
DA – Daunorubicin and Ara-C (Cytarabine) – for Acute Myeloid Leukaemia (AML)

**A Guide for
Patients**

Introduction

In this booklet we focus on DA treatment, the combination of daunorubicin and ara-C, also known as cytarabine, as well as the liposomal formulation of daunorubicin and cytarabine (also known as CPX-351 or Vyxeos). Although some healthcare professionals may use the term ara-C when referring to the generic drug cytarabine, we will use cytarabine throughout this booklet.

Acute myeloid leukaemia (AML) is one of the types of leukaemia where patients produce too many immature myeloid blast cells. Blast cells are immature cells found in the bone marrow which are not fully developed. This type of leukaemia progresses rapidly. To know more about the symptoms and diagnosis of AML, please view our booklet titled *Acute Myeloid Leukaemia (AML)*.

This booklet was compiled by Saloua Najjam, PhD. (Haematology). Thank you to our former nurse Shirley Aston, as well as Nicole Clack, CNS at Guy's Hospital, for further input and insight into this booklet and to Dr Steve Knapper of University of Wales, Cardiff for peer reviewing the booklet. We are also grateful to Julie Quigley for her valuable contribution as a patient reviewer. This booklet was updated by our Patient Information Writer, Isabelle Leach.

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 8:30am – 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.

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

What is DA?

DA – Daunorubicin and ara-C (cytarabine) – is a combination of two chemotherapy drugs. Cytarabine is also known as cytosine arabinoside (ara-C). Each works in a slightly different way and in the DA regime they are used at the optimum doses to allow the maximum effects in terms of killing cancer cells.

Daunorubicin

Daunorubicin, like other anthracyclines, is an antibiotic originally derived from the *Streptomyces peucetius* bacteria and found to be an effective anticancer drug. Anthracycline chemotherapy continues to be a key component of anticancer regimes today.

Daunorubicin interferes with the DNA and reproduction of white blood cells, including the leukaemia cells. It has antimitotic (stops cell division) and cytotoxic (kills cancer cells) activity.

Cytarabine

Cytarabine is an antimetabolite drug which works by disrupting the DNA of cancer cells, thereby slowing or stopping their growth.

Like daunorubicin, cytarabine is one of a group of drugs known as cytotoxics. Cytotoxics are drugs toxic to cancer cells and prevent

their growth and reproduction. Cytarabine is commonly used in the treatment of several acute leukaemias including AML and acute lymphoblastic leukaemia.

Key terms to remember:

Anthracycline – A drug originally used as an antibiotic, but that was subsequently found to be an effective anticancer drug.

Antimetabolite – A drug that interferes with the enzymes necessary for DNA synthesis, and therefore prevents the growth or reproduction of cells.

Antimitotic – A drug that inhibits mitosis, or cell division.

Cytotoxic – A drug that is toxic to cancer cells and prevents their growth and reproduction.



Who receives DA?

The DA combination chemotherapy regimen is given to newly-diagnosed AML patients who are considered to be medically fit enough to be treated with intensive chemotherapy.

This is generally patients below the age of 60 years and fitter patients aged between 60 and 75 years.

If you wish to have further information on AML please view our collection of patient information booklets that are available on our website at www.leukaemiacare.org.uk

How is DA administered?

Before starting treatment

Prior to starting day one of your treatment with DA, your doctor will perform a Full Blood Count (FBC), Liver Function Tests (LFTs) and Urea and Electrolytes (U&Es) tests to confirm your liver and kidneys are functioning correctly. You may also have an echocardiogram (ultrasound scan of the heart) to assess your heart function prior to starting treatment.

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

Usually a central line (PICC line, Hickman line or temporary central line) will be inserted, through which the chemotherapy can be administered. Alternatively, a small cannula can be used in your arm or hand.

Induction therapy with the DA drug combination given in the UK generally consists of daunorubicin for three days with

cytarabine being given in two main ways, either spread over ten days with two doses per day or as a continuous infusion for seven days. These regimens have been used for many years and continue to be the standard induction regimen in many countries.

In some circumstances, gemtuzumab ozogamicin (also called by the trade name Mylotarg) is now added to the DA regimen. Mylotarg has a chemotherapy drug attached to an antibody directed at CD33 on the surface of leukaemia cells; between one and three doses of Mylotarg can be added to the first cycle of DA treatment.

For more information on the drug Mylotarg, you can read our booklet. This is available on our website www.leukaemicare.org.uk or can be ordered by calling **0808 010 444**.

How is DA administered? (cont.)

Recently, an alternative formulation of DA: daunorubicin and cytarabine (liposomal), (also referred to as CPX-351 or by its trade name Vyxeos) has been approved for use in some newly-diagnosed AML patients. Vyxeos is the combination of these two drugs encapsulated in fat-like particles called liposomes. The liposomes remain in the patient's body for longer than the conventional daunorubicin and cytarabine combination, and protect daunorubicin and cytarabine from being broken down early. This makes daunorubicin and cytarabine (liposomal) potentially more effective against the cancer cells.

Daunorubicin and cytarabine (liposomal) is given as an intravenous infusion over 90 minutes, with anti-nausea medications approximately 30 minutes before the infusion to reduce the risk of nausea or vomiting. Three of these 90-minute infusions are given over five days (on days one, three and five). The amount of

daunorubicin and cytarabine (liposomal) that you will receive depends on many factors, including your height, weight, general health or any other health problems. Your doctor will determine your exact dosage and schedule.

If you are well and your blood counts are improving, you will be discharged following your first treatment of DA. The doctors will review your white cell count (WCC) and let you home when the neutrophils are greater than $1 \times 10^9/L$. Ask your medical team if you would like more information. If, following recovery from your first cycle of DA or Vyxeos therapy, it is confirmed that your leukaemia is responding to treatment, then it is likely that you will be given a second cycle. The second cycle of DA may be shorter (eight days rather than ten; or three days in the case of Vyxeos) and can sometimes be given as an outpatient.

Your chemotherapy nurse will take every precaution possible while administering DA to avoid any extravasation. This is when chemotherapy leaks out of the vein into the tissues under the skin. In the rare event that this should happen, your nurse will contact a senior member of the medical team such as your haematologist and follow local protocol for dealing with cytotoxic extravasation.

You will have daily routine blood tests while you are in hospital to monitor the effects of the chemotherapy, but tell your nurse if you experience any symptoms that you are worried about.

What are the side effects of DA?

This treatment can have serious and possibly life-threatening side effects. Therefore, it is very important that you report any side effects to your doctor straight away.

Chemotherapy is the most commonly prescribed anticancer treatment. While you are receiving DA treatment, you may become more vulnerable to infection. Side effects with the conventional combination of daunorubicin and cytarabine and the liposomal daunorubicin and cytarabine combination are similar. Symptoms of infection like fever, shivering, discomfort when you pass urine, sweats, sore throat, diarrhoea, coughing or breathlessness should be reported to your doctor or nurse to prevent them from becoming life-threatening if they are left untreated.

You can try the following methods to try and minimise the risk of infection:

- Hand washing.
- Avoidance of people with infections.
- Perform regular temperature checks using a thermometer. If your temperature exceeds 37.5°C, contact your doctor and/or hospital team immediately (if you cannot contact them for any reason, go the hospital directly).
- Stay extra clean.
- If you have a central line (also known as a Hickman line), keep the area around it clean and dry. This advice should also be followed if you have a PICC (Peripherally Inserted Central Catheter) line.
- Clean your teeth every day and check for sores in the mouth or other signs of infection.
- If you get injured and have a scratch or cut, make sure you clean it well.
- Let your doctor or hospital team know if you have a sore bottom, or whether it bleeds. If this happens, this could increase

your risk of infections.

Everyone will experience different side effects with DA treatment. It is very important that you report any new symptoms to the medical team so that these symptoms can be properly assessed and, if necessary, treated. You will have routine blood tests on most days while you are in hospital to monitor the effects of chemotherapy.

Side effects and frequencies

There are three frequencies of side effects that you may get with DA treatment: very common (may affect more than 1 in 10 people), common (may affect up to 1 in 10 people) and uncommon (may affect up to 1 in 100 people).

Very common side effects

- **Infections and low neutrophil white blood cell counts with fever** – These are the most common effects seen in patients. Because of the low neutrophil white cell counts, infections of various types such as bacterial infections, pneumonia and sepsis can

occur.

- **Bruising and bleeding** – This treatment will reduce the production of platelets which help the blood clot. Let your doctor know if you have any unexplained bruising or bleeding, such as nosebleeds, bloodspots or rashes on the skin, or bleeding gums. You are likely to need platelet transfusions at least twice per week until your bone marrow recovers from the chemotherapy (usually after four to five weeks).
- **Anaemia (low number of red blood cells** – DA chemotherapy will cause you to become more anaemic (reduces the number of red blood cells being made in the bone marrow). This is often associated with tiredness and breathlessness. Red blood cell transfusions will need to be given until your bone marrow recovers from chemotherapy (after four to five weeks).
- **Hypersensitivity reactions** – These include skin rashes and itching.
- **Pain in the muscles and joints.**

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

Top tips if you experience bleeding:

- Apply direct pressure on the bleeding site (this will apply if it is an open area of bleeding skin).
- If you have a nosebleed, apply pressure below the bridge of your nose.
- After applying pressure (where possible), contact your doctor or hospital immediately.
- If you are unable to control the bleeding, go to your hospital immediately.

- **Skin changes** – DA treatment can cause a skin rash that leaves the skin red and dry and it might be itchy. Rashes are very commonly seen following Vyxeos (CPX-351).
- **Nausea and vomiting** – Daunorubicin causes considerably more nausea and vomiting compared to cytarabine, and this side effect

varies from person to person. Your doctor can provide you with anti-nausea medication alongside your chemotherapy to prevent this. If you continue to feel or be sick, tell your nurse and your doctor may increase the dose of anti-nausea medication or change it completely.

Top tips for managing nausea:

- Eat little and often rather than large meals.
- Eat foods that appeal to you rather than forcing yourself to eat things you do not fancy.
- Eat dry food throughout the day such as toast or crackers.
- Try to avoid skipping meals as much as you can.
- Sip liquids slowly.
- Avoid foods that have a strong smell, are overly sweet, fried or fatty.
- If you experience vomiting, take sips of clear liquids such as water to replace any fluids you have lost.

- **Effects on the lungs** – You may develop shortness of breath, a cough, wheezing (fluid in the lungs) or a lung infection (pneumonia). This is more common when treatment is given at higher doses. If this is the case, your doctor can arrange tests to check your lungs.
- **Diarrhoea** – As this may be a sign of infection, you should let your nurse know if this becomes a problem during or after your treatment.
- **Mouth problems** – Your mouth may become sore or dry, or you may notice small mouth ulcers during this treatment. Drinking at least two litres of fluids a day and keeping a high standard of oral hygiene can help to reduce the risk of this happening. Your doctor can prescribe a mouthwash for you to use during treatment. Occasionally during treatment, you may experience a strange taste, sometimes described as metallic or bitter that can be treated with strongly flavoured sweets or mints.
- **Lethargy/Fatigue** – This is

when you feel tired and lacking in energy. First, talk to your nurse or doctor about it, then try to manage it by giving yourself more rest when needed, learning how to relax and maybe adopting some simple changes to your diet and exercise routine.

Tell your doctor or inform your hospital immediately if you develop the following signs and symptoms of low blood counts while you are home:

- Fever (a temperature over 37.5°C)
 - Infection
 - Nosebleeds on a regular basis
 - Easy bruising
- **Hair loss** – This is called alopecia and is caused by the toxicity of chemotherapy. It can be partial or total, but it is completely reversible as your hair will grow back when your treatment is completed. Hair does not always return to its pre-chemotherapy state and

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

can grow back a different colour or style. This hair loss happens gradually usually starting 10 to 14 days into your first course of treatment. If you would like an appointment with the wig service, this can be arranged for you. Ask a member of your medical team.

- **Tumour lysis syndrome** – This is an increase in blood uric acid levels which may cause damage to the kidneys, heart or liver. It is a result of a very large death of cancer cells.

Uncommon side effects

- **Numbness and rash in the hands and feet.**
- **Heart problems** – DA treatment, especially daunorubicin, may have a toxic effect on the heart. This may cause an irregular heartbeat, breathlessness or swelling of the legs. You should inform your nurse or doctor of any pain in the chest, palpitations or breathlessness that you experience during the treatment.

Serious and potentially life-threatening side effects

In a small proportion of patients, chemotherapy can result in very severe side effects. Side effects that may be serious or potentially life-threatening include infections, hypersensitivity and bleeding side effects. The medical team caring for you will discuss the risk of these side effects with you in more detail.

Late side effects

Some side effects may only become obvious after a number of years. Accordingly, you should discuss the details and likelihood of these late side effects with your doctor before starting treatment. Your doctor will help you assess the benefit you receive from the treatment against the risk of serious side effects. With some drugs there is also a small but real risk of developing another cancer. If any of these problems apply to you, the doctor will discuss these with you and note this on your consent form.

What happens if DA doesn't work for me?

Approximately 70-85% of younger patients will achieve complete remission following DA chemotherapy. The rates of remission are somewhat lower in older patients and those with secondary AML.

Therefore, some patients have a form of disease that is more resistant to treatment.

In these circumstances, your haematologist will be able to discuss alternative treatments. This may involve further intensive chemotherapy, discussion of clinical trial options or a switch to less intensive or palliative treatments.

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

Anthracycline

An anthracycline is a drug originally used as an antibiotic, but it was subsequently found to be an effective anticancer drug. Examples of anthracycline are daunorubicin and doxorubicin.

Antimitotic

An antimitotic drug is a drug that inhibits mitosis, or cell division.

Bilirubin

An orange-yellow substance made during the normal breakdown of red blood cells. A raised blood bilirubin level can lead to jaundice and may be an indication of problems with the liver which excretes bilirubin.

Creatinine

A waste product in the body that comes from normal wear and tear on muscles. High levels of creatinine in the body may indicate poor function of the kidneys as they excrete creatinine.

Cytotoxic

Drugs that are toxic to cancer cells and prevent their growth and reproduction.

Extravasation

Accidental leakage of certain medicines into the body from an IV drip in the vein. If you develop redness, soreness or pain at the

injection site at any time please let your doctor or nurse know straightaway.

Induction Therapy

Treatment intended to kill the majority of the leukaemia blasts in the blood and bone marrow and to restore normal blood cell production.

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) or chronic (develops slowly).

Tumour Lysis Syndrome

The rapid destruction of a large number of white blood cells that can increase blood uric acid levels which may cause damage to the kidneys, heart or liver.

Prophylaxis

Treatment given, or action taken, to prevent disease.

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**

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Leukaemia Care
YOUR Blood Cancer Charity