Acute Promyelocytic Leukemia

Take Control

Phases of Treatment
Available Resources & Clinical Trial Research
Reviewed by a Distinguished Medical Advisory Board
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Patient Resource Cancer Guide: Acute Promyelocytic Leukemia

Co-Editors-in-Chief

James O. Armitage, MD
Professor, Internal Medicine, Section of Hematology & Oncology,
The Nebraska Medical Center University Hospital
Past President of the American Society of Clinical Oncology
Past President of the American Society of Bone Marrow Transplantation

Charles M. Balch, MD, FACS
Professor of Surgery, University of Texas Southwestern Medical Center
Editor-in-Chief, Patient Resource LLC
Past President of the Society of Surgical Oncology

Editorial Submissions: Editorial submissions should be sent to prp@patientresource.com.

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A diagnosis of acute promyelocytic leukemia (APL) is overwhelming, and you may have many questions about the disease and its treatment. Your doctor and health care team are the best resources for helping you learn more about APL. This guide is designed to provide information that supports what your doctor has already told you and helps you think about what additional topics you’d like to discuss with your doctor.

APL is a subtype of acute myelogenous (or myeloid) leukemia (AML), one of four major types of leukemia. Leukemias are known as hematologic cancers (or hematologic malignancies) because they affect blood cells. AML is defined as acute because it develops and progresses quickly, in contrast to a chronic leukemia, which progresses more slowly. AML is myelogenous (or myeloid) because it begins in immature cells that are responsible for producing normal red blood cells, platelets, and white cells (granulocytes).

AML is not a common cancer. An estimated 13,780 cases of AML will be diagnosed in 2012, which represents a small fraction of the number of breast or prostate cancers diagnosed this year. APL is even less common, accounting for about one of every 12 to 20 cases of AML. The risk of AML is higher for older people, but the APL subtype occurs more often in people who are younger than 65 years of age.

Learning how AML develops can help you better understand APL.

Development of AML

All blood cells begin as stem cells in one of either two lines of blood cells: lymphoid or myeloid. In people with healthy blood production, both lymphoid and myeloid stem cells mature and become distinct kinds of blood cells. Lymphoid stem cells develop into white blood cells (lymphocytes), and myeloid stem cells develop into red cells, white cells (granulocytes), and platelets.

Each kind of blood cell has important functions in the body. With AML, immature white blood cells, or myeloblasts grow without control. This uncontrolled growth causes an excess build-up of malignant myeloblasts (also known as leukemia cells); this build-up is similar to how cancer cells form a tumor in other types of cancer (for example, in the breast or colon). However, with AML and other hematologic cancers, the collection of leukemia cells does not usually form a tumor. Instead, the uncontrolled growth of leukemia cells results in fewer healthy blood cells for two reasons: the leukemia cells do not become healthy blood cells and as they increase in number, they crowd out healthy blood cells. The decreased in healthy blood cells can lead to:

- Anemia, caused by a low number of red blood cells
- Reduced ability of the body to fight infection, caused by a low number of white blood cells
- Problems with blood clotting, caused by a low number of platelets
- Leukemia cells can leave the bone marrow, enter the bloodstream, and travel throughout the body, affecting other organs.

Classification of AML

While most cancers are staged according to the extent of disease and the prognosis (likelihood of cure), hematologic cancers are classified according to morphology, or

See WHAT IS APL?, page 4
the appearance of the leukemia cells when they are examined with use of a microscope. AML is classified according to the French-American-British (FAB) system into eight subtypes, referred to as M0 through M7, according to morphology and how mature the leukemia cells are at the time of diagnosis. With advances in technology, researchers have discovered that changes within the DNA structure of the leukemia cells is another important factor in classifying AML. These changes are known as chromosomal changes or cytogenetic changes. Determining the subtype of AML is important because the type of treatment and the prognosis vary according to subtype.

APL is classified as AML subtype M3 in the FAB system. In the WHO system, which is genetic based, APL is classified as APL with t(15;17)(q22;q12); PML-RARα. APL gets its name from the stage at which the leukemia cells stopped maturing. The cytogenetic changes or cytogenetic changes. Determining the subtype of AML is important because the type of treatment and the prognosis vary according to subtype.

APL is a complex disease, and it can be challenging to understand it because many terms and concepts are unfamiliar or complicated. Terms are defined at the end of articles, not only to help you as you read this guide but also to help you recognize terms used by your doctor and other members of your health care team. You are encouraged to talk to your health care team about anything you don’t understand and to ask questions to help you better prepare for treatment and recovery (Table 1).

**What is APL?** continued from Page 3

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**Definitions of Terms**

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute myelogenous (myeloid) leukemia</td>
<td>An aggressive (fast-growing) disease in which too many myeloblasts (immature white blood cells that are not lymphoblasts) are found in the bone marrow and blood.</td>
</tr>
<tr>
<td>Anemia</td>
<td>A condition in which the number of red blood cells is below normal.</td>
</tr>
<tr>
<td>Bone marrow</td>
<td>The soft, sponge-like tissue in the center of most bones. It produces white blood cells, red blood cells, and platelets.</td>
</tr>
<tr>
<td>Cytogenetic</td>
<td>The study of chromosomes and chromosomal abnormalities.</td>
</tr>
<tr>
<td>Morphology</td>
<td>The science of the form and structure of organisms (plants, animals, and other forms of life).</td>
</tr>
<tr>
<td>Myeloblasts</td>
<td>A type of immature cell that forms in the bone marrow.</td>
</tr>
<tr>
<td>Red blood cell</td>
<td>A cell that carries oxygen to all parts of the body. Also called erythrocyte and RBC.</td>
</tr>
<tr>
<td>Platelet</td>
<td>A tiny piece of a cell found in the blood that breaks off from a large cell found in the bone marrow. Platelets help wounds heal and prevent bleeding by forming blood clots. Also called thrombocyte.</td>
</tr>
<tr>
<td>Stem cell</td>
<td>A cell from which other types of cells develop. For example, blood cells develop from blood-forming stem cells.</td>
</tr>
<tr>
<td>White blood cell</td>
<td>A type of immune cell. Most white blood cells are made in the bone marrow and are found in the blood and lymph tissue. White blood cells help the body fight infections and other diseases. Granulocytes, monocytes, and lymphocytes are white blood cells. Also called leukocyte and WBC.</td>
</tr>
</tbody>
</table>

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**Table 1. Questions to Ask Your Doctor**

- How much experience do you have treating this type of cancer?
- Should I get a second opinion?
- What treatment choices do I have?
- Are there other tests that need to be done before we can decide on treatment?
- Which treatment do you recommend and why?
- What are the risks and side effects to the treatments that you recommend?
- Should we consider a stem cell transplant? When?
- What should I do to be ready for treatment?
- How long will treatment last? What will it involve? Where will it be done?
- How will treatment affect my daily activities?
- Are there any specific factors that might affect my prognosis?
- What is the outlook for my survival?
- What would we do if the treatment doesn’t work or if APL recurs (comes back)?
- What type of follow-up will I need after treatment?
Diagnosis of APL

APL is the most distinctive subtype of AML and requires specific treatment. An accurate diagnosis of APL is essential in order to begin appropriate treatment as soon as possible. But first, AML must be diagnosed, and then testing is done to determine the subtype. Your doctor probably made a preliminary or confirmed diagnosis of APL on the basis of several laboratory studies on your blood and bone marrow. In order to make a definite diagnosis of APL, the genetic abnormality that is the distinguishing feature of AML must be identified. Experts recommend, however, that treatment should not be delayed while waiting for confirmation of the diagnosis; instead, treatment should begin as soon as APL is suspected, to help avoid serious complications. If diagnostic testing indicates a different subtype of AML, treatment can be changed, with few or no harmful effects.

Diagnosis of AML
One of the first tests done to determine if a person has AML (or any type of leukemia) is a complete blood count (CBC) and differential. This test tells your doctor the number of red blood cells, white blood cells, and platelets in the bloodstream. In a person with leukemia, the numbers of these different types of blood cells are low because of the increased number of leukemia cells (also referred to as blasts). But low blood cell counts can be caused by many conditions, so additional tests are needed. Microscopic examination of a sample of fluid or tissue from your bone marrow is done to look for leukemia cells. The specialist reviewing the sample will study various characteristics of the cells to determine the subtype of AML. APL is defined by an abundance of cells that have not matured properly and have stopped their development at the promyelocyte stage.

If your doctor suspects APL, he or she will also order tests that show how long it takes for your blood to clot. These tests are very important because bleeding disorders, known as coagulopathy, are common with APL. Bleeding disorders can be serious, and treatment must be started immediately before excess bleeding becomes life-threatening.

The confirmation of a diagnosis of APL requires cytogenetic analysis, or the evaluation of chromosomes. Cytogenetic analysis can be done with several testing methods, including karyotyping, fluorescent in situ hybridization (FISH), immunostaining, and reverse transcription–polymerase chain reaction (RT-PCR). The results of RT-PCR can show the distinguishing feature of APL even when other tests cannot. RT-PCR is done on a sample of fluid or tissue obtained from the bone marrow. RT-PCR is also known as molecular testing.

What is the Distinguishing Feature of APL?
Changes in two chromosomes are the hallmark feature of APL. In nearly all cases of APL, there is a translocation of chromosomes 15 and 17, which means that some of the genes from chromosomes 15 and 17 have broken off and attached themselves to each other. The break in chromosome 15 disrupts the PML gene, or the promyelocytic leukemia gene, and the break in chromosome 17 interrupts the RARα gene, or the retinoic acid receptor alpha gene. Because of the translocation, these two genes become fused together to become an abnormal gene called PML/RARα. This abnormal gene produces a protein that stops myeloid cells from maturing past the promyelocyte stage. The translocation of chromosomes 15 and 17 is abbreviated as t(15;17).

How Does the Presence of t(15;17) Affect Treatment Options?
Since the discovery of the genetic abnormality as the distinguishing feature of APL, treatment involves the use of molecularly targeted agents. The exact ways these agents work in APL is somewhat unclear, but they seem to activate the RARα and PML genes to allow promyelocytes to mature into healthy blood cells, to cause leukemia cells to die, and to correct the genetic abnormality itself.

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**Definitions of Terms**

<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blasts</td>
<td>An immature blood cell.</td>
</tr>
<tr>
<td>CBC (complete blood count)</td>
<td>A test to check the number of red blood cells, white blood cells, and platelets in a sample of blood.</td>
</tr>
<tr>
<td>Chromosome</td>
<td>Part of a cell that contains genetic information. Except for sperm and eggs, all human cells contain 46 chromosomes.</td>
</tr>
<tr>
<td>Coagulopathy</td>
<td>Bleeding disorders in which there is a problem with the body’s blood clotting process. These disorders can lead to heavy and prolonged bleeding after an injury.</td>
</tr>
<tr>
<td>PML gene</td>
<td>Promyelocytic leukemia gene. The PML gene provides instructions for a protein that acts as a tumor suppressor, which means it prevents cells from growing and dividing too rapidly or in an uncontrolled way. Normally located on chromosome 15, APL can cause a rearrangement of genetic material between chromosomes 15 and 17, fusing part of the gene on chromosome 15 with part of another gene on chromosome 17.</td>
</tr>
<tr>
<td>PML/RARα gene</td>
<td>The abnormal gene caused by the rearrangement of chromosomes 15 and 17 and the distinguishing feature of APL. The abnormal gene produces a protein that causes myeloblasts to stop their development at the stage of the promyelocyte. As a result, excess promyelocytes accumulate in the bone marrow and normal white blood cells cannot form.</td>
</tr>
<tr>
<td>Promyelocyte</td>
<td>Immature white blood cells.</td>
</tr>
<tr>
<td>RARα gene</td>
<td>Retinoic acid receptor alpha gene, located on chromosome 17 and provides instructions for making a transcription factor called the retinoic acid receptor, alpha (RARα). In APL, this gene is disrupted and part of it becomes attached to chromosome 15.</td>
</tr>
<tr>
<td>Translocation</td>
<td>A genetic change in which a piece of one chromosome breaks off and attaches to another chromosome. Sometimes pieces from two different chromosomes will trade places with each other.</td>
</tr>
</tbody>
</table>
The identification of t(15;17) as the driver of APL and the discovery of treatment targeting this genetic abnormality transformed APL from a rapidly fatal disease to the most curable subtype of AML. Now, appropriate treatment leads to complete remission in about nine of every 10 people with newly diagnosed APL.

The success in remission and cure rates over the past decade is also due to a change in the goal of treatment. The goal was once to achieve a hematologic response, which was defined as a return to normal blood cell counts and no evidence of leukemia cells in the bone marrow. However, studies showed that relapse occurred in many people who had a complete hematologic response. Researchers believed that relapse occurred because leukemia cells were still present but at an amount that was too low to be detected with standard testing. This low level of leukemia cells is known as minimal residual disease.

Advances in technology now allow for a goal of molecular response, which is defined as no evidence of the PML/RARα gene on RT-PCR testing. Molecular response is much more precise, and complete molecular response (or remission) is associated with lower relapse rates and higher survival rates than complete hematologic response. Because of the importance of response to outcome, your doctor will monitor disease response at several points during treatment.

Components of Treatment: Chemotherapy and a Molecularly Targeted Agent

Treatment of APL involves conventional chemotherapy, such as that used for other types of cancer, as well as one of two molecularly targeted agents, or drugs that are directed at the molecular cause of APL. Conventional chemotherapy drugs are also known as cytotoxic drugs because they kill cells. Chemotherapy drugs are designed to kill cancer cells but they can also harm healthy cells. The dosing of chemotherapy drugs is carefully studied to determine the dose that has the greatest effect against cancer cells while minimizing damage to healthy cells. The type of conventional chemotherapy drug used is usually an anthracycline. Drugs in the anthracycline class are used to treat several types of cancer, especially leukemias. These drugs act by damaging the DNA in cancer (or leukemia) cells, which causes the cells to die.

The molecularly targeted agents used as part of treatment of APL are all-trans retinoic acid (ATRA), a substance that is related to vitamin A, and arsenic trioxide. Treatment with either of these drugs is often referred to as differentiation therapy because the drugs help promyelocytes to differentiate, or continue their maturation process. ATRA is the first differentiation therapy to be used for any type of cancer. Arsenic trioxide targets the fused, abnormal gene (PML/RARα gene) and acts by promoting differentiation as well as by causing leukemia cells to die.

Three Phases of Treatment

Treatment of APL is divided into three phases, each with its own goal. These phases are induction, consolidation, and maintenance therapy (Table 1). Many clinical trials have been done to evaluate the effectiveness of various drug regimens for each phase. Researchers have found that it is extremely important to use the regimen in the three phases exactly as they were used in a clinical trial; for example, the induction regimen from one trial should be used only with the consolidation and maintenance regimens used in the same trial. The exact regimen and doses used during each phase of treatment are modified according to the risk for relapse, which is determined by the white blood cell count at the time of diagnosis.

<table>
<thead>
<tr>
<th>Treatment Phase</th>
<th>Goal</th>
<th>Possible Drugs Used</th>
</tr>
</thead>
</table>
| Induction       | • Destroy as many leukemia cells as possible  
                  • Get blood cell counts back to normal levels  
                  • Eliminate all signs of the leukemia for an extended period of time | ATRA  
                  Cytarabine  
                  Daunorubicin  
                  Idarubicin |
| Consolidation   | Convert hematologic response into durable molecular response | Molecularly targeted agents  
                  Cytarabine  
                  Daunorubicin  
                  Idarubicin  
                  Mitoxantrone |
| Maintenance     | Maintain molecular remission | 6-mercaptopurine (6-MP)  
                  ATRA  
                  Methotrexate |

*Treatment drugs according to guidelines developed by the National Comprehensive Cancer Network.

See TREATMENT OF APL, page 7
Treatment of APL continued from Page 6

**Induction Therapy**

Induction therapy is started immediately after diagnosis and has three goals: kill as many leukemia cells as possible, restore blood cell counts to normal, and eliminate all signs of disease for an extended period of time. Thus, the overall goal is to induce or cause a complete hematologic response.

Induction therapy usually involves treatment with ATRA and anthracycline-based chemotherapy, either idarubicin or daunorubicin and cytarabine. Both combinations have had similar effectiveness in clinical trials. ATRA is taken orally (as a pill), and conventional chemotherapy drugs are given intravenously (through a vein in the arm). The drugs are given on specific days in a cycle and the cycle is repeated until a complete hematologic response is achieved.

Your doctor will assess the hematologic response to treatment by determining blood cell counts in a sample of bone drawn from your arm and by evaluating the appearance of blood cells in a sample of bone marrow. Testing on bone marrow is usually done 4-6 weeks after the blood cell counts have returned to normal. RT-PCR testing to monitor response is not done during induction therapy, as it usually takes a longer period of time for a molecular response to occur. Induction therapy leads to complete hematologic response in most people with APL.

During induction therapy, you may receive other types of treatment, known as supportive care. Supportive care involves treatments that prevent, control, or relieve complications and that may improve your quality of life by managing side effects. For people with APL, the supportive care measure used most often is transfusion of fresh frozen plasma and platelets, which helps prevent or control hemorrhage or other possible bleeding disorders. Bleeding complications occur most frequently in the induction therapy phase of treatment. Bleeding complications can be serious, but treatment with ATRA and transfusions has reduced the number of people with APL who are adversely affected by these complications.

**Consolidation Therapy**

The goal of consolidation therapy is to convert the hematologic response to a durable molecular response. Several combinations of ATRA may be combined with other drugs for use as consolidation therapy, or conventional chemotherapy drugs may be used. (see Table 1, page 6). Consolidation therapy may involve lower doses of drugs than those used in induction therapy and is usually given in two to four cycles.

The molecular response is assessed at the end of consolidation therapy. If molecular testing indicates a complete response (molecular remission), maintenance therapy is begun. Molecular testing after consolidation is very important, as it can help predict the likelihood of relapse. Positive molecular testing—the continued presence of t(15;17) and the PML/RARA gene—after consolidation therapy has been shown to be associated with increased risk of relapse; conversely, negative molecular testing—a complete molecular response—has been associated with long-term relapse-free survival. Additional cycles of consolidation therapy can be given if molecular remission has not occurred.

**Maintenance Therapy**

The goal of maintenance therapy is to ensure that molecular remission is maintained over time. Several studies have shown that using maintenance therapy after consolidation therapy decreases the likelihood of relapse, especially for people with a high risk of relapse. The role of maintenance therapy is unclear, however, for people with low risk of relapse. If recommended by your doctor, maintenance therapy is started only after molecular remission has been shown by RT-PCR. The regimen used during maintenance therapy is usually ATRA in some combination with a cytotoxic agent, and lower doses may be used. Maintenance therapy is usually continued for 1-2 years.

If you receive maintenance therapy, your doctor will likely want to continue to monitor your response to treatment. Once molecular testing of a bone marrow sample indicates molecular remission, further testing usually can be done on peripheral blood samples or blood drawn from your arm. Clinical guidelines recommend monitoring with molecular testing at least every 3 months for 2 years for individuals who are at high risk for relapse. Your doctor will decide what testing intervals are best for your particular case. If molecular testing is positive, it is recommended that testing be repeated within 4 weeks and that treatment for relapsed APL be started only if the second test is also positive.

**Treatment of Relapsed APL**

Relapse occurs in up to 30% of people with APL. Arsenic trioxide is an effective treatment.
for relapsed APL, according to recommendations from cancer experts.

A small number of relapses will be associated with APL in the central nervous system (CNS). Relapse with CNS disease usually occurs in people who have very high white blood cell counts. A treatment option is to deliver chemotherapy drugs directly into the CNS, which is known as intrathecal therapy. Intrathecal therapy may be done as a preventive measure in people with very high white blood cell counts after a second hematologic remission has been achieved. Your doctor can discuss with you the benefits and risks of intrathecal therapy and whether it is necessary or the best option in your particular case. Stem cell transplants, otherwise known as bone marrow transplants, were once recommended for relapsed disease. However, they are now done far less frequently because of the success achieved with ATRA and arsenic trioxide. Stem cell transplant is currently recommended after second-line therapy has produced a second molecular remission. This procedure is high risk and may not be appropriate for some people.

**Complications and Treatment Side Effects**

Your health care team will monitor you closely during your treatment to prevent and/or control complications and to manage side effects immediately. Make sure to tell your doctor or another member of your health care team if you have any symptoms of side effects. There are many drugs available to manage side effects so you can be more comfortable during treatment and have a better quality of life. In addition, some side effects can be more serious, and early recognition of these effects means they can be treated sooner.

Conventional chemotherapy drugs are associated with a range of side effects, but it is important to remember that side effects do not necessarily occur in everyone who receives the same chemotherapy drug, and that the severity of a side effect will also differ among people. The most common side effects for anthracycline drugs are nausea and vomiting, diarrhea, abdominal cramps, alopecia (hair loss), and infection. Studies have also indicated that anthracyclines can have a late effect on the heart. This side effect usually occurs months or years after treatment has stopped. Talk to your doctor about what follow-up is best to detect any cardiac effects early.

The most common side effects of ATRA are headache, nasal stuffiness, dry red skin, nausea and vomiting, and swelling of the hands and feet. The most common side effects of arsenic trioxide are nausea and vomiting, fatigue, headache, rash, and swelling of the hands and feet. In addition, arsenic trioxide can affect your heart rhythm, and the levels of essential minerals in your blood (such as potassium, magnesium, and calcium) should be monitored before and during treatment with ATRA, to ensure that they stay within a range that will help minimize the risk of this potentially serious side effect. Your doctor will probably order routine blood work and electrocardiograms to monitor any negative effects of the drug. Early interventions may help resolve any negative effects of the drug.

Both ATRA and arsenic trioxide have been associated with a less common but more serious side effect, APL differentiation syndrome, which is characterized by fever, shortness of breath, and weight gain. If these symptoms occur, chest x-rays can confirm the diagnosis of the syndrome. Treatment with a corticosteroid (dexamethasone) is effective at resolving the signs and symptoms of APL differentiation syndrome. If your white blood cell count is very high, your doctor may decide to treat you with dexamethasone to prevent APL differentiation syndrome.

### Definitions of Terms

<table>
<thead>
<tr>
<th>Term</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Anthracycline</td>
<td>A type of antibiotic that comes from certain types of Streptomyces bacteria. Anthracyclines damage the DNA in cancer cells, causing them to die.</td>
</tr>
<tr>
<td>APL differentiation syndrome</td>
<td>Formerly known as retinoic acid syndrome, this can be caused by treatment with ATRA and arsenic trioxide. Symptoms can include fluid buildup, low blood pressure and kidney damage. It can often be controlled through a corticosteroid.</td>
</tr>
<tr>
<td>Complete remission</td>
<td>The disappearance of all signs of cancer in response to treatment. This does not always mean the cancer has been cured. Also called complete response.</td>
</tr>
<tr>
<td>First-line therapy</td>
<td>Initial treatment used to reduce a cancer. First-line therapy is followed by other treatments, such as chemotherapy, radiation therapy, and hormone therapy to get rid of cancer that remains.</td>
</tr>
<tr>
<td>Fresh frozen plasma</td>
<td>The clear, yellowish, fluid part of the blood that carries the blood cells. The proteins that form blood clots are in plasma. Plasma can be frozen and preserved quickly after donation to help prevent or control bleeding disorders, which can occur with APL.</td>
</tr>
<tr>
<td>Hemorrhage</td>
<td>Loss of blood from damaged blood vessels. A hemorrhage may be internal or external, and usually involves a lot of bleeding in a short time.</td>
</tr>
<tr>
<td>Intrathecal therapy</td>
<td>Treatment in which anticancer drugs are injected into the fluid-filled space between the thin layers of tissue that cover the brain and spinal cord.</td>
</tr>
<tr>
<td>Relapse</td>
<td>The return of a disease or the signs and symptoms of a disease after a period of improvement.</td>
</tr>
<tr>
<td>Refractory</td>
<td>Failure to respond to standard treatment.</td>
</tr>
<tr>
<td>Second-line therapy</td>
<td>Treatment that is given when initial treatment (first-line therapy) doesn’t work, or stops working.</td>
</tr>
</tbody>
</table>
Clinical trials are a vital part of the cancer research process and are done to determine whether new cancer treatments are more effective than the current standard treatment.

You should learn all you can about APL so that you can better understand how the disease develops and what to expect during treatment and recovery. Because this type of leukemia is relatively rare, educational resources are limited, but some major cancer organizations offer detailed information on APL (Table 1). Online information about APL is often found in resources on AML or leukemia, but it is important to remember that APL is treated very differently from other subtypes of AML.

As with all types of cancer, a clinical trial may offer an opportunity to receive a newer treatment. Clinical trials are a vital part of the cancer research process and are done to determine whether new cancer treatments are more effective than the current standard treatment. Many of today's standard treatments for cancer are based on the results of earlier clinical trials. Individuals who take part in a clinical trial may receive the standard treatment or be among the first to receive a new treatment.

A clinical trial is an option and you may decide that it is not the best choice for you. To make an informed decision about volunteering for a clinical trial, learn as much as possible about clinical trials and weigh the advantages and disadvantages of participating.

Read about clinical trials in general as well as about specific trials for your type of cancer. Some people may think that a clinical trial is not an option for them because their doctor didn't recommend it. However, if your doctor does not ask you about clinical trials, you may raise the discussion yourself. Ask your physician and medical team about trials that may be appropriate for you.

One of the most important considerations in deciding whether to volunteer for a clinical trial is to weigh the advantages and disadvantages. Make sure you understand the details of the particular trial you're considering; asking several questions can help you in this decision-making process (Table 2). Your physician can tell you about specific benefits and risks that may be associated with the particular trial that he or she recommends.

The decision to participate in a clinical trial is a personal one and is yours to make. Many individuals with APL or other types of cancer have found it helpful to talk about the decision with family members or friends. Ask your physician or a member of your medical team about clinical trial resources available online or in your local community. In addition, a number of government and private organizations provide listings of clinical trials and information about the trials on their websites.

### Table 1. Online Resources

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<tr>
<th><strong>APL</strong></th>
<th><strong>Resources Available</strong></th>
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<tr>
<td><strong>American Cancer Society:</strong> <a href="http://www.cancer.org">www.cancer.org</a> <strong>Leukemia—Acute Myeloid (AML) Detailed Guide</strong></td>
<td><strong>Clinical Trial Searches</strong></td>
</tr>
<tr>
<td><strong>American Society of Clinical Oncology (ASCO) patient site:</strong> <a href="http://www.cancer.net">www.cancer.net</a> <strong>Leukemia—Acute Myeloid—AML</strong></td>
<td><strong>The Center for Information and Study on Clinical Research Participation:</strong> <a href="http://www.searchclinicaltrials.org">www.searchclinicaltrials.org</a> <strong>CenterWatch:</strong> <a href="http://www.centerwatch.com">www.centerwatch.com</a> <strong>Clinical Trials Search:</strong> <a href="http://www.clinicaltrialssearch.org">www.clinicaltrialssearch.org</a> <strong>Coalition of Cancer Cooperative Groups (Trial Check):</strong> <a href="http://www.cancertrialshelp.org">www.cancertrialshelp.org</a> <strong>National Cancer Institute:</strong> <a href="http://www.cancer.gov/clinicaltrials/search">www.cancer.gov/clinicaltrials/search</a> <strong>National Institutes of Health:</strong> <a href="http://www.clinicaltrials.gov">www.clinicaltrials.gov</a></td>
</tr>
</tbody>
</table>

**Table 2. Questions You Should Ask to Help You Decide Whether to Volunteer for a Clinical Trial**

- Why do the doctors who designed the trial believe that the treatment being studied may be better than the one being used now? Why may it not be better?
- What are my other options (standard treatments, other studies)? What are their advantages and disadvantages?
- What were the results of any previous studies of this treatment?
- What are the possible side effects or risks of the new treatment? What are the possible benefits?
- How will the doctor know if the treatment is working?
- How long will I be in the trial?
- What kinds of tests and treatments are involved?
- How could the trial affect my daily life?
- Will I have to travel somewhere to receive treatment? Will I be compensated for travel expenses?
- How often will I have to come to the hospital or clinic?
- Will I have to be hospitalized? If so, how often and for how long?
- What type of long-term follow-up care is part of the study?
- Will I continue to be under the care of my doctor or will I be seeing a different one (or both)?
- Are there others participating in the study I could speak to?
- Will I have to pay for any of the treatments or tests?
- What costs will my health insurance cover?

*From the websites of the National Cancer Institute ([www.cancer.gov](http://www.cancer.gov)) and the American Cancer Society ([www.cancer.org](http://www.cancer.org)).
Perseverance Through Lengthy Treatment Gave Survivor New Perspective

Carol Lauer is Executive Vice President for GfK Interscope—a marketing, research and sales consulting firm for consumer goods. In 2004, she helped found Interscope, which joined the global market research firm—GfK—in 2010. She is grateful to have lived to have these opportunities because in 1997, at the age of 37, Carol was diagnosed with acute promyelocytic leukemia (APL). After almost a year in treatment and more than 130 days in hospitals, she still remains in remission. Carol and her husband Dan Lauer have been married for 25 years and they live and work in Westport, Connecticut. Carol enjoys golf and walking her Labrador retriever, Bolt. She also volunteers for the Bloch Cancer Hotline.

When I was diagnosed with leukemia, it hit me out of the blue. I had the classic symptoms—bruising and bleeding—but was otherwise very healthy. I began to hemorrhage and was admitted to the hospital for testing. When my doctors came to talk to me after the blood tests, they told me the bad news—I had leukemia. The good news was that it was one of the best types because it was highly curable.

Looking back now after all these years, I have the benefit of perspective, but at the time I went to the hospital and my doctor told me I was really sick, it was very scary. I had a bone marrow biopsy to confirm the type of leukemia I had and was diagnosed with APL. My white blood cell count was so low that I had multiple infections and I ended up staying in the hospital for a month.

The oncologist who supervised my treatment was a confident and talented young physician. He looked me straight in the eye and said, “We know how to cure this. All you have to do is to survive the treatment.” The treatment was no walk in the park, but hearing those words on my first day of chemotherapy, I knew if I could just stay positive and get through it, I was going to be fine.

One of my coping mechanisms was to learn everything I could possibly know about my disease. I researched several options for treatment and I finally chose a center that was running an impressive clinical trial in which I could participate. They also had an entire floor of leukemia patients so the level of experience was comforting.

My treatment began with all-trans-retinoic acid (ATRA) right away—even before chemotherapy. I was then enrolled in the clinical trial and given monoclonal antibodies prior to receiving the chemotherapy—and again when I completed my treatment.

My chemotherapy—Ara-C (Cytarabine) and idarubicin (Idamycin)—began in April 1997, and that itself was no problem. It was 7 days afterward when all my cells were wiped out that I would get sick. The second round of chemotherapy was in July and my third was in August. During that final round of chemotherapy, I had fungal pneumonia and became critically ill. My hospital stay was close to 6 weeks. I really didn’t know if I was going to make it.

I was back in the hospital once again for the month of November due to a cytomegalovirus infection that was probably a result from one of the blood transfusions. Finally, I began to recover and when I completed the second round of monoclonal antibodies in January, I was finished with all of my treatment.

Throughout my therapy, I had wonderful support. My husband Dan was amazing. We lived in a different city from where I was treated, and he never missed a day seeing me in the hospital. I couldn’t work, and yet the people at the company where I was employed couldn’t have been more compassionate.

Surprisingly, one of the hardest times for me emotionally was when I knew I was basically okay. I went back to work a year after my diagnosis and the relative importance of some of the items we were trying to market seemed absurd to me in comparison to what I had been through. So I cut back my work schedule and I volunteered a great deal for my church. I used the time to contemplate what I wanted to do with my life.

In the years that followed, I didn’t change much about what I was doing. Through my experience, I did emerge, however, with a profound sense of gratitude and a better perspective. Starting my company also gave me a fresh lease on my work. I enjoy what I do, but I learned there are more important things than work. One of my oncologists told me that someday I would look back on this period of my life and it would all seem like a bad dream. It was a long time ago now for me . . . and she was right.