

No. 26 in a series providing the latest information for patients, caregivers and healthcare professionals

Highlights

- Acute promyelocytic leukemia (APL) is a unique subtype of acute myeloid leukemia (AML). APL cells have a very specific abnormality that involves chromosomes 15 and 17, leading to the formation of an abnormal fusion gene called *PML/RAR α* . This mutated gene causes many of the features of the disease.
- Promyelocytes are immature white blood cells. In APL, these cells are overproduced and accumulate in the bone marrow. Signs, symptoms and complications of APL result from the overproduction of promyelocytes and the underproduction of healthy blood cells.
- Treatment with a drug called all-*trans* retinoic acid (ATRA) targets chromosomal abnormality. Arsenic trioxide (ATO) as a single agent has also proven successful in APL treatment. The combination of ATRA and ATO has been FDA-approved for the treatment of adults with newly diagnosed low-risk disease characterized by the presence of the t(15;17) translocation or *PML/RAR α* gene expression. Other drug therapies that have increased remission and cure rates include anthracyclines and gemtuzumab ozogamicin (GO).
- Because of advances in diagnosis and treatment of this disease, APL is now considered the most curable form of adult leukemia. Cure rates of 90 percent have been reported from centers specializing in APL treatment.

About AML

Leukemia is a cancer of the marrow and blood. The four major types of leukemia are acute myeloid leukemia (AML), chronic myeloid leukemia (CML), acute lymphoblastic leukemia (ALL) and chronic lymphocytic leukemia (CLL). Each of the main types of leukemia is further classified into subtypes. Acute promyelocytic leukemia (APL) is a unique subtype of AML (approximately 600-800 new cases each year in the US).

In myeloid leukemia, a cancerous change begins in the bone marrow, in a stem cell that normally would develop into a blood cell—a red blood cell, some type of white blood cell or a platelet.

Acute promyelocytic leukemia (APL) gets its name from immature white blood cells called promyelocytes that accumulate in the marrow and crowd out other healthy cells. These cells are myeloblasts that have stopped maturing. (Healthy myeloblasts turn into myelocytes and eventually become mature white blood cells called granulocytes: neutrophils, basophils, and eosinophils).

APL cells have a specific chromosome abnormality that involves a translocation of chromosome 15 and chromosome 17, abbreviated as t(15;17), which creates an abnormal fusion gene called *PML/RAR α* . This abnormality is present in about 95 percent of patients diagnosed with APL.

The World Health Organization (WHO) classification is the main system used to classify AML into subtypes. The WHO developed this system to include chromosomal abnormalities and genetic mutations, which are known to affect prognosis (the likely outcome of the disease). These genetic factors help provide both doctor and patient with more reliable information about the patient's prognosis and also help predict the patient's response to treatment. Information about a person's AML subtype helps the doctor recommend a specific treatment plan. The WHO classification is usually revised every eight years. The revised 2016 classification incorporates

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new scientific and clinical information (see **Table 1**, below). **For the full WHO AML classification, please visit www.LLS.org/booklets to see the free booklet *Acute Myeloid Leukemia*.**

Table 1. World Health Organization AML Classification

Acute Myeloid Leukemia (AML) and Related Neoplasms		
AML with Recurrent Genetic Abnormalities	Inversion and/or Translocation	Gene
AML with	t(8;21)(q22;q22.1)1	<i>RUNX1-RUNX1T1</i>
AML with	inv(16)(p13.1q22) or t(16;16)(p13.1;q22)	<i>CBFB-MYH11</i>
Acute promyelocytic leukemia (APL)	t(15;17)	<i>PML-RARα</i>
AML with	t(9;11)(p21.3;q23.3)	<i>MLLT3-KMT2A</i>
AML with	t(6;9)(p23;q34.1)	<i>DEK-NUP214</i>
AML with	inv(3)(q21.3q26.2) or t(3;3)(q21.3;q26.2)	<i>GATA2, MECOM(EV11)</i>
AML (megakaryoblastic) with	t(1;22)(p13.3;q13.3)	<i>RBM15-MKL1</i>
AML with	N/A	mutated <i>NPM1</i>
AML with	N/A	Biallelic mutations of <i>CEBPA</i>

Source: World Health Organization (WHO) classification. WHO categorizes AML into groups based on recent discoveries in cytogenetic and clinical features of AML. Abbreviations: t, a translocation between chromosomes; inv, an inversion in a chromosome; q, the long arm of a chromosome (the lower half); p, the short arm of a chromosome (the upper half).

Treatment for APL differs from all other AML treatments. Because of advances in diagnosis and treatment, APL has been transformed from the most fatal to the most curable form of acute leukemia in adults.

This Fact Sheet provides current information about diagnosis, treatment, and new treatments being investigated in clinical trials, along with support resources.

Causes and Incidence

Most APL cells have a specific chromosome abnormality involving a balanced translocation (swapping) between chromosomes 15 and 17 t(15;17), resulting in the abnormal fusion gene *PML/RARα*. This abnormality is a distinguishing feature of APL that causes the symptoms of the disease; it is also a key target of treatment.

Among adults over age 20, APL represents approximately 7 percent of AML cases. There are approximately 1,100 new cases of APL each year in the United States. According to data from the National

Cancer Institute (NCI) SEER (Surveillance, Epidemiology, and End Results Program) registry, for the period from 2013 to 2017, the age-adjusted annual incidence of newly diagnosed cases was 0.34 per 100,000 persons—about 1 case per 294,000 persons. During that period, the median age of APL diagnosis was 51 years. The median age of AML diagnosis is 68 years. Hispanics have the highest incidence rate of APL, while Asian and Pacific Islanders have the lowest rate.

With current treatment, APL has become one of the most curable types of acute leukemia. People with APL who receive treatment often have a normal or near-normal quality of life.

Please visit www.LLS.org/booklets to see the free LLS booklet *Understanding Genetics*.

Signs and Symptoms

It is common for people with APL to feel a loss of well-being because of the underproduction of normal blood cells as well as with the accumulation of leukemic cells in the bone marrow.

Common signs and symptoms of APL include

- Pale complexion, caused by anemia
- Signs of bleeding caused by a very low platelet count, including
 - Black-and-blue marks or bruises occurring for no reason or because of a minor injury
 - The appearance of pinhead-sized red spots on the skin, called “petechiae”
 - Prolonged bleeding from minor cuts
- Fatigue
- Mild fever
- Swollen gums
- Frequent minor infections
- Loss of appetite
- Weight loss
- Discomfort in bones or joints
- Enlarged spleen and liver
- Neurologic symptoms such as headache, confusion and visual changes (associated with APL that involves the central nervous system [CNS])

Bleeding. A low platelet count and low amounts of clotting factors predispose patients to bleeding. In addition, patients with high white blood cell (WBC) counts at diagnosis are at increased risk for bleeding. Bleeding in the brain or lungs is serious and can be fatal. This kind of serious bleeding is usually preceded by minor bleeding, such as nosebleeds, blood in the urine, or bruises.

Infection. Severe infection may be present at the time of diagnosis for some patients, due to low white blood cell counts. Infection may become more common and often more serious during treatment, when the bone marrow is completely suppressed.

Diagnosis

When a patient is suspected of having leukemia, obtaining an accurate diagnosis of the type of leukemia is important. The exact diagnosis helps the doctor estimate how the disease will progress and determine the appropriate course of treatment. Some of the tests used for making a diagnosis may also be repeated during and after therapy to measure the effects of treatment.

Blood and Bone Marrow Tests. A change in the number and appearance of blood cells helps the doctor make an accurate diagnosis. APL cells may look similar to normal immature white cells. However, their development is incomplete.

Blood samples are generally taken from a vein in the patient's arm. Samples of marrow cells are obtained by bone marrow aspiration and biopsy. The cells from the blood and marrow samples are examined under a microscope.

Cytogenetic Tests. "Karyotyping" and "fluorescence in situ hybridization (FISH)" are tests used to identify certain changes in chromosomes and genes. "Polymerase chain reaction (PCR)" is a test used to study cells in a sample of blood or marrow to look for certain changes in the structure or function of genes. A diagnosis of APL requires demonstration of the t(15;17) translocation or presence of the *PML/RAR α* gene.

In APL, promyelocytes (immature white cells) are overproduced and accumulate in the bone marrow. Promyelocytes are unable to mature, which leads to a significant reduction of white blood cells and prevents the development of other normal blood cells. Signs, symptoms and complications of APL result

from the overproduction of promyelocytes and the underproduction of healthy blood cells.

Doctors use the results of blood and bone marrow tests to identify abnormal APL cells. A prompt diagnosis of APL is vital because appropriate treatment must be started immediately in order to avoid the serious and potentially life-threatening complications (especially bleeding in the brain or lungs) associated with the disease.

Coagulation Tests. When APL is suspected, doctors may order "coagulation status" tests along with other laboratory tests and imaging scans, to help assess the clotting status of the patient's blood. Coagulation refers to the blood's ability to form clots when necessary. This process is impaired in APL patients because patients have fewer platelets and clotting factors in the blood. Coagulation disorders can lead to heavy and prolonged bleeding after an injury. Coagulation tests help prevent or diagnose serious conditions such as deep-vein thrombosis, pulmonary embolism and strokes. See the *Glossary* on page 9 for more information on these terms.

Please visit www.LLS.org/booklets to see the free LLS booklet *Understanding Lab and Imaging Tests*.

Treatment Planning

Treatment decisions are based on the patient's age, general health and APL risk classification.

APL is classified into the two following categories of risk, based on the patient's white blood cell count at diagnosis:

- Low risk—white blood cell (WBC) count of 10,000 white blood cells per microliter of blood (10,000/microliter) or less
- High risk—WBC count greater than 10,000/microliter

Typically, patients with low-risk disease are treated with less intensive regimens than those used for patients at high risk. Nonetheless, every patient's medical situation is different and should be evaluated individually by an experienced hematologist-oncologist, a doctor who specializes in treating blood cancers. It is important for you and members of your medical team to discuss all treatment options, including treatments being studied in clinical trials.

Please visit www.LLS.org/booklets to see the free LLS publication *Choosing a Blood Cancer Specialist or Treatment Center*.

Treatment

Treatment goals for APL are

- To cure the disease
- To control symptoms
- To decrease the risk of complications

Treatment of APL is divided into three phases, each with its own objectives. The treatment phases of APL are (1) induction, (2) consolidation, and (3) maintenance therapy.

Induction therapy starts immediately after diagnosis and has three goals:

- To target the translocation t(15;17) that causes the abnormal fusion gene *PML/RAR α* and to kill as many APL cells as possible
- To bring blood cell counts to normal or near-normal levels
- To decrease or eliminate all APL-related symptoms for an extended time

When these goals are accomplished, the result is called a complete hematologic response (CHR).

Consolidation therapy follows induction. Its main goal is to convert the complete hematologic response into a molecular response (or remission). A molecular response is defined as “no evidence of the *PML/RAR α* gene by PCR testing.” Additional cycles of consolidation therapy can be administered if molecular response is not achieved.

Maintenance therapy aims to ensure that molecular response is maintained over time. Maintenance therapy may use lower doses of drugs or drug combinations than those used in previous treatment. This phase of therapy usually lasts 1 to 2 years. During maintenance therapy, the treatment team will continue to monitor the patient’s response at regular intervals. The frequency of testing will depend on the patient’s individual case. Maintenance therapy is not required in all cases of APL. Patients with low risk APL who achieve molecular response are not required to have maintenance therapy.

Obtaining a complete molecular response is the main goal of APL treatment, which is being adopted as a study objective in current clinical trials for the disease.

Drug Therapy

Although highly curable with current therapies, APL is still linked to a significant incidence of early death (during the initial course of treatment) due to characteristic bleeding complications associated with the disease. After doctors have examined a patient’s blood and bone marrow tests, if a diagnosis of APL is suspected, treatment should be started immediately. This is because of potential bleeding into the brain or lungs, a possible fatal complication of APL. For this reason, treatment with drug therapy should be started even before the presence of the translocation t(15;17) or the *PML/RAR α* gene has been confirmed.

All-trans retinoic acid (ATRA)—Also called tretinoin (Vesanoid®), this treatment is given orally. This drug, a vitamin A derivative, has become a standard component of induction therapy for APL. ATRA targets and eliminates the *PML/RAR α* abnormality. This treatment causes a marked decrease in the concentration of leukemic blast cells in the marrow, and a remission frequently follows.

Used alone, ATRA can induce a short-term remission in at least 80 percent of patients. Treatment with ATRA must be followed by or given with arsenic trioxide (ATO) and/or chemotherapy to ensure that the remission will be long-lasting. ATRA often minimizes the side effects of chemotherapy because blood cell counts may be improved and the number of leukemic cells may be decreased at the time that chemotherapy is started.

Arsenic Trioxide (ATO)—The brand name of this drug is Trisenox® and it is given by slow intravenous (IV) injection. Studies have shown that the combination of ATO and ATRA is superior to the former standard of care treatment which combined ATRA with anthracyclines (chemotherapy) for patients with low-risk APL. The possibility of receiving optimal treatment with ATO and ATRA without the addition of chemotherapy drugs may be particularly beneficial to children and older patients who are more susceptible to the toxic effects of anthracycline exposure.

The combination of arsenic trioxide with tretinoin has been FDA-approved for the treatment of adults with newly diagnosed low-risk APL characterized by the presence of the t(15;17) translocation or *PML/RAR α* gene expression. Sometimes ATO is administered daily, and other times it is given only on certain days with rest days in between as part of what is called a “treatment cycle.”

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ATO is also the recommended therapy for patients who do not achieve a molecular response at the end of consolidation or who relapse later in the treatment. For patients with high-risk APL, combinations of ATO, ATRA, and anthracyclines are commonly used.

Anthracyclines—These chemotherapy agents interact directly with the DNA in the nucleus of leukemic cells, interfering with cancer cell survival. There are several types of anthracyclines; daunorubicin (Cerubidine®) and idarubicin (Idamycin®) are the drugs most commonly used in the treatment of APL, typically in combination with ATRA. The initial remission rate of APL patients treated with ATRA and an anthracycline, such as idarubicin, is about 90 percent. The combination of ATRA and idarubicin is known as AIDA.

Antimetabolites—These chemotherapy agents prevent leukemic cells from growing by substituting for their DNA or RNA building blocks. For people with high-risk APL (white cell counts greater than 10,000/microliter at diagnosis), the antimetabolite cytarabine (Cytosar-U®) may be added to induction or consolidation regimens. Cytarabine (also called Ara-C or cytosine arabinoside) is sometimes given with ATRA and an anthracycline.

Table 2. Common Side Effects Associated with APL Treatment

Medication	Side Effect
All- <i>trans</i> -retinoic acid (ATRA) – Tretinoin	Differentiation syndrome Pseudotumor cerebri High triglycerides (type of fat) High white blood cell counts Changes in liver function
Arsenic trioxide (ATO)	Differentiation syndrome QT interval prolongation Irregular heartbeat Changes in liver function Electrolyte imbalance Nausea/vomiting Peripheral neuropathy High white blood cell counts
Anthracyclines (idarubicin/daunorubicin)	Low blood counts Damage to the heart Irregular heartbeat Liver function tests Nausea/vomiting Mouth sores Hair loss Skin rash
Antimetabolites (cytarabine)	Headache Low blood counts Nausea and vomiting Mouth sores

See the section below, *APL Treatment Side Effects and Supportive Care* and the *Glossary* on page 9 for definitions of some of the terms listed in this table.

APL Treatment Side Effects and Supportive Care

APL treatment can cause unwanted and unpleasant side effects (see **Table 2** above). Side effects may be caused by the drug type and dose used, length of treatment and the patient’s overall health. Management of side effects is important. If you have any concerns about your side effects, talk to your doctor to get help. Most side effects are temporary and resolve when treatment is completed. However, patients with APL may need specific kinds of supportive care.

Differentiation Syndrome. Treatment for APL is often associated with a variety of symptoms and abnormal conditions, including fluid retention, labored breathing, fever, fluid accumulation around the heart or lungs, and episodes of low blood pressure. This group of symptoms is known as “differentiation syndrome.” Patients should be closely monitored for the development of these symptoms because differentiation syndrome, along with hemorrhage (bleeding), are the leading causes of death

during induction therapy. Differentiation syndrome is often caused by all-*trans*-retinoic acid (ATRA) or arsenic trioxide (ATO) treatment. It occurs in approximately 15 to 25 percent of patients during their first treatment. Not everyone gets this syndrome. Patients with a white blood count higher than 10,000/microliter are at a higher risk for this condition. Early recognition and the prompt start of corticosteroid therapy with dexamethasone or prednisone are essential to manage this potential complication.

Pseudotumor cerebri. This disorder, also known as intracranial hypertension, is related to high pressure in the brain that causes signs and symptoms of a brain tumor – hence the term “pseudo” (or false) tumor. It happens when the fluid that surrounds the spinal cord and the brain—called cerebrospinal fluid—accumulates abnormally in the brain, causing pressure and pain. Pseudotumor cerebri can be a rare side effect of ATRA therapy and is most often observed in children and adolescents. The main symptom of this disorder is headache. Pseudotumor cerebri can be treated with the use of painkillers, glaucoma drugs that might reduce production of cerebrospinal fluid, steroids to reduce inflammation, and/or diuretic medication to reduce fluid buildup. Sometimes the temporary discontinuation of ATRA is necessary.

High White Blood Cell (WBC) Count. Elevated WBC counts, also known as “hyperleukocytosis,” is a frequent side effect that occurs in APL patients receiving ATO and/or ATRA therapy. A WBC count higher than 10,000/microliter is considered elevated. This side effect is generally managed with medications such as hydroxyurea, gemtuzumab ozogamicin (Mylotarg®) and anthracyclines (idarubicin and daunorubicin).

Changes in Liver Function. Liver enzymes can become elevated as a result of therapy with ATO, ATRA and/or gemtuzumab ozogamicin. Liver function should be routinely monitored during APL treatment. If needed, therapy can be temporarily discontinued until liver function returns to normal.

QT Interval Prolongation. The use of arsenic trioxide (ATO) can affect electrolyte levels. Electrolytes are essential minerals in the blood such as potassium, magnesium, and calcium. Electrolyte imbalance can cause a heart rhythm disorder known as “QT interval prolongation.” This disorder causes a fast heartbeat that may lead to sudden fainting or seizures. Electrolytes

should be monitored before and during APL treatment to ensure that they stay within a normal reference range. The doctors on your treatment team may order routine blood work and electrocardiograms to monitor any negative effects of ATO or other drugs.

Bleeding. The ability to form blood clots (a process called “coagulation”) is impaired in APL patients because they have decreased numbers of platelets and clotting factors. This condition, also known as “coagulopathy,” can cause a tendency toward prolonged or excessive bleeding that may occur spontaneously, after an injury, or during medical or dental procedures. It is important to screen for this problem with specific blood tests as part of the initial workup of newly diagnosed patients as well as before any invasive procedure. When coagulopathy symptoms are present, patients are supported with transfusion therapy that contains platelets or fresh frozen plasma. Plasma is the liquid part of the blood that carries the blood cells. The proteins that form blood clots are found in the plasma. Plasma can be frozen and preserved after blood donation to help prevent and control bleeding disorders, which frequently occur in APL.

Other side effects caused by APL treatment include nausea, vomiting, electrolyte imbalance, peripheral neuropathy and veno-occlusive disease (VOD). Please see the *Glossary* on page 9 for definitions of some of these terms.

Childhood APL

Approximately 4 to 8 percent of all AML cases in children are APL. In children and adolescents, APL shares many features with APL in adults. Pediatric patients are, however, more likely to present with high-risk features, including an elevated white blood cell count at diagnosis.

Typically, pediatric patients are treated with the same or very similar regimens as those used for adult patients. The standard approach for children with APL is induction therapy followed by consolidation and then maintenance therapy. Treatment outcomes are similar in adult and pediatric patients, although recent studies have indicated that very young children may be at higher risk of relapse. Both pediatric and adult APL rarely spreads to the brain or spinal cord (the central nervous system); however, CNS APL is more common in both groups who have relapsed APL. In CNS treatment, chemotherapy into the spinal canal (called “intrathecal chemotherapy”) may be given (see *Central Nervous System (CNS) APL* on page 7).

The successful use of the drug combination ATRA and ATO holds great promise in the treatment of pediatric APL. The possibility of receiving optimal treatment with these two agents without the addition of chemotherapy drugs may be of particular benefit to pediatric patients, who are extremely sensitive to the toxic effects of chemotherapy. Chemotherapy in children may cause organ damage, delayed growth, and other health problems later in life. However, treatment with ATRA can, particularly in children, cause side effects such as pseudotumor cerebri. (See *Pseudotumor cerebri* on page 6 for more information on pseudotumor cerebri.)

Children who receive intensive chemotherapy including anthracyclines (such as doxorubicin, daunorubicin and idarubicin) are at an increased risk of developing heart problems and should receive ongoing monitoring of cardiac function. Anthracyclines may cause abnormal heartbeat, weakness of the heart muscle and congestive heart failure. Ongoing monitoring of cardiac function in children is critical. Periodic examination of kidney function and auditory exams are also recommended. Children with APL should have their care coordinated by pediatric hematology-oncology specialists and be treated in cancer centers or hospitals with appropriate supportive care facilities and services. Chemotherapy-free regimens are currently under study in clinical trials for treatment of children with APL (see *Treatments Undergoing Investigation* in the next column).

Please visit www.LLS.org/booklets to see *Learning & Living with Cancer: Advocating for your child's educational needs for information about planning for your child's entry or return to school following diagnosis and treatment*. Visit www.LLS.org/FamilyWorkbook to find additional information about long-term and late effects in the chapter, *Beyond Treatment*.

Central Nervous System (CNS) APL

A small number of patients with APL develop disease in their cerebrospinal fluid, the watery fluid that bathes the brain and the spinal cord. Symptoms of CNS APL are headaches and various neurologic manifestations, such as confusion and visual changes. CNS APL is most often diagnosed in patients thought to be in remission. It is associated with patients who have a high white blood cell count (greater than 10,000/microliter) at diagnosis and/or those who have had a previous CNS hemorrhage, because the risk for CNS relapse is higher in these

patients. This type of APL is treated with “intrathecal therapy,” which involves spinal taps and chemotherapy injections into the spinal fluid.

Treatment for Patients with Relapsed or Refractory APL

Despite high remission rates after induction therapy, treatment resistance and relapse do occur in some patients, just as they do in some patients with other types of AML. Therefore, long-term follow-up care of patients in remission is required to identify those who are cured and those who may require further therapy.

Arsenic trioxide (Trisenox®), given intravenously, is FDA-approved for induction of remission and consolidation in patients with APL who are refractory to or have relapsed after retinoid and anthracycline chemotherapy, and whose APL is characterized by the presence of the t(15;17) translocation or *PML/RAR α* gene expression.

Stem Cell Transplantation. A small number of APL patients have persistent minimal residual disease (MRD) at the end of consolidation therapy. These patients may benefit from arsenic trioxide (Trisenox®) or GO (gemtuzumab ozogamicin), followed by autologous or allogeneic stem cell transplantation.

Please visit www.LLS.org/booklets to see the free LLS booklet *Blood and Marrow Stem Cell Transplantation* for more information.

Treatments Undergoing Investigation

New approaches to APL treatment are being studied in clinical trials that hold the promise of increasing the rate of remission, reducing deaths and treatment-related toxicity. Many clinical trials are being supported by LLS research programs.

Clinical Trials. Every new drug or treatment regimen goes through a series of studies called “clinical trials” before it becomes part of standard therapy. Clinical trials are carefully designed and reviewed by expert clinicians, researchers and patient advocates to ensure safety and scientific accuracy. Participation in a carefully conducted clinical trial may be the best available treatment option and should be considered each time treatment is discussed with the doctor. Patient participation in past clinical trials has resulted in the therapies we have today.

LLS Information Specialists, available at (800) 955-4572, offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. When appropriate, patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.

Research Approaches. Numerous approaches are under study in clinical trials for the treatment of patients with APL.

Oral arsenic trioxide (ATO)—An oral version of ATO (in clinical trials) that patients could give to themselves would be much easier than the current treatment method. ATO is now given in intravenous (IV) form in a hospital or center, and is inconvenient, requiring frequent patient visits for administration and maintenance. In addition, studies have reported an observed increase in the rate of central venous catheter-associated thrombosis (blood clot in a blood vessel) in APL patients, compared with other leukemia patients. For these reasons, an oral version of ATO has been developed and is being studied in clinical trials where it has shown promising results and fewer toxic side effects than ATO administered intravenously.

Gemtuzumab ozogamicin (GO) (Mylotarg®)—This medication is under study for the treatment of APL in combination with other agents. Gemtuzumab ozogamicin (GO) is an antibody-drug conjugate that pairs the antitumor antibiotic calicheamicin to an anti-CD33 antibody and is currently FDA-approved for the treatment of adults with newly diagnosed AML whose tumors express the CD33 antigen; it is also approved for pediatric patients who are at least 2 years old who have CD33-positive AML, and who have experienced a relapse or who have not responded to initial treatment. GO is administered via IV through a slow injection.

Tamibarotene—Tamibarotene is under study as a single agent and in combination with other drugs. This drug is a synthetic retinoid recently approved in Japan for the treatment of relapsed or refractory APL. Early studies suggest that this agent may be a more powerful inducer of APL cell differentiation than ATRA.

Chemotherapy-Free Regimen for Pediatric Patients—The combination of ATRA and ATO, without the inclusion of chemotherapy agents, is being further investigated

in children with newly diagnosed APL by the Children's Oncology Group and other cooperative oncology groups worldwide. This may not only reduce children's exposure to the toxic effects of anthracyclines (chemotherapies) and reduce long-term side effects but may also increase treatment efficacy in a patient group with higher prevalence of high-risk disease.

Patient Care Strategy Study to Decrease Patient Mortality in APL—This study, sponsored by the Eastern Cooperative Oncology Group (ECOG), is evaluating a new patient care strategy that aims to reduce the APL mortality rate associated with the immediate period after diagnosis. This strategy includes the use of simplified patient guidelines along with APL expert support to enable patients to have access to appropriate and timely medical care.

We encourage you to contact an Information Specialist at (800) 955-4572 for more information about specific treatments under study in clinical trials.

Long-Term Follow-up and Treatment Outcomes

Long-term follow-up is an important aspect of care for APL patients to prevent and treat any complications caused by the disease or its treatment. It is recommended that patients be monitored for molecular relapse every 3 months for 2 years after the end of consolidation treatment. This can be done through PCR testing using peripheral blood samples. If blood tests indicate the cancer has returned, a bone marrow biopsy will be done to confirm a relapse. It is important that patients also be routinely monitored for late and long-term treatment side effects that can affect their well-being and quality of life.

The likely outcome of a disease—the prognosis—depends on many factors. Each patient's risk factors affect his or her prognosis and are evaluated individually. While APL in adults is very successfully treated, some studies suggest that cure rates may be lower than reported when this disease is not treated in specialized centers by healthcare professionals with experience in treating APL.

Because of advances in diagnostic techniques and modern treatments, APL is now considered the most curable subtype of AML in adults, with complete remission rates of 90 percent following treatment and cure rates of approximately 80 percent reported in clinical trials.

Feedback. Please visit www.LLS.org/PublicationFeedback to provide suggestions about this booklet.

Acknowledgement

The Leukemia & Lymphoma Society appreciates the review of this material by

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Glossary

Anthracycline. Type of chemotherapy that kills cancer cells by destroying the cancer's DNA, preventing the cancer cells from dividing and proliferating.

Deep Vein Thrombosis (DVT). The formation of a blood clot in a deep vein of the leg or lower pelvis. Symptoms may include pain, swelling, warmth and redness in the affected area.

Electrolytes. Electrolytes are chemicals in the body that regulate important physiological functions. Examples of electrolytes are sodium, chloride, magnesium, potassium and calcium. Electrolyte imbalance causes a variety of symptoms that can be severe. This condition can be caused by loss of body fluids through prolonged vomiting, diarrhea, sweating or high fever. Arsenic trioxide (ATO) can cause electrolyte imbalance in APL patients.

Peripheral Neuropathy. A condition of the nervous system that can cause pain, numbness, tingling, swelling or muscle weakness in different parts of the body, particularly the extremities. Peripheral neuropathy may be caused by cancer or cancer treatment; for example, patients being treated with the drug ATO can experience this side effect. Peripheral neuropathy usually begins in the hands or feet and it can get better after treatment, or it can get worse over time.

Pulmonary Embolism. A pulmonary embolism is a blockage in an artery of the lungs. An embolism can be caused by blood clots or other substances, such as fat globules, infected tissue, or cancer cells.

Stroke. Loss of blood flow to part of the brain, which causes damage to brain tissue. Strokes are caused by blood clots and broken blood vessels in the brain. Symptoms include dizziness, numbness, weakness on one side of the body, and problems with talking, writing, or understanding language.

Translocation. A genetic change in which a piece of one chromosome breaks off and attaches to another chromosome. In a balanced translocation, pieces of two different chromosomes break off and "trade places" with each other. This happens in APL and is expressed as t(15;17).

Triglycerides. The major form of fat stored by the body. Triglycerides come from the food we eat and are also produced naturally by the body. Elevated triglyceride levels are considered a risk factor for hardening of the arteries, a condition known as atherosclerosis. Some drugs for cancer treatment, such as the medication ATRA used in APL therapy, can affect triglyceride levels.

Veno-occlusive Disease (VOD). Veno-occlusive disease (VOD) occurs when the small blood vessels that lead into the liver or are inside the liver become blocked. In APL patients, VOD can be caused by the administration of the medication gemtuzumab ozogamicin (GO).

We're Here to Help

LLS is the world's largest voluntary health organization dedicated to funding blood cancer research, education and patient services. LLS has chapters throughout the United States and in Canada. To find the chapter nearest to you, visit our website at www.LLS.org/chapterfind or contact:

The Leukemia & Lymphoma Society
3 International Drive, Suite 200
Rye Brook, NY 10573

Contact an Information Specialist at (800) 955-4572
Email: infocenter@LLS.org

LLS offers free information and services for patients and families touched by blood cancers. The following entries list various resources available to you. Use this information to learn more, to ask questions, and to make the most of your healthcare team.

Consult with an Information Specialist. Information Specialists are master's level oncology social workers, nurses and health educators. They offer up-to-date disease, treatment and support information. Language services (interpreting and translation) are available. Please contact our Information Specialists or visit our website for more information.

- Call: (800) 955-4572 (Monday through Friday, from 9 am to 9 pm ET)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org/InformationSpecialists
- Visit: www.LLS.org/InformationSpecialists

Clinical Trials (Research Studies). Research is ongoing to develop new treatment options for patients. LLS offers help for patients and caregivers in understanding, identifying and accessing clinical trials. When appropriate, patients and caregivers can work with Clinical Trial Nurse Navigators who will help find clinical trials and personally assist them throughout the entire clinical trial process. Visit www.LLS.org/CTSC for more information.

Free Information Booklets. LLS offers free education and support booklets that can either be read online or ordered. Please visit www.LLS.org/booklets for more information.

LLS Health Manager™ App. This free mobile app helps you manage your health by tracking side effects, medication, food and hydration, questions for your doctor, and more. Export the information you've tracked in a calendar format and share it with your doctor. You can also set up reminders to take medications, hydrate, and eat. Visit www.LLS.org/HealthManager to download for free.

Financial Assistance. LLS offers financial support including insurance premium and medication co-pay assistance, as well as travel and other needs, to eligible individuals with blood cancer. For more information, please

- Call: (877) 557-2672
- Visit: www.LLS.org/finances

Información en Español. (LLS information in Spanish). Please visit www.LLS.org/espanol for more information.

Telephone/Web Education Programs. LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit www.LLS.org/programs for more information.

LLS Community. The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Visit www.LLS.org/community to join.

One-on-One Nutrition Consultations. Access free one-on-one nutrition consultations provided by a registered dietitian who has experience in oncology nutrition. Dietitians assist callers with information about healthy eating strategies, side effect management and survivorship nutrition. They also provide additional nutrition resources. Please visit www.LLS.org/nutrition to schedule a consultation or for more information.

Weekly Online Chats. Moderated online chats can provide support and help cancer patients to reach out and share information. Please visit www.LLS.org/chat for more information.

Podcast. *The Bloodline with LLS* is here to remind you that after a diagnosis comes hope. Listen in as patients, caregivers, advocates, doctors and other healthcare professionals discuss diagnosis, treatment options, quality-of-life concerns, treatment side effects, doctor-patient communication and other important survivorship topics. Visit www.LLS.org/TheBloodline for more information and to subscribe.

LLS Chapters. LLS offers support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection Program* (a peer-to-peer support program), in-person support groups, and other great resources. For more information about these programs or to contact your chapter, please

- Call: (800) 955-4572
- Visit: www.LLS.org/ChapterFind

Other Helpful Organizations. LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. Please visit www.LLS.org/ResourceDirectory for more information.

Advocacy. The LLS Office of Public Policy (OPP) engages volunteers in advocating for policies and laws that encourage the development of new treatments and improve access to quality medical care. For more information, please

- Call: (800) 955-4572
- Visit: www.LLS.org/advocacy

People Suffering from Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time—for example, if you feel depressed every day for a 2-week period. For more information, please

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov. Enter “depression” in the search box

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