
ATRA and anthracycline based therapy for Acute Myeloid Leukaemia (AML)

**A Guide for
Patients**

Introduction

In this booklet, we describe the use of ATRA (All-trans retinoic acid), known as Tretinoin (Vesanoid®) along with the chemotherapy drugs idarubicin and mitoxantrone.

Booklet 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 leukaemia patient, Bruce Bain, for their 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 **support@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 is ATRA and anthracycline based therapy?

All-trans retinoic acid (ATRA), known as Tretinoin (trade name is Vesanoid®) is the acid form of vitamin A, which is used with chemotherapy for induction of remission in patients with confirmed acute promyelocytic leukaemia (APL). The combination of ATRA with anthracycline chemotherapy is sometimes referred to as the 'AIDA' treatment regimen.

ATRA + idarubicin and ATRA + mitoxantrone are both combination treatments, which include the chemotherapy drugs idarubicin or mitoxantrone along with ATRA and are used to induce remission in patients with acute promyelocytic leukaemia (APL).

The sooner treatment starts, the better the outcome.

Idarubicin

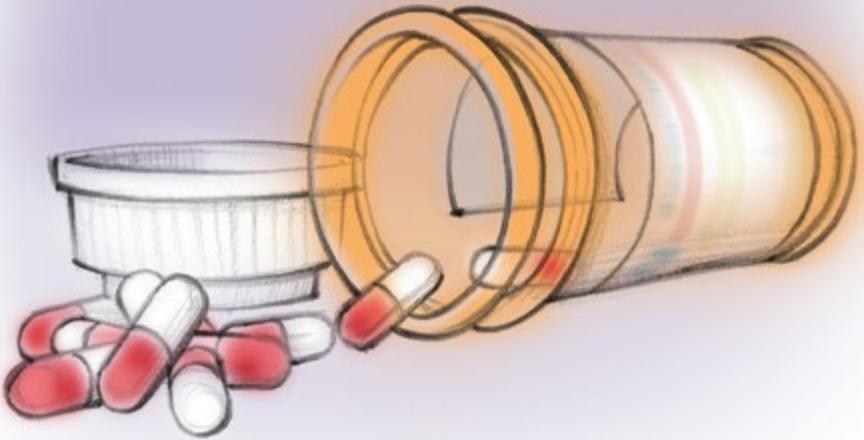
Idarubicin may also be known as Zavedos.

This drug can be supplied as capsules or powder in a solution for injection and licensed for the treatment of haematological cancers such as leukaemia, lymphoma and multiple myeloma. In the treatment of APL, it is almost always administered intravenously. This means it put through a tube or needle directly

into the vein.

Mitoxantrone

Like idarubicin, mitoxantrone is a chemotherapy drug. It is a dark blue solution which comes in vials containing different amounts. It is given as an intravenous infusion, meaning that the solution is delivered via a vein.



Who receives ATRA and anthracycline based therapy?

You may be offered this type of treatment if you have been diagnosed as having APL.

Acute promyelocytic leukaemia (APL) is a subtype of acute myeloid leukaemia (AML), which is considered as a rare blood cancer.

Acute myeloid leukaemia is a fast-developing blood cancer disease that requires immediate treatment.

Chemotherapy is the most commonly used anti-cancer treatment, although other types of cancer treatments like targeted therapies using monoclonal antibodies, stem cell transplants, radiotherapy, supportive therapy and steroids may sometimes be used.

When you see your consultant regarding your treatment, they will explain to you whether you will receive chemotherapy or another type of treatment, or a combination of the two.

No pre-medication is required with these two combination treatments. However, your treating

doctor may prescribe some drugs, only during the induction period, to prevent tumour lysis syndrome and/or nausea.

What is Tumour Lysis syndrome?

Tumour Lysis syndrome is a complication that is sometimes caused by chemotherapy drugs. Chemotherapy uses cytotoxic (anti-cancer) drugs to kill cancer cells. As cells break down, they release a product called uric acid which is normally cleared by the kidneys. When lots of these cells are broken down very quickly, the kidneys cannot cope with the increase of this uric acid. This can then lead to an imbalance of chemicals in the blood which can in turn cause problems for the kidneys or the heart.



How is ATRA and anthracycline based therapy administered?

Before treatment

Before starting ATRA and anthracycline treatment, your doctor will make some clinical pre-assessments such as:

- To confirm with you the diagnosis of APL and discuss the use of combination therapy.
- To record your weight and height.
- To run a full blood count (FBC).
- To run liver function tests (LFTs) and a measure of kidney function (U&Es).
- To remove a small amount of liquid bone marrow for analysis.
- For female patients of childbearing potential, a pregnancy test will be carried out to rule out pregnancy prior to starting therapy.
- To record your heart's rhythm, using an electrocardiogram (ECG) test to check that your heart is working normally.
- To explain the availability of facilities for management of

complications.

These tests will be performed to ensure that you are medically fit to start your treatment. Some chemotherapy drugs can have an effect on your heart.

As a patient, you will need to read and sign a consent form regarding the receipt of verbal and written information in relation to your disease, treatment and potential side effects.

APL patients will be treated in the hospital for induction and consolidation chemotherapy, spaced by a short time at home. Consolidation treatment may sometimes be given on an 'outpatient basis' such as in a Haematology Day Unit. As this is a combination treatment, your consultant will be deciding on what suits you best regarding the dose and frequency of given drugs.

How ATRA and idarubicin are administered during induction chemotherapy?

ATRA:

From day one of treatment, you will be given ATRA orally usually twice-daily for a period of up to 60 days. Sometimes ATRA treatment will be started even before the doctors have fully confirmed the diagnosis of APL, while the results of tests are pending, as it is important not to delay this important therapy.

Idarubicin:

Your clinical nurse will administer intravenously a concentrated solution of idarubicin (this is called an IV bolus), via a fast running drip. During the first cycle of treatment, this is usually given on four 'non-consecutive days' e.g., days two, four, six and eight of treatment. If your white blood cell count is high, the first dose of idarubicin may be given on the same day as starting the ATRA.

Following your induction chemotherapy, you will be monitored daily. Blood tests will be taken. When your blood results are recovering, you may be sent home for a short period. This will depend on whether there is any active infection and on how you are feeling. A repeat bone marrow test will usually be performed at this point to confirm that you have achieved remission.

After a short rest at home, you will need to return to hospital for consolidation therapy. There are three consolidation chemotherapy cycles that usually follow induction chemotherapy, and which consist of giving ATRA along with idarubicin and mitoxantrone.

How is ATRA and anthracycline based therapy administered? (cont.)

How are ATRA and Idarubicin administered during the first consolidation phase?

ATRA:

You will be given ATRA capsules twice-daily for 15 consecutive days.

Idarubicin:

You will usually receive a lower dose of idarubicin (in comparison to that given in induction treatment) for four consecutive days. This is usually done intravenously.

How are ATRA and Mitoxantrone administered during the second consolidation phase?

ATRA:

Again, during this second phase of consolidation, ATRA capsules are given orally for 15 consecutive days.

Mitoxantrone:

You usually receive an intravenous infusion of mitoxantrone (a dark blue solution) for five consecutive days.

How are ATRA and Idarubicin administered during the third (final) consolidation phase?

ATRA:

As for the first two consolidation phases, ATRA capsules are usually given for 15 consecutive days.

Idarubicin:

During this last consolidation phase, idarubicin is usually given intravenously as a single dose on the first day of treatment. This dose is the equivalent of one of the doses received during induction chemotherapy.

What are the side effects of ATRA and anthracycline based therapy?

Any renal (kidney) and/or hepatic (liver) impairment you have before or during the treatment with idarubicin and mitoxantrone will be taken into consideration by your treating doctor and the doses of these drugs may be lowered by up to 50% as a result. Renal impairment is measured and confirmed by the level of creatinine in the blood or urine. Liver function is measured by the level of bilirubin and liver enzymes in the blood.

ATRA may have some side effects which include:

- Headaches
- Dry eyes, skin and mouth
- Bone pain
- Feeling sick (nausea)

A small proportion of patients with APL who receive ATRA along with chemotherapy drugs develop what we call differentiation syndrome (previously sometimes called 'ATRA syndrome').

What is ATRA syndrome?

ATRA syndrome is a significant complication that APL patients may develop during the first 10 days of treatment with ATRA during induction chemotherapy. It is more likely to happen if the white blood cell count is very high.

What are the symptoms of ATRA syndrome?

ATRA syndrome may be suspected and confirmed if you have a fever for unexplained reasons, you gain weight, you show an inflammation in the lungs (called acute respiratory distress syndrome) that is associated with fluid gathering in the tissue and space around the air sacs of the lung (this is called interstitial pulmonary infiltrates) and leakage of fluid from the vascular system into tissue fluid (called capillary leak syndrome).

What are the side effects of ATRA and anthracycline based therapy? (cont.)

How is ATRA syndrome treated?

As soon as ATRA syndrome is suspected, your doctor may need to stop ATRA administration for a period of time and will usually commence steroid therapy (e.g. intravenous injection of dexamethasone) until all symptoms are gone. Your doctor may also start diuretic treatment with furosemide to treat the excess of fluid in the body (Oedema).

Idarubicin as a cytotoxic drug has more serious side effects, which could be grouped into common, uncommon or rare ones.

Common side effects

- **Discolouration of urine into red or pink for the first few times following your injections** - This is something you shouldn't worry about, but please talk to your haematology team if this bothers you in any way.
- **Bruising or bleeding** - The platelet number is reduced by this treatment. Platelets are involved in the formation of blood clot. You should inform your doctor or nurse if you have any unexplained bruising or bleeding, such as nosebleeds, bloodspots or rashes on the skin, or bleeding gums. You may need a platelet transfusion.
- **Anaemia (low number of red blood cells)** - While having this treatment you are likely to become anaemic. This may make you feel tired and breathless. Let your nurse know if these symptoms are a problem, so your doctor may decide on giving a blood (red cell) transfusion
- **Neutropenia (low white blood cell count)** - This will increase the risk of infections in the aftermath of chemotherapy until the blood count recovers. The medical team will advise you on special precautions to help reduce the risk of infection

during the 'neutropenic period'.

- **Nausea and vomiting (feeling sick)** - This will generally be prevented by your doctor giving you anti-sickness tablets.
- **Mucositis** - this is inflammation of the lining of your mouth and gut due to chemotherapy.
- **Fatigue and Lethargy** - Chemotherapy can make you feel tired and lacking in energy. Your nurse will help you on how to manage it during and after chemotherapy.

Uncommon side effects

- **Extravasation** - This is accidental leakage from the vein into the surrounding tissue. This usually happens when the medication passes from the blood vessel into the tissue around the blood vessels and beyond. Depending on the substance, extravasation could result in anything from a very mild skin reaction to

severe necrosis. If extravasation happens, your nurse will contact a senior member of the medical team such as your cancer doctor and follow local protocol for dealing with cytotoxic extraversion.

- **Alopecia** - Partial or complete hair loss. This is a temporary side effect as your hair will grow back when your treatment is completed.
- **Diarrhoea** - This could be easily treated by your doctor giving you anti-diarrhoea medicine.

Rare side effects

- **Irregular heartbeats** - If you experience these, it should be reported to your nurse or doctor immediately.
- **Liver toxicity** - This may affect your liver function tests, but this usually returns to normal once your treatment is completed.

Mitoxantrone as a cytotoxic drug

What are the side effects of ATRA and anthracycline based therapy? (cont.)

has a very similar side effect profile to idarubicin and may give the following side effects:

- Diarrhoea, constipation, nausea
- Partial or complete hair loss
- Heavy menstrual periods
- Feeling tired and depressed

Serious and potentially life-threatening side effects

In a small proportion of patient's chemotherapy can result in very severe side effects which may rarely result in death. The medical team caring for you will discuss the risk of these side effects with you in more details.

Sex and contraception

It is recommended that you protect yourself and your partner from the toxicity of chemotherapy drugs. During sexual intercourse, while you are having the course of chemotherapy, you or your partner should wear a condom.

Chemotherapy is dangerous to unborn babies and this will also protect you and your partner from any chemotherapy drugs that may be present in semen or in the vagina. You should inform your doctor immediately if you suspect that you may be pregnant.

Fertility

This chemotherapy may affect your ability to have children and this will be discussed with you before the start of the treatment.

What happens if ATRA and anthracycline based therapy doesn't work for me?

ATRA and anthracycline chemotherapy works well in the majority of newly-diagnosed APL patients. In the event that APL does not respond well to ATRA and anthracycline chemotherapy, or in the event that the APL should return at a later point (relapse), the combination of ATRA with Arsenic trioxide (ATO) may be offered as alternative therapy.

Overall, following the outcome of your treatment with ATRA, your consultant is the best person to discuss with and to decide on the next step to take.

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

Anthracyclines

A member of a family of chemotherapy drugs that are also antibiotics, so called 'antitumour antibiotics'. They prevent cell division by disrupting the structure of DNA. They are derived from certain types of Streptomyces bacteria.

Antineoplastic

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

Bilirubin

An orange-yellow substance made during the normal breakdown of red blood cells.

Chemotherapy

A type of cancer treatment that uses one or more drugs to kill growing cancer cells.

Creatinine

A chemical waste molecule that is generated from muscle metabolism – the blood creatinine level is useful as a measure of kidney function.

Extravasation

When a chemotherapy medication or other drug leaks outside the vein onto or into the skin, causing a reaction.

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

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.leukaemicare.org.uk
support@leukaemicare.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**

www.leukaemiacare.org.uk

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Registered charity
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YOUR Blood Cancer Charity

