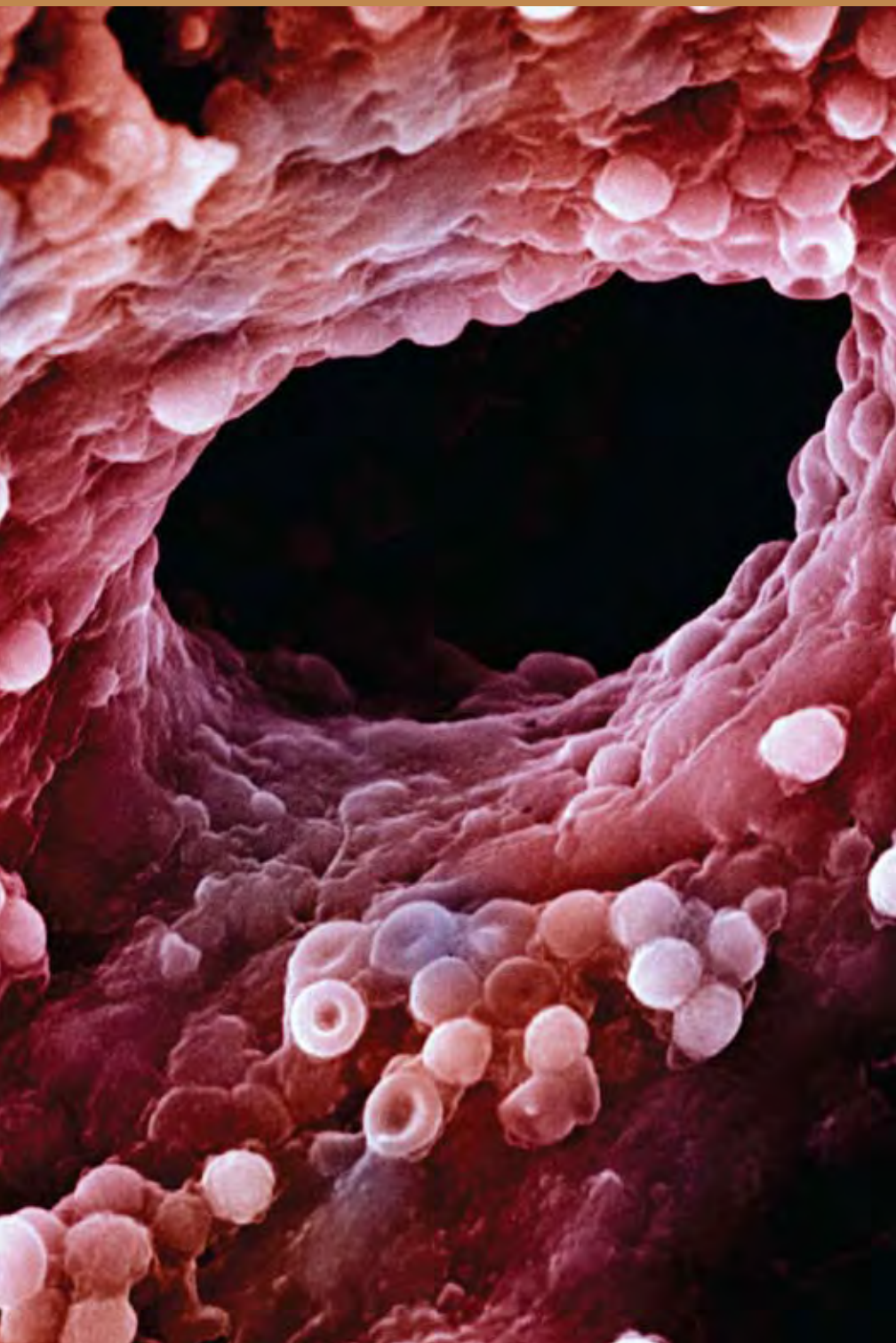


Blood and Lymph Cancers

Highlights from the 2009 Annual Meeting of the American Society of Clinical Oncology

Edited by

Kenneth C. Anderson, MD

Harvard Medical School and Dana-Farber Cancer Institute
Boston, Massachusetts

contents continued on the following page

◀ Inside a blood vessel with red and white blood cells

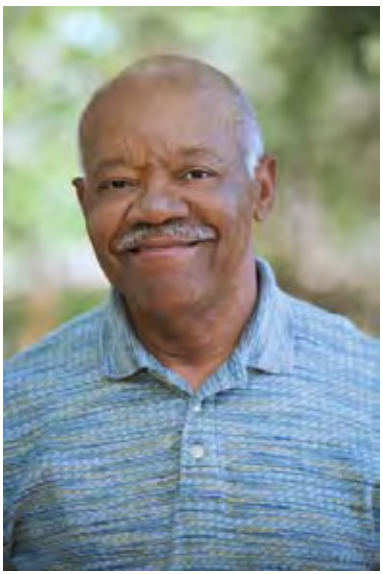
The major forms of blood and lymph cancers are leukemia, lymphoma, and multiple myeloma, all of which we discuss in this chapter. Each year, approximately 140,000 Americans are diagnosed with some form of blood or lymph cancer. Thanks to more effective treatments, survival has increased dramatically in the past 30 years for people with this diagnosis.

Leukemia is a cancer that causes the body to produce large numbers of abnormal white blood cells that do not function properly. White blood cells are an important part of our immune system, which protects us from infection and other diseases.

There are several different types of leukemia. In this chapter, we discuss:

- Acute myelogenous leukemia (AML)
- Chronic myelogenous leukemia (CML)
- Chronic lymphoblastic leukemia (CLL)

A major difference among these cancers is how they grow. The chronic forms of leukemia grow slowly, and the acute forms grow quickly.



Lymphoma is a general term for a group of cancers that originate in the lymphocytes, a type of white blood cell. The largest group of this type of cancer is called non-Hodgkin lymphomas (NHLs). There are 40 or more types of NHLs, each with a different treatment approach. This chapter includes studies on the following NHLs:

- Follicular lymphoma
- Diffuse large B-cell lymphoma
- Cutaneous T-cell lymphoma

Multiple myeloma (also known as myeloma or plasma cell myeloma) is a cancer of the plasma cells. Plasma cells, most of which are in the bone marrow, are an important part of the immune system.

Leukemia

COMBINATION TREATMENT WITH VORINOSTAT FOR AML

Adding the drug vorinostat (Zolinza) to other chemotherapies may help shrink cancer.

A combination of standard chemotherapy drugs and the newer drug vorinostat (Zolinza) appears to be an effective way to treat people with AML, according to the results of a recent clinical trial. However, it is important to note that these are very early results of a small study that must be confirmed in larger clinical trials.

Vorinostat is a new drug that has been used to treat a blood cancer called cutaneous T-cell lymphoma when it does not respond to other medications. Vorinostat is also being studied as a treatment for other types of cancer.

Thirty-three people were treated with a combination of idarubicin (Idamycin and others), cytarabine (Cytosar-U and others), and vorinostat. This was the first treatment they received for their cancer. Some of these patients had AML, whereas others had myelodysplastic syndrome (MDS).

MDS is a group of conditions in which the bone marrow does not make enough healthy blood cells. Although MDS is not leukemia, having MDS can increase the risk of developing leukemia. Doctors sometimes refer to cases of MDS as “pre-leukemia.”

The cancer completely disappeared in more than 75 percent of the people treated with the combination. However, it is too early to know whether this treatment can extend the lives of people with MDS or AML.

CYTARABINE AND DAUNORUBICIN FOR AML

Treatment with higher-than-usual doses of daunorubicin (Cerubidine and others) may help younger people who have AML to live longer.

In people younger than age 55 who have AML, higher-than-usual doses of the cancer drug daunorubicin (Cerubidine and others) may do a better job of shrinking tumors than the standard dose of daunorubicin. This new method of treatment, which is sometimes called dose-intensification therapy, may also help these people survive longer.

Approximately 600 people who had newly diagnosed AML took part in a clinical trial to test this new treatment. They were given daunorubicin—commonly used to treat acute leukemias—plus the medication cytarabine. About half of these patients received the standard dose of daunorubicin. The others received double the standard dose of daunorubicin.

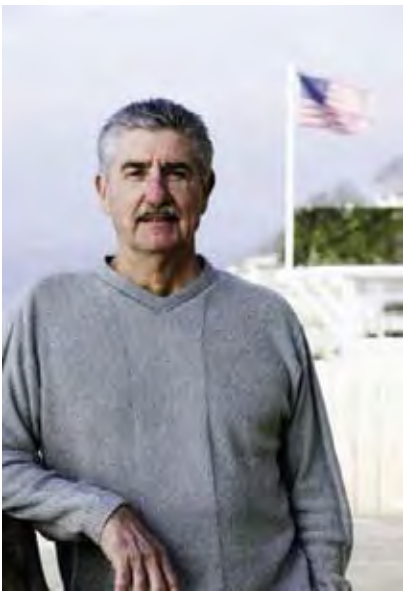
The cancer disappeared in about 70 percent of the people who received the higher-dose treatment. It shrank in less than 60 percent of those who received the lower dose. The new treatment also helped patients survive longer (almost 24 months) than did the standard treatment (almost 16 months).

Among the patients who were younger than age 55, the higher dose extended their survival by about one year over the regular dose. However, among the patients who were older than age 55, there was no real difference in survival between the two treatments.

OMACETAXINE FOR RESISTANT CML

A new drug may offer hope to certain people whose leukemia no longer responds to treatment.

The relatively new drugs imatinib (Gleevec), dasatinib (Sprycel), and nilotinib (Tasigna) are effective treatments for people with leukemias that have mutations, or changes, in certain genes. However, over time, the cancer cells may resist these medications, making them ineffective. A gene mutation may be one of the reasons why leukemia cells resist the treatment of these medications.



Mutations are changes in the DNA that makes up a gene. (DNA is the genetic material inside the cell.) Sometimes these mutations have no effect at all, and other times they can be harmful. One harmful genetic mutation is the T315I mutation. This gene mutation is often responsible for the aggressive growth of cancer in CML.

According to the early results of a clinical trial, a new drug called omacetaxine is showing promise in treating people who have CML and the T315I mutation. Forty people with CML and the T315I mutation received injections (shots) of omacetaxine. In thirty-four of these patients (85 percent), 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.) After one year of treatment, nearly 90 percent of the patients were still alive.

About half of patients whose leukemia resists treatment with imatinib have genetic mutations. Of those patients, about 10 percent have the T315I mutation.

OFATUMUMAB FOR RESISTANT CLL

For people with CLL that no longer responds to treatment, the new drug ofatumumab may be beneficial.

CLL is the most common type of leukemia in adults. People who have CLL are often treated with fludarabine (Fludara, Oforta, and others) or alemtuzumab (Campath). However, sometimes this cancer does not respond to treatment with these drugs. The cancer may be resistant at the beginning of treatment or may become resistant during treatment. So, doctors continue to search for better ways to treat people with CLL.

Ofatumumab belongs to a newer class of drugs called monoclonal antibodies. Often compared to guided missiles, monoclonal antibodies zero in on cancer cells whose surface harbors a "target molecule." This molecule is an important key in the development of a cancer cell. Other monoclonal antibodies have proved to be effective, among them rituximab (Rituxan), used to treat several types of lymphoma, and trastuzumab (Herceptin), used to treat breast cancer.

More than 150 people with CLL took part in a clinical trial to study ofatumumab. Of them, 59 patients had CLL that was resistant to both fludarabine and alemtuzumab, and nearly 80 had CLL that was resistant to just fludarabine.

About 90 percent of the people in the study received eight weekly treatments with ofatumumab intravenously (through a blood vein). In the group with CLL that was resistant to both fludarabine and alemtuzumab, the tumor shrank in 42 percent of patients. This benefit lasted about six-and-a-half months. Those who had cancer that was resistant to just fludarabine appeared to benefit from treatment as well.

Because less than 25 percent of people with CLL that is resistant to current treatments benefit from other medications, researchers are optimistic about these early results. If the results with ofatumumab are confirmed in other clinical trials, doctors may have another option for treating these patients. Ongoing clinical trials for people with CLL are studying ofatumumab in combination with other already approved drugs.

Lymphoma

VACCINE TREATMENT FOR FOLLICULAR LYMPHOMA

A personalized vaccine seems to slow the growth of follicular lymphoma, a common type of NHL.

A new vaccine appears to delay the return of a common type of NHL called follicular lymphoma, according to the results of a recent clinical trial. This new treatment is a vaccine called BiovaxID.

BiovaxID is made individually for each person by collecting lymphoma cells during removal of the lymph nodes. (Lymph nodes are a linked system of small bean-shaped structures throughout the body that filter out and destroy bacteria and other harmful substances.) The lymphoma cells are processed to create proteins that can be used to help the immune system kill the cancer cells. These proteins are returned to the patient in the form of a vaccine.

More than 100 people took part in this clinical trial. About 75 of them were treated with the new vaccine. The others were given a placebo (in this case, a look-alike liquid containing no active ingredient). In all of these patients, the lymphoma had been in remission (that is, all signs of the cancer had disappeared) for at least six months after they were treated with standard chemotherapy.

Although the patients are still being evaluated, early results

show that the vaccine is beneficial. It took the lymphoma nearly 14 months longer to return in those who received the vaccine than in those who did not (44 months versus nearly 31 months). The vaccine seemed to cause no serious side effects among the people who received it.

Researchers are very encouraged by these early results. However, further studies on this vaccine are still needed before it would become available as a treatment option. Doctors would like to learn whether this vaccine could be used to treat people whose lymphoma is in remission after treatment with the targeted drug rituximab. They also would like to see whether combining this vaccine with rituximab can make it even more effective.

RITUXIMAB FOR NON-HODGKIN LYMPHOMAS

Treatment with rituximab may help some people with certain lymphomas to live longer.

Rituximab is a monoclonal antibody that has been used to treat certain types of NHLs, such as diffuse large B-cell NHL (DLBCL) and follicular lymphoma. This drug zeros in on and destroys cells that have a molecule called CD20 on their surface. That molecule is found on most lymphoma cells. According to several recent clinical trials, rituximab may help stop the growth of follicular lymphoma; it may also extend the lives of those with DLBCL.

In the first study, more than 200 people who had DLBCL received the combination of rituximab and an aggressive form of treatment that included five chemotherapy drugs. Three years after treatment, about 80 percent of these people are still alive. Furthermore, in 75 percent of all patients, the lymphoma has stopped growing.

Further studies with this new combination treatment are needed to confirm these early encouraging results. Future clinical trials will also try to determine whether transplantation

is still a worthwhile addition to such effective therapy.

The second clinical trial studied rituximab in combination with two different chemotherapies to see which one was the most effective way to stop DLBCL from growing. Nearly 400 people with DLBCL took part. Before these patients joined the study, their lymphoma had returned after autologous stem cell transplant.

Half of the patients were treated with rituximab plus ifosfamide (Ifex and others), carboplatin (Paraplatin and others), and etoposide (Toposar, VePesid, and others). The other patients were treated with rituximab plus dexamethasone, cytarabine, and cisplatin (Platinol and others).

In both groups, the tumor disappeared or shrank in more than 60 percent of patients. The time it took for the tumor to continue growing was about the same in both groups as well. Researchers concluded that there seems to be no major difference between these two treatments for DLBCL.

In the third study on rituximab, researchers found that extra doses of this drug may help some people who have follicular lymphoma go longer without a relapse (return of cancer symptoms after a period of improvement). The benefits of rituximab appear to last for many years after the end of treatment.

More than 150 people with follicular lymphoma were treated with four weekly doses of rituximab. Some of those

whose lymphoma shrank or did not grow were given four additional doses of rituximab at two-month intervals, whereas others were not.

Those who were treated with the extra doses of rituximab went for two years without a relapse, compared with one year for those who were not treated with the extra doses. Eight years after treatment, 25 percent of those who received the extra doses of rituximab were still in remission.

Researchers noticed even more of a benefit to prolonged treatment in people who had not been treated before they joined the study and whose tumor shrank after 12 weeks of taking rituximab. Eight years after the study, the cancer had not returned in 45 percent of people in this group.

The researchers believe that these extra doses of rituximab may be a safe and effective way to keep follicular lymphoma from returning. However, further studies are needed to learn whether additional treatment with rituximab can extend the lives of people with follicular lymphoma.

ROMIDEPSIN FOR CUTANEOUS T-CELL LYMPHOMA

Romidepsin may be a promising way to treat people who have a type of lymphoma that usually affects the skin first.

Cutaneous T-cell lymphoma (CTCL) is a type of NHL that begins in the skin as an itchy, red rash that can thicken or form a tumor. CTCL can affect other organs as well as the lymph nodes. According to the early results of two clinical trials, a new drug called romidepsin may prove to be an effective way to treat people with this type of lymphoma.

Romidepsin belongs to a new class of cancer drugs known as histone deacetylase inhibitors. This type of drug causes a chemical change that stops tumor cells from multiplying.

More than 150 people with CTCL took part in two clinical trials to study romidepsin. The first clinical trial included

nearly 100 people whose lymphoma did not respond to or no longer responded to earlier treatment. The second clinical trial included 71 people with CTCL. All of the patients were treated intravenously with romidepsin once a week for three weeks out of every four.

Similar results were noted in both clinical trial groups. The tumor shrank in about 40 percent of the patients. Also, nearly two-thirds of all the participants with moderate to severe itching experienced significant relief with the use of romidepsin.

The most common side effects of romidepsin appeared to be nausea and fatigue. In most cases, these side effects were generally mild.

Multiple Myeloma

THALIDOMIDE COMBINATION FOR MULTIPLE MYELOMA

Combining thalidomide (Thalomid) with standard chemotherapy may be an effective way to treat older adults with multiple myeloma.

Bortezomib (Velcade) has been approved in combination with other drugs to treat people with multiple myeloma that does not or no longer responds to other treatment. Now, according to the results of a recent clinical trial, adding thalidomide to standard chemotherapy containing bortezomib may also be a worthwhile way to treat older adults who are newly diagnosed with multiple myeloma.

In Italy, more than 350 patients with multiple myeloma who were older than 65 took part in this study. About half of them received a standard chemotherapy combination called VMP—Velcade (bortezomib), melphalan (Alkeran), and prednisone. The others were treated with VMP plus thalidomide, a treatment referred to as VMPT.

The tumor disappeared in 21 percent of the people who received VMP. However, the tumor disappeared in 35 percent of those who received VMPT. In another 16 percent of those who received VMPT, the tumor shrank by at least 50 percent.

These older adults seemed to do better with lower doses of bortezomib. The lower doses reduced side effects and helped the patients stick with their treatment longer.

However, researchers did not find that one treatment was better than the other in helping to stop the tumor from growing or in extending the lives of patients. These people will be followed to find out whether the newer treatment turns out to improve survival.

On the Horizon

CNTO 328 FOR RESISTANT MULTIPLE MYELOMA

For people whose myeloma no longer responds to treatment, CNTO 328 in combination with dexamethasone may be a promising alternative.

Doctors have tried to find an effective treatment for relapsed and refractory multiple myeloma, which is myeloma that returns and stops responding to treatment. A new combination of drugs may be a step in the right direction.

CNTO 328 is a new monoclonal antibody that appears to work well with a drug called dexamethasone. Dexamethasone is used to treat leukemia and lymphoma and to reduce some side effects caused by other cancers and their treatment.

Approximately 35 people with resistant multiple myeloma took part in this very small clinical trial. They had already received at least two treatments (including bortezomib) for their myeloma. The tumor shrank in about 30 percent of patients who received CNTO 328 and dexamethasone. The cancer did not start growing again for an average of more than five months after treatment.

Researchers are encouraged by these very early results. Further clinical trials with CNTO 328 and dexamethasone are being performed.

CARFILZOMIB AND TANESPIMYCIN FOR RESISTANT MULTIPLE MYELOMA

Two new drugs appear to be promising for the treatment of relapsed and refractory multiple myeloma, although the studies are very early.

Carfilzomib and tanespimycin may benefit people who have multiple myeloma that no longer responds to other treatments, according to the results of two small clinical trials. However, these results are preliminary and will have to be confirmed in further clinical trials.

In the first study, 39 people whose myeloma resisted treatment with other drugs, including bortezomib and thalidomide, were given carfilzomib. The tumor shrank in about 25 percent of these patients. The tumor neither shrank nor grew in another 41 percent of patients who received this new drug.

Researchers plan to expand this clinical trial of carfilzomib to include 250 more people with resistant multiple myeloma. They also plan to test a higher dose of the drug to try to improve the results.

In the second study, the combination of tanespimycin plus bortezomib was given to nearly 70 people with resistant

multiple myeloma. These patients had already tried several other treatments, but their myeloma did not respond or no longer responded to them.

The tumor shrank in more than 25 percent of these patients. The results were even better in those who had never been treated with bortezomib. The tumor shrank in almost 50 percent of these patients. All of the people in this study were still alive 18 months after they were treated with tanespimycin and bortezomib.

In other clinical trials, this promising combination is being compared with bortezomib alone in people who have resistant multiple myeloma. The new treatment also is being tested in people who are newly diagnosed with multiple myeloma.

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.*