TREATMENT UPDATE:

Blood Cancers

CANCER*CARE* CONNECT® BOOKLET SERIES

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This special edition of the Cancer*Care* Connect Booklet Series highlights cutting-edge research presented at the 2019 Annual Meeting of the American Society of Hematology, which took place December 7-10 in Orlando, Florida.

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

The information contained in this e-booklet is intended for discussion with your doctor. They can let you know whether these advances in the treatment of blood cancers affect your treatment plan and whether a clinical trial is right for you.

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.

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Treatment Update: Blood Cancers

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All people depicted in the photographs in this booklet are models, used for illustrative purposes only.

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 Hematology. The information contained in these pages is intended for discussion with your doctor. They 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 22 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

In compiling this report, we used content from the Cancer*Care* Connect Education Workshop titled "Update from the 2019 American Society of Hematology (ASH) Annual Meeting" held on December 19, 2019. We are indebted to the following individuals who were featured on this workshop:

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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 making a decision about 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 of the risks and benefits of the trial, including any possible side effects.
- Many clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- Participation is voluntary and does not affect your access to treatment in other settings. 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 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.

Leukemia

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

- **Research showed that treatment with an oral formulation of azacitidine improved overall survival and relapse-free survival when used as maintenance therapy in patients with acute myeloid leukemia** (page 8).
- **Two trials are evaluating the safety and efficacy of APR-246 in combination with azacitidine for the treatment of TP53-mutated myelodysplastic syndromes and acute myeloid leukemia** (page 9).
- **Trial results confirmed the clinical benefit of the immunotherapy drug blinatumomab in the treatment of children and young adults with B-cell acute lymphoblastic leukemia** (page 9).
- **In certain patients with chronic lymphocytic leukemia/ small cell leukemia, trial results showed the benefit of a longer duration of ibrutinib plus venetoclax combination therapy** (page 10).

Maintenance treatment with oral formulation of azacitidine improved outcomes in AML

According to research from the phase III QUAZER trial, patients with acute myeloid leukemia (AML) who were in remission after induction chemotherapy showed improved overall survival and relapse-free survival when treated with CC-486, a formulation of the chemotherapy azacitidine that is taken orally.

What Patients Need to Know

Azacitidine is designed to slow the production of leukemia cells and help the bone marrow produce more healthy and normal-functioning cells.

Investigational drug being studied for treatment of TP53-mutated myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML)

Investigators from two phase Ib/II clinical trials presented positive data on the investigational drug APR-246 used in combination with the chemotherapy azacitidine in the treatment of patients with TP53-mutated MDS and AML.

In past research, APR-246 has demonstrated significant clinical activity in a wide variety of cancers, including MDS and AML, both as a monotherapy and in combination with other therapies.

What Patients Need to Know

The p53 gene is the most frequently mutated gene in human cancer. These mutations are often associated with resistance to anti-cancer drugs.

Clinical benefit of blinatumomab confirmed in treatment of children and young adults with B-ALL

Trial results showed that, compared with standard chemotherapy, the immunotherapy drug blinatumomab significantly improved survival in children and young adults with B-cell acute lymphoblastic leukemia (B-ALL) who still had residual disease (remaining cancer cells) following induction therapy.

What Patients Need to Know

Researchers say the results support blinatumomab as a new standard of care for high- and intermediate-risk relapsed B-ALL patients who are preparing to receive a bone marrow transplant.

Longer-duration combination therapy of benefit in treatment of CLL/SLL

In a study of patients with previously untreated high-risk chronic lymphocytic leukemia/small cell leukemia (CLL/SLL), trial results showed that a longer duration of ibrutinib plus venetoclax reduced the rate of undetectable minimal residual disease (MRD) in the bone marrow.

What Patients Need to Know

Ibrutinib inhibits the function of a type of protein called BTK that can cause cancer cells to grow. Venetoclax targets a different protein, BCL-2, which is overexpressed (too high) in many patients with CLL/SLL, and can cause cancer cells to grow.

Lymphoma

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

- **The updated results from a phase II trial showed the clinical benefit of a CAR T-cell therapy as a treatment for large B-cell lymphoma** (page 11).

- **The results of a pooled analysis showed that treatment with ibrutinib at first relapse extended progression-free survival in patients with mantle cell lymphoma** (page 12).

- **Data from a phase II trial showed that the combination of obinutuzumab plus lenalidomide resulted in high "complete response" rates in previously untreated follicular lymphoma** (page 12).

- **The combination of polatuzumab-vedotin, obinutuzumab and lenalidomide resulted in a high rate of durable responses in patients with relapsed/refractory follicular lymphoma** (page 13).

Updated trial results show benefit of CAR T-cell therapy in treatment of large B-cell lymphoma

According to the updated results from the phase II ZUMA-1 trial, treatment with axicabtagene ciloleucel showed clinical benefit in overall survival in patients with refractory (not responding to treatment) large B-cell lymphoma.

Axicabtagene ciloleucel, a 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.

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.

Early treatment with ibrutinib extends progression-free survival in mantle cell lymphoma (MCL)

The updated results of a 7.5-year pooled analysis showed that treatment with ibrutinib at first relapse (compared to later therapy) extended progression-free survival and increased the likelihood of a complete response (absence of all detectable cancer) in patients with relapsed/refractory MCL.

The pooled analysis included results from three clinical trials: phase II SPARK, phase III RAY and phase II PCYC-1104.

What Patients Need to Know

Ibrutinib, a type of targeted therapy called a Bruton's tyrosine kinase (BTK) inhibitor, is approved by the FDA to treat a number of types of lymphoma and leukemia.

Combination therapy effective in previously untreated follicular lymphoma (FL)

According to data from a phase II study, the combination of the immunotherapy obinutuzumab plus the immunomodulatory agent lenalidomide resulted in early and very high rates of complete response in previously untreated patients with FL.

What Patients Need to Know

The goal of the ongoing research is to develop highly effective, well-tolerated frontline (initial) therapies that can serve as an alternative to chemotherapy for the treatment of follicular lymphoma.

"Triplet" therapy studied as treatment for relapsed/refractory FL

The results of an analysis showed that the combination of polatuzumab-vedotin, the immunotherapy drug obinutuzumab and the immunomodulatory agent lenalidomide induced a high rate of durable (long-lasting) responses in patients with relapsed/refractory follicular lymphoma.

Polatuzumab-vedotin is an antibody-drug conjugate, which is a targeted therapy combined with chemotherapy.

What Patients Need to Know

The analysis of this novel (new) combination demonstrated a safety profile consistent with the known profiles of the individual drugs.

Multiple Myeloma

Researchers reported a number of important findings in the treatment of multiple myeloma at the 2019 Annual Meeting of the American Society of Hematology:

- **Investigators reported that the evaluation of "circulating tumor DNA" may refine prognosis and add predictive value in relapsed multiple myeloma** (page 14).
- **Four-drug combinations are being studied as a possible standard of care in the treatment of multiple myeloma** (page 15).
- **As a result of the CARTITUDE-1 trial, CAR T-cell therapy has been granted a Breakthrough Therapy Designation by the FDA for the treatment of relapsed or refractory multiple myeloma** (page 15).
- **The results from a phase III trial suggest that early treatment with lenalidomide can delay smoldering multiple myeloma from progressing to symptomatic multiple myeloma** (page 16).

Analysis of "circulating tumor DNA" may add value in predicting multiple myeloma relapse

Cancer cells can shed tiny bits of DNA, which then circulate throughout the body. Investigators evaluated how the analysis of this "circulating tumor DNA" (ctDNA) through a liquid biopsy (a blood test that is able to detect cancer cells) may refine prognosis and provide added predictive value over current blood markers alone.

What Patients Need to Know

The analysis of ctDNA does not replace what is learned from other blood markers, but may be of additional value in treatment decisions.

Four-drug combinations being studied as treatment for multiple myeloma

Multiple studies are evaluating four-drug combinations (quadruplets) in the treatment of multiple myeloma. The quadruplets being studied include daratumumab and the combination of bortezomib, lenalidomide and dexamethasone (the Griffin study) and daratumumab plus the combination of bortezomib, melphalan and prednisone (the Alcyone study).

What Patients Need to Know

Additional research on efficacy (effectiveness) and safety is needed before four-drug combinations can be considered the standard of care for the treatment of multiple myeloma.

Investigational CAR T-cell therapy evaluated as treatment for relapsed/refractory multiple myeloma

The CARTITUDE-1 clinical trial evaluated the effectiveness and safety of JNJ-4528, an investigational BCMA-directed CAR T-cell therapy, in the treatment of relapsed or refractory multiple myeloma. The investigators reported that JNJ-4528 brings an early and deep response, including residual disease "negativity" (the lack of detectable residual disease).

BCMA, a cell-surface protein that helps regulate B-cell growth and survival, is overexpressed (too high) in patients with multiple myeloma.

What Patients Need to Know

In December 2019, the FDA granted JNJ-4528 a Breakthrough Therapy Designation, given to expedite the development and regulatory review of an investigational medicine that is intended to treat a serious or life-threatening condition.

Trial results suggest lenalidomide can delay progression of smoldering multiple myeloma

The standard approach to managing most patients with smoldering (showing no symptoms) multiple myeloma is observation, but the results from a phase III trial suggest that early treatment with the immunomodulatory drug lenalidomide can delay the progression to symptomatic multiple myeloma.

What Patients Need to Know

Lenalidomide was approved by the FDA in 2006 for relapsed (recurring) multiple myeloma. It was approved for newly-diagnosed patients in 2015 and as a maintenance therapy (continued treatment designed to prevent relapse) in 2017.

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 Hematology:

- **The JAK-inhibitor fedratinib was approved by the FDA in August 2019 as a treatment for myelofibrosis** (page 19).
- **A phase II trial demonstrated the benefit of an investigational BET-inhibitor in the treatment of myelofibrosis as a monotherapy or in combination with a JAK-inhibitor** (page 19).
- **The addition of navitoclax to ruxolitinib showed clinically meaningful spleen responses and improvements in symptoms in the treatment of certain patients with myelofibrosis** (page 20).
- **According to the result of a phase II trial, pegylated-interferon-α leads to high response rates in essential thrombocythemia and polycythemia vera after treatment with hydroxyurea** (page 20).

JAK-inhibitor fedratinib approved by the FDA for treatment of myelofibrosis

The JAK-inhibitor fedratinib was approved by the FDA in August 2019 for patients with intermediate-2 or high-risk primary or secondary myelofibrosis. Another JAK-inhibitor, ruxolitinib, was approved by the FDA in 2011 for treatment of the same conditions.

What Patients Need to Know

The approval was based on the phase III JAKARTA study, which found that after treatment with fedratinib, patients with primary or secondary myelofibrosis achieved symptom improvement and a significant reduction of spleen enlargement.

Investigational BET inhibitor evaluated as treatment for myelofibrosis

According to data from the phase II MANIFEST trial, the investigational drug CPI-0610 demonstrated symptom improvement, reduction of spleen enlargement and reduction in bone marrow fibrosis (lesions) when used as monotherapy or in combination with the JAK inhibitor ruxolitinib in the treatment of patients with myelofibrosis.

What Patients Need to Know

CPI-0610 is an oral bromodomain and extra-terminal domain (BET) inhibitor. Previous studies have shown that BET inhibitors constrain the growth and survival of tumor cells. Additional analysis is needed to confirm the benefit of CPI-0610 in the treatment of myelofibrosis.

Navitoclax shows benefit in ruxolitinib-resistant myelofibrosis

The addition of navitoclax to the JAK inhibitor ruxolitinib showed clinically meaningful spleen responses and symptom improvement in the treatment of patients with myelofibrosis who developed resistance to ruxolitinib. The ongoing phase II study will further assess navitoclax alone or in combination with ruxolitinib for patients with myelofibrosis.

What Patients Need to Know

Navitoclax is an inhibitor of BCLXL, BCL2 and BCLW, proteins which can prevent apoptosis (a process that eliminates damaged, potentially dangerous cells).

Pegylated-interferon-α associated with high response rates in hydroxyurea-resistant ET and PV

According to results of a phase II study, treatment with pegylated-interferon-α resulted in an overall response rate of approximately two-thirds in patients with high-risk essential thrombocythemia (ET) and polycythemia vera (PV) that is resistant or intolerant to hydroxyurea.

What Patients Need to Know

Researchers also found that a mutation of the calreticulin (CALR) gene was associated with higher complete response rates in patients with ET, suggesting that mutational status may help identify which patients would benefit most from treatment with pegylated-interferon-α.

Resources

CancerCare®
800-813-HOPE (800-813-4673)
www.cancercare.org

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

Be the Match® Patient Services
800-627-7692
www.bethematch.org

Blood & Marrow Transplant Information Network
888-597-7674
www.bmtinfonet.org

The Bone Marrow Foundation
800-365-1336
www.bonemarrow.org

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

CLINICAL TRIALS WEBSITES

EmergingMed
www.emergingmed.com

National Cancer Institute
www.cancer.gov

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

National Bone Marrow Transplant Link
800-546-5268
www.nbmtlink.org

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

The Leukemia & Lymphoma Society
800-955-4572
www.lls.org

Leukemia Research Foundation
847-424-0600
www.allbloodcancers.org

Lymphoma Research Foundation
800-500-9976
www.lymphoma.org

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