCR
Oral, Head and Neck Cancers
Associate Professor of Medicine, Hematology and Medical Oncology, Assistant Professor, Otolaryngology, Icahn School of Medicine at Mount Sinai, Mount Sinai Hospital

Edith P. Mitchell, MD, FACP, FCPP
Clinical Trials
Clinical Professor of Medicine and Medical Oncology, Department of Medical Oncology, Director, Center to Eliminate Cancer Disparities, Associate Director, Diversity Affairs, Sidney Kimmel Cancer Center at Jefferson, 116th President National Medical Association

Eileen M. O' Reilly, MD
Pancreatic Cancer
Winthrop Rockefeller Chair in Medical Oncology, Section Head Hepatopancreaticobiliary/Neuroendocrine Cancers, Gastrointestinal Oncology Service Associate Director, David M. Rubenstein Center for Pancreatic Cancer, Attending Physician, Member, Memorial Sloan Kettering Cancer Center, Associate Professor, Weill Cornell Medical College

Carolyn D. Runowicz, MD
Ovarian Cancer
Executive Associate Dean for Academic Affairs, Professor, Department of Obstetrics and Gynecology, Herbert Wertheim College of Medicine, Florida International University

Susan Slovin, MD, PhD

Prostate Cancer

Attending Physician, Genitourinary Oncology Service, Sidney Kimmel Center for Prostate and Urologic Diseases, Memorial Sloan Kettering Cancer Center, Professor of Medicine, Department of Medicine, Weill College of Cornell University

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 and provide evidence about newer treatment approaches, such as immunotherapy and targeted therapy. 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 2019 Annual Meeting of the American Society of Clinical Oncology:

- **The results of recent research did not support the continuation of temozolomide therapy beyond 6 cycles in people with newly-diagnosed glioblastoma** (page 10).
- **A phase III trial showed benefit in combining temozolomide with radiotherapy in IDH-mutated anaplastic gliomas** (page 11).
- **An investigational drug is being studied to treat recurrent or progressive IDH1-mutated gliomas** (page 11).
- **A phase II trial found benefit in combining an investigational immunotherapy with standard therapy in the treatment of glioblastoma** (page 12).

Data does not support prolonged temozolomide as maintenance therapy in newly diagnosed glioblastoma

A retrospective analysis of four separate studies concluded that continuing temozolomide beyond 6 cycles did not result in improvement in overall survival for people with newly-diagnosed glioblastoma. The patients whose outcomes were analyzed had glioblastoma that had not progressed (advanced) following the initial 6 cycles of temozolomide.

What Patients Need to Know

Temozolomide, a chemotherapy taken in pill form, is typically prescribed following a 6-week course of radiation.

Adding temozolomide to radiotherapy studied in anaplastic gliomas

The phase III CATNON trial studied adding the chemotherapy temozolomide to radiotherapy in patients with anaplastic gliomas. While giving concurrent temozolomide did not increase survival in trial participants as a whole, there was a trend towards a benefit in IDH-mutated tumors.

What Patients Need to Know

Mutations in the IDH gene are "molecular markers" that are known to be of great significance in the development of gliomas.

Investigational drug for treatment of IDH1-mutated gliomas being studied

A first-in-human phase I trial is evaluating the investigational drug DS-1001b in the treatment of patients with recurrent or progressive IDH1-mutated gliomas. The trial is designed to assess the drug's safety, tolerability and anti-tumor activity.

What Patients Need to Know

The blood-brain barrier keeps harmful substances away from the brain, but also prevents many anticancer drugs from reaching brain tumors. DS-1001b has been shown to have high blood-brain permeability, meaning that it can effectively cross this barrier.

Investigational immunotherapy shows benefit as part of glioblastoma combination therapy

The latest results from an ongoing phase II trial showed that the investigational immunotherapy SurVaxM extended survival when used as part of combination treatment for glioblastoma. SurVaxM is a synthetic compound that stimulates the immune system to target survivin, a cancer molecule that is present in glioblastoma and many other cancers.

What Patients Need to Know

The trial participants were treated with SurVaxM in combination with standard therapy—surgery, radiation and the chemotherapy temozolomide.

Breast Cancer

Researchers reported a number of important findings in breast cancer treatment at the 2019 Annual Meeting of the American Society of Clinical Oncology:

- **A phase III trial showed the combination of alpelisib and fulvestrant prolonged progression-free survival when used to treat advanced breast cancer with the PIK3CA mutation** (page 14).
- **The MONALEESA-7 trial showed that a combination of targeted therapy and standard-of-care endocrine therapy improved overall survival in premenopausal women with advanced HR-positive, HER2-negative breast cancer** (page 14).
- **The novel regimen of neratinib plus capecitabine increased progression-free survival in women with metastatic HER2-positive breast cancer** (page 15).
- **The SOPHIA trial showed that the novel drug margetuximab, in combination with chemotherapy, improved clinical benefit in heavily pretreated HER2-positive metastatic breast cancer** (page 15).
- **Immunotherapy, in combination with chemotherapy, was studied as first-line treatment of locally advanced or metastatic triple-negative breast cancer in a phase III trial** (page 16).

Investigational drug evaluated in treatment of advanced breast cancer with PIK3CA mutation

In treatment of advanced breast cancer with the PIK3CA mutation, data from the phase III SOLAR-1 trial showed that the investigational drug alpelisib, used in combination with the hormone therapy fulvestrant, prolongs progression-free survival (PFS), compared with fulvestrant alone.

What Patients Need to Know

PIK3CA mutations are present in approximately 40 percent of ER-positive metastatic breast cancers. These mutations result in the PI3K pathway being hyper-active, which drives cancer cell growth and increases resistance to hormonal therapies.

Combination of targeted therapy and standard-of-care endocrine therapy studied in advanced HR-positive breast cancer

The international phase III MONALEESA-7 trial found that adding the targeted therapy ribociclib to endocrine therapy significantly improved overall survival for premenopausal women with advanced hormone receptor (HR)-positive, HER2-negative breast cancer, compared with endocrine therapy alone.

After 42 months of follow-up, the survival rate was 70 percent for women treated with the combination therapy, compared with 46 percent for women who received endocrine therapy alone.

What Patients Need to Know

MONALEESA-7 is the first trial to focus exclusively on premenopausal women with advanced breast cancer that had not previously been treated with endocrine therapy.

Global trial shows combination of neratinib and capecitabine increased PFS in women with metastatic HER2-positive breast cancer

In the global phase III NALA trial, the treatment of metastatic HER2-positive breast cancer with the targeted therapy neratinib plus the chemotherapy capecitabine significantly improved progression-free survival as compared with the combination of lapatinib (a targeted therapy) and capecitabine.

The results of the trial also showed a trend toward improved overall survival.

What Patients Need to Know

In the trial, the novel (new) regimen of neratinib plus capecitabine was given to 662 women who had received at least two prior HER2-directed treatments for metastatic breast cancer.

Phase III trial shows combination of margetuximab and chemotherapy has clinical benefit in pretreated HER2-positive metastatic breast cancer

Compared to the combination of trastuzumab and chemotherapy, the results of the phase III SOPHIA trial showed margetuximab plus chemotherapy led to significant improvements in progression-free survival in the treatment of HER2-positive metastatic breast cancer that had progressed after treatment with trastuzumab, pertuzumab and chemotherapy.

What Patients Need to Know

Margetuximab is a novel anti-HER2 antibody. The improved clinical benefit of margetuximab plus chemotherapy was enhanced in women with the low-affinity CD16A-158F gene. This gene is known to prevent treatment with trastuzumab from being effective.

Immunotherapy evaluated as first-line treatment of triple-negative breast cancer in phase III trial

In previously untreated women with locally advanced or metastatic triple-negative breast cancer, the phase III IMpassion130 trial showed the immunotherapy atezolizumab, in combination with the chemotherapy nab-paclitaxel, resulted in improved median survival compared to placebo plus nab-paclitaxel.

What Patients Need to Know

IMpassion130 is the first phase III trial to show the clinical benefit of immunotherapy as a first-line treatment for metastatic triple-negative breast cancer.

Colorectal Cancer

Researchers reported a number of important findings in colorectal cancer treatment at the 2019 Annual Meeting of the American Society of Clinical Oncology:

- **Researchers are studying how analyzing "circulating tumor DNA" may be of benefit in the detection, diagnosis and treatment of colorectal cancer** (page 17).
- **The duration of post-surgery chemotherapy was studied in the treatment of high-risk stage II colon cancer** (page 18).
- **Up-front chemotherapy may lead to better outcomes in the treatment of colon cancer** (page 18).
- **The results of the phase III TRIBE2 trial showed the superiority of FOLFOXIRI as a first-line treatment approach for inoperable metastatic colorectal cancer** (page 19).

"Circulating tumor DNA" analysis being researched as tool in colorectal cancer

Colorectal tumors can shed tiny bits of DNA, which then circulate throughout the body. Researchers are seeking to learn how analysis of this "circulating tumor DNA" (ctDNA) can help detect, diagnose and treat colorectal cancer.

What Patients Need to Know

While the research is at an early stage, analysis of ctDNA has the potential for a number of uses in colorectal cancer. One potential use is checking the blood for ctDNA after surgery, to see if any disease remains in the body. This analysis would allow doctors to be more certain about which patients would benefit from post-surgery chemotherapy.

Duration of post-surgery chemotherapy regimens evaluated in high-risk stage II colon cancer

As a treatment for high-risk stage II colon cancer, the results of a recent analysis suggest that three months of CAPOX (capecitabine plus oxaliplatin) given after surgery may be as effective as six months of CAPOX and result in less toxicity. The analysis was conducted by the IDEA (International uration Evaluation of Adjuvant Chemotherapy) Collaboration.

What Patients Need to Know

There were no significant differences in the five-year recurrence rate for patients who received either three or six months of treatment with CAPOX, which is given in pill form. However, the analysis showed that six months of intravenous treatment with FOLFOX (folinic acid, fluorouracil and oxaliplatin) was more effective than three months of FOLFOX treatment.

Up-front chemotherapy evaluated in treatment of colon cancer

The standard of care for resectable (surgically operable) stage I, II or III colon cancer is to remove the tumor with surgery, followed by treatment with chemotherapy for between three and six months.

The international FOxTROT trial evaluated whether colon cancer patients could benefit from six weeks of up-front (neoadjuvant) chemotherapy, followed by surgery and 18 weeks of chemotherapy.

What Patients Need to Know

Although the results were not conclusive, researchers found a promising trend toward fewer cancer recurrences over a two-year period in patients who received chemotherapy before surgery.

Chemotherapy regimen FOLFOXIRI evaluated as first-line approach for metastatic colorectal cancer

In the treatment of unresectable (inoperable) metastatic colorectal cancer, the phase III TRIBE2 trial showed the clinical superiority of FOLFOXIRI plus the targeted therapy bevacizumab, as compared with sequential treatment with FOLFOX plus bevacizumab followed by FOLFIRI plus bevacizumab.

The results were consistent with the results of the TRIBE trial and support the use of FOLFOXIRI plus bevacizumab as a first-line (initial) approach in the treatment of unresectable metastatic colorectal cancer

What Patients Need to Know

FOLFOXIRI, FOLFOX and FOLFIRI are all chemotherapy regimens. FOLFOXIRI consists of folinic acid, 5-fluorouracil, oxaliplatin and irinotecan. FOLFOX is FOLFOXIRI without irinotecan, and FOLFIRI is FOLFOXIRI without oxaliplatin.

Leukemia

Researchers reported a number of important findings in leukemia treatment at the 2019 Annual Meeting of the American Society of Clinical Oncology:

- **The ADMIRAL trial evaluated gilteritinib in the treatment of relapsed/refractory FLT3-positive acute myeloid leukemia** (page 21).
- **A phase III trial indicated that flumatinib may be superior to imatinib in the first-line treatment of chronic-phase CML, when compared with imatinib** (page 21).
- **Treatment-free remission was evaluated in chronic-phase CML after second-line treatment with the TKI nilotinib** (page 22).

Targeted therapy gilteritinib shown to prolong survival in FLT3-postive AML

The results of the phase III ADMIRAL trial showed that the targeted therapy gilteritinib significantly prolonged overall survival in people with FLT3-positive relapsed (returned) or refractory (resistant to treatment) acute myeloid leukemia (AML), compared with chemotherapy.

What Patients Need to Know

The trial showed that the clinical benefit of gilteritinib was maintained even if additional (non-FLT3) gene mutations were present.

Flumatinib compared to imatinib in treatment of chronic myelogenous leukemia (CML)

According to the results of a phase III trial, the targeted therapy flumatinib may have superior effectiveness in the first-line (initial) treatment of chronic-phase CML, when compared with imatinib. In chronic-phase CML, the leukemia is slow-growing and generally responds well to treatment.

What Patients Need to Know

Flumatinib, a tyrosine kinase inhibitor (TKI), is a derivative of imatinib. Imatinib was the first TKI used for the treatment of CML. Researchers found that flumatinib and imatinib had comparable safety profiles.

Treatment-free remission in chronic-phase CML evaluated after second-line treatment with nilotinib

Updated results from the ENESTop trial showed that about half of patients with chronic-phase CML remained in treatment-free remission 3.7 years after stopping second-line treatment with the TKI nilotinib. Trial participants were previously treated with the TKI imatinib.

What Patients Need to Know

ENESTop is one of three trials evaluating treatment-free remission in people with chronic-phase CML after second-line treatment with nilotinib.

Lung Cancer

Researchers reported a number of important findings in lung cancer treatment at the 2019 Annual Meeting of the American Society of Clinical Oncology:

- **Two trials found benefit in treating non-small cell lung cancer (NSCLC) with immunotherapy prior to surgery** (page23).
- **The results of a phase I trial indicated that an anti-HER3 antibody drug conjugate decreased tumor size in EGFR-positive NSCLC** (page 24).
- **A phase III trial showed that adding ramucirumab to erlotinib significantly reduced the risk of disease progression or death in EGFR-positive NSCLC** (page 24).
- **The results of a phase III trial showed that adding durvalumab to radiation and chemotherapy decreased the risk of recurrence in unresectable NSCLC** (page 25).

Immunotherapy prior to surgery found to be beneficial in the treatment of NSCLC non-small cell lung cancer

The results of two trials showed there was clinical benefit in giving immunotherapy prior to surgery in the treatment of non-small cell lung cancer (NSCLC). The Lung Cancer Mutation Consortium LCMC3 trial evaluated atezolizumab, while the NEOSTAR trial evaluated nivolumab and a combination of nivolumab and ipilimumab.

What Patients Need to Know

Atezolizumab, nivolumab and ipilimumab are all types of immunotherapy known as "immune checkpoint inhibitors." Atezolizumab and nivolumab work by releasing a molecular "brake" known as PD-L1 that prevents the body's immune system from attacking tumors. Ipilimumab seeks out and locks onto CTLA-4, a protein that normally helps keep immune system cells (called T-cells) in check. By blocking the action of CTLA-4, ipilimumab is thought to help the immune system destroy cancer cells.

Novel anti-HER3 drug evaluated in phase I trial for treatment of NSCLC with EGFR mutation

According to research from a phase I trial, the novel (new) anti-HER3 antibody drug conjugate U3-1402 appeared to decrease tumor size in cases of NSCLC with a mutation of the EGFR (epidermal growth factor receptor) gene.

What Patients Need to Know

HER3 (human epidermal growth factor receptor 3) is overexpressed in the majority of EGFR-mutated lung cancers. Targeting HER3 is being explored as a treatment option for patients whose NSCLC has become resistant to treatment with tyrosine kinase inhibitors (TKIs).

Clinical benefit shown by adding ramucirumab to erlotinib in treatment of EGFR-positive NSCLC

The phase III RELAY trial showed that adding ramucirumab to erlotinib reduced the risk of disease progression or death by 40 percent in patients with EGFR-positive non-small cell lung cancer, compared to treatment with erlotinib alone.

What Patients Need to Know

Ramucirumab is a drug designed to cut off the blood supply that tumors need to grow. Erlotinib is a targeted therapy that is often used in the treatment of EGFR-positive NSCLC.

Immunotherapy drug added to chemoradiation reduces risk of recurrence in unresectable NSCLC

The phase III PACIFIC trial found that adding the immunotherapy durvalumab to radiation and chemotherapy significantly decreased the recurrence of lung cancer in patients with stage III unresectable (inoperable) non-small cell lung cancer.

What Patients Need to Know

Durvalumab, a type of immune checkpoint inhibitor, works by interfering with a molecular "brake" known as PD-1 or PD-L1 that prevents the body's immune system from attacking cancer cells.

Lymphoma

Researchers reported a number of important findings in lymphoma treatment at the 2019 Annual Meeting of the American Society of Clinical Oncology:

- **The phase II Smart Start trial evaluated a targeted therapy regimen in the treatment of a specific type of DLBCL** (page 26).
- **In people with DLBCL, maintenance treatment with rituximab provided no additional benefit after successful R-CHOP therapy** (page 27).
- **The immunotherapy combination of lenalidomide plus rituximab demonstrated clinical activity in the treatment of follicular lymphoma and marginal zone lymphoma** (page 27).
- **Targeted therapy plus immunotherapy was evaluated as treatment of CLL in people with comorbidities** (page 28).

Targeted therapy combination evaluated in treatment of non-germinal center DLBCL

The first-of-its-kind phase II Smart Start trial evaluated a targeted therapy regimen of rituximab, lenalidomide and ibrutinib in the treatment of a specific type of diffuse large B-cell lymphoma (DLBCL).

What Patients Need to Know

Treatment with the targeted therapy regimen resulted in an 84.6 percent overall response rate and a 38.5 percent complete response rate when given, prior to chemotherapy, to newly-diagnosed patients with non-germinal center DLBCL.

No additional benefit shown in rituximab as maintenance treatment in DLBCL

According to the results of a phase II trial, people with diffuse large B-cell lymphoma who achieve complete remission after treatment with R-CHOP received no additional disease-free survival benefit from undergoing maintenance treatment with the immunotherapy rituximab.

What Patients Need to Know

R-CHOP is a regimen that consists of rituximab, the chemotherapies cyclophosphamide, doxorubicin and vincristine and the steroid prednisone.

Phase III trial shows clinical benefit of combination immunotherapy in treatment of FL and MZL

The results of the phase III MAGNIFY trial showed that the immunotherapy combination of lenalidomide plus rituximab demonstrated clinical activity in the treatment of follicular lymphoma (FL) and marginal zone lymphoma (MZL).

What Patients Need to Know

The lenalidomide/rituximab combination produced responses even in people who had previously experienced early relapse (return of their lymphoma) and whose FL or MLZ was refractory (resistant to treatment).

Targeted therapy and immunotherapy combination evaluated in previously-untreated CLL

In the treatment of chronic lymphocytic leukemia (CLL), the phase III CLL14 trial compared the targeted therapy venetoclax plus the immunotherapy obinutuzumab with the chemotherapy chlorambucil plus obinutuzumab. The trial participants were people whose CLL had not been previously treated, and who also had comorbidities (other chronic health conditions).

What Patients Need to Know

Researchers concluded that venetoclax plus obinutuzumab induced minimal residual disease (MRD) negativity, resulting in improved progression-free survival. Negative MRD status means that no cancer can be detected, even with the use of sophisticated diagnostic tests.

Melanoma

Researchers reported a number of important findings in melanoma treatment at the 2019 Annual Meeting of the American Society of Clinical Oncology:

- **An analysis of pooled data showed that there was clinical benefit to neoadjuvant (before surgery) therapy in stage III melanoma** (page 29).
- **The results of a phase III trial showed that adjuvant (post-surgery) immunotherapy reduced the risk of recurrence in stage III melanoma** (page 30).
- **The combination of nivolumab and ipilimumab led to durable responses in patients with metastatic melanoma and asymptomatic brain metastases** (page 30).

Neoadjuvant therapy of benefit in stage III melanoma

Pooled data from six trials showed that neoadjuvant treatment with immunotherapy or targeted therapy was associated with a high clinical response rate in stage III melanoma. The researchers evaluated data from neoadjuvant therapy trials of anti-PD-1 immunotherapy or anti-BRAF/MEK-targeted therapy.

What Patients Need to Know

PD-1 inhibitors target proteins that can prevent the body's immune system from attacking tumors. BRAF and MEK inhibitors target proteins that exist in melanomas that have a mutation of the BRAF gene.

Post-surgery therapy with ipilimumab reduces risk of recurrence in stage III melanoma

An analysis of findings from the phase III EORTC trial showed that the immunotherapy ipilimumab, given post-surgery, resulted in a 25 percent reduction in the risk of recurrence or death for patients with stage III melanoma, as compared with placebo.

What Patients Need to Know

Ipilimumab, which is given intravenously, seeks out and locks onto CTLA-4, a protein that normally helps keep immune system cells (called T-cells) in check. By blocking the action of CTLA-4, ipilimumab is thought to help the immune system destroy melanoma cells.

Immunotherapy combination studied in metastatic melanoma with brain metastases

According to data from the phase II CheckMate-204 trial, the combination of the immunotherapies nivolumab and ipilimumab led to durable (long-lasting) responses in people with metastatic melanoma who had asymptomatic (showing no symptoms) brain metastases.

What Patients Need to Know

Brain metastases begin as cancer in a different part of the body, spreading to the brain over time. More than half of people with metastatic melanoma will experience at least one brain metastasis during the course of their disease

Myeloproliferative Neoplasms

Researchers reported a number of important findings in the treatment of myeloproliferative neoplasms (MPNs) at the 2019 Annual Meeting of the American Society of Clinical Oncology:

- **Based on the results of the JAKARTA trial, the FDA has approved the JAK inhibitor fedratinib for the treatment of intermediate-2 or high-risk primary or secondary myelofibrosis** (page 32).
- **The investigational drug CPI-0610 is being evaluated as a treatment for refractory myelofibrosis** (page 32).
- **The effectiveness and safety of the targeted therapy tagraxofusp is being evaluated in the treatment of intermediate or high-risk myelofibrosis** (page 33).

FDA approves fedratinib for treatment of certain types of myelofibrosis

In August 2019, the Food and Drug Administration (FDA) approved fedratinib for the treatment of patients with intermediate-2 or high-risk primary or secondary myelofibrosis (MF), including post-polycythemia vera and post-essential thrombocythemia MF. The approval was based on the results of the JAKARTA trial.

What Patients Need to Know

Fedratinib is a Janus kinase (JAK) inhibitor, a type of drug that works by inhibiting the activity of one or more of the Janus kinase family of enzymes. Ruxolitinib, another JAK inhibitor, was approved for post-polycythemia vera and post-essential thrombocythemia MF in 2011.

Investigational drug shows clinical benefit in treatment of refractory myelofibrosis

Interim results from the phase II MANIFEST trial indicated that the investigational drug CPI-0610 showed signs of beneficial clinical activity in the treatment of refractory (resistant to treatment) myelofibrosis, both as a monotherapy (a drug used alone) and in combination with the JAK inhibitor ruxolitinib.

What Patients Need to Know

CPI-0610 prevents bromodomain and extraterminal (BET) proteins from attaching to certain cancer-causing genes, which may "turn off" the genes and stop them from making new cancer cells.

Targeted therapy tagraxofusp being evaluated as treatment for relapsed/ refractory myelofibrosis

A multicenter, phase I/II trial is evaluating the effectiveness and safety of tagraxofusp in the treatment of people with intermediate or high-risk myelofibrosis (MF) that has relapsed or is refractory (resistant) to treatment with a JAK inhibitor. Trial participants also include people who, because of side effects, could not tolerate the continued use of a JAK inhibitor as a treatment for MF.

What Patients Need to Know

Tagraxofusp, also called SL-401, is a targeted therapy directed at the interleukin-3 receptor CD123, which is expressed (present) on a variety of malignancies, including myelofibrosis.

Oral, Head and Neck Cancers

Researchers reported a number of important findings in the treatment of oral, neck and head cancers at the 2019 Annual Meeting of the American Society of Clinical Oncology:

- **Induction chemotherapy was shown to be of benefit in the treatment of locally advanced nasopharyngeal carcinoma** (page 35).
- **The KEYNOTE-048 trial demonstrated overall survival benefit of pembrolizumab plus chemotherapy as initial therapy for squamous cell cancer of the head and neck** (page 35).
- **The immunotherapy toripalimab is being studied in phase II trial as treatment of metastatic nasopharyngeal cancer that has not responded to other therapies** (page 36).

Induction chemotherapy effective in treatment of nasopharyngeal carcinoma

Induction chemotherapy with cisplatin followed by the combination of chemotherapy and radiation appeared to offer survival benefits for people with locally advanced nasopharyngeal carcinoma, compared with the combination of chemotherapy and radiation alone.

What Patients Need to Know

The results of a phase III randomized trial showed no significant difference in the rate of serious adverse events in the group that received induction chemotherapy.

Superior overall survival demonstrated by pembrolizumab as initial treatment of SCCHN

The final analysis from the phase III KEYNOTE-048 trial showed that the immunotherapy pembrolizumab plus chemotherapy demonstrated superior overall survival as an initial treatment for squamous cell cancer of the head and neck (SCCHN), as compared to a regimen of cisplatin, 5-FU and cetuximab.

Pembrolizumab blocks the programmed death receptor-1 (PD-1) pathway, which cancer cells can use to hide from cells that attack and destroy them.

What Patients Need to Know

In June 2019, the Food and Drug Administration (FDA) approved pembrolizumab, in combination with the chemotherapy regimen 5-FU, as treatment for SCCHN.

PD-1 checkpoint inhibitor evaluated as treatment for metastatic nasopharyngeal cancer

A phase II trial is evaluating the safety and effectiveness of the immunotherapy toripalimab in treatment of metastatic nasopharyngeal cancer that has not responded to other therapies. Toripalimab, like pembrolizumab, is a PD-1 checkpoint inhibitor.

What Patients Need to Know

In the trial, toripalimab demonstrated encouraging clinical activity and a manageable safety profile, especially in patients who had received only one prior line of therapy.

Ovarian Cancer

Researchers reported a number of important findings in ovarian cancer treatment at the 2019 Annual Meeting of the American Society of Clinical Oncology:

- **Multiple studies indicated that PARP inhibitors may be substituted for chemotherapy for women with relapsed ovarian cancer, regardless of platinum-sensitivity status** (page 37).
- **The EWOC-1 trial showed that a combination of chemotherapies was better than single-agent chemotherapy in treatment of ovarian cancer in elderly women** (page 38).

Substituting PARP inhibitors for chemotherapy studied in treatment of relapsed ovarian cancer

A number of clinical trials evaluated the substitution of PARP inhibitors for chemotherapy in the treatment of relapsed ovarian cancer, including:

- **SOLO3.** In this phase III trial, women with BRCA-mutated, platinum-sensitive relapsed ovarian cancer gained significant clinical benefit from treatment with the PARP inhibitor olaparib, as compared with chemotherapy.
- **AVANOVA.** The results of this phase II trial showed that the combination of the PARP inhibitor niraparib plus the targeted therapy bevacizumab significantly improved progression-free survival in women with platinum-sensitive relapsed ovarian cancer.

- **CLIO.** This phase II trial showed favorable results of olaparib therapy versus standard-of-care chemotherapy in the treatment of platinum-resistant relapsed ovarian cancer.

What Patients Need to Know

PARP is a type of enzyme that helps repair DNA. In cancer treatment, PARP inhibitors are used to prevent cancer cells from repairing their damaged DNA. This can cause the cancer cells to die, especially those with defective DNA repair pathways, such as BRCA1/2-associated ovarian cancers.

Combination of chemotherapies better in treatment of ovarian cancer in elderly women

According to the results of the EWOC-1 trial, elderly women with stage III/IV epithelial ovarian cancer had better survival outcomes when treated with the combination of carboplatin and paclitaxel, compared to single-agent carboplatin.

What Patients Need to Know

The primary endpoint of the study was the ability of the women to complete six chemotherapy courses without disease progression, discontinuation of treatment or death.

Pancreatic Cancer

Researchers reported a number of important findings in pancreatic cancer treatment at the 2019 Annual Meeting of the American Society of Clinical Oncology:

- **A phase III trial found that the PARP inhibitor olaparib delays disease progression in BRCA-mutated metastatic pancreatic cancer** (page 40).
- **An independent review of the APACT trial results found that adding nab-paclitaxel to gemcitabine as adjuvant treatment did not prolong disease-free survival** (page 40).
- **An analysis showed that the anticoagulant rivaroxaban substantially reduced venous thromboembolism in people with pancreatic cancer** (page 41).

PARP inhibitor delays disease progression in metastatic pancreatic cancer with inherited BRCA mutation

The results of POLO, a large phase III trial, found that the PARP inhibitor olaparib is effective at delaying disease progression in people with metastatic pancreatic cancer who have an inherited BRCA mutation.

What Patients Need to Know

PARP is a type of enzyme that helps repair DNA. In cancer treatment, PARP inhibitors are used to prevent cancer cells from repairing their damaged DNA. This can cause the cancer cells to die, especially those with the cancer-predisposition genes BRCA1 or BRCA2.

Addition of nab-paclitaxel to gemcitabine in adjuvant treatment evaluated

The global phase III APACT trial evaluated the chemotherapy combination of nab-paclitaxel plus gemcitabine versus gemcitabine alone in the adjuvant (post-surgery) treatment of pancreatic cancer.

What Patients Need to Know

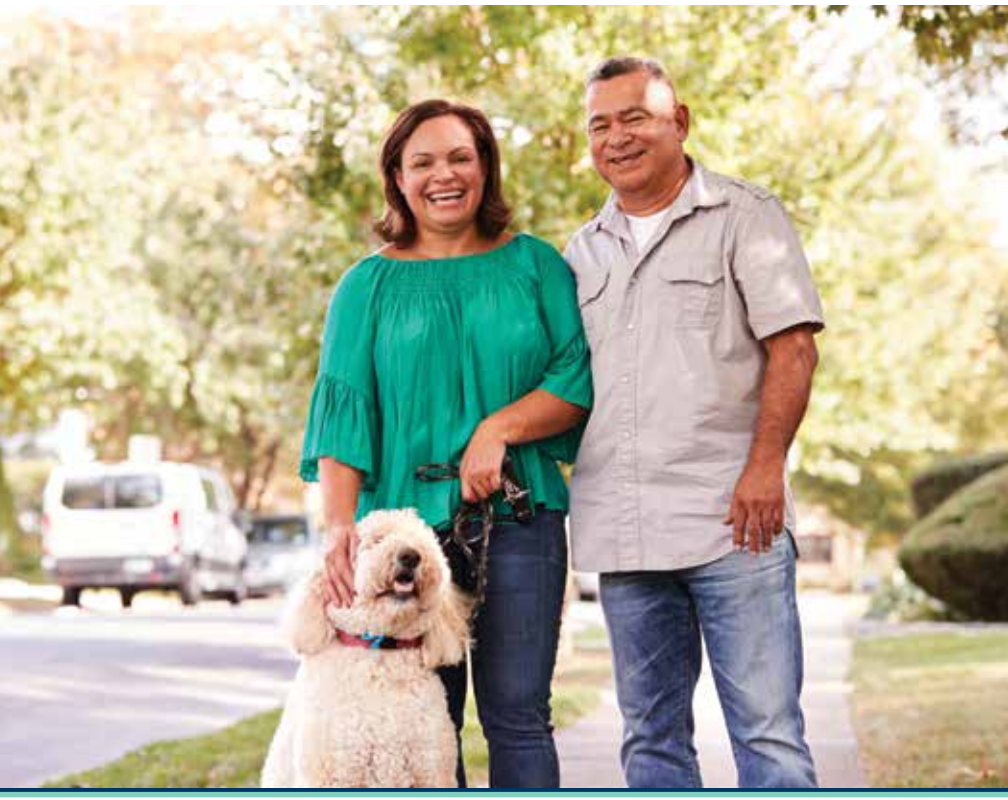
An independent review of the trial results found that adding nab-paclitaxel to adjuvant gemcitabine did not significantly prolong disease-free survival.

Rivaroxaban reduces VTE in patients with pancreatic cancer

According to the results from a subgroup analysis of the CASSINI study, rivaroxaban substantially reduces venous thromboembolism (VTE) in people with pancreatic cancer, without increasing the incidence of major bleeding events.

What Patients Need to Know

Rivaroxaban is an anticoagulant used to treat deep vein thrombosis (DVT) and pulmonary embolism. The findings indicate the potential benefit of including rivaroxaban as part of a systemic treatment regimen for pancreatic cancer.



Prostate Cancer

Researchers reported a number of important findings in prostate cancer treatment at the 2019 Annual Meeting of the American Society of Clinical Oncology:

- **The androgen receptor inhibitors enzalutamide and apalutamide were evaluated in separate trials as a supplement to testosterone suppression therapy for metastatic hormone-sensitive prostate cancer** (page 43).
- **The phase III ARAMIS trial evaluated the addition of the investigational drug darolutamide to testosterone suppression therapy in men with nonmetastatic castration-resistant prostate cancer** (page 43).
- **Results of TOPARP-B, a phase II trial, suggested that olaparib delays disease progression in metastatic castration-resistant prostate cancers that have DNA repair defects** (page 44).

Androgen receptor inhibitors evaluated in treatment of metastatic hormone-sensitive prostate cancer

Two trials evaluated the use of androgen receptor inhibitors, in combination with standard-of-care testosterone suppression therapy, for the treatment of metastatic hormone-sensitive prostate cancer.

Results of the phase III ENZAMET trial showed that 80 percent of men with metastatic hormone-sensitive prostate cancer were alive three years after being given the anti-androgen drug enzalutamide, along with testosterone suppression therapy.

Similar results were found in the phase III TITAN trial, which evaluated the anti-androgen drug apalutamide in combination with testosterone suppression therapy.

What Patients Need to Know

Both enzalutamide and apalutamide block male hormones from attaching to prostate cancer cells. As a result, these drugs can slow the growth of (or destroy) prostate tumors.

Investigational drug studied as treatment for nonmetastatic castration-resistant prostate cancer

ARAMIS, a phase III trial, showed the addition of the investigational drug darolutamide to testosterone suppression therapy delayed the spread of nonmetastatic castration-resistant prostate cancer to other parts of the body. Darolutamide, like enzalutamide and apalutamide, is an androgen receptor inhibitor.

What Patients Need to Know

The ARAMIS trial also found that darolutamide reduced pain progression by approximately 40 percent, as compared with placebo.

PARP inhibitor studied as treatment for certain metastatic castration-resistant prostate cancers

The phase II TOPARP-B trial found that the PARP inhibitor olaparib seemed to exhibit antitumor activity and delay disease progression in the subset of metastatic castration-resistant prostate cancers with DNA repair defects.

Tumors with defects in the BRCA1/2 gene were most sensitive to olaparib, but responses were also seen in tumors with other types of defects.

What Patients Need to Know

Olaparib blocks proteins called PARP; by doing so, the drug prevents cancer cells from repairing their damaged DNA, which can cause cancer cells to die.

Sarcoma

Researchers reported a number of important findings in sarcoma treatment at the 2019 Annual Meeting of the American Society of Clinical Oncology

- **A phase III trial found that adding a targeted therapy to chemotherapy in the treatment of soft-tissue sarcoma did not increase survival** (page 45).
- **A phase III trial is evaluating standard versus histology-driven chemotherapy in the treatment of soft tissue sarcomas** (page 46).
- **An international phase III trial showed no clinical benefit in adding pre-operative radiotherapy to surgery in the treatment of retroperitoneal sarcoma** (page 46).

Adding targeted therapy to chemotherapy did not increase survival in soft-tissue sarcoma

The phase III ANNOUNCE trial studied the combination of the chemotherapy doxorubicin and the targeted therapy olaratumab in treatment of advanced soft-tissue sarcoma, compared to treatment with doxorubicin alone.

What Patients Need to Know

The results of ANNOUNCE found that adding olaratumab to chemotherapy did not increase survival. In April 2019, olaratumab was withdrawn from the market.

Standard versus tailored chemotherapy evaluated in treatment of soft-tissue sarcoma

A randomized phase III clinical trial is evaluating the treatment of localized high-risk soft-tissue sarcoma (STS) with the standard chemotherapy (epirubicin plus ifosfamide) compared to chemotherapy tailored to the specific type of STS.

What Patients Need to Know

This trial is designed to verify the hypothesis that a tailored approach is associated with an overall 30 percent reduction in the risk of relapse.

Adding pre-operative radiotherapy to surgery alone did not show benefit in retroperitoneal sarcoma

STRASS, an international phase III randomized trial, evaluated the effectiveness of pre-operative radiotherapy plus surgery compared with surgery alone in the treatment of retroperitoneal (abdominal) sarcoma.

What Patients Need to Know

The results of the trial failed to show a benefit of pre-operative radiotherapy in the treatment of retroperitoneal sarcoma. However, an exploratory analysis indicated that pre-operative radiotherapy may benefit patients being treated for liposarcoma, a subtype of retroperitoneal sarcoma.

Resources

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

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

Cancer.Net
888-651-3038
www.cancer.net

Cancer Support Community
888-793-9355
www.cancersupportcommunity.org

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

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

National Library of Medicine
888-346-3656
www.nlm.nih.gov

CLINICAL TRIALS WEBSITES

EmergingMed
www.emergingmed.com

National Cancer Institute
www.cancer.gov/clinicaltrials

This booklet was supported by Gilead and Takeda Oncology.

CANCERcare®

Help and Hope

WWW.CANCERCARE.ORG

800-813-HOPE (4673)