LATEST NEWS IN BLOOD CANCER RESEARCH

# Highlights from the 2017 Annual Meeting of the American Society of Hematology

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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. 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 25 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 2017 American Society of Hematology (ASH) Annual Meeting" held on March 15, 2018. We are indebted to the following individuals that 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.

# Leukemia

**Researchers reported a number of important findings in leukemia treatment at the 2017 Annual Meeting of the American Society of Hematology:**

- **In April 2017, the FDA (U.S. Food and Drug Administration) approved the targeted therapy midostaurin, in combination with chemotherapy, for the treatment of certain adult patients with newly diagnosed acute myeloid leukemia (AML)** (page 9).
- **The targeted therapy enasidenib was approved by the FDA in August 2017 for the treatment of relapsed or refractory AML that has a mutation of the IDH2 gene** (page 9).
- **Venetoclax, a targeted therapy, has received breakthrough therapy designation from the FDA as treatment, in combination with chemotherapy, for some patients with previously-untreated AML** (page 10).
- **Chimeric antigen receptor (CAR) T-cell immunotherapy is being studied in clinical trials for the treatment of AML** (page 10).
- **The FDA has granted accelerated approval to the targeted therapy bosutinib for the treatment of certain types of chronic myeloid leukemia (CML)** (page 11).
- **A global trial assessed the duration of "major molecular response" in CML after treatment is halted** (page 11).
- **A combination of targeted therapies for the treatment of chronic lymphocytic leukemia (CLL) is being studied in a phase III trial** (page 12).

- **The targeted therapies ibrutinib and venetoclax were studied in a UK trial for treatment of relapsed or refractory CLL** (page 12).
- **A phase II trial evaluated the targeted therapy ibrutinib, in combination with standard chemo-immunotherapy, as treatment for CLL** (page 13).

## Targeted therapy midostaurin approved for FLT3 mutation-positive AML

Midostaurin was approved by the FDA in April 2017 to treat adult patients with newly-diagnosed, FLT3 mutation-positive AML, to be used in combination with chemotherapy. Midostaurin is the first targeted therapy approved by the FDA to treat any form of AML.

The presence of the FLT3 mutation is determined by an FDA-approved diagnostic test.

### What Patients Need to Know

The FLT3 gene makes a protein that encourages cell growth. Approximately 30 percent of people with AML have a mutation of this gene, resulting in the increased growth of cancer cells. Midostaurin works by targeting (blocking) the action of the FLT3 protein.

## FDA approves enasidenib for the treatment of AML patients with a mutation of the IDH2 gene

Enasidenib, a targeted therapy, was approved by the FDA in August 2017 for the treatment of adult patients with AML that has relapsed or is refractory (not responding to treatment) and that has a mutation of the IDH2 gene.

A mutation of the IDH2 gene stops cells from maturing in the way they should. Enasidenib works by helping leukemia cells mature into normal cells.

### What Patients Need to Know

Enasidenib is the first therapy approved for relapsed or refractory AML with the IDH2 mutation. The presence of the IDH2 mutation is detected by an FDA-approved test.

## Venetoclax receives FDA "Breakthrough Therapy" designation for previously untreated AML in elderly patients

In July 2017, the targeted therapy venetoclax was granted an FDA Breakthrough Therapy designation for use in combination with low dose cytarabine (a chemotherapy drug) in elderly patients who have not received previous treatment for their AML and who are not candidates for high-dose chemotherapy.

### What Patients Need to Know

The FDA's Breakthrough Therapy designation is a process designed to expedite the development and review of drugs that may demonstrate substantial improvement over available therapy.

## Chimeric antigen receptor (CAR) T-cell therapy being studied for treatment of AML

CAR T-cell immunotherapy, which uses a person's own T-cells (a type of white blood cell) to target cancer cells, is being studied in an ongoing phase I clinical trial.

The drug being studied targets a receptor called CD123, which can be "overexpressed" in AML and other types of leukemia, causing cancer cells to grow.

### What Patients Need to Know

Certain steps are followed in CAR T-cell therapy, including 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.

## Accelerated approval granted to bosutinib for treatment of Philadelphia chromosome-positive CML

Based on findings from a phase III trial, in December 2017 the FDA granted an accelerated approval to the targeted therapy bosutinib as a first-line (initial) treatment for patients with Philadelphia chromosome-positive CML.

The Philadelphia chromosome is an abnormality that forms BCR-ABL, a new "fusion" gene. Cells with the BCR-ABL gene make an abnormal protein that fuels the growth of cancer cells.

### What Patients Need to Know

Bosutinib is a tyrosine kinase inhibitor (TKI), which can stop the protein made by the BCR-ABL gene from working, causing CML cells to die. There are four other drugs of this type used to treat CML: imatinib, nilotinib, dasatinib and ponatinib.

## Effectiveness of halting TKI therapy in CML patients studied

The effectiveness of halting tyrosine kinase inhibitor (TKI) therapy is a key question in the management of CML. The global EURO-SKI trial assessed the duration of "major molecular response" (MMR) after treatment of CML with a TKI is halted.

A major molecular response in CML means that the amount of abnormal protein in the blood made by the fusion gene BCR-ABL is very low.

### What Patients Need to Know

The EURO-SKI study showed that halting TKI therapy is safe and feasible for about 50 percent of patients. A higher probability of MMR is associated with patients who received TKI therapy for at least 5 years before halting this therapy.

## Combination of targeted therapies for treatment of CLL being studied in phase III trial

The phase III MURANO trial studied the progression-free survival of patients with CLL who were treated with a combination of the targeted therapies venetoclax and rituximab, as compared to treatment with rituximab and the standard chemo-immunotherapy drug bendamustine.

### What Patients Need to Know

The results of the trial showed that the combination of venetoclax and rituximab significantly increased the likelihood of progression-free survival.

## UK trial evaluates combination of targeted therapies ibrutinib and venetoclax in treatment of CLL

According to the United Kingdom CLARITY trial, combining the targeted therapies ibrutinib and venetoclax appeared to be safe and effective in treating patients with relapsed (recurred) or refractory (not responding to treatment) CLL.

### What Patients Need to Know

One-third of patients in the trial had no detectable disease after six months of treatment with the two targeted therapies, and no additional safety concerns were reported.

## Targeted therapy combined with chemo-immunotherapy studied for treatment of CLL

A phase II trial evaluated the targeted therapy ibrutinib, combined with standard chemo-immunotherapy, for the treatment of CLL.

Data from the trial showed that the combination induced negative "minimum residual disease" (MRD) status in the bone marrow for a significant percentage of trial participants. Negative MRD status means that no cancer can be detected, even with the use of sophisticated diagnostic tests.

### What Patients Need to Know

The chemo-immunotherapy regimen consisted of fludarabine, cyclophosphamide and rituximab (FCR). No new safety issues were identified for either ibrutinib or FCR.

# Lymphoma

**Researchers reported a number of important findings in lymphoma treatment at the 2017 Annual Meeting of the American Society of Hematology:**

- **Based on the results of a phase III trial, the FDA has approved the addition of the targeted therapy brentuximab vedotin, used in combination with chemotherapy, as a first-line treatment of advanced Hodgkin lymphoma (HL)** (page 15).
- **The targeted therapy acalabrutinib has been approved for the treatment of mantle cell lymphoma (MCL) that has progressed after previous therapy** (page 15).
- **Follow-up data was reported on the effectiveness of the CAR T-cell therapy axicabtagene ciloleucel in the treatment of large B-cell lymphoma** (page 16).

## Results of phase III trial leads to approval of targeted therapy drug in advanced HL

A multinational phase III clinical trial called Echelon-1 evaluated the addition of the targeted therapy brentuximab vedotin to the standard chemotherapy treatment of doxorubicin, bleomycin, vinblastine, and dacarbazine in treatment of patients with advanced Hodgkin lymphoma (HL).

Researchers reported that patients with advanced HL who were treated with a first-line regimen that included brentuximab vedotin had a 23 percent reduction in the risk of disease progression, death, or the need for additional therapy, compared with patients who received a standard first-line chemotherapy regimen.

### What Patients Need to Know

In March 2018, the FDA granted approval of brentuximab vedotin, in combination with chemotherapy, for the treatment of adults with previously untreated advanced HL.

## Accelerated approval granted to targeted therapy acalabrutinib for treatment of MCL

In October 2017, the FDA granted accelerated approval to the targeted therapy acalabrutinib for the treatment of adults with mantle cell lymphoma (MCL) whose cancer has progressed after receiving at least one prior therapy.

### What Patients Need to Know

Another targeted therapy, ibrutinib, was approved for the treatment of MCL in 2013. Both ibrutinib and acalabrutinib can cause problems with bruising and bleeding, but research indicates that acalabrutinib may be less likely to do so.

## Follow-up data reported on effectiveness of CAR T-cell therapy in treatment of large B-cell lymphoma

Axicabtagene ciloleucel, a chimeric antigen receptor (CAR) T-cell therapy , was approved by the FDA in October 2017 for the treatment of adult patients with relapsed or refractory (not responding to treatment) large B-cell lymphoma who had previously received at least two other kinds of therapy.

Follow-up data from the ZUMA-1 study indicated that, after a single infusion, 42 percent of patients in this population continued to respond to therapy after more than one year, including 40 percent with a complete remission.

### 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.

# Multiple Myeloma

**Researchers reported a number of important findings in the treatment of multiple myeloma at the 2017 Annual Meeting of the American Society of Hematology:**

- **A phase III trial showed that adding the targeted therapy daratumumab to standard therapy lowered the risk of disease progression in patients with newly diagnosed multiple myeloma** (page 17).
- **A curative approach for the treatment of high-risk smoldering multiple myeloma (SMM) was studied in a phase II trial** (page 18).
- **A phase I/II study showed encouraging results for previously treated multiple myeloma patients when given an investigational anti-BCMA monoclonal antibody** (page 19).
- **Initial phase I trial data showed impressive results of a CAR T-cell therapy in the treatment of relapsed or refractory multiple myeloma** (page 19).

## Phase III trial shows effectiveness of daratumumab in combination with standard regimen

Findings from the phase III ALCYONE trial showed a 50 percent lower risk for disease progression or death when the targeted therapy daratumumab was added to the standard regimen of bortezomib, melphalan, and prednisone in patients newly diagnosed with multiple myeloma.

Daratumumab targets a protein (CD38) that is often "overexpressed" on multiple myeloma cells.

### What Patients Need to Know

Daratumumab was approved by the FDA in 2016 for the treatment of patients with multiple myeloma who have received at least one prior therapy. The ALCYONE trial results showed it also improves outcomes in patients with newly diagnosed multiple myeloma, when used in combination with the standard regimen.

## Early treatment with combination therapy studied for smoldering multiple myeloma

Smoldering multiple myeloma (SMM), an asymptomatic plasma cell disorder, is often not treated when initially diagnosed; rather, it is monitored through blood and urine tests to determine if it is progressing and if treatment should begin.

The phase II ASCENT trial evaluated a new treatment strategy for SMM, consisting of initial therapy using a combination of a corticosteroid and the targeted therapies lenalidomide and dexamethasone, followed by high-dose therapy and stem cell transplantation, and finally by maintenance therapy with lenalidomide and dexamethasone.

### What Patients Need to Know

The results of the ASCENT trial and a prior phase III study showed that early treatment with lenalidomide and dexamethasone may significantly improve progression-free survival (PFS) in patients with SMM.

## Investigational drug for the treatment of relapsed/refractory multiple myeloma studied

The DREAMM-1 trial showed that an investigational drug produced positive results, in terms of response rate and progression-free survival, in a group of multiple myeloma patients whose cancer had recurred (relapsed) or was not responding to prior therapies (refractory).

The drug is a monoclonal antibody that targets a protein called B-cell maturation antigen (BCMA).

### What Patients Need to Know

Because of the positive results of the trial, in November 2017 the FDA awarded the investigational drug Breakthrough Therapy designation, a process designed to expedite the development and review of drugs that may demonstrate substantial improvement over available therapy.

## CAR T-cell immunotherapy being studied in phase I/II trial

A phase I/II trial of the investigational CAR T-cell immunotherapy bb2121 showed impressive results, in terms of effectiveness and safety, in treating multiple myeloma that has recurred or is resistant to treatment. The therapy targets the B-cell maturation antigen (BCMA).

### What Patients Need to Know

CAR T-cell therapy is an approach in which T-cells are removed from the patient and genetically modified so that the T-cells can target a particular protein often found on cancer cells. These reprogrammed T-cells are re-introduced into the patient with the goal of improving the immune system's anti-cancer response.

# Myeloproliferative Neoplasms

**Researchers reported a number of important findings in the treatment of myeloproliferative neoplasms (MPNs) at the 2017 Annual Meeting of the American Society of Hematology:**

- **The results of a phase III trial showed that ruxolitinib provided rapid and durable clinical benefits as a second-line therapy for polycythemia vera (PV)** (page 21).
- **Pegylated interferon-alpha-2a was studied in patients with PV or essential thrombocythemia (ET) whose cancer has become resistant to the chemotherapy hydroxyurea** (page 21).
- **The investigational drug idasanutlin demonstrated significant clinical activity and was well-tolerated in a phase I trial of patients with refractory PV** (page 22).
- **A phase II trial showed the investigational drug sotatercept safely increases hemoglobin levels in patients with myelofibrosis** (page 22).

## Ruxolitinib studied as second-line therapy for advanced PV

RESPONSE 2, a global phase III trial, compared ruxolitinib to the best available therapy in patients with advanced polycythemia vera (PV) whose disease is resistant to the chemotherapy hydroxyurea.

The results showed that ruxolitinib provided rapid and durable clinical benefits as a second-line therapy and was superior to the best available therapy at controlling the volume of red blood cells and improving spleen enlargement.

### What Patients Need to Know

The RESPONSE 2 trial also included patients who could not continue to take hydroxyurea due to side effects. Results from the trial indicated that ruxolitinib was generally well tolerated.

## Pegylated interferon-alpha-2a studied as treatment option for hydroxyurea-resistant PV and ET

The phase II clinical trial MPD-RC 111 studied how patients with polycythemia vera (PV) or essential thrombocythemia (ET) responded to treatment with pegylated interferon-alpha-2a after becoming resistant to treatment with the chemotherapy hydroxyurea.

Pegylated interferon-alpha-2a is an antiviral medication approved by the FDA to treat hepatitis C and hepatitis B.

### What Patients Need to Know

The results of the MPD-RC 111 trial showed that patients with PV and ET were responsive to pegylated interferon, which potentially provides another treatment option for patients who are no longer able to benefit from hydroxyurea.

## Investigational drug idasanutlin studied as treatment for refractory PV

Data from a phase I trial showed that the investigational drug idasanutlin, given as a monotherapy or in combination with the anti-viral drug pegylated interferon, demonstrated significant clinical activity and was well tolerated after multiple cycles of exposure in patients with refractory polycythemia vera (PV).

### What Patients Need to Know

The data also showed a normalization of the hematologic profile (the balance of red blood cells, white blood cells and platelets) and an improvement in patient symptoms with the administration of either monotherapy and combination therapy.

## Study shows investigational drug safely raises hemoglobin levels in patients with myelofibrosis

A phase II trial showed that the investigational drug sotatercept safely increased hemoglobin levels in patients with myeloproliferative neoplasm (MPN)-associated myelofibrosis, both when used alone and in combination with the JAK1 inhibitor ruxolitinib.

### What Patients Need to Know

Ruxolitinib is the only therapy approved by the FDA for the treatment of myelofibrosis. It initially causes a decline in hemoglobin levels (which can lead to anemia) before those levels return to a new, lower baseline.


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# 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**
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www.allbloodcancers.org

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