
Treatment for Acute Promyelocytic Leukaemia (APL)

A Guide for
Patients

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

Acute promyelocytic leukaemia (APL, sometimes referred to as ‘AML M3’) is one of the subtypes of acute myeloid leukaemia (AML).

Although this type of blood cancer is highly aggressive, there is an outstanding rate of remission if it is diagnosed and treated early. The drugs used for treating APL are ATRA (all trans retinoic acids), anthracycline-based chemotherapy (usually Idarubicin and Mitoxantrone) and Arsenic Trioxide (ATO).

This booklet was compiled by one of our medical writers Saloua Najjam, PhD. and peer reviewed by one of our medical professionals who is specialised in leukaemia therapy, Dr Steven Knapper, University Hospital of Wales, Cardiff. We are also grateful to Julie Quigley, AML patient reviewer, for her valuable contribution.

If you would like any information on the sources used for this booklet, please email communications@leukaemiacare.org.uk for a list of references.

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About Leukaemia Care

Leukaemia Care is a national charity dedicated to ensuring that people affected by blood cancer have access to the right information, advice and support.

Our services

Helpline

Our helpline is available 9.00am - 10.00pm on weekdays and 9.00am - 12.30pm on Saturdays. If you need someone to talk to, call **08088 010 444**

Nurse service

We have two trained nurses on hand to answer your questions and offer advice and support, whether it be through emailing **nurse@leukaemicare.org.uk**, over the phone on **08088 010 444** or via LiveChat.

Patient Information Booklets

We have a number of patient information booklets like this available to anyone who has been affected by a blood cancer. A full list of titles – both disease specific and general information titles – can be found on our

website at **www.leukaemicare.org.uk/resources/filter-by-resource-type/information-booklets**

Support Groups

Our nationwide support groups are a chance to meet and talk to other people who are going through a similar experience. For more information about a support group local to your area, go to **www.leukaemicare.org.uk/our-support-groups**

Buddy Support

We offer one-to-one phone support with volunteers who have had blood cancer themselves or been affected by it in some way. You can speak to someone who knows what you are going through. For more information on how to get a buddy call **08088 010 444** or email **care@leukaemicare.org.uk**

Online Forum

Our online forum, www.healthunlocked.com/leukaemia-care, is a place for people to ask questions anonymously or to join in the discussion with other people in a similar situation.

Patient and carer conferences

Our nationwide conferences provide an opportunity to ask questions and listen to patient speakers and medical professionals who can provide valuable information and support.

Website

You can access up-to-date information on our website, www.leukaemicare.org.uk, as well as speak to one of our care advisers on our online support service, LiveChat (9am-5pm weekdays).

Campaigning and Advocacy

Leukaemia Care is involved in campaigning for patient well-being, NHS funding and drug and treatment availability. If you would like an update on any of the work we are currently doing or want to know how to get involved, email advocacy@leukaemicare.org.uk

Patient magazine

Our free quarterly magazine includes inspirational patient and carer stories as well as informative articles by medical professionals. To subscribe go to www.leukaemicare.org.uk/resources/subscribe-to-journey-magazine

What are the drugs for APL?

The drugs used most frequently in APL treatment are ATRA (All Trans Retinoic Acid), anthracyclines and arsenic trioxide (ATO).

All-trans retinoic acid (ATRA)

ATRA, known as Tretinoin (trade name is Vesanoid) is the acid form of vitamin A, used with chemotherapy in induction of remission in patients with confirmed acute promyelocytic leukaemia (APL).

Anthracyclines

These are members of a family of chemotherapy drugs that are also antibiotics. They prevent cell division by disrupting the replication of DNA.

Examples of anthracyclines that are used along with ATRA to treat APL are Idarubicin and Mitoxantrone.

For further information on this, please view one of our patient information booklets titled **ATRA and Anthracycline-based chemotherapy**.

Arsenic trioxide (ATO)

Marketed under the name of Trisenox, this is a 'non-chemotherapy' antineoplastic drug. ATO is gradually being used more often, in combination with ATRA, in the treatment in APL. Currently, it is used mainly for the treatment of patients who relapse, or where there is a sub-optimal response to front line ATRA/anthracycline treatment. Older, frailer patients, or patients with pre-existing medical problems such as heart disease, may be treated first-line with ATO/ATRA instead of ATRA/anthracycline.



What receives these drugs?

Patients who have been diagnosed with APL will receive the combination of the drugs mentioned previously, depending on how the treatment progresses.

Because APL is highly aggressive, if you are suspected to be suffering from it, your doctor will often need to commence you on ATRA treatment before final confirmation of the diagnosis. This would not be harmful, but on the contrary, will potentially shorten the time you are at risk from the complications of the disease such as bleeding and blood clots, thus improving the survival rate.

At present, APL has a cure rate of more than 90%; mainly thanks to all continuing progress that has been made with clinical trial studies to test and improve APL treatment.

To read more about symptoms and diagnosis of this blood cancer, please refer to one of our patient information booklet titled **Acute Promyelocytic Leukaemia**. You can order our booklets by contacting the patient services team on **08088 010 444** or **care@leukaemiacare.org.uk**

How are these drugs administered?

APL treatment will start as soon as routine clinical pre-assessments, including full blood count assessments (FBC) which generally show low number of white and red blood cells and platelets, and a bone marrow aspirate and biopsy, are done.

After being diagnosed with APL, you will have to stay in hospital and most patients will combination 'induction' therapy with ATRA and anthracycline chemotherapy (Idarubicin). This is the standard first-line therapy and is generally followed by three courses of consolidation therapy (ATRA with either Idarubicin or Mitoxantrone). ATRA in this combination therapy targets the faulty gene PML/RARA, which is responsible for stopping promyelocytes from maturing into normal white blood cells.

Patients who don't achieve with ATRA and anthracycline-based chemotherapy, will generally

receive second line therapy using Arsenic trioxide (ATO) and ATRA. Arsenic trioxide is also be given to patients who have relapsed APL.

ATRA

ATRA is manufactured under the name of Vesanoid and it is given to APL patients as yellow/brown capsules for oral administration. ATRA is taken twice-daily. With this treatment, effective contraception must be used for at least one month before and after treatment as well as during treatment.

Anthracyclines

Idarubicin and Mitoxantrone are two the Anthracyclines that will be administered alongside ATRA, through an intravenous infusion. An intravenous infusion is when liquid substances are directly injected into a vein. Both drugs are well tolerated, but both cause myelosuppression (lowering of the blood count lasting days to

How are these drugs administered? (cont.)

weeks which may require red cell and platelet transfusion and causes an increased risk of infection). A small number of patients develop dose-related cardiotoxicity (toxic to the heart).

Because of how aggressive APL is, supportive therapy is given during the first month to prevent early death, primarily due to the risks of abnormal bleeding and clotting. Supportive therapy includes platelet transfusions (if the number of platelets) and transfusions of blood clotting factors in the form of fresh frozen plasma (FFP) or fibrinogen infusions (fibrinogen is an important protein involved in blood clotting).

Arsenic trioxide (ATO)

This drug is administered by intravenous infusion. A small proportion of patients receiving ATO develop abnormalities of electrical conduction in the heart. For this reason, during

ATO treatment, there is regular monitoring of the ECG (electrocardiogram - heart tracing) and close monitoring of blood chemical levels (particularly potassium and magnesium which are important for electrical conduction in the heart). Sometimes it is necessary to also give potassium and/or magnesium supplements.



What are the side effects of these drugs?

Chemotherapy is the most commonly prescribed anti-cancer treatment but, while you are having it, you are vulnerable to infections. Symptoms of infection like fever, shivering, discomfort when you pass urine, sweats, sore throat, diarrhoea, cough or breathlessness should be reported to your doctor or nurse.

Everyone will experience different side effects from induction chemotherapy and although you may experience them occasionally, it is important to report them so that they can be monitored and treated. You will have a routine blood test to monitor the effects of the chemotherapy.

Side effects of ATRA

ATRA is not a chemotherapy drug; however, it may have some side effects:

- Headache
- Dry eyes, skin and mouth

- Bone pain
- Feeling sick (nausea)

Differentiation Syndrome (previously called 'ATRA syndrome')

This happens in a relatively small proportion of patients but requires immediate treatment. It is associated with both ATRA and ATO treatment. It comes with a number of symptoms like fever, difficulty in breathing, accumulation of fluid in the space that surrounds the lungs, an excess of white blood cells, low blood pressure (hypotension), excess of fluid in cavities and tissues, weight gain, hepatic, renal and multi-organ failure. It is treated with steroids (usually dexamethasone) and sometimes it is necessary to temporarily stop the ATRA treatment until symptoms subside.

Side effects of anthracyclines

- Loss of appetite, nausea, vomiting, diarrhoea
- Inflammation of the mucous membrane of the mouth (stomatitis), dry mouth
- Excess of fluid in cavities and tissues (oedema)
- Difficulty in breathing (dyspnoea)
- Dizziness, temporary loss of consciousness due to low blood pressure (syncope), malaise
- Infection, fever (pyrexia)
- Blood disorders including low red blood cells count (anaemia), low white blood cells count (leucopenia), and low platelets count (thrombocytopenia)
- Partial or complete hair loss (alopecia)
- Superficial reddening of the

skin (erythema) and rash, severe itching (pruritus)

- Injection-site reactions including phlebitis (inflammation of the walls of a vein)

There is a risk of 'extravasation' with the administration of Mitoxantrone. Extravasation is when a chemotherapy medication or other drug leaks outside the vein onto and/or into the skin, causing a reaction. If you experience any signs of extravasation, such as burning, pain, pruritus, erythema, swelling, blue discolouration, or ulceration, the administration of the drug should be stopped immediately.

Side effects of arsenic trioxide (ATO)

Common side effects:

- Diarrhoea
- Differentiation syndrome with

What are the side effects of these drugs? (cont.)

symptoms like fever, difficulty in breathing (dyspnoea), weight gain, accumulation of fluid in the space that surrounds the lungs or the heart (pleural or pericardial effusions). This can be treated with high dose steroids

- Excess of glucose in the blood (hyperglycaemia), deficiency of potassium in the blood (hypokalaemia)
- Irregular heartbeats, musculoskeletal pain, tingling or pins and needles (paraesthesia)
- Fatigue

Uncommon side effects:

- Abdominal pain
- Abnormal rapid heartbeat (tachycardia)
- Inflammation of the blood vessel (vasculitis)
- Low blood pressure

(hypotension)

- Excess of fluid in cavities and tissues (oedema)
- Inflammation of the walls of air sacs in the lungs (pneumonitis)
- Seizures
- Renal (kidney) failure
- Blurred vision
- Rash



What happens if these drugs do not work for me?

APL is cured in more than 90% of patients who have been diagnosed on time and treated without delay.

The majority of patients who do not respond optimally to first-line ATRA/anthracycline therapy, or who relapse at a later point, make a good response to second-line ATO/ATRA treatment with long-term cure. In these circumstances it is sometimes necessary to consider a stem cell transplant (formerly known as 'bone marrow transplant') either using the patient's own harvested stem cells (autologous transplant) or from a matched donor (allogeneic transplant).

Your consultant will be able to discuss these treatments, and circumstances in which they might become necessary.

Leukaemia Care offers nationwide support groups for people affected by a diagnosis of a blood or lymphatic cancer. Visit www.leukaemiacare.org.uk, or call **08088 010 444**, to find out more and to find a group near you.

Glossary

Acute

Disease or condition that arrives suddenly and progress quickly.

Antibiotics

Drugs that destroy harmful bacteria.

Antineoplastic drug

A drug that inhibits or prevents the growth and spread of tumours or malignant cells.

Coagulation cascade

The chain reaction of chemical reactions that involves a number of proteins in the formation of a blood clot.

Chemotherapy

Type of therapy that uses chemical substances, especially in the treatment of cancer and that have cytotoxic activity (toxic to cancer cells).

Corticosteroids

Medicines used to treat inflammation. In APL they are used in the treatment of

differentiation syndrome.

DNA

Deoxyribonucleic acid, a self-replicating material within each cell that carries the genetic information.

Erythema

Superficial reddening of the skin, usually in patches.

Intravenous Infusion

Administration of fluids into a vein using a steel needle or plastic catheter.

Leukaemia

A cancer of the blood with many different subtypes. Some forms are acute (develop quickly) and others are chronic (develop slowly). Leukaemia is an excess number of abnormal cells in the blood, usually white blood cells, which stop the bone marrow working properly.

Pruritus

Itching

Promyelocytes

There are cells in the bone marrow at an intermediate stage of development between myeloblasts and mature granulocytes (neutrophils) of the blood.

Remission

When no leukaemia cells are found in the blood or bone marrow and the bone marrow is working normally after the treatment is finished.

Useful contacts and further support

There are a number of helpful sources to support you during your diagnosis, treatment and beyond, including:

- Your haematologist and healthcare team
- Your family and friends
- Your psychologist (ask your haematologist or CNS for a referral)
- Reliable online sources, such as Leukaemia Care
- Charitable organisations

There are a number of organisations, including ourselves, who provide expert advice and information.

Leukaemia Care

We are a charity dedicated to supporting anyone affected by the diagnosis of any blood cancer.

We provide emotional support through a range of support services including a helpline, patient and carer conferences, support group, informative website, one-to-one buddy service and high-quality patient information. We also have a nurse on our help line for any medical queries relating to your diagnosis.

Helpline: **08088 010 444**
www.leukaemiacare.org.uk
care@leukaemiacare.org.uk

Bloodwise

Bloodwise is the leading charity into the research of blood cancers. They offer support to patients, their family and friends through patient services.

020 7504 2200
www.bloodwise.org.uk

Cancer Research UK

Cancer Research UK is a leading charity dedicated to cancer research.

0808 800 4040
www.cancerresearchuk.org

Macmillan

Macmillan provides free practical, medical and financial support for people facing cancer.

0808 808 0000
www.macmillan.org.uk

Maggie's Centres

Maggie's offers free practical, emotional and social support to people with cancer and their families and friends.

0300 123 1801
www.maggiescentres.org

Citizens Advice Bureau (CAB)

Offers advice on benefits and financial assistance.

08444 111 444
www.adviceguide.org.uk

Leukaemia Care is a national charity dedicated to providing information, advice and support to anyone affected by a blood cancer.

Around 34,000 new cases of blood cancer are diagnosed in the UK each year. We are here to support you, whether you're a patient, carer or family member.

Want to talk?

Helpline: **08088 010 444**

(free from landlines and all major mobile networks)

Office Line: **01905 755977**

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