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 2022 Annual Meeting of the American Society of Hematology, which took place December 10-13 as both a virtual and in-person event.

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.

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

TABLE OF CONTENTS

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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 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 2022 American Society of Hematology (ASH) Annual Meeting" held on December 15, 2022. 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 2022 Annual Meeting of the American Society of Hematology:

- **According to results from a phase III trial, induction chemotherapy prior to allogeneic hematopoietic cell transplantation may not be necessary in some patients with relapsed/refractory AML (page 6).**
- **Results from a phase III trial showed double induction with daunorubicin is of no additional benefit in newly diagnosed AML (page 7).**
- **The addition of blinatumomab to consolidation chemotherapy resulted in a significantly better overall survival in certain patients with newly-diagnosed B-lineage ALL (page 8).**
- **Asciminib showed early promise as frontline therapy for CML-CP (page 8).**

Salvage chemotherapy prior to stem cell transplant evaluated in treatment of AML

In patients with relapsed/refractory acute myeloid leukemia (AML), the phase III ASAP trial showed that, prior to allogeneic hematopoietic stem cell transplant, intensive induction (salvage) chemotherapy does not provide a benefit over watchful waiting and less intensive sequential conditioning.

What Patients Need to Know

The results suggested that some patients may be able to omit salvage chemotherapy and the associated side effects before undergoing allogeneic (from a donor) hematopoietic stem cell transplant.

Double induction with daunorubicin showed no benefit in newly diagnosed AML

According to results from the phase III Dauno-Double trial, double induction with daunorubicin did not lead to higher remission rates or longer survival than single induction in patients with newly diagnosed acute myeloid leukemia.

What Patients Need to Know

Daunorubicin is given, along with the chemotherapy cytarabine, as part of the "7 + 3" regimen. This regimen consists of cytarabine given daily for 7 days, followed by an anthracycline (such as daunorubicin), given daily for 3 days. This treatment is administered intravenously (into a vein), in an in-patient hospital setting.

Addition of blinatumomab to consolidation therapy showed benefit in treatment of B-Lineage ALL

Results from the phase III ECOG-ACRIN E1910 trial showed that the addition of blinatumomab (Blincyto) to consolidation chemotherapy resulted in a significantly better overall survival in patients newly diagnosed with B-lineage acute lymphoblastic leukemia (ALL). Blinatumomab is a type of immunotherapy called a bispecific T-cell engager (BiTE).

What Patients Need to Know

The patients in the trial were MRD negative (no disease detected) after intensification chemotherapy. The results suggested that the addition of blinatumomab to consolidation chemotherapy represents a new standard of care in B-lineage ALL.

Asciminib showed early promise for the frontline treatment of CML-CP

Results from the phase II ASCEND-CML trial indicated that asciminib (Scemblix) showed promise for the frontline (initial) treatment of chronic phase chronic myeloid leukemia (CML-CP). Asciminib is a type of drug called a kinase inhibitor. It works by blocking the action of an abnormal protein that signals cancer cells to multiply.

What Patients Need to Know

In October 2021, the FDA granted approval to asciminib for the treatment of Philadelphia chromosome-positive CML in chronic phase, previously treated with two or more tyrosine kinase inhibitors.

Lymphoma

Researchers reported a number of important findings in the treatment of lymphoma at the 2022 Annual Meeting of the American Society of Hematology:

- **Findings from the ALPINE trial showed that, compared with ibrutinib, treatment with zanubrutinib improved progression-free survival in relapsed/refractory CLL or SLL (page 10).**
- **In certain cases of MCL, results of the TRIANGLE trial suggested that ibrutinib may replace autologous stem cell transplantation after chemoimmunotherapy (page 10).**
- **New data was presented on bispecific antibodies for the treatment of LBCL, FL and B-cell lymphomas; three treatments were subsequently approved by the FDA (page 10).**
- **In the treatment of FL, a phase III trial showed that rituximab significantly prolongs the time to initiation of new treatment compared with the watch-and-wait approach (page 11).**

Ibrutinib and zanubrutinib compared in treatment of CLL and SLL

Compared with ibrutinib, treatment with zanubrutinib reduced the risk of progression or death by 35% in patients with relapsed/refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL). The results were from the phase III ALPINE trial.

What Patients Need to Know

In January 2023, the FDA approved zanubrutinib (brand name Brukinsa) for the treatment of CLL or SLL. Both zanubrutinib and ibrutinib are BTK inhibitors, which cause the death of malignant B-cells.

Adding ibrutinib to chemotherapy may become standard of care for MCL

Although longer follow-up is needed, results from the phase III TRIANGLE trial suggested that chemotherapy plus the BTK inhibitor ibrutinib may be the new standard of care for the first-line treatment of mantle cell lymphoma (MCL), rather than chemotherapy plus an autologous stem cell transplant (ASCT).

What Patients Need to Know

The trial also found that when ibrutinib was added to ASCT, the 3-year failure-free survival was significantly superior to ASCT alone.

Three bi-specific antibodies approved by the FDA

Standard antibody drugs (a type of immunotherapy) aim at a single disease target. Bispecific antibodies aim at two disease targets, increasing the treatment's potency against cancer. New data was presented on bispecific antibodies for the treatment certain lymphomas.

What Patients Need to Know

Since the ASH meeting, three bispecific antibodies have been approved by the FDA:

- In December 2022, mosunetuzumab-axgb (brand name Lunsumio), was approved for the treatment of relapsed or refractory follicular lymphoma (FL) after at least two lines of systemic therapy.
- In May 2023, epcoritamab (brand name Epkinly) was approved for the treatment of diffuse large B-cell lymphoma (DLBCL) after at least two lines of systemic therapy.
- In June 2023, glofitamab-gxbm (brand name Columvi) was approved, after at least two lines of systemic therapy, for the treatment of relapsed or refractory DLBCL or large B-cell lymphoma (LBCL) arising from FL.

For FL, rituximab may allow longer time to initiation of chemotherapy

In certain patients with follicular lymphoma (FL), the phase III Watch & Wait trial showed that the monoclonal antibody rituximab significantly prolongs the time to initiation of new treatment with chemotherapy. The comparison was to the watch-and-wait approach.

What Patients Need to Know

Based on these results, researchers concluded that early treatment with rituximab, either as induction alone or induction and maintenance, should be considered a standard treatment option for patients with asymptomatic, low-tumor-burden FL.

Multiple Myeloma

Researchers reported a number of important findings in the treatment of multiple myeloma at the 2022 Annual Meeting of the American Society of Hematology:

- **In October 2022, the FDA granted approval to teclistamab-cqyv the for the treatment of relapsed/refractory multiple myeloma (page 12).**
- **It was announced in November 2022 that belantamab, used for the treatment of relapsed/refractory multiple myeloma, is in the process of being withdrawn from the U.S. market by its manufacturer (page 13).**
- **An analysis showed that continuing lenalidomide for more than 3 years after stem cell transplant is associated with improved progression free survival (page 14).**
- **In a phase I/II trial, the investigational drug talquetamab demonstrated efficacy in the treatment of relapsed/refractory multiple myeloma (page 14).**

Teclistamab approved for pre-treated relapsed/refractory multiple myeloma

On October 25, 2022, the FDA granted accelerated approval to teclistamab (Tecvayli) for the treatment of patients with relapsed or refractory multiple myeloma who have received at least four prior lines of therapy, including a proteasome inhibitor, an immunomodulatory agent and an anti-CD38 monoclonal antibody.

What Patients Need to Know

Teclistamab is a first-in-class, bispecific T-cell engager antibody that is administered subcutaneously (beneath the skin). Bispecific antibodies aim at two cancer targets, increasing the treatment's potency.

Belantamab being withdrawn from US market

In November 2022, the manufacturer of belantamab (Blenrep) announced that the drug was in the process of being withdrawn from the U.S. market. Belantamab, used in the treatment of relapsed/refractory multiple myeloma, is an antibody drug conjugate that targets BCMA (B-cell maturation antigen).

What Patients Need to Know

The withdrawal was at the request of the FDA following disappointing results from a large confirmatory trial. In that trial, known as DREAMM-3, belantamab failed to show an improvement in progression-free survival (PFS).

Longer maintenance with lenalidomide shown to provide clinical benefit

According to researchers who analyzed data from the Myeloma XI trial, continuing lenalidomide (Revlimid) maintenance beyond 3 years after stem cell transplant is associated with improved progression free survival.

What Patients Need to Know

A current analysis suggests that continuing lenalidomide maintenance beyond 4-5 years may no longer have ongoing benefit.

Investigational drug demonstrated efficacy in relapsed/refractory multiple myeloma

In the phase I/II MonumenTAL-1 trial, the investigational drug talquetamab demonstrated efficacy (effectiveness) in patients with heavily pretreated relapsed/refractory multiple myeloma. Talquetamab, a bispecific antibody, received Breakthrough Therapy designation from the FDA in June 2022.

What Patients Need to Know

A Breakthrough Therapy designation is for a drug that treats a serious or life-threatening condition and preliminary evidence indicates the drug may demonstrate substantial clinical improvement compared to available therapies.

Myeloproliferative Neoplasms

Researchers reported a number of important findings in the treatment of myeloproliferative neoplasms (MPNs) at the 2022 Annual Meeting of the American Society of Hematology:

- **Rusfertide, an investigational drug now in phase III trials, has been shown to effectively control hematocrit levels and reduce the need for phlebotomy in patients with polycythemia vera (page 16).**
- **Momelotinib, a JAK inhibitor that reduces symptoms of myelofibrosis, is expected to be approved by the FDA in 2023 (page 18).**
- **There is promising data on combining other therapies with ruxolitinib in the treatment of myelofibrosis (page 18).**
- **Results from a phase III trial showed that pacritinib can increase hemoglobin in some patients with myelofibrosis (page 19).**

Rusfertide shown to control hematocrit levels in PV

A primary goal of therapy for polycythemia vera (PV) is to maintain a hematocrit level below 45%, which is proven to decrease a patient's risk of forming a blood clot. The hematocrit level is the ratio of the volume of red blood cells to the total volume of blood.

Phlebotomy (blood-letting) is often the therapy of choice to maintain hematocrit levels below 45%. According to research results, twice-weekly injections with the investigational drug rusfertide effectively controlled hematocrit levels and significantly reduced the need for phlebotomy.

What Patients Need to Know

Studies of ruxolitinib in PV patients also show a decrease over time in JAK 2 mutation (allele burden), identified as the primary driver of the disease.

Investigational drug momelotinib shows benefit in the treatment of MF

The JAK inhibitor momelotinib has been found to reduce symptoms of myelofibrosis (MF), including improving fatigue, decreasing pain and reducing spleen size. Momelotinib is expected to be approved by the FDA in 2023.

What Patients Need to Know

Momelotinib also potentially increases hemoglobin (a protein in red blood cells that carries oxygen) so that some transfusion-dependent patients may no longer require blood transfusions

Combining ruxolitinib with other therapies being studied for treatment of MF

There is promising data on combining the JAK inhibitor ruxolitinib with other investigational therapies for the treatment of myelofibrosis. A description of those therapies:

- Navitoclax blocks some of the enzymes that keep cancer cells from dying.
- Pelabresib promotes anti-tumor activity by inhibiting the function of certain proteins.
- Parsaclisib may stop the growth of cancer cells by blocking PI3K enzymes needed for cell growth.

The evaluation of these combination therapies is ongoing.

What Patients Need to Know

There are other drugs for use in combination with ruxolitinib in earlier stages of development.

Pacritinib shown to increase hemoglobin as well as platelets in people with MF

The kinase inhibitor pacritinib is approved by the FDA for the treatment of patients with myelofibrosis and severe thrombocytopenia, a condition that occurs when the blood's platelet count is too low. Results from the ongoing phase III PACIFICA trial showed that pacritinib can not only increase platelets but can also increase hemoglobin in some patients.

What Patients Need to Know

An increase in hemoglobin is associated with the reduction or elimination of anemia-related blood transfusions.

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

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.allbloodcancers.org

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

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