Treatments in Acute Lymphoblastic Leukaemia (ALL)

A Guide for Patients

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

Acute lymphoblastic leukaemia (ALL) is a blood cancer that affects the lymphocytic cells. The term acute does not describe how serious the leukaemia is, it refers to how quickly it progresses. Because of this, immediate treatment is often needed.

This booklet looks at the treatment options for patients with ALL including chemotherapy, CNS treatment, TKIs, immunotherapy and CAR-T therapy. If you have any questions about any of the treatments - who has it, when and how do you receive it and possible side effects - this booklet covers the basics for you.

For more tailored advice, talk to your haematologist, clinical nurse specialist or hospital pharmacist.

This booklet was written by our Patient Information Writer Isabelle Leach, and reviewed by Robert Marcus and Clare Rowntree. Thank you to Diane Bone for providing valuable feedback 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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In this booklet

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@leukaemiacare.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 **https://www.leukaemiacare.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 **https://www.leukaemiacare.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**, 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@leukaemiacare.org.uk**

Patient magazine

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

What is ALL and how is it treated?

Acute lymphoblastic leukaemia (ALL), also known as acute lymphocytic leukaemia, is so called because ALL usually begins 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.

There are two main types of lymphocytes called B-cells and T-cells. Healthy B-cells produce antibodies that seek out and immobilise bacteria, viruses, and toxins which invade the body. Healthy T-cells destroy the invading organisms that have been tagged by the B-cells as well as cells that have become cancerous.

If you would like more information on ALL, you can order one of our booklets by calling **08088 010 444** or via the website **www.leukaemiacare.org.uk**

There are main phases in the treatment of ALL which are generally recognised and used by doctors internationally. They are as follows:

- **Induction of remission therapy -** This is the first treatment given for three to four weeks after diagnosis. The aim is to destroy the majority of the leukaemia blasts cells and return the blood counts to normal levels.
- **Intensification of remission therapy -** A combination of drugs which may be given depending on the subtype of your ALL. Several courses of intensification therapy may be recommended.
- **Maintenance of remission therapy -** This treatment can be given orally or intravenously for two to three years generally at lower doses and with fewer side effects.
- **Relapsed or refractory re-induction chemotherapy -** This is given to patients for whom ALL has returned (relapse) or those who did not respond to

induction therapy (refractory).

- **Central nervous system preventive treatment -** Drugs are given to prevent the leukaemia cells in the blood from spreading to the brain or spinal cord.

Steroids are often also given to help improve the effectiveness of the chemotherapy. You may also be given a targeted therapy drug which attacks specific components of the leukaemia cells. Some patients will need to have an allogeneic stem cell transplant (ASCT), either from a sibling or an unrelated donor.

There are two types of stem cell transplant: **allogeneic** and **autologous**. You can find out more information about stem cell transplants in our booklets.

The treatments covered in this booklet include:

Drugs used in induction

- Vincristine
- Daunorubicin
- Cyclophosphamide
- Cytarabine (and CNS treatment)
- Asparaginase

Drugs used in maintenance

- Mercaptopurine
- Methotrexate

New and experimental agents

- Tyrosine kinase inhibitors (TKIs) and Philadelphia chromosome-positive (Ph-positive) ALL
- Immunotherapy including chimeric antigen receptor T-cell (CAR-T) therapy
- Inotuzumab ozogamicin
- Rituximab
- Blinatumomab

Patients with ALL can be characterised according to their genetic analysis. An important group of ALL patients have the Philadelphia chromosome (Ph) and are described as Ph-positive. The remaining patients can also be classified based on their genetic information which may be helpful in determining if extra treatment such as an ASCT may be required. Patients without the Ph are described as Philadelphia chromosome-negative (Ph-negative).

What is ALL and how is it treated? (cont.)

ALL is predominantly a disease of children with around 60% of patients aged less than 20 years old. Approximately 10% of patients are aged 20 to 44 years, with the remaining being aged 45 years and older.

The use of intensive chemotherapy has led to a significant improvement in outcome for children with ALL. In adults, the results of treatment are less encouraging because of the high-risk characteristics of ALL and the significant toxicity (harmful effect) associated with chemotherapy in adults. However, there have been recent improvements for outcomes in adults, and there may be the possibility of an ASCT if chemotherapy alone is unsuccessful. But, despite being a curative option, this represents a very intensive treatment and requires a matching donor, which means that not all patients are suitable for this form of treatment.

What tests will you be given before you have chemotherapy?

Tests which are carried out to diagnose ALL include:

Full blood count

- This will show low levels of red blood cells and normal levels of white blood cells and platelets as the bone marrow has been infiltrated by the immature leukaemic blast cells. The full blood count may vary at diagnosis.
- The white blood cell count and platelet count should be regularly monitored during treatment with your chemotherapy.

Blood film (also called peripheral blood smear)

This is a thin layer of blood smeared on a glass microscope slide and stained to allow the various blood cells to be seen with a microscope. This will show the immature leukaemic blast cells to confirm the diagnosis, although these are not always seen at first presentation.

Bone marrow test

A needle is used to remove a sample of bone marrow from the hip bone (bone marrow aspiration) to check for leukaemia blast cells and determine which type of white blood cells they came from. Depending on the subtype of ALL found, your doctor can refine your diagnosis and plan your treatment. The main ALL subtypes are as follows:

- **Precursor B-cell ALL:** Most common type
- **Precursor T-cell ALL:** More likely to affect young adults and is more common in men

Once ALL has been diagnosed, tests are performed to determine any spread to the central nervous system (CNS), which includes the brain and spinal cord, or other parts of the body. These tests will help identify the features of the leukaemia and the best treatment for you.

Other tests which may be carried out include:

- Imaging tests such as a chest X-ray and/or a CT scan.
- Lumbar puncture: This test collects a sample of spinal fluid to see if the ALL has spread to the spinal fluid.
- Magnetic resonance imaging: Imaging procedure that involves a magnet, radio waves, and a computer to make a series of detailed pictures of areas inside the body. This is only done for patients with suspected CNS disease.

Remission and ALL treatments

With treatment of intensive chemotherapy, the best outcome is to achieve remission. By definition, remission occurs when the following conditions are met:

- Blood cell counts returned to normal (haematological remission).
- Less than 5% of blasts are present in the bone marrow (cytogenetic remission). Cytogenetic refers to the cell's chromosomes.
- No evidence of disease in the blood cells and/or bone marrow is seen at all (molecular

What is ALL and how is it treated? (cont.)

remission). MRD is said to be negative in this case.

The term MRD refers to the leukaemic cancer cells left in the body after remission (no symptoms or signs of disease), and its value helps predict how likely it is that the patient will relapse. Monitoring of MRD is now routine in the management of almost all children with ALL and in many adults with ALL.

If you would like more information on minimal residual disease, take a look at our Know Your Rights toolkit at: http://bit.ly/KnowYourRightsToolkitLC

What are the shared side effects for ALL treatments?

Side effects which are common in most of the ALL chemotherapy treatments include:

Infections

Chemotherapy can reduce the number of your white blood cells which makes getting an infection more likely. Symptoms and signs of infection include a body temperature over 37.5°C, a sore throat, a cough, chills, feeling unwell, diarrhoea or the need to pass urine frequently. In this case, you should contact the hospital straight away on the relevant telephone number given to you. Sometimes the infection can be severe and enter your blood (sepsis) and you may go into septic shock, so it is important that you listen to your body and see a doctor when you feel ill.

Your white blood cell numbers will usually be restored to normal before your next cycle of treatment. Regular blood tests to monitor your white blood cell levels will indicate if they are still low and your doctor may alter your treatment schedule if needed.

Tumour lysis syndrome

Tumour lysis syndrome occurs when the rapid destruction of large numbers of white blood cells through treatment increases

blood uric acid levels, which may cause damage to your kidneys, heart or liver. Hyperuricaemia (high levels of uric acid in the blood) can also be caused by a rapid destruction of the cancer cells.

During the first week of treatment, your doctor will check your blood uric acid and urea levels several times as these may rise significantly if there is rapid destruction of large numbers of leukaemia cells. Should this be the case, you will receive fluids and the drug allopurinol to avoid you developing very high levels of uric acid.

Your doctor will then continue to monitor your blood uric acid level and be prepared to use such supportive and pharmacological measures as may be necessary to control the problem. To prevent the occurrence of tumour lysis syndrome, the patient should be fully hydrated and receive anti hyperuricaemic therapy, such as allopurinol or rasburicase, to counteract the effect of the breakdown of a large number of white cells or tumour bulk.

For each of the ALL treatments, the specific side effects which you are likely to encounter commonly have been determined by a haematologist to give you an idea of what you might normally expect. These common side effects are included in the sections for each treatment.

What other important information do you need to consider?

Pregnancy, breast feeding, contraception and loss of fertility

Chemotherapy has been reported to harm the foetus following maternal or paternal exposure. While there are very few studies of the use of chemotherapy in pregnant women, studies in animals have shown toxic effects in the offspring. Women and men of childbearing potential should use appropriate contraception methods during treatment.

Breast feeding is not recommended for patients receiving chemotherapy.

Treatment with chemotherapy

What is ALL and how is it treated? (cont.)

may permanently reduce fertility in men and women. It is often possible to collect and store sperm for male patients prior to starting chemotherapy. However, it is rarely possible to delay ALL treatment in order for women to have their eggs harvested.

If you have any questions or would like some advice or emotional support, information can be found at **fertilitynetworkuk.org**

Immunisations

Vaccinations with live pathogens should not be administered during treatment as this can lower the body's resistance to infection, and there is a chance that you may get the infection the immunisation is meant to prevent. In the United Kingdom, live vaccines include rubella, mumps, measles, BCG, yellow fever and shingles. However, you can have the flu vaccine, and it would be advisable for those who live with you to also be immunised against flu.

Additionally, you can be in contact with people who have had live vaccines, but you need to avoid people who have had oral (taken by mouth) live vaccines.

Vincristine

Vincristine (generic name) is available under the brand names of Oncovin® and Vincasar PFS®.

Who is given vincristine?

Vincristine can be used either alone or in combination with other cancer chemotherapy drugs for the treatment of leukaemias, including ALL.

How are you given vincristine?

Vincristine is administered by intravenous (IV) infusion at weekly intervals.

Are there any tests you need before and while you are taking vincristine?

A complete set of blood tests will be carried out prior to starting treatment and periodically during treatment to monitor the function of your organs such as your kidneys and liver.

Given vincristine's toxicity can manifest itself as numbness and tingling of fingers and toes, a periodic physical examination, which includes a check of your reflexes, will be carried out to detect if the dose of vincristine needs to be decreased.

What are the specific side effects for vincristine?

Specific side effects for vincristine include:

- Constipation
- Numbness
- Tingling in hands or feet
- Sore mouth
- Jaw pain
- Muscle pain or joint pain

The full list of side effects for vincristine is available on the European Medicines Agency website or is also available on the Macmillan website.

Daunorubicin

Daunorubicin is an effective anti-cancer drug and a key component of anti-cancer regimens. You may be given a very similar drug to this called doxorubicin.

Who is given daunorubicin?

In ALL, daunorubicin is used in patients for inducing remission and treating ALL in children, as part of combination chemotherapy.

How does daunorubicin work?

Daunorubicin is a type of chemotherapy called an anti-cancer antibiotic. It blocks an enzyme called topoisomerase 2, which is essential for cells to duplicate themselves and survive. Daunorubicin therefore prevents the cancer cells from dividing and thriving.

How are you given daunorubicin?

Since daunorubicin is extremely irritating to human tissues, it should always be diluted and administered through a large vein, and the infusion should be kept free flowing.

When do you have daunorubicin?

Daunorubicin is used mainly for the induction of remission in both adults and children with ALL.

What tests will you be given before you have daunorubicin?

Before starting treatment with daunorubicin, blood tests will be performed to check:

- The levels of your white blood cells, red blood cells and platelets.
- Substance and enzyme levels to confirm your liver and kidneys are working correctly.
- You may also be given an echocardiogram to check your heart function.

Are there any tests while you are taking daunorubicin?

Your doctor will monitor your progress with the following tests:

- Liver and kidney enzyme levels to monitor how well your liver and kidneys are working.

- Because daunorubicin has the potential to be toxic to the heart, an echocardiogram will be made at the beginning and end of treatment. Cardiotoxicity may develop suddenly and can be irreversible.

What are the specific side effects for daunorubicin?

Common side effects seen with daunorubicin include:

- Bruising
- Bleeding gums or nose bleeds (due to low levels of platelets)
- Anaemia (low levels of red blood cells)
- Diarrhoea, nausea, vomiting
- Abdominal pain
- Colitis (due to inflammation of the lining of the colon)
- Bone marrow failure (resulting in low levels of white blood cells, red blood cells blood, and platelets)
- Fatigue (tiredness and weakness)
- Hair loss (always reversible)

These side effects may be different if you are having daunorubicin with other cancer treatments.

The full list of side effects for daunorubicin is available on the European Medicines Agency website or is also available on the Macmillan website.

Cyclophosphamide

Cyclophosphamide is a chemotherapy drug that becomes active when it enters the body and sticks to the cancer cells.

Who is given cyclophosphamide?

Cyclophosphamide is used in patients with ALL alone or in combination with other anti-cancer drugs.

How does cyclophosphamide work?

Cyclophosphamide is part of a group of drugs called alkylating agents. Cyclophosphamide interferes with DNA activities to achieve its anti-cancer properties. In addition, cyclophosphamide has an immunosuppressant effect at lower doses. It has been shown to contribute to the activation of T-cells which destroy the cells that have become cancerous.

How are you given cyclophosphamide?

Cyclophosphamide is administered to you intravenously.

The doses of cyclophosphamide must be determined for each patient because both the doses and duration of treatment periods will depend on the combination therapy regimen you are having, your general health, liver/kidney/bone marrow function, and the results of laboratory monitoring.

To prevent and reduce the risk of bone marrow suppression by cyclophosphamide, you may be given something to help stimulate the growth of blood cells.

To reduce the risk of cyclophosphamide toxicity affecting the bladder, patients should be given adequate amounts of fluid to drink or infused intravenously, before, during and immediately after administration of cyclophosphamide.

When do you have cyclophosphamide?

In the treatment of ALL, cyclophosphamide is used to initiate remission, for intensification and as preparation of the bone marrow prior to transplantation.

What tests will you be given before and while you have cyclophosphamide?

Prior to your treatment with cyclophosphamide, clinical tests, biochemical tests and blood tests will be carried out. Other than the regular monitoring of your white blood cell count and platelet count during your treatment, there are no other tests required while you are taking cyclophosphamide.

What are the specific side effects for cyclophosphamide?

Common side effects which occur with cyclophosphamide include:

- A decrease in numbers of neutrophils (white blood cells involved in fighting infection)
- Cystitis (bladder inflammation) causing blood in the urine
- Bone marrow suppression (low levels of white blood cells, red blood cells, and platelets)
- Hair loss

The full list of side effects for cyclophosphamide is available on the European Medicines Agency website or is also available on the Macmillan website.

Cytarabine

Cytarabine is an anti-cancer drug commonly used as part of combination chemotherapy regimens for the treatment of leukaemia and lymphomas.

How does cytarabine work?

Cytarabine inhibits the synthesis of DNA. It also works as an antiviral and immunosuppressant drug.

How are you given cytarabine?

Cytarabine is normally given as an IV infusion. Cytarabine is given in four-day blocks as a short bolus infusion.

For CNS (central nervous system) prophylaxis, cytarabine may be administered by intrathecal infusion into the spinal cord so that the drug reaches the cerebrospinal fluid which surrounds the brain and spinal cord. This acts as a preventative treatment to stop cancer cells spreading to the CNS (more information about CNS treatment can be found in the next section of the booklet, on page 20).

When do you have cytarabine?

In the treatment of ALL, cytarabine is used for intensification of remission as part of combination therapy, as well as high-dose cytarabine for the induction of remission in Ph-positive ALL. Your doctor will be able to determine the best regimen for you.

What tests will you be given before you have cytarabine?

Before starting treatment with cytarabine, the following blood tests will be performed to check:

- The levels of all your blood cells
- Substance and enzyme levels to confirm your liver and kidneys are working correctly

Are there any tests while you are taking cytarabine?

During the course of your treatment with cytarabine, your doctor will monitor your progress at the following times:

- For patients with pre-existing

drug-induced bone marrow suppression, cytarabine induction therapy must be accompanied by daily blood cell counts and platelet counts. In addition, bone marrow examinations should be performed frequently after blasts have disappeared from the peripheral blood.

- Periodic checks of bone marrow, liver and kidney functions should be performed in patients receiving cytarabine.
- Both hepatic and renal function should be monitored during cytarabine therapy. In patients with pre-existing liver impairment, cytarabine should be administered only with utmost care.

What are the specific side effects for cytarabine?

Common side effects that have been reported in association with cytarabine therapy are:

- Anaemia
- Abdominal pain
- Nausea, vomiting and diarrhoea
- Dysphagia (difficulty swallowing)
- Oral/anal inflammation or ulceration
- Increased levels of liver enzyme (reversible)
- Skin irritation/ulceration
- Burning pain of palms and soles

Side effects for cytarabine are dose-dependent.

The full list of side effects for cytarabine is available on the European Medicines Agency website or is also available on the Macmillan website.

CNS treatment

What is the CNS?

The human nervous system is divided into the central nervous system (CNS) and the peripheral nervous system, so called because of their location in the body. The CNS includes the brain and spinal cord.

What is CNS prophylaxis?

Therapy for patients with ALL can be broadly classified as including induction, intensification, maintenance, and CNS prophylaxis or treatment.

CNS prophylaxis is treatment intended to stop cancer cells spreading to the brain and spinal cord. Chemotherapy is given as a preventive treatment. It kills leukaemia cells that may be in the brain and spinal cord, even though no cancer cells can be detected, because tiny numbers of cells could be present in your CNS and could continue to grow.

Who is given CNS treatment?

All patients with ALL will receive CNS treatment to keep the leukaemia cells from spreading to the CNS (CNS prophylaxis) or to treat the leukaemia if it has already spread to the CNS.

How is CNS treatment given?

CNS prophylaxis is often started during induction therapy and continued through the other phases of treatment. It may include one or more of the following:

- **Intrathecal chemotherapy:** Chemotherapy is injected directly into the spinal fluid, usually during a lumbar puncture, meaning that the chemotherapy only affects your CNS.
- Methotrexate is used most often, but cytarabine or a steroid may be used as well.
- **High-dose IV chemotherapy:** This is administered by IV infusion over usually 24 hrs in ALL treatment and requires a stay in hospital as large amounts of fluid will be given to you before and after the infusion to reduce the risk of

any side effects.

What are the side effects of CNS treatment?

Side effects might include:

- Headache
- Nausea and vomiting
- Fever

Asparaginase

Asparaginase (or L-asparaginase) is an important anti-cancer drug for the treatment of ALL and other blood cancers.

Who is given asparaginase?

Asparaginase is currently used in combination with other anti-cancer drugs to treat ALL in children and adult patients.

How does asparaginase work?

Asparaginase is an enzyme which breaks down asparagine in the body into aspartic acid and ammonia. By doing this, asparaginase reduces the circulation levels of asparagine in the body. All body cells need asparagine to make proteins and stay alive. Normal cells have the ability to make asparagine for themselves. However, unlike normal cells, leukaemia cells and other cancer cells are unable to make asparagine, and rely on the asparagine available in the blood for survival.

When administered to patients, asparaginase breaks down asparagine in the body and since the cancer cells cannot make more asparagine, they are unable to make proteins and cannot survive.

How are you given asparaginase?

Asparaginase can be given by IV injection, by intramuscular injection or by subcutaneous (given under the skin) injection. Most regimens in the United Kingdom now use PEG-asparaginase which is a form of asparaginase to which a substance called PEG has been attached to enable the drug to stay in the body longer.

When do you have asparaginase?

Your haematologist will determine your schedule and dose of asparaginase.

What tests will you be given before and while you have asparaginase?

The following tests are assessed before treatment with asparaginase is started, and then

maintained regularly throughout treatment to monitor the patient's condition.

Initially the tests are performed to check your organs are working well enough to withstand treatment and to provide a baseline for monitoring throughout treatment.

- White blood cell, red blood cell and platelet counts should be performed to assess the bone marrow. Platelet count is important for blood clotting.
- Liver and kidney function tests
- Serum amylase (enzymes secreted by the pancreas to help digest food)

During your treatment with asparaginase, the following tests will be performed to monitor any side effects:

- Serum amylase and blood sugar levels to exclude hyperglycaemia (high blood sugar level) and severe pancreatitis (inflammation of the pancreas). Hyperglycaemia may be treated with insulin, if needed.

What are the specific side effects of asparaginase?

Common side effects reported with asparaginase include:

- Hypersensitivity reactions (rashes, urticaria, itching, swelling of the face and lips)
- Nausea, vomiting and diarrhoea
- Abdominal pain
- Fatigue
- Blood coagulation abnormalities
- Altered levels of liver and pancreas enzymes

Severe side effects can include:

- Thrombosis
- Liver failure
- Pancreatitis

Side effects are generally reversible.

The full list of side effects for asparaginase is available on the European medicines agency website or is also available on the Macmillan website.

Mercaptopurine

Mercaptopurine (also called 6-mercaptopurine) is indicated for the treatment of acute leukaemias in adults, adolescents and children.

How does mercaptopurine work?

Mercaptopurine is a chemotherapy drug which stops human cells making and repairing DNA by interfering with the metabolism of purine, one of the components for DNA. It therefore prevents cancer cells from growing and multiplying.

How are you given mercaptopurine?

Mercaptopurine is supplied as tablets. The number of mercaptopurine tablets you will need to take will vary according to the results of your blood tests. Your doctor will discuss this with you. Your treatment may be administered during a stay in hospital, or as an outpatient.

When do you have mercaptopurine?

Mercaptopurine tablets are usually taken once a day, preferably in the evening. The length of time you will take mercaptopurine will depend on a the protocol you are on.

Are there any tests you need before and while you are taking mercaptopurine?

The following tests are assessed before treatment is started, and then maintained regularly throughout treatment to monitor your condition:

- Regular full blood count tests - While mercaptopurine suppresses your bone marrow in order to destroy the cancerous immature blast lymphocyte cells, it also supresses the healthy bone marrow. Your doctor will use these results to determine the best dose of mercaptopurine to use going forward.
- Liver function tests when required.

What are the specific side effects for mercaptopurine?

The main side effect of treatment

with mercaptopurine is bone marrow suppression leading to low levels of white blood cells and platelets.

Due to the lose doses of mercaptopurine that are given, other side effects are rare, but can include:

- Nausea and vomiting
- Biliary stasis (bile formed by the liver that cannot flow into the small intestine to help digestion)
- Hepatotoxicity (toxic effect on the liver cells)

The full list of side effects for mercatopurine is available on the European Medicines Agency website or is also available on the Macmillan website.

Methotrexate

Methotrexate is available under the brand names of Maxtrex™, Otrexup™ or Trexall™.

Who is given methotrexate?

Methotrexate is used for intensification and maintenance of remission in patients with ALL, as well as a wide range of cancers.

How does methotrexate work?

Methotrexate is a chemotherapy drug and immunosuppressant that stops cells making and repairing DNA, by disrupting several of the DNA components. Therefore, it prevents cancer cells from growing and multiplying. However, it also damages the DNA of some normal cells which results in side effects for the patient.

How are you given methotrexate?

Methotrexate is either given in high doses over 24 hours once every 15 days or as a low-dose maintenance dose every week. Methotrexate is available as tablets for oral administration. Doses of 100mg or more of methotrexate are usually administered parenterally (by a subcutaneous, intramuscular or IV) or a maximum of 12.5mg would be administered via the intrathecal route (the spinal cord).

When methotrexate is administered as part of a combination of chemotherapies, the dosage of methotrexate should be reduced to take into account any overlapping toxicities with the other drugs in the chemotherapy regimen.

When do you have methotrexate?

Your doctor will be able to determine the best regimen for you. In ALL, methotrexate is used for intensification and maintenance therapy in a variety of combination chemotherapy regimens.

What tests will you be given before and while you have methotrexate?

Prior to starting your treatment

with methotrexate, you will have blood tests to check your blood cell levels and to confirm your liver and kidneys are working properly. During your treatment, these will continue to be monitored.

What are the specific side effects for methotrexate?

The most common side effects of methotrexate include:

- Headaches
- Loss of appetite
- Mouth sores
- Tiredness
- Cough
- Hair loss
- Bruising easily (due to low platelet count)
- Anaemia (due to low number of red blood cells)

The incidence and severity of side effects with methotrexate are considered to be dependent on the dose administered. Most side effects are reversible when detected at an early stage.

The full list of side effects for methotrexate is available on the European Medicines Agency website or is also available on the Macmillan website.

TKIs and Ph-positive ALL

What is Ph-positive ALL?

Ph-positive ALL is a form of ALL which occurs in patients with the Philadelphia chromosome. This is the most common genetic abnormality in adult patients with ALL. The genetic abnormality is a fusion of a portion of chromosome 9 on chromosome 22.

The Ph-positive gene is only present in 3% to 5% of children with ALL compared with 25%-40% of adults with ALL. Ph-positive ALL is classified as a high risk subset of ALL, associated with a low response rate and high risk of relapse.

How does age determine the prognosis of Ph-positive ALL?

The age of a patient with Ph-positive ALL at diagnosis gives a good indication of the patient's prognosis. Five-year survival rates are around 80% for children less than five years old, but only 50% to 60% in adolescents and young adults. For patients aged 45 to 54 years, these survival rates decrease to almost 30%, and 15% in older adults.

This worsening prognosis with increasing age is thought to be due partially to the fact that the Ph-positive ALL chromosome abnormality is more common in older patients. Ph-positive ALL occurs in only 5% of patients less than 20 years old, 33% in patients aged 40 years, 49% in patients older than 40 years old, and then decreases slightly to 35% in patients older than 60 years.

Another reason for the difference in prognosis of patients with Ph-positive ALL is the inability of the older patients to tolerate standard chemotherapy regimens given that they may have other diseases as well.

What are the treatments available for Ph-positive ALL?

The prognosis for patients with Ph-positive ALL has considerably improved since the TKI imatinib was added to chemotherapy. Complete remissions have

been reached in close to 95% of newly diagnosed Ph-positive ALL patients. Unfortunately, some resistance to imatinib has been reported in a number of patients with Ph-positive ALL, but newly developed TKIs such as dasatinib, nilotinib and ponatinib are showing good efficacy in the treatment of imatinib-resistant patients with Ph-positive ALL. Current study results show that ponatinib has a broader spectrum of action than dasatinib and nilotinib, but dasatinib is the most toxic.

Imatinib, dasatinib and ponatinib are approved for the treatment of Ph-positive ALL.

How have TKIs changed the treatment of Ph-positive ALL?

Before the use of TKIs, Ph-positive ALL was considered to be a high-risk subgroup of ALL, associated with low response rate, high risk of relapse and the worst prognosis. However, the combination of imatinib with chemotherapy has substantially improved the outlook for patients with Ph-positive ALL, achieving complete remission in nearly all cases and increasing survival rates.

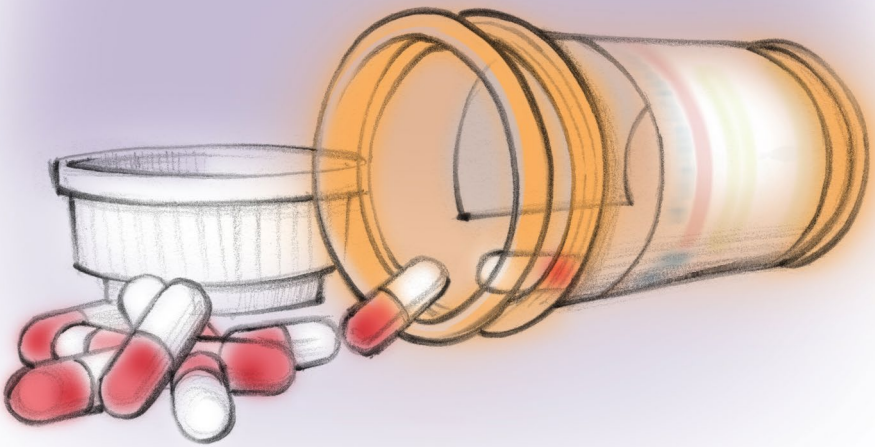
With standard chemotherapy alone, the prognosis in both children and adults was poor with long term survival rates of approximately 10%. Following the addition of the TKIs to chemotherapy, long term survival rates of 30% to 50% have been reported.

For those patients who can tolerate it, intensive chemotherapy administered with a TKI will yield complete remission in 100% of patients (including leukaemia cells anywhere in the body, i.e. MRD negative). Reduced intensity chemotherapy administered with a TKI will still achieve a complete remission of 100% (but not including leukaemia cells anywhere in the body, i.e. MRD-positive). Nevertheless, adding a TKI to reduced-intensive chemotherapy offers an option for the less robust patients such as the elderly.

Recommendation from recent

TKIs and Ph-positive ALL (cont.)

studies is therefore to give intensive chemotherapy combined with a TKI to patients with Ph-positive ALL who are strong enough to tolerate it. The TKI should be administered at the same time as the chemotherapy, and continued indefinitely. An ASCT should be reserved for patients in first remission who have not achieved complete remission at three months or later.



Immunotherapies

What is an immunotherapy?

Immunotherapy is a type of treatment that boosts the body's natural defences to fight cancer. It uses substances made by the body or in a laboratory to improve or restore the function of the immune system.

The immune system is a defence mechanism comprising of many biological structures and processes to protect the body against disease. Part of this system are the white blood cells called lymphocytes. There are two main types of lymphocytes called B-cells and T-cells:

- B-cell lymphocytes (B-cells) produce antibodies that seek out, immobilise and label invading organisms or cancers cells.
- T-cell lymphocytes (T-cells) move around the body to find and destroy the invading organisms or cancerous cells that have been tagged by the B-cells. The body then stores some of the T-cells, so that if it comes across the organism again, it can recognise and destroy it immediately.

Immunotherapy uses the body's own immune system to fight the cancer. There are several types of immunotherapy that have been developed to fight cancer, including checkpoint inhibitors, cytokines and vaccines, but these are not yet available as treatments for ALL.

At present, only monoclonal antibodies can be used to treat ALL. These antibodies are developed in the laboratory to be all the same type (hence monoclonal). They are synthesised to find a specific protein either on the cancer cells or sometimes another target protein on cells of the immune system with the aim of damaging the cancer cells.

What is CAR-T therapy?

CAR T-cell therapy is a new cancer treatment in which the patient's own immune cells are removed from the patient, genetically modified so they can recognise the tumour, and then re-infused into the patient so they can attack the cancer.

In CAR T-cell therapy, the CAR-T stands for chimeric antigen receptor T-cell. Chimeric, which describes an organism that

contains cells from two or more different species, refers to the protein that is made of different types of gene (i.e. the T-cell) and antigen refers to the antigen on the tumour cell. The term antigen applies to a foreign substance in the body which makes the immune system produce an immune response, especially the production of antibodies.

Who can receive CAR-T therapy?

The first trials of CAR T-cell therapy looked mainly at blood cancers such as ALL and chronic lymphocytic leukaemia (CLL). These cancers develop from B-cell lymphocytes. Therefore, researchers developed CAR T-cells to target a protein on the surface of the B-cell called CD19. This protein is on the surface of nearly all B-cells making CAR T-cells particularly effective against cancers derived from B-cells.

What is anti-CD19 CAR-T therapy?

An anti-CD19 CAR T-cell is a human T-cell which has been genetically engineered to recognise a CAR T-cell that is specific for CD19. CD19 is an antigen found on cancerous and normal-B cells, but not on other normal cells in the body.

Anti-CD19 CAR T-cell therapy has shown great promise in the treatment of B-cell ALL. The anti-CD19 agent tisagenlecleucel (Kymriah) is the first CAR T-cell therapy to be approved in the United States for the treatment of patients up to 25 years of age with B-cell ALL that is refractory or in second or later relapse. In Europe, this anti-CD19 CAR T-cell drug has been licenced and approved by NICE.

What is the difference between allogeneic vs autologous?

Allogeneic relates to cells or tissues which are genetically dissimilar and have come from a matched donor. Autologous relates to cells or tissues which are genetically the same and have been derived from the same individual.

In the case of CAR-T cell therapy, the treatment so far is autologous since the patient's own T-cells are collected, modified genetically and returned to patients on a case-by-case basis. However,

Immunotherapies (cont.)

if this treatment is to reach as many as patients as possible, the time-consuming nature of the procedure, the cost to generate one product for one patient and the problems for patients who do not have enough T-cells to complete the process need to be addressed.

Pharmaceutical companies are already involved in centralised manufacturing of patient-derived CAR-T cells and are planning widespread distribution. However, for this to succeed, strategies to avoid immune responses to allogeneic CAR-T cells leading to rejection need to be developed.

What cancers could CAR-T therapy treat?

In recent years, a number of clinical trials have assessed the feasibility of CAR T-cell therapy for the treatment of B-cell cancers including B-cell non-Hodgkin lymphoma, chronic lymphocytic leukaemia and Hodgkin lymphoma, as well as B-cell ALL. Results from these trials have been promising. While there are some technical difficulties to be resolved, large Phase 3 trials are likely to be planned in order to generate the results required for approval of CAR T-cell therapy for the relevant conditions. A phase 3 trial is a large clinical trial (more than 100 patients) that collects information on a drug's safety and effectiveness using different populations and different dosages, and by comparing it to other known drugs for the same condition.

What are the difficulties with CAR-T therapy?

Despite the clinical success of CAR T-cells for the treatment of B-cell ALL, there are a number of difficulties to be overcome in the development of CAR T-cells:

- Relapse caused by the CAR T-cells no longer being able to detect the specific antigen on the cancer cells.
- Adapting the success of CAR T-cell therapy for B-cell ALL for solid tumours such as breast or lung cancer as it is presenting a number of technical problems.
- Determining the suitable dosage range of CAR T-cells, and establishing if it is the same in different diseases.
- Ensuring the CAR T-cells only

target the protein on cancer cells, not healthy cells.

- Determining the best way to manage patients who have received CAR T-cell therapy, particularly whether CAR T-cell therapy and ASCT will fit together for patients who are eligible for bone marrow transplant.

What clinical trials of CAR-T therapy in ALL are ongoing?

Full details of these trials can be found on the ClinincalTrial.gov website.

What is known about future approval and access to CAR-T therapy?

The first CAR T-cell therapy to be approved in the United States and in the UK is the anti-CD19 agent tisagenlecleucel (Kymriah) for the treatment of patients up to 25 years of age with B-cell ALL that is refractory or in second or later relapse.

Additionally, the Food and Drug Administration have granted Priority Review for Kymriah for the treatment of adult patients with relapsed or refractory diffuse large B-cell lymphoma who are ineligible for or have relapsed after ASCT.

The regulatory applications for approval of Kymriah in Europe and the US are based on the results from two pivotal Phase 2 clinical trials called JULIET and ELIANA. Both trials are international, enrolling patients from the US, Canada, Australia, Japan and Europe.

1. JULIET is investigating the efficacy and safety of CTL019 (Kymriah) in adult patients with relapsed or refractory diffuse large B-cell lymphoma. The study includes 116 participants and is no longer recruiting. The trial is planned to finish in February 2023.

2. ELIANA is investigating the efficacy and safety of CTL019 (Kymriah) in children with relapsed and refractory B-cell ALL. The study includes 81 participants and is no longer recruiting. The trial is planned to finish in November 2021.

Full details of these trials are available at **https://clinicaltrials.gov** (JULIET: NCT02445248 and

Inotuzumab ozogamicin

Inotuzumab ozogamicin (sold as Besponsa™ by Wyeth Pharmaceuticals) is a humanised monoclonal antibody against the CD22 protein (inotuzumab), which has been linked to a toxic compound (ozogamicin or calicheamicin).

Clusters of differentiation (CD) are proteins on the surface of a cell, which are recognised by specific sets of antibodies, and used to identify the cell type, stage of differentiation and activity of a cell.

Who is given inotuzumab ozogamicin?

Inotuzumab ozogamicin has been approved in the UK for the treatment of patients with relapsed or refractory CD22-positive B-cell precursor ALL.

How does inotuzumab ozogamicin work?

CD22 (cluster of differentiation-22) is a protein found on the surface of B-cells that prevents the overactivation of the immune system. It is seen in large numbers on immature B cells which characterise ALL and is present in >90% of patients with ALL.

The purpose of creating monoclonal antibodies is that they can detect and bind to a desired target, which in this case is the CD22 on the immature B-cells. The toxic agent ozogamicin then destroys the DNA of the immature B-cells to stop them multiplying.

When used as medications, the name given to these monoclonal antibody drugs all end in -mab. This targeted approach improves the specificity of the chemotherapy and spares the normal B-cells.

How are you given inotuzumab ozogamicin?

Inotuzumab ozogamicin should be administered under the supervision of an experienced haematologist in premises where full resuscitation equipment is available.

For patients who have

lymphoblasts circulating in the blood, the use of a combination of hydroxyurea, steroids, and/or vincristine to reduce the blast cells to less than 10,000/mm^3 prior to the first dose of treatment is recommended.

Inotuzumab ozogamicin for injection is available and should be administered in cycles of three to four weeks.

For patients proceeding to ASCT:

- Two cycles are recommended.
- A third cycle may be considered for patients who do not achieve a complete remission or have some minimal residual disease (MRD) after two cycles.

For patients not proceeding to ASCT:

- A maximum of six additional cycles may be administered.
- Patients who do not achieve complete remission within three cycles should discontinue treatment.

When do you have inotuzumab ozogamicin?

Inotuzumab ozogamicin is only currently approved as relapsed or refractory re-induction chemotherapy.

Inotuzumab ozogamicin should be administered in cycles of three to four weeks. Pre-medication with a corticosteroid, an antipyretic (drug to lower temperature), and antihistamine is recommended prior to dosing.

For patients with a large tumour mass, hydration and pre-medication to reduce uric acid levels are recommended prior to dosing.

During, and for at least one hour after the end of an infusion, patients should be observed for symptoms of infusion-related reactions.

What tests will you be given before you have inotuzumab ozogamicin?

Prior to the first dose of

Inotuzumab ozogamicin (cont.)

inotuzumab ozogamicin, all patients should have liver tests including levels of liver enzymes (such as alanine aminotransferase, aspartate aminotransferase, total bilirubin, and alkaline phosphatase) to confirm the liver is functioning normally.

Are there any tests while you are taking inotuzumab ozogamicin?

In all patients, liver tests should be monitored prior to and following each dose of inotuzumab ozogamicin.

Patients who develop abnormal liver tests, liver enzyme levels and clinical signs and symptoms of hepatotoxicity (toxic effect on liver) should be monitored more frequently.

For those patients who proceed to ASCT, liver tests should be monitored closely during the first month post-ASCT and less frequently thereafter. Elevation of liver tests may require dosing interruption, dose reduction, or permanent discontinuation of inotuzumab ozogamicin.

What are the specific side effects for inotuzumab ozogamicin?

The most common side effects which occur with inotuzumab ozogamicin include:

- A decrease in numbers of all white blood cells
- Anaemia (low level of red blood cells)
- Fatigue
- Haemorrhage (low levels of platelets)
- Nausea
- Headache
- Abdominal pain
- Increased level of liver enzymes

Infusion related reactions

Infusion related reactions have been reported in approximately 10% of patients receiving inotuzumab ozogamicin. For this reason, pre medication

with a steroid, antipyretic, and antihistamine is recommended prior to dosing with inotuzumab ozogamicin. Patients should be monitored closely during, and for at least one hour after the end of, the infusion for the potential onset of infusion related reactions, which could include symptoms such as hypotension (low blood pressure), hot flushes, or breathing problems.

If an infusion related reaction does occur with inotuzumab ozogamicin, the infusion should be interrupted, and appropriate medical management should be started. Depending on how severe the infusion related reaction is, the infusion should be stopped, or steroids and antihistamines can be administered.

The full list of side effects for inotuzumab ozogamicin is available on the European Medicines Agency website or is also available on the Macmillan website.

Rituximab

Rituximab is available under the brand names of MabThera™, Truxima™, or Rituxan™.

Who is given rituximab?

Recent studies have shown that the combining of rituximab with chemotherapy has improved outcomes in previously-untreated CD20 positive ALL.

How does rituximab work?

Rituximab is a monoclonal antibody which binds to the CD20 protein on the surface of B cells. By attaching to CD20, rituximab causes the death of B-cell lymphocytes.

How are you given rituximab?

Rituximab is given as an IV infusion.

To prevent any allergic reactions, patients should be given an antihistamine and an anti-pyretic before each infusion or injection. Administration of rituximab should be supervised by a haematologist or another healthcare professional experienced in the management of patients with ALL.

When do you have rituximab?

In previously-untreated adults below the age of 60 with Ph-negative ALL, rituximab has shown clinical improvement when combined with intensive induction chemotherapy regimens.

What are the specific side effects for rituximab?

The most common side effects which occur with rituximab include:

- Infusion-related reactions
- Low levels of white blood cells
- Low levels of neutrophils
- Low levels of platelets
- Rash
- Hair loss
- Fatigue
- Nausea

- Headaches

The full list of side effects for rituximab is available on the European Medicines Agency website or is also available on the Macmillan website.

Blinatumomab

Blinatumomab (sold as Blincyto® by Amgen) is a bi-specific monoclonal antibody which contains two binding sites (CD3 and CD19) and whose actions result in the selective disintegration of tumour cells.

On 19 June 2018, the EMA granted blinatumomab full approval for Ph-negative relapsed or refractory B-cell precursor ALL.

Who is given blinatumomab?

Blinatumomab is indicated for the treatment of adults with Ph-negative relapsed or refractory B-precursor ALL. Its approval was expanded on 29 March 2018 to include the treatment of adults and children with B-cell precursor acute lymphoblastic leukaemia who are in remission but still have MRD.

How does blinatumomab work?

Blinatumomab is a bi-specific monoclonal antibody which means it has been made to have two ways of sticking to cancer cells:

1. One binding site that targets the CD19 protein present on the B-cell precursors on the cancer cell
2. The other binding site attracts CD3-positive cytotoxic T-cells to direct the immune system to act against the tumour cells which are present on the CD19 protein.

These two binding sites on blinatumomab result in the selective disintegration of tumour cells. CD19 is a protein marker for normal and cancerous B-cells. CD3 is the protein marker for T-cells and its function is to help activate the T-cells.

How are you given blinatumomab?

Treatment should be initiated and supervised by a haematologist experienced in the treatment of haematological malignancies.

Patients normally receive two cycles of treatment. Generally, for the first cycle, hospitalisation is recommended for the first 14 days as a minimum, and the first two days of the second cycle.

Blinatumomab solution for infusion is administered as a continuous IV infusion.

When do you have blinatumomab?

Blinatumomab is currently only approved for treatment of adults with Ph-negative relapsed or refractory B-cell precursor ALL, and patients normally receive two cycles of treatment.

Blinatumomab may be discontinued temporarily or permanently in the event of the following severe or life-threatening events. If the treatment is interrupted for less than seven days, the same cycle should be continued to a total of 28 days of infusion. If the treatment is interrupted for more than seven days, a new cycle should be started.

Are there any tests needed before and while you are taking blinatumomab?

During treatment with blinatumomab, the following monitoring tests should be carried out to prevent the complications of:

- Cytokine release syndrome: Signs and symptoms of this inflammatory reponse (swelling) will generally appear within two days of starting treatment and patients should be closely monitored.
- Infusion reactions: Patients should be observed closely for infusion reactions, especially during the initiation of the first and second treatment cycles and treated appropriately.
- A neurological examination should be done prior to starting treatment, and the nervous system should be clinically monitored throughout the treatment period.
- Kidney function and fluid balance in the first 48 hours after the first infusion should be monitored as this can be an indication of tumour lysis syndrome.
- Neutropenia and febrile neutropenia: neutrophil numbers should be monitored

Blinatumomab (cont.)

through white blood cell counts as well as any symptoms of fever.

- The pancreas should be monitored for signs and symptoms of pancreatitis, including any inflammation.

What are the specific side effects for blinatumomab?

Data from two large studies in adults with Ph-negative relapsed or refractory B-cell precursor ALL were used to analyse the most common side effects, which include:

- Infusion-related reactions
- Headache
- Anaemia
- Oedema (swelling of tissues of the body due to fluid retention)
- Low levels of neutrophils
- Low levels of platelets
- Increased levels of liver enzymes
- Cough
- Rash

The full list of side effects for blinatumomab is available on the European Medicines Agency website or is also available on the Macmillan website.

Glossary

Allogeneic Stem Cell Transplant

A stem cell transplant of cells from a matching donor.

Anaemia

Low levels of red blood cells.

Antigen

A foreign substance in the body which makes the immune system produce an immune response, especially the production of antibodies.

Antipyretic

A drug to lower temperature.

Biliary Stasis

Bile formed by the liver that cannot flow into the small intestine to help digestion.

Blood Lactate Dehydrogenase

An enzyme that turns sugar into energy for all cells in the body and is released into the bloodstream when the cells are damaged.

Bolus Injection

A single large dose injection.

Bone Marrow Failure

Very low levels of white and red blood cells and platelets.

Central Nervous System

The part of the nervous system that includes the brain and spinal cord.

Chimeric

This describes an organism that contains cells from two or more different species.

Colitis

Inflammation of the lining of the colon.

Dysphagia

Difficulty swallowing.

Fatigue

Tiredness and weakness.

Haematopoiesis

The process by which blood cells are formed.

Hyperuricemia

High levels of uric acid in the blood.

Intensification

Treatment to consolidate remission.

Intramuscular Injection

An injection into a muscle,

Glossary (cont.)

normally the buttock or upper thigh.

Oedema

Swelling of tissues of the body due to fluid retention.

Platelets

Small blood cells that help the body form clots.

Pro-drug

A drug which is inactive outside the body but becomes active when transported into cells.

Prophylaxis

Treatment given, or action taken, to prevent disease.

Refractory (leukaemia)

Leukaemia in which treatment does not result in a remission or that gets worse within six months of the last treatment. However, the leukaemia may be stable.

Relapse

A relapse is when a patient initially responds to leukaemia treatment but, after six months or more, response stops. This is also sometimes called a recurrence.

Sepsis

An infection in the blood with septic shock.

Toxicity

Harmful effect.

Tumour Lysis Syndrome

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

Tell us what you think!

If you would like to give us some feedback about this patient information booklet, please hover over the code to the right using your phone or tablet's camera. Click the link as it appears and this will take you to a short web form to fill in.

Suitable for Android, iPhone 7 and above.

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.leukaemiacare.org.uk

support@leukaemiacare.org.uk

Leukaemia Care,
One Birch Court,
Blackpole East,
Worcester,
WR3 8SG

Registered charity
259483 and SC039207

Leukaemia Care
YOUR Blood Cancer Charity

Health & care information you can trust
The Information Standard Certified Member