
MidAC for Acute Myeloid Leukaemia (AML)

**A Guide for
Patients**

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

Mitoxantrone and cytarabine (also known as cytosine arabinoside or Ara-C) are two licensed drugs that can be used together as a combination therapy (named MidAC) for the treatment of acute myeloid leukaemia (AML).

For more information, or if you are unsure about anything, please talk to your consultant, haematologist, clinical nurse specialist or hospital pharmacist.

This booklet was compiled by Saloua Najjam and peer reviewed by one of our medical professionals. This booklet has then been updated by our Patient

Information Writer, Isabelle Leach, and reviewed by Dr Steve Knapper. We are also grateful to Ian Micklewright and his valuable contribution as a patient reviewer.

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 – 5:00pm Monday – Friday and 7:00pm – 10:00pm on Thursdays and Fridays. If you need someone to talk to, call **08088 010 444**.

Alternatively, you can send a message via WhatsApp on **07500068065** on weekdays 9:00am – 5:00pm.

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** or over the phone on **08088 010 444**.

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/support-and-information/help-and-resources/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/support-and-information/support-for-you/find-a-support-group/**

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@leukaemiacare.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.

Webinars

Our webinars provide an opportunity to ask questions and listen to patient speakers and medical professionals who can provide valuable information and support. For information on upcoming webinars, go to **www.leukaemiacare.org.uk/support-and-information/support-for-you/onlinewebinars/**

Website

You can access up-to-date information on our website, **www.leukaemiacare.org.uk**.

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@leukaemiacare.org.uk**

Patient magazine

Our magazine includes inspirational patient and carer stories as well as informative articles by medical professionals: **www.leukaemiacare.org.uk/communication-preferences/**

What is MidAC?

MidAC is the abbreviation for the combination of mitoxantrone and cytarabine for the treatment of patients with acute myeloid leukaemia (AML).

Mitoxantrone is an anthraquinone chemotherapy drug similar in structure to an anthracycline. Like anthracyclines, mitoxantrone is an antimetabolite which interferes with the synthesis of DNA, and prevents growth or reproduction of cells, including the leukaemia cells. It was developed in the 1970s as a safer alternative to anthracyclines which can be damaging to the heart (cardiotoxic).

Apart from the treatment of patients with AML, mitoxantrone can also be used on its own or in combination with other drugs for the treatment of patients with chronic myeloid leukaemia (CML), non-Hodgkin's lymphoma and the advanced stages of breast and prostate cancer. Mitoxantrone also suppresses the immune system and is used to treat relapsing multiple sclerosis. Its ability to damage

the DNA of cells becomes more effective when it is combined with other antimetabolites such as etoposide, doxorubicin and cytarabine.

Cytarabine (also known as cytosine arabinoside or Ara-C) is also an antimetabolite chemotherapy drug and works by blocking the functions of DNA and stopping the growth of leukaemia cells in the body. It is commonly used to treat blood cancers especially AML, acute lymphoblastic leukaemia (ALL) and non-Hodgkin's lymphoma.

Three doses of cytarabine are generally used in leukaemia chemotherapy regimens:

- High-dose cytarabine of 2000 to 3000mg/m² of body surface area, twice daily over three or five days.
- Intermediate-dose cytarabine of 1000 to 2000mg/m², twice daily over three or six days.
- Low-dose cytarabine of a regimen of either 20mg given twice daily for 10 days subcutaneously, or a similar

dosage of 20mg/m² for 10 days.

While mitoxantrone is used less frequently than doxorubicin or daunorubicin, it continues to be an important component for the treatment of AML as it is understood to be less cardiotoxic than anthracyclines; however, more evidence is needed.

For more information about the causes, symptoms, diagnosis and clinical features of AML, please see our information booklet on the website at www.leukaemiacare.org.uk

Who receives MidAC?

The most common use of MidAC is as a consolidation regimen in AML patients who are already in remission.

However, other patients who can receive MidAC as either induction or consolidation treatment are:

- Patients with AML who require induction and consolidation treatment.
- Patients with refractory or relapsed AML.
- Patients with relapsed acute lymphoblastic leukaemia.

How is MidAC administered?

Before starting treatment with MidAC, the following clinical assessments are carried out:

- Measurements of your weight and height.
- Full blood count, liver function tests, and urea/electrolyte levels to measure the function of your kidneys (these tests will be performed before each treatment cycle).
- A pregnancy test for all female patients of child-bearing age.
- Electrocardiogram (ECG) to check that your heart is working normally.
- Bone marrow biopsy to check how many leukaemia cells are in your bone marrow.

You will then need to read and sign a consent form summarising the receipt of verbal and written information about your disease, treatment and potential side effects.

- Mitoxantrone ($10\text{mg}/\text{m}^2$) is given daily over an hour on days one to five.

- Cytarabine ($1000\text{mg}/\text{m}^2$) is given twice daily over two hours on days one to three.

Mitoxantrone and cytarabine are both given as intravenous infusions where diluted solutions of the drugs are administered directly into a vein over a period of time.

In order for both infusions to be delivered easily, you will normally have a venous access device fitted. This allows delivery of the infusions directly into a vein without the need of a new needle puncture every time you have treatment. The device will also allow you to receive nutrients or have blood samples taken when required.

Types of devices that are commonly used include subcutaneously tunnelled central catheters (Hickman-type devices) or peripherally inserted central catheters (PICC lines). They can remain in place for months and can be used throughout your treatment.

How is MidAC administered? (cont.)

A tunnelled central catheter insertion requires a minor surgical procedure usually under local anaesthetic. A silicone catheter is surgically implanted into the large vein which drains into your heart. The catheter is tunnelled under the skin, so that the opening to the catheter is sticking out of the skin on your chest.

Having a PICC line inserted means that the catheter usually goes in the arm. A needle is used to put the PICC into a vein in the arm, and the catheter is threaded via the needle so that it ends in a large vein in the chest near your heart. The needle is then removed. Having a PICC line will not require you to have any surgery. The external portion of the PICC line is taped to the arm and covered with a transparent dressing.

Your doctor or nurse will be able to provide you with more information about these devices.

In general, you receive treatment with MidAC in hospital and you

may have to stay in until your blood counts recover. However, if you are feeling well you may be able to go home for periods and be monitored closely as an outpatient until your blood counts recover. This usually takes about four weeks, but this may be different for everyone.

What are the side effects of MidAC?

Everyone will experience separate side effects with MidAC treatment as each patient is different. Common side effects that you may experience during treatment with MidAC are:

- **Nausea and vomiting:** The severity of these side effects will vary from person to person. An injection of anti-sickness medication can be given before your treatment. You will also be given some anti-sickness tablets to take home.
- **Sore mouth:** You may develop a sore mouth and mouth ulcers. Analgesic, anti-bacterial mouthwashes and topical ointments may help. To help prevent oral infections, brush your teeth at least twice a day and drink plenty of fluids.
- **Bone marrow suppression:** Your bone marrow is where your blood cells (red blood cells, white blood cells, and platelets) are produced to replace those that naturally die. Chemotherapy interferes with this process and the number of the cells in your blood can become lower than normal. This

can lead to the following:

- **Anaemia due to low red blood cell levels.** This may make you feel tired and breathless. Let your doctor know if these symptoms become a problem, you may need a blood transfusion.
- **Bruising or mild bleeding due to low platelet levels.** Platelets are a type of blood cell which help to stop bleeding. Let your doctor know if you have any unexplained bruising or bleeding such as nosebleeds, bloodspots or rashes on the skin, or bleeding gums.
- **Increased risk of infection due to low levels of white blood cells.** If you have any signs of infection, such as fever, shivering, breathlessness, a sore throat, cough, needing to pass urine often, diarrhoea or a temperature of 37.8°C or above, contact your doctor or nurse straight away as it is important to treat it as soon as possible.

What are the side effects of MidAC? (cont.)

- **Hair loss:** Your hair may thin and you may lose your hair. The hair falls out gradually 10 to 14 days following your first course of treatment. The time scale varies from person to person. However, hair loss is normally temporary and your hair will start to grow back after chemotherapy ends.
- **Fatigue:** You may feel tired and lacking in energy. It is often worse towards the end of treatment and for some weeks after the treatment has finished. Take rests when necessary. Gentle exercise such as walking can help.
- **Injection site reaction:** Inflammation with pain, redness or swelling of the veins or skin at the injection site.
- **Diarrhoea and constipation:** Let your medical team know as they will be able to offer you medications for treatment and to prevent further complications, for example if your bottom becomes sore. In the meantime, try using unscented wet wipes instead of toilet paper as this can provide some relief.
- **Discoloured urine:** Your urine may become green in colour due to the mitoxantrone. This is normal and temporary, and not a cause for concern.
- **Cardiomyopathy, which is disease of the heart muscle:** Cardiac examinations are recommended after a total dose of 160mg/m² of mitoxantrone.
- **Cytarabine syndrome:** This is an allergic reaction which manifests itself by fever, skin rash, nausea, muscle and bone pain and conjunctivitis. It usually occurs six to 12 hours after administration of cytarabine. This will not affect everyone and will disappear soon after the cytarabine infusions stop. The use of steroids has been shown to be helpful in preventing or treating this syndrome.

Fertility, pregnancy and breastfeeding

There are no human studies of the effect of MidAC on fertility. However, both mitoxantrone and cytarabine increase the risk of

absence of menstruation and lack of sperm in the semen. Please discuss with your doctor the option of preserving your eggs or sperm before treatment begins.

Cytarabine and mitoxantrone can cause chromosome damage in the sperm, and men undergoing MidAC treatment are advised to use a reliable contraceptive method during, and at least six months after, treatment. Women must be advised to avoid becoming pregnant and should have a negative pregnancy test prior to each dose of treatment. They are advised to use effective contraception during treatment with MidAC and for at least four months after stopping treatment.

Mitoxantrone and cytarabine can cause abnormalities to the baby. MidAC should not be used in pregnant women, or in those who may become pregnant.

It is not known whether cytarabine is excreted in breast milk, but mitoxantrone is excreted in breastmilk, and has

been detected in breast milk for up to one month after the last dose of treatment. Women who are taking MidAC are advised not to breastfeed.

What happens if MidAC doesn't work?

If after your treatment with the mitoxantrone and cytarabine, your AML has not gone into remission or you have relapsed after achieving remission, your consultant is the best person to discuss what other treatments are available for you, and help you decide the next course of action. With knowledge of your genetic results, your physical condition and any new treatments available, your consultant can recommend the best options for you.

Mitoxantrone and cytarabine is not the first-line treatment for the induction or consolidation of AML. Therefore, other options that may be available to you include:

- Combination of an anthracycline drug, such as daunorubicin or doxorubicin with cytarabine. This is an

effective induction treatment. Additionally, a targeted drug may be added such as an FLT3 inhibitor. This will depend on the genetic abnormalities associated with your AML.

- Your induction can be repeated with the addition of another drug such as etoposide, cladribine or clofarabine.
- For younger patients and those patients who can withstand it, an allo-SCT to help destroy remaining leukaemia cells in the body can be performed to prevent further relapse. An allo-SCT involves the transplantation of bone marrow stem cells from a matching donor such as sibling, parent or child. The allo-SCT helps re-establish a healthy bone marrow.

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

Glossary

Acute Lymphoblastic Leukaemia (ALL)

A leukaemia in which lymphocytes start multiplying uncontrollably in the bone marrow, resulting in high numbers of abnormal, immature lymphocytes. Lymphocytes are a type of white blood cell involved in the immune response.

Acute Myeloid Leukaemia (AML)

A rapid and aggressive cancer of the myeloid cells in the bone marrow.

Allogeneic Stem Cell Transplant (allo-SCT)

The transplant of stem cells from a matching donor.

Amino Acids

Organic molecules which are the building blocks for making proteins.

Anaemia

A condition where the number of red blood cells are reduced. Red blood cells contain haemoglobin

and transport oxygen to body cells. This may be due to a lack of iron, leukaemia, or sickle cell disease.

Anthracycline

An antibiotic derived from the bacteria *Streptomyces peucetius* and found to be an effective anticancer drug.

Antraquinones

A class of natural and synthetic compounds with a wide range of applications. Besides their use as colourants, anthraquinone products can be used as laxatives or anti-inflammatory agents. Current medical indications include arthritis, multiple sclerosis and cancer.

Antimetabolite

A drug that interferes with DNA synthesis, and therefore preventing growth or reproduction of cells.

Bone Marrow

The soft-blood forming tissue that fills the cavities of bones

Glossary (cont.)

and contains fat, immature and mature blood cells, including white blood cells, red blood cells and platelets.

Bone Marrow Biopsy

A collection of a sample of bone marrow from the hip bone, generally under local anaesthesia. A bone marrow surgical instrument with a cylindrical blade, called a trephine, is used to remove a one or two-centimetre core of bone marrow in one piece.

Chemotherapy

Drugs that work in different ways to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.

Chromosomes

Thread-like structures which carry the genes, and are located in the nuclei of every cell in the body. There are 46 chromosomes (23 pairs) in humans.

Chronic Myeloid Leukaemia (CML)

A leukaemia in which the myeloid

cells start multiplying in the bone marrow leading to large numbers of abnormal, immature myeloid cells called blasts, which prevent the bone marrow from producing enough healthy blood cells of all types.

Complete Remission

Complete remission has occurred when:

- Blood cell counts have returned to normal
- Less than 5% of abnormal, leukaemia cells are still present in the bone marrow

Consolidation Treatment

Treatment following remission intended to kill any cancer cells that may be left in the body.

DNA (Deoxyribonucleic Acid)

A thread-like chain of amino acids found in the nucleus of each cell in the body which carries genetic instructions used in the growth, development and functioning of the individual's cells.

Electrocardiogram (ECG)

A test that records the electrical signals in your heart to detect any heart problems and monitor the heart's status.

Electrolytes

Salts and minerals in the blood that help conduct electrical impulses in the body. They include sodium, potassium, chloride and bicarbonate among others.

First-line Treatment

The first treatment given for a disease. It is generally the treatment accepted by the medical profession as the best initial treatment for a given type and stage of cancer.

Genes

Genes are made up of DNA which stores the genetic information required to make human proteins.

Induction Treatment

The first treatment after diagnosis intended to kill the majority of the leukaemia cells and stimulate remission.

Leukaemia

A group of cancers that usually begin in the bone marrow and result in high numbers of abnormal blood cells. These cells are not fully developed and are called blasts or leukaemia cells. Depending on the type of blood cell involved, there are different types of leukaemia with varying characteristics, such as being acute (develops quickly) and chronic (develops slowly).

Myeloid

Relates to bone marrow.

Non-Hodgkin's Lymphoma

A group of blood cancers that includes all types of lymphoma except Hodgkin lymphomas. Lymphoma is a cancer that starts in the white blood cells called lymphocytes, which are part of the body's immune system.

Red Blood Cells

Small blood cells that contain haemoglobin and carry oxygen and other substances to all tissues of the body.

Glossary (cont.)

Refractory Condition

A condition for which treatment does not result in a remission. However, the condition may be stable.

Relapse Condition

Relapse occurs when a patient initially responds to treatment, but after six months or more, the response stops. This is also sometimes called a recurrence.

Stem Cell

The most basic cell in the body that has the ability to develop into any of the body's specialised cell types, from muscle cells to brain cells. However, what makes these stem cells reproduce uncontrollably, as in cancer, is thought to be linked to chromosome abnormalities.

Stem Cell Transplant

The transplant of stem cells derived from part of the same individual or a donor.

Targeted Drug

A drug that is designed to specifically interrupt the leukaemia cells from growing in

the body without simultaneously harming healthy cells the way conventional chemotherapy drugs do.

Urea

The breakdown product of proteins in the body which is excreted in the urine.

White Blood Cells

White blood cells are one of the types of cells found in the blood and bone marrow, along with red blood cells and platelets. White blood cells create an immune response against both infectious disease and foreign invaders. Granulocyte white blood cells, include the neutrophils (protect against bacterial infections and inflammation), eosinophils (protect against parasites and allergens) and basophils (create the inflammatory reactions during an immune response). Other white blood cells include lymphocytes (recognise bacteria, viruses and toxins, to which they produce antibodies) and monocytes (clear infection products from the body).

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

Blood Cancer UK

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

0808 2080 888
www.bloodcancer.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.leukaemicare.org.uk

support@leukaemicare.org.uk

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Leukaemia Care is registered as a charity in England and Wales (no.1183890) and Scotland (no. SC049802).
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Leukaemia Care
YOUR Blood Cancer Charity