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 2023 Annual Meeting of the American Society of Hematology, which took place December 9-12 in San Diego, California.

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 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 resource navigation, 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.

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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 21 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 "Updates from the 2023 American Society of Hematology (ASH) Annual Meeting" held on December 14, 2023. 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 2023 Annual Meeting of the American Society of Hematology:

- **Zanubrutinib, compared with bendamustine plus rituximab, was evaluated in the treatment of CLL and SLL (page 6).**
- **In the treatment of relapsed/refractory CLL and SLL, results from a phase III trial showed zanubrutinib to be superior to ibrutinib (page 7).**
- **According to a phase III trial, ibrutinib plus venetoclax significantly improved progression-free and overall survival in untreated CLL, compared to FCR (page 8).**
- **Revumenib is an investigational therapy being studied as a treatment for acute leukemias with a certain genetic abnormality (page 8).**

Phase III trial showed superiority of BTK inhibitor in treatment of CLL and SLL

A biomarker subgroup analysis of the phase III SEQUOIA trial showed broad superiority of the kinase inhibitor zanubrutinib over bendamustine plus rituximab in the first-line treatment of chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL).

What Patients Need to Know

Kinase proteins send signals to the cell's control center that help tumor cells grow. Kinase inhibitors block these proteins. Zanubrutinib inhibits the function of a type of kinase called Bruton's tyrosine kinase (BTK). Bendamustine is a chemotherapy; rituximab is a monoclonal antibody.

Sustained progression-free survival seen with zanubrutinib in relapsed/refractory CLL and SLL

An extended follow-up of the ALPINE phase III trial confirmed sustained superior progression-free survival of zanubrutinib (compared with ibrutinib) for the treatment of relapsed or refractory (resistant to treatment) CLL and SLL.

What Patients Need to Know

Zanubrutinib is a BTK inhibitor. Ibrutinib is a tyrosine kinase inhibitor (TKI).

Results on untreated CLL reported from the FLAIR trial

Results from the phase III FLAIR trial showed that the TKI ibrutinib, in combination with the BCL-2 inhibitor venetoclax, significantly improved progression-free and overall survival compared to FCR in untreated CLL.

What Patients Need to Know

FCR is a combination therapy containing the chemotherapies fludarabine and cyclophosphamide and the monoclonal antibody rituximab.

Investigational drug studied for acute leukemia with certain genetic abnormality

In a phase II trial, the investigational targeted therapy revumenib showed clinical benefit in relapsed or refractory acute leukemia with a genetic marker known as KMT2Ar.

What Patients Need to Know

Revumenib could help more patients with hard-to-treat leukemias proceed to stem cell transplant.

Lymphoma

Researchers reported a number of important findings in the treatment of lymphoma at the 2023 Annual Meeting of the American Society of Hematology:

- **Axicabtagene ciloleucel studied as a first-line therapy for high-risk LBCL (page 9).**
- **Accelerated approval granted to lisocabtagene maraleucel for the treatment of follicular lymphoma (page 10).**
- **Chemotherapy-free treatment for newly-diagnosed DLBCL evaluated in the Smart Stop trial (page 11).**
- **Adding ibrutinib to standard immunochemotherapy evaluated in the treatment of mantle cell lymphoma (page 11).**

Updated analysis showed benefit of axi-cel in the treatment of high-risk LBCL

An updated analysis of the phase II ZUMA-12 trial showed that axicabtagene ciloleucel (axi-cel) demonstrated a high rate of durable responses, with no new safety concerns, in the treatment of high-risk large B-Cell lymphoma (LBCL).

What Patients Need to Know

Axicabtagene ciloleucel, a CAR T-cell therapy, may benefit patients with high-risk LBCL after standard first-line chemoimmunotherapy.

CAR T-cell therapy approved for FL based on TRANSCEND trial

The TRANSCEND FL trial evaluated lisocabtagene maraleucel, a CAR T-cell therapy, as a second-line treatment for high-risk relapsed or refractory (resistant to treatment) follicular lymphoma (FL).

Based on a person's specific situation, CAR T-cell therapy may be conducted on an outpatient basis or require a hospital admission. The process:

- Blood is drawn from the patient via an intravenous catheter (a flexible tube).
- T-cells are isolated from the rest of the blood.
- In a laboratory, the T-cells are genetically re-engineered by adding a chimeric antigen receptor to their surface.
- The modified T-cells (which are now CAR T-cells) are expanded to number in the hundreds of millions.
- The CAR T-cells are infused back into the patient where they target and destroy cancer cells.

What Patients Need to Know

On May 15, 2024, the FDA granted accelerated approval to lisocabtagene maraleucel for the treatment of relapsed or refractory FL after two or more prior lines of systemic therapy.

Chemotherapy-free treatment evaluated in newly-diagnosed DLBCL

The Smart Stop trial demonstrated that the combination of lenalidomide, tafasitamab, rituximab and acalabrutinib is highly effective as an initial chemotherapy-free treatment for newly-diagnosed diffuse large B-cell lymphoma (DLBCL).

What Patients Need to Know

Lenalidomide is a type of immunotherapy called an immunomodulator. Tafasitamab and rituximab are monoclonal antibodies, lab-generated proteins that target specific substances on the surface of the lymphoma cells, triggering an immune response. Acalabrutinib is a kinase inhibitor, designed to block proteins that help cancer cells grow.

Ibrutinib compared to ASCT in untreated mantle cell lymphoma

Although longer follow-up is needed, results of the phase III TRIANGLE study suggested the tyrosine kinase inhibitor ibrutinib may replace autologous stem cell transplantation (ASCT) after chemoimmunotherapy in younger patients with untreated mantle cell lymphoma. The trial also found clinical benefit when ibrutinib was added to ASCT, compared to ASCT alone.

What Patients Need to Know

In an autologous stem cell transplant, the person receives their own stem cells, rather than stem cells from a donor.

Multiple Myeloma

Researchers reported a number of important findings in the treatment of multiple myeloma at the 2023 Annual Meeting of the American Society of Hematology:

- **The phase III IsKia trial evaluated the efficacy and safety of isatuximab-carfilzomib-lenalidomide-dexamethasone in the treatment of multiple myeloma (page 12).**
- **Results from the Perseus trial supported a new standard of care for transplant-eligible patients with newly diagnosed multiple myeloma (page 13).**
- **A cohort study of the KarMMa-2 trial reported durable responses in patients with high-risk multiple myeloma treated with the CAR T-cell therapy idecabtagene vicleucel (page 14).**
- **Results from a phase II trial confirmed the efficacy of daratumumab plus KRd as induction and consolidation therapy when given with double transplant in patients with high-risk, newly diagnosed multiple myeloma (page 14).**

Phase III IsKia trial evaluated addition of isatuximab to combination therapy

In transplant-eligible, newly diagnosed multiple myeloma patients, the addition of the monoclonal antibody isatuximab to carfilzomib, lenalidomide and dexamethasone (KRd) induction and consolidation therapy significantly improved minimal residual disease (MRD) rates compared to KRd alone. The benefit was also shown in high-risk multiple myeloma patients, and no new safety concerns were identified.

What Patients Need to Know

Monoclonal antibodies are lab-generated proteins that target specific substances on the surface of the lymphoma cells, triggering an immune response.

New standard of care supported in the treatment of multiple myeloma subgroups

According to the phase III Perseus trial, adding the monoclonal antibody daratumumab to the combination of bortezomib, lenalidomide and dexamethasone showed significant clinical benefit in the treatment of transplant-eligible patients with newly diagnosed multiple myeloma, with no new safety concerns identified.

What Patients Need to Know

The results support this 4-drug combination as the new standard of care for treating transplant-eligible, newly diagnosed multiple myeloma.

CAR T-cell therapy showed benefit in relapsed multiple myeloma

Treatment with the chimeric antigen receptor (CAR) T-cell therapy idecabtagene vicleucel demonstrated durable responses in the treatment of high-risk multiple myeloma that relapsed within 18 months of frontline therapy.

What Patients Need to Know

The results were from cohort 2B of the phase II KarMMa-2 trial. Cohort studies are a type of longitudinal study, an approach that follows research participants over a period of time.

4-drug therapy along with transplantation improved outcomes in high-risk multiple myeloma

In the treatment of high-risk, newly diagnosed multiple myeloma, results from the phase II IFM 2018-04 trial confirmed that the addition of daratumumab to the combination of carfilzomib, lenalidomide and dexamethasone improved response rate and progression free-survival when given with double transplantation.

What Patients Need to Know

Double transplantation is a type of transplant in which a patient receives two courses of systemic therapy, each course followed by an infusion of their own healthy blood-forming stem cells.

Myeloproliferative Neoplasms

Researchers reported a number of important findings in the treatment of myeloproliferative neoplasms (MPNs) at the 2023 Annual Meeting of the American Society of Hematology:

- **The phase III FREEDOM2 trial evaluated the safety and efficacy of fedratinib in patients with myelofibrosis previously treated with ruxolitinib (page 16).**
- **An international phase III trial evaluated navitoclax plus ruxolitinib versus ruxolitinib plus placebo in untreated myelofibrosis (page 17).**
- **In the treatment of myelofibrosis, a long-term follow-up suggested disease modification with the combination of selinexor plus ruxolitinib (page 18).**
- **Results of the MANIFEST-2 phase III trial showed clinically meaningful improvement in spleen volume with the combination of pelabresib and ruxolitinib in the treatment of myelofibrosis (page 18).**

Fedratinib demonstrated superior results in previously-treated myelofibrosis

For people with myelofibrosis previously treated with ruxolitinib, results from the phase III FREEDOM2 trial showed fedratinib demonstrated superior spleen volume reduction and symptom response rates compared with ruxolitinib, with no new safety concerns identified.

What Patients Need to Know

Both ruxolitinib and fedratinib target mutations in the JAK2 gene and block its faulty processes.

Investigational drug studied for treatment of myelofibrosis

According to findings from the international phase III Transform-1 trial, ruxolitinib plus navitoclax may be twice as effective at spleen volume reduction compared with ruxolitinib alone in the initial treatment of intermediate- or high-risk myelofibrosis.

What Patients Need to Know

Ruxolitinib, a JAK inhibitor, is considered the standard of care for most people with primary or secondary myelofibrosis. Navitoclax is an investigational drug, not yet approved by the FDA. It is a BCL-2 inhibitor, targeting a protein that causes cancer cells to grow.

Combination of selinexor and ruxolitinib has potential benefit in treatment of myelofibrosis

A long-term follow-up from XPORT-MF-034 showed evidence of potential disease modification when selinexor was combined with ruxolitinib in the initial treatment of myelofibrosis. The combination was generally well tolerated.

What Patients Need to Know

Selinexor is a Selective Inhibitor of Nuclear Export (SINE). It works by inhibiting the action of proteins involved in cancer cell growth.

Improvement in spleen volume shown with combination of pelabresib and ruxolitinib

As an initial treatment for myelofibrosis, the combination of pelabresib and ruxolitinib demonstrated a clinically meaningful improvement in spleen volume when compared with placebo plus ruxolitinib. The results were from the phase III MANIFEST-2 study.

What Patients Need to Know

Pelabresib is an investigational BET inhibitor. The inhibition of BET proteins disrupts processes essential for tumor cell growth and survival.

Resources

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

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

NMDP
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 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

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

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

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

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