



A Report From the American Society of Clinical Oncology 2007 Annual Meeting

Blood and Lymph Cancers

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The major forms of blood and lymph cancers are **lymphoma**, **leukemia**, and **multiple myeloma**. These cancers affect the way the body makes blood and provides immunity from other diseases. Thanks to more effective radiation treatment and chemotherapy, the five-year survival rates for people with blood cancers have increased dramatically in the past 30 years.

This year, approximately 250,000 Americans will be diagnosed with some form of blood or lymph cancer. What causes these cancers is still unknown. Researchers are trying to identify when and why the body starts producing abnormal cells and how those cells begin invading the body's blood system. As these questions are answered, the information is used to improve prevention and treatment options.

Targeted Treatments for Lymphoma

Targeted treatments are a new class of drugs that offers an effective approach to cancer therapy. One category of targeted treatments is the **monoclonal antibody**. Unlike drugs that destroy both cancerous and healthy cells, monoclonal antibodies target only the cancerous cells. They are used to deliver radiation, chemotherapy, or other types of treatment directly to the tumor. These drugs also stimulate the body's immune system to attack cancer cells.

TOSITUMOMAB (BEXXAR) FOR FOLLICULAR LYMPHOMA

Tositumomab (Bexxar) is a monoclonal antibody that has been approved by the U.S. Food and Drug Administration for treatment of non-Hodgkin's lymphoma (NHL). NHL is a general term for more than two dozen types of cancer that can arise in the body's **lymph nodes**, spleen, and other organs of the immune system. Tositumomab zeros in on and destroys cells that have a molecule called CD20 on their surface. That molecule is found on most lymphoma cells.

Researchers from the University of Michigan tested tositumomab in about 75 people who had not been treated

before for their follicular lymphoma, a type of NHL. Patients received a single one-week course of treatment. Eight years after treatment, approximately 85 percent of these patients were still alive. Also, half survived without their cancer growing. Overall, the drug seemed to slow or stop the growth of cancer in 95 percent of the patients treated.

The Michigan researchers believe that tositumomab should now serve as a standard against which other treatment approaches should be compared.

TOSITUMOMAB FOR DIFFUSE LARGE B-CELL LYMPHOMA

Tositumomab was also studied in people with **relapsed** diffuse large B-cell lymphoma, another type of NHL, who received an **autologous stem cell transplant (ASCT)**. In ASCT, bone marrow is taken from the person with cancer. The marrow contains immature cells, called stem cells, that can mature into red blood cells, white blood cells, and other essential cells produced by healthy bone marrow. With the stem cells on reserve, doctors give the patient high doses of chemotherapy to destroy their remaining cancerous bone marrow. Afterward, the reserved stem cells are transplanted back to the person in the hope that mature, healthy bone marrow cells will develop.

What's New, What's Important

- Tositumomab (Bexxar) may prolong the lives of people with follicular lymphoma and diffuse large B-cell lymphoma, two types of non-Hodgkin's lymphoma.
- Denileukin diftitox (Ontak) is an effective drug for treating people with cutaneous T-cell lymphoma (CTCL), a type of lymphoma that affects the skin.
- A new combination treatment of lenalidomide (Revlimid) plus low-dose dexamethasone seems to help people with multiple myeloma live longer than the standard high-dose approach and may become a new standard of care.

In this clinical trial, tositumomab was added to a chemotherapy treatment plan before ASCT. All of the 40 people in the clinical trial had received at least two chemotherapy treatments before transplant and were thought to have cancer that would respond to further chemotherapy. Researchers found that after their transplant, more than two-thirds of patients who received this combination treatment showed no evidence of disease. Three years after treatment, about 80 percent of patients were still alive. Study of this promising drug is continuing.

DENILEUKIN DIFTITOX (ONTAK) FOR CUTANEOUS T-CELL LYMPHOMA

The results of a clinical trial of a drug called denileukin diftitox (Ontak) have been encouraging for the treatment of cutaneous T-cell lymphoma (CTCL), a type of lymphoma that affects the skin. Findings on its value and safety as a treatment show that this drug, which was approved by the U.S. Food and Drug Administration in 1999, benefits people with persistent or recurrent CTCL whose cancer cells **overexpress** a substance called CD25. Tumors that overexpress CD25—which means that they contain a large amount of CD25—are said to be CD25-positive.

Researchers from cancer centers in Australia, Germany, and the United States tested two different doses of denileukin diftitox in a group of patients, nearly 70 percent of whom were over the age of 65. About 145 people who had CD25-positive CTCL received one of three treatments: a low dose of denileukin diftitox, a higher dose of denileukin diftitox, or a **placebo** (inactive substance). Nearly 100 patients with CD25-negative CTCL received just a placebo. All of the people in both groups had received no more than three previous treatments before joining the study, which



is the largest clinical trial involving people with CTCL.

The growth of the cancer was slowed or stopped in 17 of the 45 patients who received the low dose of the drug and in 27 of the 55 patients who received the higher dose of the drug. These results were much better than those in the placebo group. Both doses of denileukin diftitox significantly improved the average time patients went without the cancer growing: more than two years for those treated with the drug and only about four months for those treated with a placebo. Even though up to eight treatment cycles were planned, positive responses were seen in many patients after five or more treatment cycles.

The side effects did not differ among the groups. The only real exception was the occurrence of nausea, which was more common in those who received the higher dose of the drug than in those who received a placebo (15 percent versus 2 percent). However, researchers reported that side effects noticeably decreased after the first two cycles of treatment.

Combination Treatment for Multiple Myeloma

LENALIDOMIDE (REVLIMID) PLUS LOW-DOSE DEXAMETHASONE FOR MULTIPLE MYELOMA

Recent findings from a clinical trial conducted by the Eastern Cooperative Oncology Group may change the first treatment that doctors consider for people with multiple myeloma (cancer of the plasma cells, most of which reside in the bone marrow). The clinical trial has shown remarkable survival results when lenalidomide (Revlimid) is combined with low-dose dexamethasone.

Researchers from the Mayo Clinic in Rochester, Minnesota, have adopted this approach as the new standard **first-line** treatment for people with multiple myeloma who are

candidates for a bone marrow transplant. Such transplants replace cancerous cells with healthy cells.

Nearly 450 people with untreated multiple myeloma took part in the clinical trial. All of them received 25 mg of lenalidomide by mouth. Half of them also received the routine treatment of high-dose dexamethasone. The other half received the low-dose dexamethasone, which is a new approach.

More than one year after treatment, more people in the low-dose group were alive than in the high-dose group (96 percent versus 87 percent). People over the age of 65 seemed to benefit the same as younger people. In addition, the low-dose group had fewer side effects than the high-dose group, such as infection or pneumonia (experienced by 5 percent of patients in the first group versus 15 percent of patients in the second group) and thromboembolism (9 percent versus 24 percent). Thromboembolism can be a life-threatening condition. It occurs when a blood clot travels through the body's circulation.

To fully evaluate this new treatment for people with multiple myeloma, researchers need to study **response rates** over a longer period of time. However, they do believe that the low-dose combination treatment is a reasonable alternative to the previously used high-dose treatments.

New Treatments for Leukemia

NILOTINIB (TASIGNA) AND BOSUTINIB (SKI-606) FOR CHRONIC MYELOID LEUKEMIA (CML)

The drug imatinib (Gleevec) revolutionized treatment of people with a rare form of cancer called **chronic myeloid leukemia (CML)**. Even though imatinib often slows or stops the growth of cancer in people with CML, in some patients it is ineffective or causes intolerable side effects. For those patients, two new drugs—nilotinib (Tasigna) and bosutinib (SKI-606)—may be promising alternatives.

What's New, What's Important

- Two new drugs, nilotinib (Tasigna) and bosutinib (SKI-606), may be effective alternatives for people with CML who do not respond to or cannot tolerate the side effects of standard treatment with imatinib.
- Dasatinib (Sprycel), which is already approved for treating people with CML that no longer responds to imatinib, may also be effective as initial treatment, at a recommended dose of 100 mg once a day.
- The three-drug combination called FCR appears to be an effective first-line chemotherapy for people with chronic lymphocytic leukemia.
- Adding arsenic trioxide (Trisenox), a treatment with already proven benefits, to standard chemotherapy may help people with acute promyelocytic leukemia live longer without this rare cancer returning.

Nilotinib belongs to the same class of drugs as imatinib but is much more powerful than imatinib. Like imatinib, nilotinib works against CML by zeroing in on mechanisms that promote the growth of cancer cells. Specifically, the drug prevents **receptors** from sending signals to cancer cells to grow and divide. Instead of killing both healthy and unhealthy cells, the way chemotherapy does, nilotinib focuses on disrupting cancer growth, with less serious side effects.

Researchers from cancer centers in several countries, including Italy, Germany, and the United States, tested nilotinib in more than 300 people with CML. These patients either did not respond to or could not tolerate the side effects of treatment with imatinib. After at least six months, 40 percent of the people who received nilotinib had a complete **cytogenetic response**—that is, there was no longer any evidence of cancer in the patients' bone marrow. In addition, 56 percent had a major cytogenetic response, meaning that their bone marrow had begun producing normal cells and, at least to some extent,

started working properly. These positive results were achieved with few serious side effects.

In another preliminary trial, Italian researchers tested bosutinib (SKI-606) in more than 100 people with CML. For all of these patients, imatinib had become ineffective or intolerable because of side effects.

In people who had not been treated before with any drug other than imatinib, more than 90 percent (33 of 36 people evaluated) had a complete **hematologic response**—that is, their blood counts returned to normal and their spleen was no longer enlarged. (The spleen is a filtering organ that disposes of old, worn-out red blood cells.) More than 40 percent of patients who had not been treated before with any drug other than imatinib (13 of 31 people evaluated) had a major cytogenetic response. Bosutinib was not as effective in people who had been treated before with other drugs besides imatinib. These early results are encouraging, and studies are continuing.

DASATINIB (SPRYCEL) FOR CML

Another targeted drug called dasatinib (Sprycel) has shown encouraging results in people with CML that does not respond to imatinib. Like nilotinib and imatinib, dasatinib targets the **genetic** change that causes the leukemia cells to grow uncontrollably. Currently, dasatinib is approved as a **second-line** treatment in such people. But findings from M. D. Anderson Cancer Center in Houston now show that it may also be an effective first-line treatment for newly diagnosed people with the most common **stage** of CML, known as chronic phase.

About 30 people with chronic phase CML who had not already received treatment took part in the first study of dasatinib as a first-line option. They received either 100 mg of dasatinib once a day or 50 mg of dasatinib twice a day. Both doses of dasatinib were given as a pill by mouth.

After three months, 21 of the 26 patients who were evaluated had a complete hematologic response. Also, 19 of the 26

patients who were evaluated had a complete cytogenetic response. After six months, 20 of the 21 patients who were evaluated had a complete cytogenetic response.

In another clinical trial, researchers from the University of California, San Francisco, studied different dosing schedules of dasatinib to see which one was the most effective and caused the fewest side effects. This clinical trial, which included more than 650 patients with chronic phase CML, compared 50 mg or 70 mg of dasatinib given twice a day with 100 mg or 140 mg of dasatinib given once a day. After eight months of treatment, the hematologic and cytogenetic responses were similar in all four groups.

However, the 100 mg, once-a-day dose was associated with the fewest side effects, such as low blood counts (thrombocytopenia) and fluid outside the lungs (pleural effusion). Therefore, researchers now recommend 100 mg of dasatinib once daily as the best dose for people with chronic-phase CML.

It's still too early to know for sure whether dasatinib will help people with CML live longer. But researchers are very impressed with these promising results, and studies of this drug continue comparing dasatinib with imatinib as first-line treatment for people with CML.

CHEMOTHERAPY WITH FCR FOR CHRONIC LYMPHOCYTIC LEUKEMIA

A three-drug combination has shown promise as first-line treatment of people with **chronic lymphocytic leukemia (CLL)** based on the results of a clinical trial. This blood cancer arises from white blood cells called **lymphocytes**. The overproduction of these cells causes them to build up in the



blood, bone marrow, and others areas of the body, crowding out healthy blood cells.

Nearly 300 people with CLL received chemotherapy with FCR, which consists of fludarabine (Fludara), cyclophosphamide (Cytoxan, Neosar, and others), and rituximab (Rituxan). This was the first treatment these people had received for their cancer. About 75 percent of the patients completed the planned six cycles of treatment. In people who had complete or partial disappearance of tumors, the time it took for tumors to begin growing after treatment was more than six years. Five years after treatment with FCR, 70 percent of patients still had a complete disappearance of their cancer.



These impressive results with FCR were better than results with earlier treatments such as fludarabine alone or

with cyclophosphamide. Although there is some controversy about the best approach, researchers from the The University of Texas M. D. Anderson Cancer Center in Houston consider FCR the most effective first-line treatment for people with CLL. One question about FCR treatment remains: Can it prolong the lives of people with CLL, compared with other approaches? Future studies hope to answer this question.

ARSENIC TRIOXIDE (TRISENOX) FOR ACUTE PROMYELOCYTIC LEUKEMIA

Adding arsenic trioxide (Trisenox) to standard treatment may considerably extend the lives of adults with a rare type of leukemia called acute promyelocytic leukemia (APL). Most often diagnosed in young and middle-aged adults, APL is a cancer of the bone marrow in which cancerous cells eventually crowd out healthy blood cells. About 1,500 cases of APL are

diagnosed in the United States each year. Up to 30 percent of people with APL will relapse after initial, or first-line, treatment. Currently, arsenic trioxide is approved for use as second-line treatment of APL. When the standard first-line medications—which consist of tretinoin (a form of vitamin A), daunorubicin (Cerubidine and others), and cytarabine (Cytosar-U and others)—are no longer effective, arsenic trioxide is used.

Now, a new study suggests that perhaps arsenic trioxide should be used as part of the first-line treatment of APL, so more people can benefit from it.

More than 500 people with newly diagnosed APL in the United States and Canada took part in a clinical trial over six years. The study was sponsored by the National Cancer Institute and led by the Cancer and Leukemia Group B. About half of the adults in this clinical trial received two courses of arsenic trioxide in addition to standard chemotherapy. The other half received just the standard treatment.

After three years, nearly 80 percent of the people who received arsenic trioxide were alive and remained in remission (free of leukemia), compared with about 65 percent of those treated with just the standard chemotherapy. People who received arsenic trioxide plus chemotherapy also lived longer than those who did not (almost 90 percent versus nearly 80 percent). More people taking arsenic trioxide did experience infections and headaches than those who did not take arsenic trioxide (about 40 percent versus almost 30 percent).

Researchers believe that more people with APL will benefit if arsenic trioxide is given earlier in the course of treatment than it has been.

Please note: *Although the treatments discussed in this chapter are showing promise, most are still in clinical trials—some in earlier phases of research—and may not be available yet to the general public. Your doctor can help guide you as to which new medications could be right for you and whether you are eligible to take part in the clinical trials of these new treatments.*