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Latest News in Blood Cancer Research:

Highlights From the 2015 Annual Meeting of the American Society of Hematology

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This special edition of the Cancer*Care* Connect Booklet Series highlights cutting-edge research presented at the 2015 Annual Meeting of the American Society of Hematology, which took place December 5–8 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 booklet is intended for discussion with your doctor. He or she 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.

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About the Editors

In compiling this report, we used content from the Cancer*Care* Connect Education Workshop titled "Update from the 2015 American Society of Hematology (ASH) Annual Meeting" held on January 14, 2016. We are indebted to the following individuals that were featured on this workshop:

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Leukemia

Several studies reported at the 2015 Annual Meeting of the American Society of Hematology show important progress in the treatment of leukemia:

A new type of daily pill—an isocitrate dehydrogenase (IDH) inhibitor—might help people with acute myeloid leukemia (AML) who have not responded or relapsed with standard treatment. Encouraged by results from early studies with the IDH inhibitors, AG-221 and AG-120, researchers have started new clinical trials (page 3).

Midostaurin lengthens survival in previously untreated AML that has mutations in FMS-like tyrosine kinase 3 (FLT3). The U.S. Food and Drug Administration (FDA) is reviewing the study results to decide if they will approve midostaurin (page 4).

Sorafenib might help patients with FLT3-mutated AML live longer. Even though the results look promising, better quality, larger studies are needed to confirm the findings (page 5).

Adding rituximab to standard chemotherapy improves event-free survival in some newly diagnosed patients with a type of acute lymphoblastic leukemia (ALL). This regimen might become the new standard for most people with this type of ALL (page 6).

A new kind of immunotherapy-chimeric antigen receptor (CAR)-modified T-cell therapy—might help patients with ALL. More research is needed to determine the best way to use this therapy and to decrease its side effects (page 7).

A new oral tyrosine kinase inhibitor (TKI), ABL001, may be active in patients with resistant chronic myelogenous leukemia (CML). So far, patients have not had serious side effects and many had sustained remissions (page 8).

Daily dasatinib combined with pegylated-interferon alpha 2b shows activity against newly diagnosed CML. After 12 months of treatment, almost a third of patients had deep molecular remission with manageable side effects (page 9).

AG-221 and AG-120 for Relapsed AML

Patients with AML might benefit from two new oral drugs, AG-221 and AG-120, according to early results from two studies. Both studies included people with AML that had not responded to or had relapsed with standard treatments. So far, these drugs have caused few side effects.

AG-221 and AG-120 are the first examples of a new class of drugs that block (inhibit) defective forms of isocitrate dehydrogenase (IDH). IDH is an enzyme—a special type of protein that makes chemical reactions go faster—that works inside the cell's power plant (the mitochondria) to help make energy. Researchers have found defects (mutations) in two types of IDH (IDH1 and IDH2) in AML and other blood and solid cancers.

In one study, 41 percent of patients who took AG-221 had responses. Eighteen percent had complete remissions. This study included 128 adults with AML that had mutations in IDH2.

In the other study, 36 percent of patients who took AG-120 had responses and 18 percent had complete remissions. This study included 66 adults with AML that had mutations in IDH1.

What Patients Need to Know

The purpose of these studies was to find the lowest dose AG-221 and AG-120 that would still be effective. Researchers have not published the final results from these studies.

AG-221 and AG-120 are being tested in other ongoing clinical trials. Researchers are trying to find out if these IDH inhibitors will work better when combined with other drugs.

Midostaurin for FLT3-Mutated Untreated AML

Patients treated with midostaurin plus chemotherapy lived longer than patients treated with placebo plus chemotherapy, according to a clinical trial in 3,279 adults (18 to 60 years old) not previously treated for AML. To be included in the study, the patient's AML cells had to contain defects in FLT3. Midostaurin targets several kinases and is termed a "multikinase inhibitor."

When compared with the placebo group, people in the midostaurin group had longer median survival (75 months versus 26 months) and more were alive at five years (51 percent versus 44 percent). The two groups had similar rates of serious side effects. Rash and skin peeling (desquamation) were the main side effect reported with midostaurin.

Patients received midostaurin or placebo added to standard "7 + 3" chemotherapy as induction and consolidation therapies.

Patients who had a complete remission received maintenance therapy with midostaurin or placebo for one year. Over half of the patients (57 percent) had a stem cell transplant.

What Patients Should Know

Midostaurin is a pill that inhibits mutated FLT3. About one third (30 to 35 percent) of patients with AML have FLT3 mutations.

The Food and Drug Administration (FDA) has decided to do an expedited review of midostaurin to decide if it will approve it for the treatment of patients with newly diagnosed FLT3-mutated AML.

Sorafenib for FLT3-Mutated AML

Sorafenib (Nexavar) might help patients with FLT3-mutated AML live longer, according to two small clinical trials. Sorafenib is an oral drug that inhibits several kinases.

In the first study, sorafenib added to chemotherapy doubled the one year survival compared with what other studies had reported for AML chemotherapy (62 percent versus 30 percent). This study included 54 older patients (average age 67 years). Patients took sorafenib as part of induction chemotherapy and post-remission therapy. The most commonly seen side effects of sorafenib were low-grade diarrhea, fatigue, and redness, swelling, and pain on the bottom of the hands and feet.

The other study was in 80 consecutive patients in remission after stem-cell transplantation. Twenty-six patients had taken sorafenib and 54 had not. Patients treated with sorafenib had better 2 year overall survival versus patients who did not take sorafenib (83 percent versus 58 percent).

What Patients Should Know

Although the results look promising, better quality, larger studies are needed to confirm the findings. These two studies were small and they were not designed as prospective randomized controlled trials, the best quality study design for cancer therapies.

Rituximab Added to Chemotherapy for ALL

Adding rituximab (Rituxan) to conventional chemotherapy improved event-free survival in newly diagnosed patients with a type of ALL. This randomized study involved 220 patients who had CD20-positive, Philadelphia-chromosome negative, B-cell precursor ALL. CD20 is on the surface of 30-50% of ALL patients. All the patients were treated with conventional chemotherapy and half also received rituximab.

Two-year event-free survival increased from 52 percent for patients treated only with conventional therapy to 65 percent for patients who also received rituximab. After two years, the rituximab-treated group had a lower relapse rate than the group that had only received conventional therapy (18 percent versus 30 percent). The overall response rate and overall survival were similar between the two groups of patients. But adding rituximab to conventional therapy improved the overall survival of patients who had not received an allogeneic stem-cell transplant at first remission (74 percent versus 63 percent).

What Patients Need to Know

These results are making doctors consider the benefit of including rituximab with chemotherapy for ALL patients that express CD20.

Chimeric Antigen Receptor T-Cell Therapy for ALL

A new kind of immunotherapy, chimeric antigen receptor (CAR)-modified T-cell therapy, may help patients with ALL. According to a small study, CD19-targeted 19-28z CAR-modified T-cell therapy led to an impressive 82 percent complete remission rate in adults with relapsed or refractory ALL. Of the 46 people who participated in this study, 18 previously had an allogeneic stem-cell transplant. Most of these patients were young, with an average age of 45 years.

To make the CAR T-cell therapy, doctors first harvest T-cells from a patient. Then, the T-cells are modified in the laboratory to make them recognize and fight the leukemia cells. The doctors then reinfuse the modified T-cells back into the patient.

While it shows promise, this therapy can cause serious side effects. Many patients had severe cytokine release syndrome (24 percent) and serious neurotoxicity (28 percent).

What Patients Need to Know

The final results of this study have not yet been published. More research is needed to determine the best way to use this

therapy and to decrease its side effects. CAR T-cell therapy is being studied in several ongoing clinical trials for different blood cancers.

CAR T-cell therapy has to be made specifically for each patient so that it will not be rejected by their immune system. Researchers are studying ways to make a type of "off-the-shelf" CAR T-cell therapy that might work in any patient with a particular type of leukemia.

ABL001 for Chronic Myelogenous Leukemia

A new oral tyrosine kinase inhibitor (TKI), ABL001, may be active in patients with resistant CML, according to initial results from a small trial. The 59 patients in this study had chronic or accelerated phase CML which had advanced despite treatment with at least two other TKI drugs.

In this study, researchers were trying to identify the maximum dose patients could tolerate without severe side effects. This maximum tolerated dose has not yet been reached and the study is continuing. So far, patients have not had serious side effects. Many patients had sustained remissions.

The most common serious side effects were anemia, thrombocytopenia (deficiency of platelets in the blood), and neutropenia.

What Patients Need to Know

ABL001 seems to be active against cancers that have mutated and have become resistant to other TKIs. Future studies might show whether ABL001 may be useful in combination.

Dasatinib Combined With Interferon for CML

Daily dasatinib (Sprycel) combined with pegylated-interferon alpha 2b shows activity against newly diagnosed CML. At 12 months of treatment, this combination produced a 31 percent rate of deep molecular remission with manageable side effects. This was a non-comparative study that enrolled 81 patients less than 65 years old who had Philadelphia chromosome-positive CML in chronic phase.

Patient took daily oral dasatinib alone for the first three months. After that, they also received the interferon, depending on their platelet count. Almost 80 percent of patients continued treatment after one year. The trial is still ongoing.

The most commonly reported side effects were infection, skin lesion, liver abnormalities, headache, pain, psychiatric disorders, and gastrointestinal disorders. Five patients had immune disorders.

What Patients Need to Know

Dasatinib is a second generation TKI made to follow in the footsteps of the first generation TKI, imatinib (Gleevec). In previous studies, patients treated with pegylated-interferon alpha 2a and imatinib had a higher rate of molecular remission compared with patients treated with imatinib alone.

Dasatinib has an FDA-approved indication for the treatment of patients with certain types of CML with resistance or intolerance to prior therapy. The FDA has not yet approved the use of dasatinib for previously untreated patients with CML.

Lymphoma

Several studies reported at the 2015 Annual Meeting of the American Society of Hematology show progress in the treatment of lymphoma:

The two checkpoint inhibitors nivolumab and pembrolizumab seem to work against Hodgkin lymphoma. In small studies, patients with lymphomas treated with these drugs had strong remissions (page 11).

Brentuximab vedotin plus bendamustine may help people with relapsed or refractory Hodgkin lymphoma. If these results hold true in larger studies, doctors might be able to use this combination to get more patients to curative transplant (page 12).

Ibrutinib works better than chlorambucil in older patients with untreated chronic lymphocytic leukemia (CLL) and small lymphocytic lymphoma (SLL). These results suggest that ibrutinib may become a new standard first-line therapy for older people with CLL or SLL (page 13).

Venetoclax treatment produces responses and few serious side effects in patients with CLL. Researchers are continuing to study this drug in clinical trials (page 14).

Nivolumab and Pembrolizumab for Lymphoma

Checkpoint inhibitors are one class of cancer-fighting drugs that has produced much enthusiasm over the last couple of years. These drugs re-educate the immune system to recognize and help kill cancer cells. Checkpoint inhibitors, like nivolumab (Opdivo) and pembrolizumab (Keytruda), have started to show positive results in lymphoma. Nivolumab blocks programmed cell death protein 1 (PD-1). Pembrolizumab blocks PD ligand 1 (PD-L1).

In small studies, patients with lymphomas treated with nivolumab or pembrolizumab had strong remissions. These responses included complete remissions in many patients who had relapsed disease after conventional chemotherapy and autologous stem cell transplantation (ASCT). For some people, these drugs provide disease control. In others, these medicines are being used as a bridge to other forms of transplant, such as allogeneic stem cell transplantation.

What Patients Need to Know

Nivolumab and pembrolizumab are monoclonal antibodies. They work by unmasking molecules that hide cancer cells from the immune system. Ongoing and future larger clinical trials will help determine how to best use these drugs in lymphoma. Researchers are looking to see if they should be used to treat people with earlier stages of lymphoma. In the future, doctors might use checkpoint inhibitors in place of conventional chemotherapy. The hope is to shift towards less toxic, more effective cancer drugs. More clinical trials are needed before we get to that point.

Both drugs are approved by the FDA to treat people with melanoma and lung cancer. Other checkpoint inhibitors are also being studied in clinical trials.

Brentuximab Vedotin and Bendamustine for Hodgkin Lymphoma

Brentuximab vedotin (Adcetris) plus bendamustine (Treanda) helped people with relapsed or refractory Hodgkin lymphoma in a small study. Over 90 percent of patients had a response and 80 percent had a complete remission. This study included 55 patients with Hodgkin disease that had relapsed after the standard ABVD regimen of doxorubicin, bleomycin, vinblastine, and dacarbazine.

While this combination had not been directly compared with other treatments, these results seem better than the responses usually seen with the ifosfamide, carboplatin, etoposide (ICE) regimen—a standard therapy for these patients. In other studies, ICE had 50 percent overall response and 25 percent complete remission rates.

The most common side effects of brentuximab vedotin plus bendamustine were allergic-like reactions during the infusion. These allergic-like reactions included fever, chills, difficulty breathing, nausea, flushing, and low blood pressure.

What Patients Need to Know

Researchers have not yet published the final results from this study. If these results hold true in bigger, comparative studies, doctors might be able to use this combination to get more patients to curative transplant. The combination of brentuximab vedotin and bendamustine might become a new standard of care for patients with relapsed disease.

Ibrutinib for CLL and SLL

Older patients with CLL or SLL treated with ibrutinib (Imbruvica) lived longer than people treated with chlorambucil (Leukeran), in a large randomized study. After about 18 months of treatment, patients in the ibrutinib group had better median progression-free survival (not reached versus 18.9 months), two year overall survival (98 percent versus 85 percent), and overall response rate (86 percent versus 35 percent), compared with the chlorambucil group. The study is still ongoing. The most common side effects of ibrutinib were diarrhea, fatigue, cough, and nausea.

This clinical trial involved 269 adults, age 65 year or older, with previously untreated CLL or SLL. The study did not include patients with a chromosome 17p13.1 deletion or p53 mutation. The results of this study were published in the *New England Journal of Medicine* in December 2015.

What Patients Need to Know

These results suggest that ibrutinib may become a new standard first-line therapy for older people with CLL or SLL. By using ibrutinib or other active, well-tolerated oral drugs, such

as idelalisib (Zydelig), doctors are trying to change the natural course of the cancer, as early as possible. The hope is that people will be able to live longer with a better quality of life.

Ibrutinib is an oral drug that blocks the Bruton's tyrosine kinase (BTK), an enzyme that helps tumor cells grow. Ibrutinib is approved by the FDA for the treatment of patients with CLL after at least one other therapy. The FDA has also approved ibrutinib as primary therapy for patients with CLL who have a 17p13.1 chromosome deletion.

Venetoclax for CLL

Venetoclax treatment led to responses and few serious side effects in patients with CLL, according to an initial study. The study included 116 patients with relapsed or refractory CLL or SLL. Most patients (79 percent) had a response and 20 percent had complete remissions. A few patients (5 percent) achieved complete remissions with no minimal residual disease detected by sensitive molecular methods.

This study tested different doses of venetoclax to find the best dose to use in larger studies. The most common side effects of venetoclax were diarrhea, upper respiratory tract infection, nausea, low white blood cell count (neutropenia), and fatigue. Patients taking venetoclax should not be given live attenuated vaccines.

What Patients Should Know

Venetoclax targets BCL-2 to affect a cancer cell's ability to survive. The FDA has now approved venetoclax (Venclexta™) for the treatment of patients with CLL containing the chromosome 17p deletion. Researchers are continuing to study this drug in clinical trials. Your participation in clinical trials helps speed-up the application of new therapies.

Multiple Myeloma

Several studies reported at the 2015 Annual Meeting of the American Society of Hematology reported important progress in the treatment of multiple myeloma:

Adding bortezomib to lenalidomide and dexamethasone for induction therapy improves survival in patients with untreated multiple myeloma. Patients treated with this combination as induction therapy also had a better response rate and remained without evidence of disease for longer (page 16).

ASCT with high-dose chemotherapy seems to improve disease-free survival, but not overall survival in patients with untreated multiple myeloma. An ongoing study might answer the question of whether longer periods of maintenance treatment could do away with the need for ASCT (page 17).

Adding ixazomib to lenalidomide and dexamethasone improves survival in patients with relapsed multiple myeloma. Ixazomib is a new type of proteasome inhibitor that is taken as a pill once a week (page 18).

Daratumumab monotherapy may help people with relapsed or refractory multiple myeloma. Almost a third of patients had a response (page 19).

The checkpoint inhibitor pembrolizumab in combination with lenalidomide or pomalidomide seems to benefit patients with relapsed multiple myeloma. These are some of the first positive results with a checkpoint inhibitor in multiple myeloma (page 20).

Bortezomib Added to Lenalidomide and Dexamethasone for Untreated Multiple Myeloma

Adding bortezomib (Velcade) to lenalidomide (Revlimid) and dexamethasone for induction therapy improved survival in patients with multiple myeloma, according to a large study. This study included about 500 patients not previously treated for multiple myeloma and not planning to undergo an immediate autologous stem cell transplant. Patients who got the three-drug combination as induction therapy had a better response rate. They remained without evidence of disease for longer periods of time and had higher survival rates.

The only side effect increased by adding bortezomib to lenalidomide and dexamethasone was peripheral neuropathy (numbness, weakness, and pain in the hands and feet). Because this trial started years ago, doctors were giving bortezomib by intravenous injection. Doctors now may give bortezomib by subcutaneous injection which lowers the risk of peripheral neuropathy.

What Patients Should Know

These results suggest that adding the proteasome inhibitor bortezomib to the lenalidomide and dexamethasone combination may be a good option for patients with multiple myeloma.

ASCT for Untreated Multiple Myeloma

ASCT with high-dose chemotherapy improves disease-free survival but not overall survival, according to a large French study. This study included 700 patients with untreated multiple myeloma. Doctors treated all the patients with lenalidomide, bortezomib and dexamethasone. After three cycles of this triple therapy, doctors collected stem cells from all the patients. Then, half of the patients had an ASCT followed by two more cycles of the triple combination. The other half had five more cycles of the triple combination. All the patients in the study had one year of maintenance therapy with lenalidomide.

Three years later, more patients in the ASCT group than in the chemotherapy group were living without evidence of disease (61 percent versus 48 percent). Most patients (88 percent) were alive and there was no difference in overall survival in the two groups. The study is still ongoing.

What Patients Should Know

For many years, high-dose chemotherapy followed by ASCT has been the standard of care for multiple myeloma in patients younger than 65 years of age. Since the introduction of new effective therapies, researchers are trying to find out if ASCT and high-dose chemotherapy still have an important role as myeloma therapy.

This study only included one year of maintenance therapy. An ongoing U.S. trial is following the same design as the French study except that patients will continue on lenalidomide until progression. This study might answer the question of whether longer periods of maintenance treatment could do away with the need for ASCT.

Ixazomib for Relapsed Multiple Myeloma

Patients with relapsed multiple myeloma treated with ixazomib (Ninlaro), lenalidomide, and dexamethasone had longer survival rates than patients treated only with lenalidomide and dexamethasone, in a large study. Ixazomib is a new type of proteasome inhibitor that is taken as a pill once a week.

Researchers randomized 772 patients who had relapsed or refractory multiple myeloma after one to three prior therapies that did not include lenalidomide or another proteasome inhibitor (like bortezomib). Patients treated with the three drugs had high response rates and had a longer period without evidence of disease than the patients who did not get ixazomib. Ixazomib caused few side effects, including very little peripheral neuropathy. The final results of this study have not yet been published.

What Patients Should Know

The completely oral, well-tolerated regimen of ixazomib, lenalidomide, and dexamethasone sets a new standard for patients who have received at least one prior therapy. The FDA approved this triple regimen in November 2015.

The fact that ixazomib has few severe side effects suggests that it could be used also for maintenance therapy.

Daratumumab for Relapsed/Refractory Multiple Myeloma

Daratumumab (Darzalex) monotherapy helps many patients with relapsed or refractory multiple myeloma, according to follow-up results from two studies. Most of the 148 patients in these studies had received more than 3 prior therapies. Almost a third of patients (31 percent) had a response. These responses lasted about 8 months. Many of the responding patients continued on treatment for almost a year and a half. After the first one or two infusions, daratumumab had few side effects.

What Patients Should Know

Daratumumab is a monoclonal antibody that targets CD38. Myeloma cells make large amounts of CD38. The FDA has approved daratumumab to treat people with multiple myeloma who have received three or more prior therapies (including a proteasome inhibitor and an immunomodulatory drug) or with disease unresponsive to both a proteasome inhibitor and an immunomodulatory drug.

Pembrolizumab for Multiple Myeloma

The checkpoint inhibitor pembrolizumab (Keytruda) in combination with lenalidomide or pomalidomide helps patients with relapsed multiple myeloma. For the first time in multiple myeloma, studies showed that patients treated with this checkpoint inhibitor can have strong responses. The patients in these studies had been previously treated with immunomodulatory drugs and proteasome inhibitors. Many patients also had ASCT.

In one study, doctors treated 24 patients with pembrolizumab, pomalidomide (Pomalyst), and dexamethasone. Half of the patient responded to the three drug combination.

In another study, doctors treated 17 patients with pembrolizumab, lenalidomide, and low-dose dexamethasone. Most patients (76 percent) responded to treatment.

What Patients Should Know

These studies are ongoing. These are some of the first positive results with a checkpoint inhibitor in multiple myeloma. Checkpoint inhibitors are a new class of drugs that works with the body's own immune system. They are approved for the treatment of a few other cancers. Researchers hope to soon see more exciting results.

Myeloproliferative Neoplasms

Several studies reported at the 2015 Annual Meeting of the American Society of Hematology show important advances in the treatment of myeloproliferative neoplasms:

Ruxolitinib is better than best alternative treatment in patients with polycythemia vera and an enlarged spleen. New data shows that ruxolitinib seems to improve control of red blood cell and white blood cell counts, and lowers the risk of blood clots (page 21).

Long-acting anagrelide seems to benefit patients with essential thrombocythemia. Researchers made the long-acting form to try to decrease the side effects of anagrelide (page 22).

Ruxolitinib improves survival at five years compared with best available therapy in patients with myelofibrosis. Half of the patients treated with ruxolitinib had a lasting decrease in spleen volume, stable blood counts, and improved bone marrow fibrosis (page 23).

Imetelstat and PRM 151 are two new drugs that seem to be active against myelofibrosis. Some patients have experienced tumor shrinkage and symptom improvement (page 24).

Ruxolitinib for Polycythemia Vera

Updated results from a large randomized study confirmed that ruxolitinib (Jakafi) was better than best alternative treatment in people with polycythemia vera and an enlarged spleen. The new data showed that patients treated with ruxolitinib had better control of red blood cell counts

(hematocrit). These patients were less likely to need to have their blood drawn out of the body (phlebotomy) to decrease their red blood cell counts. Also, ruxolitinib treatment provided better and longer lasting control of white blood cell counts and decreased the risk of blood clots.

This study included 222 patients who needed phlebotomies to control their blood counts. According to results published in the *New England Journal of Medicine* in January 2015, ruxolitinib improved symptoms, spleen size, and quality of life.

What Patients Should Know

Mostly based on the results from this study, the FDA approved ruxolitinib for the treatment of patients with polycythemia vera who had an insufficient response to or cannot tolerate hydroxyurea. Ruxolitinib is also approved to treat people with some types of myelofibrosis. Ruxolitinib inhibits a protein known as the Janus associated kinase (JAK) 2.

Another interesting study has compared ruxolitinib with best alternative therapy in 219 patients with polycythemia vera that was intolerant to or resistant to hydroxyurea and no enlarged spleen. This study is complete but the results have not yet been published.

Long-Acting Anagrelide for Essential Thrombocythemia

Long-acting (controlled-release) anagrelide (GALE-401) seems to benefit patients with essential thrombocythemia, according to a small study. The study included 12 patients with essential thrombocythemia, three with polycythemia vera, and one with both conditions. Most of the 18 treated patients (83 percent) had a response and 61 percent had complete responses. Fourteen patients had at least one side effect. Most of the side effects were mild.

What Patients Should Know

The purpose of the study was to evaluate the safety and efficacy of long-acting anagrelide. The currently available immediate release (short-acting) form of anagrelide (Agrylin) has an FDA indication to treat people with thrombocythemia.

Ruxolitinib for Myelofibrosis

Ruxolitinib lowered the risk of death at five years by 33 percent compared with best available therapy in patients with myelofibrosis, according to the long-term follow-up from a large study. Also, after five years of treatment, about half of patients treated with ruxolitinib had a lasting decrease in spleen volume, stable blood counts, and improved bone marrow fibrosis. About one fourth of patients stopped ruxolitinib treatment because of side effects.

The 219 study participants had intermediate-2 or high-risk primary myelofibrosis, post-polycythemia vera myelofibrosis, or post-essential thrombocythemia myelofibrosis. The first results of the study were reported in the *New England Journal of Medicine* in 2012. After 48 weeks of therapy, 28 percent of patients in the ruxolitinib group and none in the best available therapy group had decreased spleen volume.

What Patients Should Know

In addition to this study, there are ongoing studies of different ruxolitinib drug combinations in people with myelofibrosis and other myeloproliferative neoplasms. Promising combinations include ruxolitinib with danazol, ruxolitinib with pegylated interferon alpha 2A (Pegasys), ruxolitinib with 5-azacitidine (Vidaza), and ruxolitinib with panobinostat (Farydak).

Imetelstat and PRM 151 for Myelofibrosis

Imetelstat and PRM 151 are two new drugs that seem to be active against myelofibrosis and other blood cancers. In a small clinical study, some patients who took imetelstat had complete and partial remissions. The drug seems to help shrink the spleen and improve other symptoms. Imetelstat blocks the activity of a protein called telomerase. People whose cancer cells have specific mutations might respond better to imetelstat. This drug may cause serious blood side effects though. One ongoing clinical trial is testing two different dose levels of imetelstat.

In another small study, some patients who took PRM-151 had decreased fibrosis and spleen size, and improved low blood counts. Most of the study participants had primary myelofibrosis. PRM-151 seems to work by reversing and maybe healing the scar tissue (fibrosis) that builds up in the bone marrow of patients with myelofibrosis. This study is still ongoing.

What Patients Should Know

Imetelstat and PRM 151 are only available through clinical trials. Talk with your healthcare team about your current therapy and ask if a clinical trial would be worthwhile.

Resources

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