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 2021 Annual Meeting of the American Society of Hematology, which took place December 11-14 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.

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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 case management, 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 2021 American Society of Hematology (ASH) Annual Meeting" held on December 16, 2021. 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 2021 Annual Meeting of the American Society of Hematology:

- **The combination of ivosidenib and azacitidine showed superior results compared to azacitidine alone in the treatment of newly diagnosed IDH1-mutated acute myeloid leukemia (page 7).**
- **Adding magrolimab to the combination therapy of venetoclax and azacitidine showed benefit in the treatment of patients with newly diagnosed high-risk AML (page 7).**
- **Findings from the ASCEMBL trial showed improved results when patients with chronic-phase chronic myeloid leukemia were treated with asciminib, as compared to treatment with bosutinib (page 8).**
- **An analysis showed patients with higher-risk myelodysplastic syndromes who received venetoclax and a hypomethylating agent (HMA) as first-line therapy had higher response rates than those receiving an HMA alone (page 8).**

Combination therapy increased overall survival in IDH1-mutated AML

The phase III AGILE trial showed the combination of ivosidenib and the chemotherapy azacitidine extended overall survival in the treatment of newly diagnosed IDH1-mutated acute myeloid leukemia (AML), as compared to azacitidine alone.

What Patients Need to Know

Ivosidenib, an IDHI inhibitor, works by slowing or stopping the growth of cancer cells.

Investigational drug studied in the treatment of acute myeloid leukemia

According to a phase I/II trial, adding magrolimab to the combination of venetoclax and azacitidine showed benefit in the treatment of patients with newly diagnosed high-risk AML. The benefit, in the form of higher response rates, was also seen in older patients and those who are not able to tolerate other forms of treatment.

What Patients Need to Know

Magrolimab, a first-in-class investigational monoclonal antibody, is designed to interfere with the recognition of a type of protein called CD47. By doing so, it blocks the signal that prevents cancer cells from being destroyed.

Asciminib evaluated in phase III trial for the treatment of CP-CML

Findings from the phase III ASCEMBL trial showed a consistent improvement in major molecular response rate and depth of response when patients with chronic-phase chronic myeloid leukemia (CP-CML) were treated with asciminib, as compared to treatment with the TKI bosutinib.

Patients in the study were treated with at least two prior rounds of TKIs (tyrosine kinase inhibitors). Asciminib is designed to overcome resistance and/or intolerance to treatment with TKIs.

What Patients Need to Know

No new or worsening adverse effects (side effects) were reported from the trial.

Analysis showed effect of venetoclax in higher-risk MDS

A retrospective analysis showed that patients with higher-risk myelodysplastic syndromes (MDS) who received venetoclax and a hypomethylating agent (HMA) as first-line therapy had higher response rates than those receiving an HMA alone.

What Patients Need to Know

Venetoclax is a type of drug called a B-cell lymphoma-2 (BCL-2) inhibitor. It works by blocking the action of a certain protein in the body that helps cancer cells survive.

Lymphoma

Researchers reported a number of important findings in the treatment of lymphoma at the 2021 Annual Meeting of the American Society of Hematology:

- **A phase III trial showed that a new drug combination improved progression-free survival in newly-diagnosed DLBCL (page 9).**
- **The experimental drug mosunetuzumab led to durable remissions for patients with relapsed/refractory follicular lymphoma (page 10).**
- **The combination of umbralisib and ublituximab was studied in the treatment of relapsed/refractory marginal zone lymphoma (page 11).**
- **A phase II trial showed that pembrolizumab in combination with a chemotherapy regimen showed benefit in the treatment of relapsed/refractory classical Hodgkin lymphoma (page 11).**

Alternative to standard of care for newly diagnosed DLBCL studied

The standard of care for newly diagnosed diffuse large B-cell lymphoma (DLBCL) is a chemotherapy regimen called R-CHOP (rituximab, cyclophosphamide, doxorubicin, vincristine and prednisone). The phase III POLARIX trial showed that replacing vincristine with polatuzumab vedotin significantly improved progression-free survival.

Polatuzumab vedotin is an antibody drug conjugate (ADC) which works by linking a chemotherapy with a monoclonal antibody. It is currently approved by the FDA for the treatment of relapsed (recurred) DLBCL.

What Patients Need to Know

Although POLARIX found no significant difference in overall survival at 2 years between the two therapies, those who received the new drug combination were less likely to need additional treatment compared with those receiving R-CHOP.

Bispecific antibody showed durable remissions in follicular lymphoma

The results of a phase I/II trial showed the experimental drug mosunetuzumab led to durable remissions for patients with relapsed or refractory (not responding to treatment) follicular lymphoma who have received at least two prior lines of therapy.

Mosunetuzumab, a bispecific antibody, brings together a target on the lymphoma cells and a target on the person's T-cells (a type of immune cell) to destroy lymphoma cells.

What Patients Need to Know

Unlike CAR T-cell therapy, mosunetuzumab is infused directly into the bloodstream without requiring the removal and modification of the patient's T-cells.

Combination treatment studied in relapsed/refractory MZL

According to results of the phase I/II UNITY-NHL trial, the combination of umbralisib and ublituximab demonstrated durable responses in patients with relapsed or refractory marginal zone lymphoma (MZL).

Umbralisib, a kinase inhibitor, works by slowing or stopping the growth of cancer cells. Ublituximab is a monoclonal antibody that attaches to specific receptors on cancer cells, causing them to disintegrate.

What Patients Need to Know

The combination of umbralisib and ublituximab resulted in an increased rate of response when compared to umbralisib given alone.

Immunotherapy in combination with chemotherapy produced high CMR in cHL

A phase II trial showed that the immunotherapy pembrolizumab, in combination with a chemotherapy regimen called ICE (ifosfamide, carboplatin and etoposide), produced a high complete metabolic response (CMR) rate in patients with relapsed/refractory classical Hodgkin lymphoma (cHL).

CMR is achieved when all detectable evidence of cancer is gone. CMR prior to autologous stem cell transplant predicts progression-free survival and overall survival.

What Patients Need to Know

A stem cell transplant is a procedure in which diseased bone marrow is replaced with healthy bone marrow. When a person with CML receives their own stem cells, the procedure is called an "autologous" stem cell transplant.

Multiple Myeloma

Researchers reported a number of important findings in the treatment of multiple myeloma at the 2021 Annual Meeting of the American Society of Hematology:

- **The GRIFFIN trial showed the addition of daratumumab to a combination regimen improved responses (page 12).**
- **Promising results were shown in combining iberdomide with dexamethasone for the treatment of heavily pretreated relapsed/refractory multiple myeloma (page 13).**
- **A CAR T-cell therapy produced durable responses in patients with relapsed/refractory multiple myeloma (page 14).**
- **An investigational drug was shown to be safe and effective in the treatment of relapsed/refractory multiple myeloma (page 14).**

Improved response shown in addition of daratumumab to combination treatment

For patients newly diagnosed with multiple myeloma, results from the GRIFFIN trial showed the addition of daratumumab to the drug combination of lenalidomide, bortezomib and dexamethasone prior to stem cell transplantation led to an improved depth of response.

Daratumumab is a monoclonal antibody. It works by helping the body to slow or stop the growth of cancer cells.

What Patients Need to Know

The improved response was also seen post-transplant when daratumumab was added to maintenance therapy with lenalidomide alone.

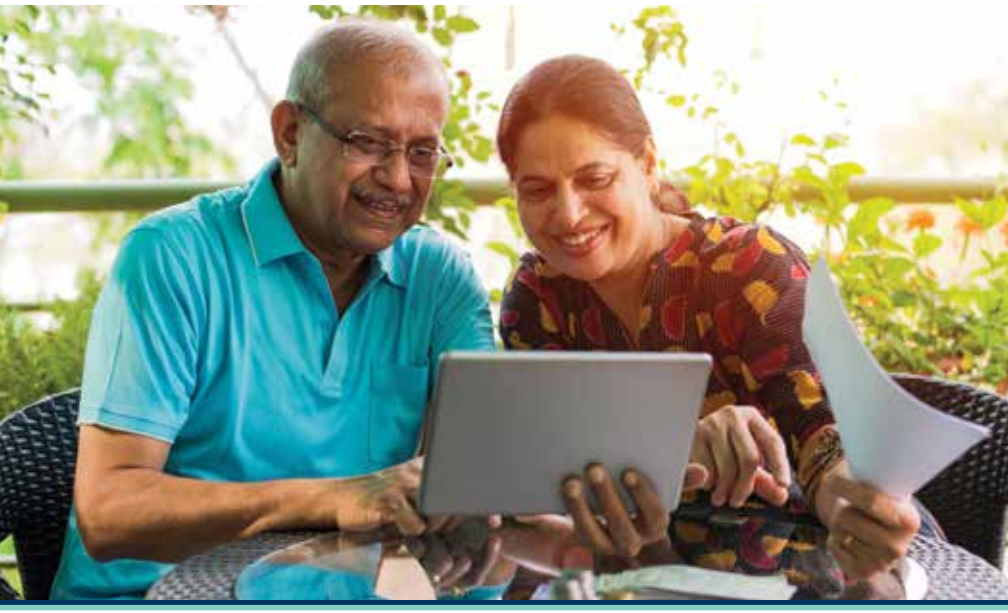
Combining iberdomide with dexamethasone evaluated

The results of the dose-expansion phase of the CC-220-MM-001 trial showed promise in combining iberdomide with the corticosteroid dexamethasone for the treatment of heavily pretreated, relapsed (recurred) or refractory (resistant to treatment) multiple myeloma.

Iberdomide is an immunomodulatory drug, designed to reduce growth signals in myeloma cells.

What Patients Need to Know

These results support the further study of iberdomide in the treatment of multiple myeloma, including as part of combination regimens.



CAR T-cell therapy produced durable responses in relapsed/refractory multiple myeloma

Results from a phase I/II trial suggested the investigational chimeric antigen receptor (CAR) T-cell therapy CT103A produced durable responses in patients with relapsed/refractory multiple myeloma, even those who had received prior BCMA CAR T-cell therapy.

What Patients Need to Know

CAR T-cell therapy follows a specific process:

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

Investigational drug studied for treatment of RRMM

In updated results from a phase I trial, the investigational drug talquetamab was shown to be safe and effective in the treatment of relapsed/refractory multiple myeloma (RRMM).

What Patients Need to Know

Further investigation of talquetamab as a monotherapy (a drug used alone) and in combination with other therapies for the treatment of RRMM is underway.

Myeloproliferative Neoplasms

Researchers reported a number of important findings in the treatment of myeloproliferative neoplasms (MPNs) at the 2021 Annual Meeting of the American Society of Hematology:

- **An analysis of trial results suggested that early treatment with ruxolitinib may improve clinical outcomes in newly diagnosed myelofibrosis (page 16).**
- **Preliminary results from a phase II trial showed pelabresib demonstrated signs of effectiveness in patients with advanced myelofibrosis (page 18).**
- **Results of the FREEDOM trial highlighted the safety and efficacy of fedratinib for myelofibrosis previously treated with ruxolitinib (page 18).**
- **According to research results, treatment of polycythemia vera with the investigational drug rusfertide significantly reduced the need for phlebotomy (page 18).**

Early treatment with ruxolitinib evaluated in newly diagnosed MF

"Watch and wait" is a common treatment approach for patients newly diagnosed with myelofibrosis (MF). An analysis of the Comfort I and II trials suggested that early treatment with the JAK inhibitor ruxolitinib may improve clinical outcomes, including fewer cytopenia events, durable spleen volume response, reduced symptom burden and overall survival.

What Patients Need to Know

The researchers concluded that additional studies to further evaluate the impact of early intervention with ruxolitinib are warranted.

Alternative to JAK inhibitors studied for treatment of advanced MF

Preliminary results from the phase II MANIFEST trial showed the investigational drug pelabresib demonstrated signs of effectiveness in patients with advanced myelofibrosis for whom a JAK inhibitor (such as ruxolitinib) is not an option.

What Patients Need to Know

In MANIFEST, pelabresib was given as a monotherapy (a drug used alone) and was found to be generally well-tolerated.

Safety and efficacy of fedratinib for treatment of MF highlighted in trial

Results of the ongoing phase IIIb FREEDOM trial highlighted the safety and efficacy (effectiveness) of fedratinib for myelofibrosis that was previously treated with ruxolitinib.

Both fedratinib and ruxolitinib are JAK inhibitors.

What Patients Need to Know

The FREEDOM trial included prospective strategies for preventing or lessening side effects, including gastrointestinal problems and thiamine level decreases.

Investigational drug studied 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, treatment with the investigational drug rusfertide effectively controlled hematocrit levels and significantly reduced the need for phlebotomy.

What Patients Need to Know

A further study of rusfertide vs. placebo is planned for patients who require frequent phlebotomies.

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

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

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

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

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