
FLAG-Ida for Acute Myeloid Leukaemia (AML)

**A Guide for
Patients**

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

FLAG-Ida is a combination chemotherapy regimen made up of fludarabine, high dose cytarabine (Ara-CO), idarubicin and granulocyte-colony stimulating factor (G-CSF) used in the treatment of acute myeloid leukaemia (AML).

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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@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**.

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

What is FLAG-Ida?

FLAG-Ida is the abbreviation for a combination of drugs which has shown to be effective for the treatment of AML. FLAG-Ida consists of fludarabine, cytarabine (Ara-C), granulocyte-colony stimulating factor (G-CSF) and idarubicin.

Fludarabine

Fludarabine is a type of chemotherapy drug called an antimetabolite. Antimetabolites interfere with the synthesis of DNA, and therefore prevent the growth or reproduction of leukaemia cells.

Fludarabine is indicated for the treatment of adult patients with chronic lymphocytic leukaemia (CLL) in combination with cyclophosphamide and rituximab (FCR), but when used as part of the FLAG-Ida combination, it has been very useful for the treatment of AML.

Fludarabine is available as a concentrated solution for injection or infusion, or as a tablet.

Cytarabine

Cytarabine (also called cytosine arabinoside or Ara-C) is also an antimetabolite chemotherapy drug that has been used for the treatment of AML for over 40 years.

Cytarabine is used in combination with other chemotherapies for the treatment of AML, acute lymphoblastic leukaemia and crises in chronic myeloid leukaemia.

Cytarabine is available as a concentrated solution for injection or infusion.

Idarubicin

Idarubicin is a drug that belongs to a group of anti-cancer drugs called anthracyclines. These drugs were originally used as antibiotics, but it was subsequently found that they were effective anti-cancer drugs. Anthracyclines work by damaging DNA of the leukaemia cells.

Idarubicin is indicated for the treatment of patients with AML and relapsed/refractory acute

lymphoblastic leukaemia (ALL).

Idarubicin is available as a freeze-dried powder to be made into a solution for injection or infusion, or as a tablet, if an injection or infusion is not possible.

G-CSF

G-CSF is a growth factor which stimulates the bone marrow to produce granulocyte white blood cells, mainly the neutrophils.

Granulocytes (white blood cells that are characterised by small granules in their cells) include the neutrophils, eosinophils and basophils. Neutrophils protect against bacterial infections and inflammation. Eosinophils protect against parasites and allergens, and basophils create the inflammatory reactions during an immune response.

G-CSFs are indicated for the improvement of neutropenia (a decrease in the number of neutrophils) caused by chemotherapy. G-CSFs are not cancer treatments, but supportive care medicines for patients with bone marrow suppression secondary to cancer and its

treatments.

G-CSFs are available as solutions for injection or infusion. It is included in the FLAG-Ida regimen from the day before the chemotherapy drugs start to try to bring the leukaemic cells into cycle and increase their sensitivity to the chemotherapy agents.

FLAG-Ida

The aim of treatment for AML is to cure the majority of patients who are able to tolerate intensive chemotherapy, as well as improve supportive care and availability of allogeneic stem cell transplants.

FLAG-Ida is a chemotherapy regimen widely used in patients with relapsed or refractory AML. It is often used in patients with refractory or relapsed AML who are awaiting an allogeneic stem cell transplant.

FLAG-Ida has also been shown to achieve complete remission in newly diagnosed patients. One course of FLAG-Ida resulted in more remissions and reduced relapse compared with the

What is FLAG-Ida? (cont.)

standard care treatment for AML of cytarabine with daunorubicin in younger patients with AML. Daunorubicin is an anthracycline drug like idarubicin. Patients treated with FLAG-Ida require more supportive care than patients receiving daunorubicin and cytarabine. The duration of neutropenia is slightly longer, they need more transfusions and antibiotics, on average spend slightly longer in hospital, and they experienced bone marrow suppression which can prevent some of them completing the full course of treatment.

The FLAG-Ida regimen is given for two cycles and includes fludarabine for four days, cytarabine for four days, idarubicin for three days and G-CSF for six days. Sometimes idarubicin is omitted from the second cycle.

High-risk AML includes a number of groups of patients:

- Those with high-risk cytogenetic abnormalities, or those with high-risk molecular features

(e.g. FLT3-ITD in the absence of an NPM1 mutation, p53 mutations, ASXL1 or RUNX1 mutations)

- Patients with secondary AML (following previous haematological conditions like MDS, MPNs) or therapy-related AML following previous chemotherapy.

Many high-risk patients now receive CPX-351 (Vyxeos) as their initial therapy.



Who receives FLAG-Ida?

Patients with AML who may benefit from the FLAG-Ida combination therapy are the following:

- Patients with relapsed or refractory AML, who may or may not be awaiting an allogeneic stem cell transplant
- Newly diagnosed patients with AML as an induction of remission (particularly those with high-risk disease features)
- Patients whose induction therapy with cytarabine and daunorubicin or daunorubicin with cytarabine and etoposide has not worked (refractory AML)

Patients with acute promyelocytic leukaemia (APL), which is a subtype of AML, should not be treated with FLAG-Ida as the combination of differentiating agents all-trans retinoic acid (ATRA) and arsenic trioxide (ATO) achieves excellent cure rates of 85% (for high-risk patients) to over 90% (for low- to intermediate-risk patients) in these patients.

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

How is FLAG-Ida administered?

Before starting FLAG-Ida treatment, the following clinical assessments will be carried out:

- Measurement of your weight and height.
- Full blood count and urea and electrolyte levels as a measure of kidney function. These tests will be performed before each treatment cycle.
- A pregnancy test will be carried out on all female patients of child bearing age two weeks before starting treatment.
- Electrocardiograms (ECGs), echocardiograms (ECHOs) or multiple-gated acquisition (MUGA) scans for patients with a cardiac history, elderly patients or those with a history of heart disease.

Details and facilities available for managing any side effects or complications will be explained to you, and patients should be informed on the importance of using adequate barrier contraception as the drugs in the FLAG-Ida regimen can be harmful

to your partner or unborn baby.

You will then 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.

For part of your induction therapy, you will be treated in the hospital for a period of around four weeks, but this may vary from person to person. Your stay in the hospital is separated by a short period of stay at home, to rest between the two given courses of FLAG-Ida.

The two cycles of FLAG-Ida include:

- The injection of G-CSF is given under the skin in the abdomen or leg for seven consecutive days (days one to seven).
- Fludarabine given via an infusion over 30 minutes once a day for five consecutive days (days two to six).
- Cytarabine given via an infusion over four hours once a day (four hours after the fludarabine) for five days (days two to six).

How is FLAG-Ida administered? (cont.)

- Idarubicin given via an infusion over one hour, once a day for three days. Sometimes idarubicin is omitted from the second cycle.

The doses of the individual chemotherapies in the FLAG-Ida regimen will be adjusted in line with your medical history and the results of your pre-treatment assessments.

The levels of creatinine and bilirubin in your blood during treatment will indicate any kidney or liver impairment, respectively. Your doctor will modify the doses within FLAG-Ida accordingly. If there are any signs of heart damage or impairment, idarubicin will be stopped.

What are the side effects of FLAG-Ida?

The side effects of FLAG-Ida may be caused by any of the drugs in the regimen.

Common side effects

- Bruising or bleeding – This treatment can reduce the production of platelets which help the blood clot. You may need platelet transfusions.
- Anaemia (low number of red blood cells) – You may become anaemic, which can make you feel tired and breathless. You will have a routine blood test every day you are in hospital to monitor your full blood count and you may require blood transfusions.
- Increased risk of serious infection – You are vulnerable to infection while you are having chemotherapy. Minor infections can become life-threatening in a matter of hours if left untreated. Symptoms of infections include fever, shivering, sweats, sore throat and diarrhoea.
- Nausea and vomiting – The

severity of this varies from person to person. Anti-sickness medication will be given along with your chemotherapy to prevent this.

- Eye irritation – This is a known side effect of cytarabine. You will be given eye drops to try and prevent this.
- Hair loss – Your hair will gradually fall out 10 to 14 days following your first course of treatment. The timescale varies from person to person. This is a temporary side effect and your hair will grow back when your treatment is completed.
- Discolouration of urine – Idarubicin, because of its red colour, may discolour your urine red or pink for the first few times following treatment.
- Fatigue – You may feel tired and lacking in energy, especially when your blood counts are low.

Uncommon side effects

- G-CSF can sometimes cause pain or an aching sensation in

What are the side effects of FLAG-Ida? (cont.)

your bones.

- Cytarabine can sometimes cause a set of symptoms during its infusion known as cytarabine syndrome. These symptoms include fever, a rash, aching in your muscles and bones, and pain in the chest. These symptoms usually occur six to 12 hours following the infusion and will stop once the infusion of cytarabine is finished.
- Diarrhoea - If this becomes a problem anti-diarrhoea tablets can be prescribed.
- Mucositis (sore mouth) - Your mouth may become sore or dry and you may develop mouth ulcers. Drinking plenty of fluids and cleaning your teeth regularly and gently with a soft toothbrush can help reduce the risk of this happening. Occasionally during treatment, you may experience a strange metallic or bitter taste. A strong flavoured sweet or mint may help with this.

Rare side effects

- Irregular heartbeat - Occasionally this can happen as a result of the idarubicin. It is quite rare and usually reversible.
- Skin changes - Sometimes after having FLAG-Ida, your skin may appear darker in colour or lightly tanned, especially around the joints. This is called hyperpigmentation. Your skin will return to normal after the treatment has been completed.
- Protecting your partner and contraception - It is recommended that you or your partner use a condom during sexual intercourse while you are having the course of chemotherapy. 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 and in the vagina.
- Fertility - This chemotherapy may affect your ability to have

children. You should discuss this with your doctor or nurse before you start treatment.

Very rare side effects

- Serious allergic reactions.
- Minor ulceration of the gastric mucosa (the mucus layer of the stomach).
- Hand-foot syndrome (redness, swelling, and pain on the palms of the hands and/or soles of the feet).
- Blockage of a blood vessel by a blood clot that has become moved from another side in the circulation (thromboembolism).
- Transfusion-associated graft-versus-host-disease (TA-GvHD) – Fludarabine weakens your immune system, so when you have a transfusion of blood products you are at a higher risk of developing TA-GvHD. This extremely rare condition can cause a severe rejection reaction. It is almost fully prevented by gamma irradiation of any of the blood products you are given once you have had

treatment with FLAG-Ida.

The addition of idarubicin to the FLAG schedule will be decided carefully by your consultant as this drug is contra-indicated in the following patients:

- Patients with severe myocardial insufficiency, who have had a recent heart attack (myocardial infarction).
- Patients with severe arrhythmia (a condition in which the heart beats with an irregular or abnormal rhythm).
- Patients who have unstable angina (a condition marked by severe pain in the chest, often spreading to the shoulders, arms, and neck).
- Patients who suffer from cardiomyopathy, which is a condition in which the heart muscle is damaged.
- Patients with a previous treatment history of cumulative doses of idarubicin or other anthracyclines.

What happens if FLAG-Ida doesn't work?

Overall, following the outcome of your treatment with FLAG-Ida, your consultant is the best person to discuss your options with and to decide on the next step to take. Your clinician will be able to discuss options with you that might include alternative chemotherapy combinations or recruitment to clinical trials of novel therapeutic options.

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 Lymphoblastic Leukaemia (ALL)

A leukaemia in which lymphocytes start multiplying uncontrollably in the bone marrow resulting in high numbers of abnormal, immature lymphocytes called blasts. 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.

Acute Promyelocytic Leukaemia (APL)

A rare sub-type of AML in which there is an increased production of immature, abnormal white blood cells called promyelocytes in the bone marrow.

Antimetabolite

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

Bilirubin

The breakdown product of red blood cells.

Bone Marrow

The soft blood-forming tissue that fills the cavities of bones and contains fat, immature and mature blood cells, including white blood cells, red blood cells and platelets.

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.

Chromosome

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

Creatinine

The breakdown product of creatine that results from the normal wear and tear of muscles in the body.

Electrolytes

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

Glossary (cont.)

FLT3-ITD (FMS-like tyrosine kinase 3-Internal tandem duplication) mutation

The mutation in a gene called FLT3 due to internal tandem duplication of the gene. FLT3 is mutated in about a third of patients with AML. Patients with FLT3-ITD mutations have lower cure rates due to an increased risk relapse.

Full Blood Count

A full blood count is performed on a blood sample using automated equipment to provide the concentration of haemoglobin in the blood, measures of the red cell components, the white cell count, including the different types of white cells, and the platelet count.

Induction

The treatment phase intended to kill the majority of the leukaemia cells in the blood and bone marrow, and to restore normal blood cell production, i.e. to induce a disease remission.

Intravenous Infusion

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

Neutrophils

White blood cells involved in fighting inflammation and infection, specifically bacterial infections.

Relapse

A relapse occurs when a patient initially responds to treatment, but the leukaemia then comes back at a later point. This is also sometimes called a recurrence.

Remission

'Complete Remission' is said to have occurred when the blood cell counts have returned to normal and there are less than 5% abnormal, immature leukaemia cells still present in the bone marrow.

TP53 (tumour protein 53) Mutation

The TP53 gene is located on chromosome 17. The TP53 protein is responsible for preventing cells from over-multiplying and switching on the destruction of cells with damaged DNA. The mutation in this gene is the most common mutation associated with human cancers.

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
support@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**

www.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
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