Long-term Remission of Acute Lymphoblastic Leukaemia (ALL) and Next Steps

A Guide for Patients

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

Long-term remission of your acute lymphoblastic leukaemia (ALL) is when your leukaemia cells can no longer be detected in your body and you have little or no symptoms of your leukaemia. If you have any questions about this, including the late side effects and the emotional impact - this booklet covers the basics for you.

The booklet was written and updated by our Patient Information Writer, Isabelle Leach, and peer reviewed by consultant haematologists.

We are also grateful to our patient reviewers, Ross Happell, Meryl Simons and Karen Collier for their contribution.

Throughout this booklet, you will see QR codes that will take you to the relevant webpage for further support. Open the camera app on your phone and hover it over the QR code to open the link (suitable for Android, iPhone 7 and above).

Alternatively, if you are not able to use QR codes and would like to be sent the relevant webpages as URLs, or you would like the list of references used for this booklet, please email **communications@leukaemiacare.org.uk.**

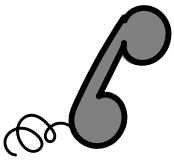
Version 1a
Reviewed: 06/2023
Updated: 04/2024
Review date: 06/2026

In this booklet

About Leukaemia Care

Leukaemia Care is the UK's leading leukaemia charity. For over 50 years, we have been dedicated to ensuring that everyone affected receives the best possible diagnosis, information, advice, treatment and support.

Our services

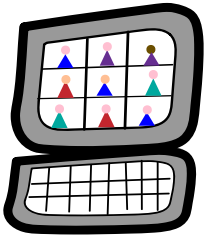


Helpline

Our helpline is available 9am to 5pm Monday to Friday. If you need someone to talk to, call **08088 010 444**.

Alternatively, you can send a message via WhatsApp on **07500 068065** on weekdays 9am to 5pm.

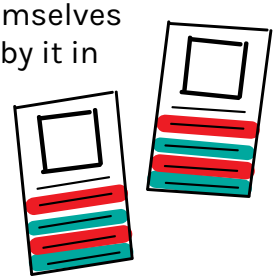
Support groups



Our nationwide support groups are a chance to meet and talk to other people who have been affected by a ALL diagnosis. For more information, scan this QR code:

Buddy support

We offer one-to-one phone support with volunteers who have had ALL 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



Counselling service

Our counselling service helps ALL patients and their loved ones access up to six sessions of counselling. To apply, scan this QR code:

Advocacy and welfare

Our advocacy and welfare officers are here to help you find the support you need for many issues surrounding a ALL diagnosis. These include insurance, benefits and clinical trials. If you would like support from our advocacy or welfare officer, email **advocacy@leukaemiacare.org.uk** or call **08088 010 444**.

Cost of living fund

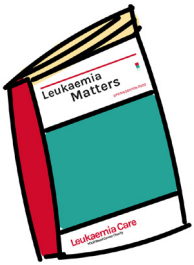
This fund provides grants to patients and families affected by ALL, to help with essential living costs. All applications must be made via the form which can be found by scanning the QR code:

Write a free will

Using our complimentary service, you can write a simple will so you know what happens to your estate when you die. To start writing your free will today, scan this QR code:

Patient magazine

Our magazine includes inspirational patient and carer stories as well as informative articles by medical professionals. To subscribe to our magazine, scan this QR code:



Glossary of medical terms

Acute leukaemia

Leukaemia which progresses rapidly and is generally aggressive. There are two types: acute lymphoblastic leukaemia and acute myeloid leukaemia.

Acute lymphoblastic leukaemia (ALL)

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

Allogeneic stem cell transplant

A procedure where bone marrow stem cells are taken from a genetically matched donor and given to the patient through an intravenous line. The donor may be related or unrelated.

Autologous stem cell transplant (ASCT)

Transplant of stem cells derived from part of the same individual.

Blast cell

An abnormal (dysplastic), immature blood cell found in the bone marrow or peripheral blood. As they are not mature, these cells are unable to fulfil their intended function. AML develops from these blast cells.

Blood transfusion

A procedure in which whole blood or one of its components is given to a person through an intravenous line into the bloodstream. A red blood cell transfusion or a platelet transfusion can help some patients with low blood counts.

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

Therapy for cancer using chemicals that stop the growth of cells.

Clinical trial

A medical research study involving patients with the aim of improving treatments and their side effects. You will always be informed if your treatment is part of a trial.

Consolidation (phase)

Treatment following remission intended to kill any cancer cells that may be left in the body (also called intensification phase).

Fatigue

Extreme tiredness, which is not alleviated by sleep or rest. Fatigue can be acute and come on suddenly or it can be chronic and persistent.

Fluorescence in situ hybridisation (FISH)

Process using fluorescent dyes to attach to certain parts of chromosomes for their identification.

Full blood count or FBC

A blood test that counts the number of different blood cells.

Graft-versus-host disease

Serious complication that occurs with allogenic stem cell transplants. It happens when the graft (donated marrow or stem cells) reacts against the host (patient receiving the stem cells).

Immunophenotyping

Process that uses antibodies to identify cells based on the types of antigens or markers on the surface of the cells. This process is used to diagnose specific types of leukaemia and lymphoma by comparing the cancer cells to normal cells of the immune system.

Immunotherapy

Treatment that uses the body's own immune system to fight the cancer.

Induction (phase)

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

Intrathecal therapy

Injection of chemotherapy into the cerebrospinal fluid that surrounds and protects the brain and spinal cord.

Maintenance

Treatment given to prevent cancer from coming back after it has disappeared following the first-line treatment.

Monoclonal antibody

Man-made antibodies created from identical cloned immune cells so that they all bind to the same protein commonly found on the leukaemia cells such as CD20.

Neutropenia

A condition in which the number of neutrophils (a type of white blood cell) in the bloodstream is decreased.

Neutrophil

A type of white blood cell that helps fight infection.

Palliative care

Also known as supportive care, this is a type of care that focusses on improving the quality of life for a patient with a life threatening illness and their loved ones.

Platelet

A disc-shaped element in the blood that assists in blood clotting.

During normal blood clotting, the platelets clump together (aggregate). Although platelets are often classed as blood cells, they are actually fragments of large bone marrow cells (megakaryocytes).

Platelet count

A normal platelet count in a healthy individual is between 150,000 and 450,000 per microlitre of blood. In general, low platelet counts increase bleeding risks. Normal platelet count 150-450 $x10^9$/l.

Red blood cells

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

Stem cells

Cells that have the potential to develop into many different or specialised cell types.

White blood cell

One of the cells the body makes to help fight infections. There are several types of white blood cells. The two most common types are the lymphocytes and neutrophils. Normal white cell count is 4-11$x10^9$/l.

Summary: What is long-term remission for ALL?

- Long-term remission of acute lymphoblastic leukaemia (ALL) is when your treatment has been successful. You are in a state of lasting remission and **you do not need any active treatment**.
- Long-term remission means that none of your previous leukaemia cells can now be detected in your body.
- Your haematology team should see you at regular intervals. They will check for any long-term side effects or signs of relapse.
- You might see different healthcare professionals according to your needs. These include your haematology doctors, your clinical nurse specialist and physiotherapists.
- **Frequency of appointments will vary based on your risk of relapse.** You should ask if you have any concerns about your appointment schedule.

What is long-term remission for ALL?

Long-term remission of your ALL is when your leukaemia cells can no longer be detected in your body. You should have little or no symptoms.

Five-year survival rates for adults up to age of 60-65 with ALL are between 30-60%. This depends on the type of ALL, patients' genetics and age above 65. This figure is the range of averages of patients still alive after five years. Survival rate is the percentage of patients who are alive at a certain time after diagnosis.

Factors that impact on your survival rate include:

- Your genetic mutations
- Your ALL subtype (T-cell versus B-cell ALL)
- Your age at diagnosis
- The number of high number of white blood cells in your blood at diagnosis
- Treatments that you have received
- Your response to treatment

After treatment, it is hoped that you remain in remission for five years or more. If this is the case, some people consider that you are 'cured' as the likelihood of relapse is very much reduced. However, haematologists would rarely commit to stating that you are 'cured' or that your leukaemia will never return.

This is because some leukaemia cells may still be in your body for many years after treatment. At each of your follow-up visits, your haematology team may perform checks for any signs of relapse.

Signs and symptoms of relapse

If you relapse, your signs and symptoms will be similar to those you experienced when you were first diagnosed. These include:

- Fatigue
- Fever and night sweats
- Unexpected weight loss or anorexia
- Easy bruising
- Frequent chest or urinary tract infections
- Enlarged lymph nodes, spleen or liver
- Pain in the bones or joints

For more information about ALL, we have two dedicated booklets, Newly diagnosed B-cell ALL and Newly diagnosed T-cell ALL. Scan the QR code to order or download our booklets:

What medical support will you have during long-term remission?

Once you are in long-term remission, your haematology team will discuss your follow-up care and recommend a schedule for your care. This will include the frequency of your follow-up visits and the tests they intend to perform at each visit.

Your haematology team will determine your follow-up care schedule based on:

- Your overall health
- Medications you have received during your treatment for ALL

As with other ALL patients, you will need regular check-up visits to detect any signs of relapse or side effects/complications caused by previous treatments.

Your follow-up visits will continue for several years. The frequency of these visits will depend on:

- The type of ALL treatments you have had
- The supportive care you need, for example, to manage your long-term side effects

If you have concerns about your health between appointments, you can ask your haematology team how to get support.

Which health professionals will you see?

At your follow-up visits, you will see your clinical nurse specialist who will ask you about any new symptoms or secondary side effects of treatment. Your test results will also be reviewed. If there are any problems, you are likely to see your haematologist.

If you have long-term physical issues, you may also see other healthcare specialists such as physiotherapists, ophthalmologists, dermatologists and counsellors. It is possible that you may see a clinical immunologist.

Sometimes you may be asked to attend separate clinics that specialise in dealing with your side effects and late effects.

What should you discuss with your haematology team?

At your follow-up visits with your haematology team, you should discuss:

- Any new symptoms of ALL or side effects from previous treatment that you have noticed.
- Side effects that may come back or new side effects (sometimes known as late effects). These will depend on:

- Different treatments that you have had
- Doses of these treatments
- Your age at which you had these treatments

- The follow-up care schedule that your haematology team have recommended for you and any concerns you have with it.

What is the frequency of your follow-up visits and which tests will you have?

At your follow-up visits, your haematology team will discuss with you how you are doing. They will also perform some tests to check if there are any changes in your remission.

Each patient will have a different follow-up care schedule. This will depend on their:

- ALL subtype
- Overall health
- Treatments received

Your follow-up care schedule should include:

Three-monthly visits with your haematology team. Most relapses happen during the first two and a half years after starting treatment.

The following tests are usually carried out during the first two years after remission:

- Physical examination (including testicular examination for males)
- Full blood count (red blood cells, white blood cells and platelets)
- Liver function tests
- Routine chemistry test to examine the function of your kidneys and other organs

- In years four and five, follow-up appointments should be half yearly. Overtime, the check-ups will become less and less frequent.
- If they feel it is necessary, your haematology team may perform bone marrow aspirations every three to six months. If a bone marrow aspiration is done, other tests may include:
    - Flow cytometry: Laboratory method that detects, identifies and counts specific cells and the elements within these cells.
    - Cytogenetic testing: Test that detects structural abnormalities in your chromosomes.
    - Fluorescent in situ hybridisation: Test that gives information about certain gene changes within your chromosomes.
    - Molecular testing: This can be used to find out how well your treatment is working and predict whether your ALL will come back.
    - MRD assessment: This gives an accurate measure of your remission status.
- Your haematology team will conduct periodic screening and examination of your skin, gastrointestinal system, kidneys, bladder, prostate, breasts, lungs, head and neck. Secondary cancers can occur following chemotherapy and a stem cell transplant. However they only occur in less than 3% of patients.

You should have a health examination at least once a year with your general practitioner. This may help discover the onset of any other medical problems or a long-term side effect. Most GPs now reach out automatically to those they know to have had cancer. It is worth contacting your GP surgery to let them know where you are at with your treatment. This will help in case your records have not been updated.

Measurable residual disease

MRD is the most important indicator of your prognosis or risk of relapse. Experts recommend your MRD is determined every three months.

MRD measures the very small amount of leukaemia still present in your body that cannot be detected by conventional methods such as viewing the cells under a microscope and/or tracking their abnormal proteins in the blood.

- MRD positive: If your leukaemia cells are still detectable in your body, you are said to be MRD positive
- MRD negative: If you have no detectable leukaemia cells in your body, you are said to be MRD negative

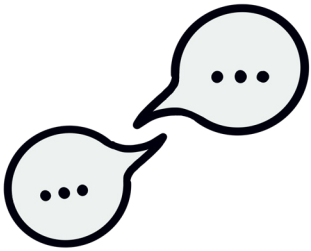
MRD gives a very accurate assessment of remission and an early detection of relapse. Measurement of MRD after treatment will let your haematology team know about your risk of relapse. Your haematology team can measure your MRD using either a blood or bone marrow sample.

Common tests for measuring MRD take place in a laboratory. They include:

- Flow cytometry
- Polymerase chain reaction (PCR) tests

Summary: What is the emotional impact of being in long-term remission?

- **Adapting to being in long-term remission may be challenging.** You might feel **reassured** that you are in long-term remission, but you may also be the **concerned** that the ALL could return.
- A common challenge to your mental health is the **uncertainty** about your future at this stage. Additionally, some people find they experience many emotions that they didn't have the time or space to express while receiving treatment.
- It is crucial to talk about any issues you have. Nothing should be a problem, and your haematology team should be able to put you in contact with someone that you can talk to. Before focussing on the next stages of your life, it is important to deal with the **emotional impact of being in long-term remission**. This will allow you to move forward.
- You may experience this time in a way that is different to others. Some people feel **happy** that their treatment is over. Others are **worried** about the future or the risk of relapse. **A mixture of positive and negative emotions is also normal.**
- You should **seek help** for with any mental health issues if you are struggling. **You are entitled to support when in remission.**



What is the emotional impact of being in long-term remission?

Adjusting to long-term remission

Adjusting to long-term remission can be difficult. You might feel pleased that you are in long-term remission, but there is also the worry that your ALL might come back. Late side effects of your ALL treatment may also be troubling thoughts.

This section is designed to provide you with information on how to live in long-term remission. It can help you begin with rebuilding your life and coping with hurdles that you could face. Before contemplating how you move forward, it is important to deal with the emotional impact of being in long-term remission.

A start to living with long-term remission is to acknowledge that your response to the news is normal. Some feel positive, some feel negative, and many feel both of these things, sometimes at the same time.

The emotions we describe may or may not apply to you, but they are common for people who are in long-term remission. If you have these emotions you should be reassured that your response is entirely normal.

Always seek help if you are concerned about your emotions or mental health.

You can receive help by talking to our Patient Services Team. Call our freephone helpline on **08088 010 444**.

Living with uncertainty

Many patients find the treatment process very challenging. As you adapt to this process and develop a routine, you may have built a good relationship with your haematology team. You may feel safe in their hands and that they are doing all that can be done for you.

When your treatment finishes, this feeling of safety may

diminish as you have less contact with your haematology team. You may feel uncertain about the future. These feelings of uncertainty may make you experience anxiety, depression and a range of other emotions.

Fears of relapse can be very troubling, but they often fade with time. You should seek formal help if this is preventing you from doing things you want or need to do.

Dealing with the emotions of being in long-term remission

As mentioned above, uncertainty is a common theme. There are topics in this section that you might find helpful moving forward.

We have worked with other patients in your position to bring together some tips to help you:

- Continue to accept support from those close to you and do not be afraid of contacting your haematology team if you have any problems.
- Making decisions and plans with those around you can help you feel more prepared for the future.

While the emotions of being in long-term remission are normal and predictable, you may be surprised by the strength of your emotions. This is not unusual.

During your treatment, you have focussed your emotional energy on coping with your day-to-day way of life. Now that you are in long-term remission, your emotions are 'catching up' with you. Remember to seek help if you feel unable to cope by yourself, such as being unable to do day-to-day things.

Being able to talk about difficult emotions can make your feelings seem more manageable. You may be tempted to try and ignore your feelings to protect yourself and others from your strong emotions. But, the energy it takes you to conceal such emotions can make coping with them more difficult. Talking

openly about your worries and fears can free up your energy for a more hopeful outlook.

You may find sharing your story in a support group or at a local cancer meeting a worthwhile way of moving forward. Alternatively, you may prefer to talk in confidence with someone who is impartial. They are used to helping people 'work through' their experience. This is not a sign of weakness but a brave and positive step in your recovery process.

A diagnosis of ALL can be a lot to take in, especially when it comes to treatment options, prognosis and remission. If you think you may benefit from counselling, we can offer funding for up to six sessions. Scan the QR code to fill in a form:

So far, this booklet has described negative emotions you may feel after reaching long-term remission. It is okay to feel happy that your treatment is over. After treatment, you may find you have a renewed sense of purpose. Relationships can become closer and more meaningful. Think about your priorities and make plans for the future that you want. This could be making more time with the people you love or new hobbies and interests.

Your transition to a new life after treatment is sometimes referred to what is sometimes called a 'new normal'. It can be a big upheaval for you. Be kind and patient with yourself until you regain your self-confidence and take in all you have been through. Friends and family may think you should go back to being your normal self as soon as your treatment has ended, but you can need time to recover both physically and emotionally. You may want to have a change of occupation, or follow a new direction in your life. Build your life into what you want it to be.

Your experience of being treated for ALL is not something that can be discounted. It is a part of who you are and your life story.

Accepting it will take time and is not something that can be rushed, even if you are keen for it to be.

Coping with stress

Handling that you are in long-term remission of ALL can be stressful. Stress may make you irritable and result in difficulty concentrating. Feeling tense or anxious can make it harder to enjoy life.

Sharing your feelings can help you to manage your stress. Letting your family or friends know how you feel will enable them to understand and help you. If you are having trouble managing life day-to-day, write a list of what you need to do. This allows you to prioritise and break down your tasks into manageable chunks. Every time you get something done, you will feel a sense of achievement and your load will seem a little lighter.

Re-adjusting back to a normal lifestyle can have profound effects on your relationships. Your relationships may have changed whilst you were being treated. Perhaps your partner took on a carer role, or maybe your children didn't spend the time with you that they did before your diagnosis.

Mindfulness

Mindfulness has emerged as a way that people can learn to live with long-term challenges and periods of uncertainty. It encourages a balanced and non-judgemental approach to your experiences in life.

Mindfulness can help you to appreciate the good times in life. You are encouraged to live day by day, rather than worrying about the future or aspects of your life that you cannot control. It is often explained in groups, but can be learned and practiced alone.

Looking after yourself

Exercise

During exercise, your brain produces chemicals called endorphins that help you manage stress, anxiety, low mood or depression. Exercise promotes better sleep. Being more active during the day helps you relax and sleep better at night.

Regular activity can help alleviate fatigue. Even a small increase in activity can help to improve your energy levels. If you have gained weight during treatment due to inactivity, exercise can help you reach a healthy weight. This will reduce your risk of getting other health problems.

If you have experienced side effects after finishing treatment, regular physical activity may help you manage these.

Healthy eating

Where possible you should eat a well-balanced diet. This will help you:

- Feel stronger
- Have more energy
- Recover without delays

You may have lost weight on treatment due to changes in taste or appetite. This may also be due to the side effects of treatment, which includes sore mouth, or nausea and sickness.

You should ensure your diet includes portions of the following:

- Fruit and vegetables
- Starchy, carbohydrate-rich foods such as bread, rice, pasta and potatoes
- Foods high in protein such as meat, poultry, fish, nuts, eggs and pulses like beans and lentils

- Milk and dairy foods such as cheese, yoghurts and cream
- Plenty of water

Relaxation exercises

You may want to try relaxation exercises. Some support groups or complementary therapy centres teach relaxation, or you can also teach yourself from the internet. Most techniques help you focus on your breathing and relax your muscles in turn. Learning this technique may also help you to get to sleep.

Other complementary therapies can help you to relax and improve your sleep. These include massage, reflexology or hypnotherapy. You may also want to try yoga or tai chi.

Practical support

Work and money

If you develop a late effect of your ALL treatment, you will probably be referred to a clinician with expertise in that area. Because some ALL treatments are associated with several late effects, you may need to see various clinicians at different hospitals. This could have an impact on your work.

You may be thinking about returning to work after treatment or you may not feel ready to restart work or be physically fit enough immediately.

If you are already in work, you will need to talk to your employer about your working arrangements. You may need to negotiate a reduction in your working hours, or to make an arrangement with your employer for times when you need to go to hospital for follow-up visits. You employers are likely to be supportive. However, Leukaemia Care and other organisations can help you if they are not.

If you are looking to return to work or are unsure about your employee rights, Leukaemia Care has useful information that can help you. We can also provide advice throughout the process. You can speak to our Advocacy Team by emailing **advocacy@leukaemiacare.org.uk** or calling **08088 010 444**.

It is important to be aware people who have had any form of cancer are covered by the Equality Act. This means that legally employers cannot discriminate against you and must make reasonable adjustments for the late effects or other physical and mental health challenges that you have.

Your ALL may also affect your finances even if you are not working. Leukaemia Care are aware that being diagnosed with ALL comes with extra costs.

For more information about the financial help that we can provide, scan the QR code to take you there:

Summary: What late side effects can occur during your long-term remission?

- **Long-term side effects** after your treatment for ALL might develop within **months** or **years** after the end of your ALL treatment.
- Your haematologist will discuss any possible late or long-term side effects that you could experience. This is because **early medical attention often can lessen any issues** that can come from late or long-term side effects.

- In this booklet, we discuss the late side effects and long-term side effects of treatments for ALL. These side effects may be physical or emotional.
- **Late and long-term side effects vary from patient to patient**, ranging from very mild to serious. Not everyone gets late effects, the risk depends on type of treatment, dose and age when treated.

What late side effects can occur during your long-term remission?

Long-term side effects after your treatment for ALL might develop within months or years after the end of your treatment. You should report these to your haematology team at your follow-up care visits. Your haematologist should discuss any possible late or long-term side effects with you. Early medical attention can often lessen any issues that can come from late or long-term side effects.

In this section, we list and discuss the late and long-term side effects of treatments of ALL. These side effects vary from patient to patient, and range from very mild to serious. Late and long-term effects can affect your quality of life.

Types of side effects

In general, side effects as a result of treatment for ALL are distinguished as acute, late, or long-term.

- **Acute side effects:** Side effects that occur during and immediately after treatment. Most are short-lived and reversible. For example, nausea and hair loss.
- **Late side effects (also called delayed side effects):** Side effects that occur a certain period after your treatment is finished. For example, cataracts may appear within 18-24 months after your treatment
- **Long-term side effects:** Side effects that are permanent and remain long after treatment is finished. For example, lung fibrosis can develop 10 years after treatment finishes.

The late or long-term side effects that you might get will be related to the ALL treatments you have received to achieve long-term remission. It can be difficult to determine the treatment that caused a late or long-term side effect.

In general, long-term side effects are treated as separate conditions. If a side effect can be linked to a specific drug, then

your haematology team will stop the drug and provide you with supportive care.

Treatments used for ALL

The main treatment for ALL is chemotherapy. In addition, you might have any the following treatments, depending on your subtype of ALL:

Chemotherapy:

- Vincristine
- An anthracycline drug such as daunorubicin, doxorubicin or idarubicin
- Cyclophosphamide or cytarabine
- Asparaginase or pegaspargase

Targeted cancer drugs:

- Imatinib
- Dasatinib
- Nilotinib
- Bosutinib
- Ponatinib

Immunotherapy:

- Blinatumumab for MRD2-positive patients and relapsed/refractory settings (MRD2 is the abbreviation for MRD after two courses of chemotherapy)
- Inotuzumab ozogamicin (only in relapsed/refractory settings)

CAR T-cell therapy:

- Tisagenlecleucel
- Brexucabtagene

Radiotherapy

Stem cell transplant

As well as your side effects relating to your ALL treatments, some treatments can cause the same side effects. An example of this is fatigue. The side effect of fatigue is caused by most of the treatments for ALL. Moreover, fatigue is one of the symptoms of ALL itself.

You will have access to supportive care at any time during your treatment. Supportive care is any medication or medical care that is not intended to treat your leukaemia. Its main objective is to treat any side effects that you have or remaining symptoms of ALL to improve your quality of life.

Late and long-term side effects

Your haematologist will discuss with you any possible late or long-term side effects that you may experience. This is because early medical attention often can decrease any issues that can come from late or long-term side effects.

Late and long-term side effects of patients who have received ALL treatment include:

- Fatigue
- Eye, hearing and mouth changes
- Skin and nail side effects
- Bone and joint issues, especially risk of tissue damage

- Endocrine and thyroid changes
- Cognitive or thinking effects
- Lung toxicity
- Heart toxicity
- Nerve side effects, especially nerve damage
- Kidney and urinary toxicity
- Secondary cancers

Most long-term side effects result from chemotherapy and radiotherapy. Immunotherapies and CAR T-cell therapy have only recently been developed in the last 10 years. Data on their long-term use has not been compiled as yet.

Details of these late and long-term side effects together with any treatments or supportive care to manage them are shown below:

Fatigue

Fatigue can occur during treatment, but it can also last for years after treatment is finished. Fatigue in this context is a tiredness or feeling of exhaustion which leaves you unable to work or perform your usual activities.

The reasons why persistent fatigue occurs following treatment for cancer are not yet fully understood. It is thought that fatigue may be related to chronic inflammation or an imbalance in the central nervous system or hormonal systems.

- Chemotherapies (vincristine) often cause fatigue during and after treatment.
- Radiotherapy can cause fatigue that increases over time, irrespective of the site of treatment.
- Stem cell transplants are aggressive treatments that can cause fatigue lasting for up to one year.

- Stress or depression. Fatigue, stress and depression are often linked and it may not be clear as to which started first. Fatigue is one of the major symptoms of depression.

Supportive care can be very helpful for dealing with fatigue.

Cataracts

Cataracts are areas of clouding of the lens of the eye that interfere with light passing through it. They cause blurred vision, sensitivity to light, glare, double vision and poor vision at night.

Chemotherapy, hormone therapy, immunotherapy, radiotherapy and steroid drugs can all lead to an increased risk of cataracts. Treatment is the surgical removal of the clouded lens and replacement with an artificial plastic lens. You will normally have local anaesthesia and be able to go home the same day.

Dry eye syndrome

Dry eye syndrome is a common condition which results from inflammation of the cornea and conjunctiva of the eye. This leads to a decrease in tear production.

Dry eye syndrome is common after radiotherapy and a sign of chronic graft-versus-host disease after a stem cell transplant. Graft versus-host disease is a condition following a stem cell transplant where the donated stem cells react against the patient receiving the stem cells. It can affect any part of the eye, but typically causes inflammation of the conjunctiva and tear glands.

Dry eyes are prone to eye infection. Symptoms of dry eye include dry gritty eyes, pain, light sensitivity and excessive watering of your eyes. Treatments include artificial tears or ointments to lubricate the eye.

Hearing changes

Some chemotherapy drugs and high doses of radiation can cause hearing loss. This can occur months or years after exposure.

If you have noticed any impairment in your hearing, you should speak to your consultant or GP. You will be referred to specialised audiology services.

Mouth changes

If you have had certain chemotherapy drugs or radiation treatment to your head or neck, you may notice late side effects such as dry mouth, gum infections, tooth loss or bone loss of your jaw. Other symptoms include mouth sores, changes in taste or smell and sensitivity to hot or cold foods. Treatment includes pain killers, antibacterial mouth washes and antibiotics.

Skin changes

Chemotherapy and radiotherapy can cause several skin problems. The most common ones include dry skin, hyperpigmentation (increased skin colour) and an increased skin response to ultraviolet light (photosensitivity).

In patients having had a stem cell transplant, graft-versus-host disease can cause a number of late side effects such as a rash, blisters on the face, ears, palms, and soles, and sclerosis (hardening) of the skin.

Dry skin reactions can be effectively improved with moisturising creams and lotions. Photosensitivity is best managed with the use of sun cream, protective clothing and moisturising after-sun creams.

Nail changes

Chemotherapy can cause discolouration of the nails, single white

transverse bands on the nail plate, and haemorrhages under the nails. More serious nail changes include reddening and swelling around the nail, abscesses under the nail, and onycholysis (detachment of the nail plate from the bed). These result in pain, discomfort, and impair manual activities.

Nail side effects are common with anthracyclines and tyrosine kinase inhibitors. Be aware of any changes on your nails after your chemotherapy treatment. Talk to your haematology team about side effects that you may be experiencing. They can help you treat and prevent complications, such as nail loss and secondary infections.

Bone changes

Chemotherapy treatments responsible for bone damage include methotrexate, imatinib and steroids. The effect of these treatments on the bone can be direct such as in the case for imatinib. However damage to the bone can be through altered ovarian function and hormonal status.

Decreases in bone mineral density occurs naturally with aging. However, reduction in sex steroid levels that occurs with treatments used in ALL is also an important factor in bone loss. For example, ovarian failure results in bone loss within two years. Severe reduction in bone mineral density is called osteoporosis. This can lead to bone fractures, particularly in patients who received chemotherapy at a young age.

Hormone replacement therapy should be prescribed. This must be done with care in patients with a family history of breast cancer or clotting events.

If you have bone damage you should have regular check-ups to test your bone mineral density. You can also minimise the risk of bone loss by limiting your alcohol intake and not smoking. In addition, weight bearing exercises, as well as calcium and vitamin D can help preserve your bone density.

Joint changes

Chemotherapy drugs, steroids and radiotherapy can lead to muscle weakness, scar tissue and bone loss. This may cause a loss of motion in your joints. If you are at risk because of your previous cancer treatment, you will be monitored for early signs of joint changes to prevent worsening.

Death of bone cells caused by interruption of the blood supply to the bone can result from radiation therapy or chemotherapy. These joint changes are most common in the hip and shoulder, but can affect other joints. Joint changes can cause considerable pain and disability depending on the joints involved.

Treatment consists of good pain relief and improving the use of the joints with physiotherapy. Surgery and joint replacement can be used if required.

Endocrine changes

The endocrine system is a network of glands that produce hormones. These hormones control vital body functions including growth, how the body generates energy, sleep and reproduction.

Chemotherapies and radiation to the head and neck area can result in temporary or permanent damage to the endocrine system. This damage can lead to early menopause, infertility, under active thyroid and weight gain. Hormone replacement therapy should be prescribed.

Thyroid changes

The most common effect of radiation is to make the thyroid gland become underactive. This leads to a reduction of thyroid hormone production and a slowing of the body's metabolism. This causes fatigue, feelings of being cold, slow pulse rate, weight gain, and sometimes hoarseness. An underactive thyroid is a

permanent side effect. You will be prescribed thyroxine tablets for life and you should have your thyroid function monitored yearly.

If a nodule is discovered at your yearly thyroid test, you should have a biopsy and surgery to remove the nodule, if required.

Decreased fertility

Chemotherapy and radiotherapy can result in premature ovarian failure and early menopause. Men can have lowered testosterone levels and sperm counts. These changes result in a permanent decrease in fertility for both genders.

Male fertility

Chemotherapy can slow down or stop sperm production either temporarily or permanently. In addition, it can affect the ability to have an erection and ejaculate.

Chemotherapy drugs most commonly implicated in affecting sperm production are cyclophosphamide and cytarabine. Recovery can take many years.

Testosterone secretion is usually less affected by chemotherapies. Testosterone regulates sex drive and sperm production, muscle mass, bone mass and fat distribution. Male patients should be offered the opportunity to store sperm before treatment for their ALL starts. This may not always be possible if you need immediate treatment.

Pelvic radiotherapy can affect:

- Sperm production
- Testosterone secretion
- Nerves necessary for sustained erection

The cells that produce sperm are sensitive to chemotherapy or radiotherapy. Those that produce testosterone however are more

resilient. Males rarely require hormone replacement treatment.

Female fertility

The ovaries are very sensitive to chemotherapy. Some drugs may cause either rapid and permanent ovarian failure or a period of normal fertility followed by an early menopause. Some drugs, particularly cyclophosphamide, are more damaging to the ovaries than others. Chemotherapy drugs that affect ovarian function are similar to those affecting sperm production. They include cyclophosphamide and cytarabine.

Radiotherapy produces severe dose-related damage to the ovarian tissue. This affects both egg production and hormone producing cells. It may cause immediate permanent sterility, temporary cessation of periods or lead to an early menopause. The probability of infertility from a given dose of radiotherapy increases with:

- Age
- Simultaneous use of chemotherapy

In addition, high doses of radiotherapy decreases the functional lining of the uterus. This can lead to an increased risk of early pregnancy loss.

Fertility preservation before treatment is not as simple for women as it is for men. Egg collection depends on your fertility levels and number of eggs in your ovaries. Treatment for ALL normally starts relatively quickly after your diagnosis. You should freeze your eggs if you can before receiving treatment.

Your haematology team should inform you about the potential effects on your fertility at the time of diagnosis. When a child is having ALL treatment, their parents should be given this information.

Cognitive function effect

Cognitive function is the name given to all the mental processes that allow us to carry out any task. Patients may commonly notice that their short-term memory and concentration are diminished. This usually settles after treatment, but can occasionally be a long-term effect.

Radiation therapy to areas including the brain can cause difficulties in the months or years after treatment. These late effects may include:

- Verbal memory loss
- Issues with concentration
- Speed of processing of information
- Personality changes

Following cancer treatment, you will have regular check-up appointments. Any cognitive function or brain changes should be assessed to determine if these are late side effects. Referral for physical, occupational, or speech therapy should be made for late side effects.

Lymphoedema

Patients who have had radiation treatment as part of their conditioning regimen are at risk of lymphoedema as a late effect.

Lymphoedema is a condition where the lymph fluid from the lymphatic system does not drain into the blood vessels as it should. This is because of radiation damage to the lymphatic vessels. The lymphatic fluid builds up in the tissues causing swelling. It can develop many years after treatment.

Lymphoedema may range from causing mild discomfort to severe painful swelling. Treatment for lymphoedema is lymphatic

drainage massage together with physiotherapy, compression garments, exercise and diet.

Lung toxicity

Chemotherapies such as high doses of cyclophosphamide and radiation therapy to the chest can cause lung damage. Chronic graft-versus-host disease after a stem cell transplant is also known to have an effect on the lungs.

Lung damage can cause shortness of breath, wheezing, fever, dry cough, congestion and feeling tired. These symptoms usually begin to improve after around two to three weeks after treatment.

Months or years after radiotherapy, patients may develop serious side effects including:

- Pneumonitis is an inflammation of the walls of the alveoli (air sacs) in the lungs.
- Pulmonary fibrosis is a build-up of scar tissue in the lungs. Pulmonary fibrosis occurs six to 24 months after the pneumonitis. However, pulmonary fibrosis may develop several years after radiation therapy is finished. Pulmonary fibrosis can lead to chronic pulmonary insufficiency, where the lungs can no longer take in enough oxygen or expel enough carbon dioxide to keep the body healthy.

Oxygen therapy can be given for serious breathing trouble. It is normally administered through a mask that fits over your mouth and nose.

Risk of lung damage is increased by smoking, pre-existing lung problems such as asthma, onset of treatment at a young age and administration of cancer drugs anthracyclines that increase the effect of radiotherapy.

Heart toxicity

The heart can be affected by a number of chemotherapy drugs used to treat ALL as well as by radiotherapy when the heart is in the radiotherapy field.

The most common drugs implicated in late cardiotoxicity are the anthracyclines. These drugs are used in many treatment combinations for patients with ALL. They include doxorubicin (adriamycin), daunorubicin, idarubicin and epirubicin. They are often administered as part of combination chemotherapy. Their toxic effects on the heart is dependent on the dose you receive.

Anthracyclines may have a direct toxic effect on the heart muscle preventing it pumping effectively. This may become apparent within one year of finishing treatment.

In case of severe heart damage, the use of medications such as beta-blockers and angiotensin converting enzyme (ACE) inhibitors might delay the progression of your cardiotoxicity, and also reverse part of the damage. These drugs might have to be continued for life.

Radiotherapy can have a number of effects on the heart, but the exact cause of it is not clear. It can cause damage to the heart muscles (cardiomyopathy), coronary artery disease, valvular disease (damage to one of the four heart valves), and disease of the heart conduction system and pericardium (membrane enclosing the heart).

Kidney toxicity

Certain chemotherapy drugs can change your kidney function. They affect people in different ways. This can occur for months or years after treatment. Long-term kidney toxicity has been reported after as long as 35 years in patients who have received methotrexate, cyclophosphamide and radiotherapy as children.

When your kidneys are not functioning properly, the kidney tubule cells can be damaged and lead to infection of your kidney. Cyclophosphamide can cause renal tubular necrosis. Methotrexate is used at high doses in the treatment of ALL and can cause chronic kidney disease. Interferon-alpha can cause glomerulonephritis. This is inflammation of the tiny filters in your kidney.

Early detection of the side effects of chemotherapy on the kidney is important to prevent progression to end stage renal disease.

Liver toxicity

Hepatotoxicity is the injury to the liver or impairment of liver function caused by exposure to drugs, alcohol or environmental toxic products. Certain chemotherapy drugs can cause damage to liver cells by inhibiting how they produce DNA and stopping their cells divide. Drugs used to treat ALL which are toxic to the liver are methotrexate and cytarabine. Methotrexate has been associated with non-alcoholic fatty liver, fibrosis and cirrhosis. These liver complications may be reversed within months after treatment is stopped.

6-mercaptopurine used in the maintenance treatment of ALL can result in toxicity of the liver cells and obstruction of the bile duct. Cytarabine has also been linked to the slowing or stalling of bile flow.

Veno-occlusive disease

Veno-occlusive disease (VOD) occurs in 2% of patients with B-cell relapsed or refractory ALL. It is a result of the small blood vessels in and around the liver becoming blocked. VOD develops in the first few weeks after a SCT and can be mild or severe. It is a potentially fatal form of hepatic injury.

Symptoms of VOD include:

- Jaundice (your skin and whites of the eyes become yellow and your urine is dark yellow)
- Liver tenderness (under the ribs on the right side of the body)
- Liver enlargement
- Ascites (abnormal build-up of fluid in the abdomen).
- Sudden weight gain

The main cause of VOD was thought to be an acute side effect to inotuzumab ozogamicin. VOD is now thought to be a late onset side effect in patients who undergo an allogeneic SCT.

Treatment includes supportive care, intensive care and specific treatment with the drug defibrotide. The mechanism of defibrotide is not yet fully understood.

Nerve side effects

Certain anticancer drugs can cause temporary or permanent peripheral neuropathy. This is the damage or dysfunction of one or more nerves resulting in numbness, tingling, muscle weakness and pain in the area supplied by the nerves. Peripheral neuropathy can develop weeks after starting chemotherapy, or may show a gradual onset but may last from months to years after the chemotherapy is finished.

Drugs used to treat ALL that causes peripheral neuropathy are the vinca alkaloids such as vincristine. Long-term peripheral neuropathy causes disorders of co-ordination, balance and speech, insomnia and depression.

It is important to let your doctor know immediately if you experience any of these symptoms so your medication can be adjusted to relieve the condition. Peripheral neuropathy can

last for many years after the end of treatment and dramatically reduce quality of life.

Secondary cancers

Secondary cancers have become one of the most serious late side effects of treatment for ALL, both in children and adults. A secondary cancer is the development of a new primary cancer of a different type to the original cancer, generally years after treatment. For example, patients who have had treatment for ALL may develop a thyroid cancer 15 years after their treatment.

Secondary cancers are often mistakenly considered to be related to the first cancer. Alternatively, they are thought to be the spread of the first cancer to other areas in the body. If a cancer is a spread of the first cancer to other areas in the body, they should be called metastasis. Importantly, they will have the same type of cells as the original cancer i.e. leukaemia cells.

Secondary cancers often occur years after the original treatment using chemotherapy or radiotherapy.

Any chemotherapy whose mechanism of action is to damage the DNA of cells may result in secondary cancers in the future. Chemotherapies most likely to cause this damage are:

- Alkylating drugs (cyclophosphamide)
- Anthracycline drugs (daunorubicin and doxorubicin)

Radiotherapy is also known to break DNA strands leading to gene mutation and cancer transformation.

What supportive care could you have during your long-term remission?

Supportive care is available for you at any time during your treatment. Supportive care describes any medication or medical care that is not meant for the treatment of your leukaemia. The purpose of supportive care is to help you with side effects of treatment (e.g. sleep disturbance) or any remaining symptoms from your ALL. This includes medication or different treatment strategies like counselling or physiotherapy. The purpose of supportive care is to improve your quality of life.

In the previous chapter, we included any medication that could treat or help with your late or long-term side effects. If no treatment is available, then supportive care can help.

Supportive care is not only limited to the physical impact of your ALL symptoms. It will provide support for matters that are:

- Psychological
- Social
- Spiritual

Classes or workshops in mindfulness, relaxation techniques and the above can help you manage with concerns such as fatigue, cognitive function, nerve side effects.

Fatigue

Fatigue is a very common and troublesome side effect of ALL treatment. It can be caused directly by the drugs or it can have different causes such as the psychological and emotional stress of diagnosis. Fatigue is often frustrating as it cannot be treated with medicines.

Solutions to decrease your level of fatigue are available. These include pacing yourself, improving the quality of your sleep and reducing your alcohol intake.

Make sure you discuss your fatigue with your haematology team. It is very common for it to continue after treatment. There are fatigue services if it affects you in the long-term, or particularly severely, but waiting lists can be long.

Infection

You should be aware that you are still vulnerable to infections even after treatment. This is because most treatments have an effect on other aspects of your immune system.

You should already be aware of the symptoms of infections. Common symptoms of infection include:

- Fever – a raised temperature (38°C or higher)
- Aching muscles
- Diarrhoea
- Headaches
- Excessive tiredness

You should seek help as soon as possible if you experience any of these symptoms. Your haematology team should have given you a specific phone number and instructions on what to do if you are aware of symptoms of infection.

Prevention of infections

Simple precautions can help you reduce your risk of infection. These are:

- Washing your hands.
- Limiting your time in crowds, especially if there is an epidemic of flu or other illness.
- Following food safety advice and not keeping food after use-by dates. Cleanliness in the kitchen is important.

Specific advice on how to protect yourself from COVID-19 infection is available on our website. It is constantly updated. Scan the QR code to take you there:

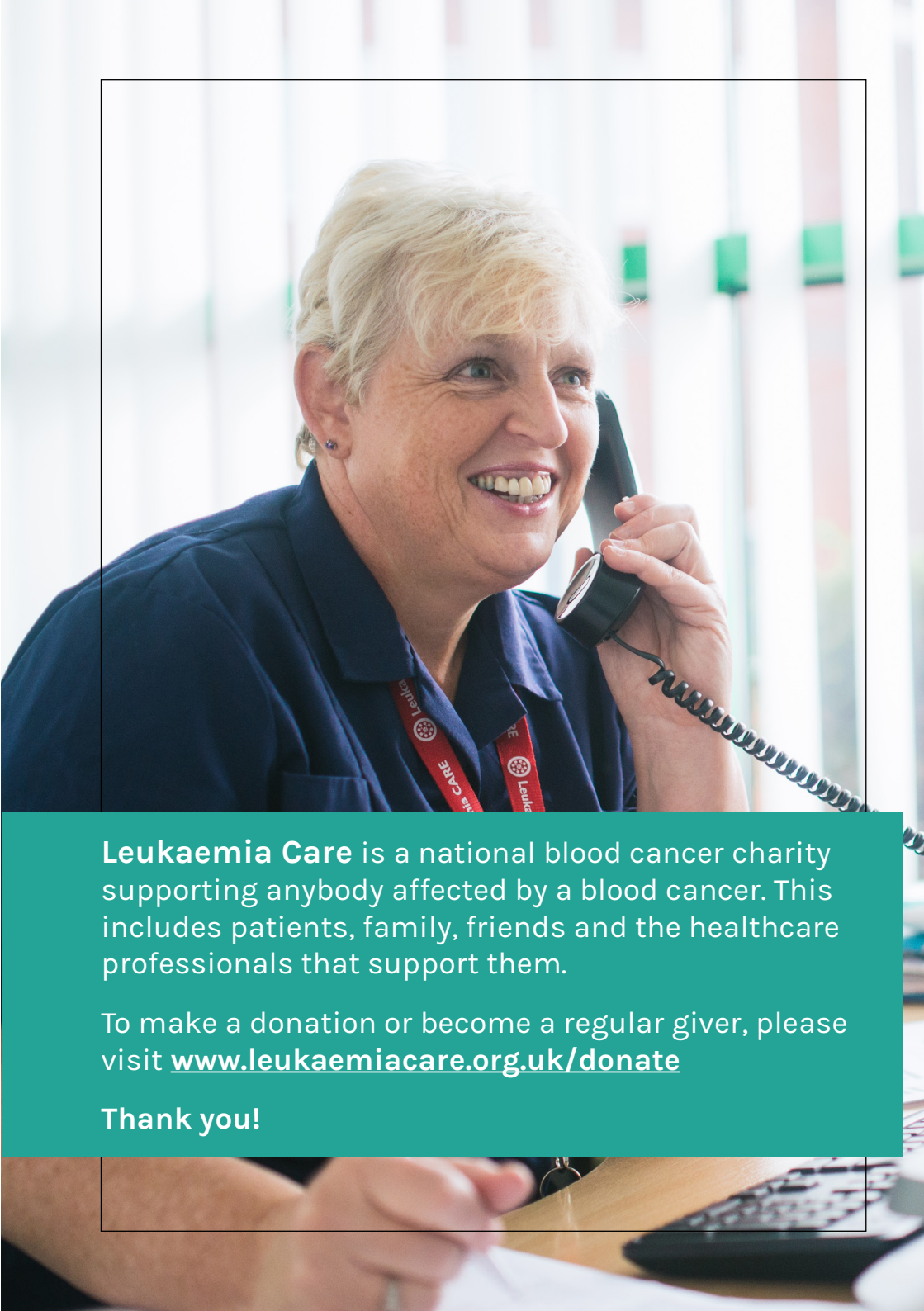
Antibiotics normally used to treat infections can also be used to prevent them where applicable. Most common antibiotics and antifungals used are:

- Trimethoprim/sulfamethoxazole (cotrimoxazole) for pneumocystis pneumonia prophylaxis
- Aciclovir to prevent viral infections

Support with transfusions

Supportive care also includes in the event of a relapse:

- Blood transfusions (red cells or platelets) if your bone marrow is unable to make normal blood cells.
- Injections of growth factors will help if you need to produce more white blood cells. Transfusion of white blood cells carries a high risk of side effects and will not performed.



Leukaemia Care is a national blood cancer charity supporting anybody affected by a blood cancer. This includes patients, family, friends and the healthcare professionals that support them.

To make a donation or become a regular giver, please visit **www.leukaemiacare.org.uk/donate**

Thank you!

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

Leukaemia Care

Leukaemia Care is the UK's leading leukaemia charity. For over 50 years, we have been dedicated to ensuring that everyone affected receives the best possible diagnosis, information, advice, treatment and support. We are here for everyone affected by leukaemia and related blood cancer types – such as myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPN). We believe in improving lives and being a force for change. To do this, we have to challenge the status quo and do things differently.

Helpline: **08088 010 444**
www.leukaemiacare.org.uk
support@leukaemiacare.org.uk

Blood Cancer UK

Leading charity into the research of blood cancers.

0808 2080 888
www.bloodcancer.org.uk

Cancer Research UK

Leading charity dedicated to cancer research.

0808 800 4040
www.cancerresearchuk.org

Macmillan

Provides free practical, medical and financial support for people facing cancer.

0808 808 0000
www.macmillan.org.uk

Maggie's Centres

Offers free practical, emotional and social support to people with cancer and their loved ones.

0300 123 1801
www.maggiescentres.org

Citizens Advice Bureau (CAB)

Offers advice on benefits and financial assistance.

08444 111 444
www.adviceguide.org.uk

How you can help us

If you've been affected by ALL, sharing your story can help others going through a similar situation and help the public to better understand.

Scan the QR to share your story:

Alternatively, you can email our Communications Team at communications@leukaemiacare.org.uk.

We are continually working to make sure our information is up to date and includes everything you need to help feel supported and empowered to advocate for yourself. With this, it is important for us to listen to any feedback you might have about our long-term remission of ALL and next steps booklet.

Scan the QR to take you to our shop to leave a review of our booklet:

Alternatively, you can email our Information Team at information@leukaemiacare.org.uk, call our office line on **01905 755 977** or write a letter to our Head Office at **Leukaemia Care, One Birch Court, Blackpole East, Worcester, WR3 8SG**.

Take on a challenge for Leukaemia Care

We have a range of fundraising challenges that you can get involved in to help us continue to provide care and support to those affected by a leukaemia, MDS or an MPN.

Running, swimming, cycling and adrenaline challenges are available to take part in, both in the UK and abroad. There really is something for everyone.

If you're interested in taking part in a challenge, speak to a member of our Fundraising Team by emailing fundraising@leukaemiacare.org.uk or calling **01905 755977**.

Alternatively, scan this QR code to find out all the ways you can get involved with Leukaemia Care:

"It was a pleasure to meet you and to take part in my first half marathon together with the Leukaemia Care team! I'm a scientist and work in immunology research. A dear family member passed away from leukaemia seven years ago this month, so I did this in his memory. I smashed my goal of under two hours with a final time of 1:53! I'm extremely happy, thank you so much for all your hard work and it was great to see you cheering us on along the track. I loved the look of the vests too! See you again, next year maybe!" **- Alexandru Bacita ran London Landmarks for Leukaemia Care in 2022**

Your gift today will ensure that Leukaemia Care can continue to offer support to leukaemia patients and those who love them

Yes, I want to make a regular gift to Leukaemia Care of £5 or £ ☐ a month starting on the 1st ☐ or the 15th ☐ of each month (please tick one).

Please note: the minimum for a direct debit is £2 a month.

Title: .....

First name or initial(s): ..... Surname: .....

Full home address: .....

.....

Postcode: ..... Phone: .....

Email: .....

☐ **Gift Aid Declaration: Please tick here if you want Leukaemia Care to reclaim the tax that you have paid on all your donations you make in the future or have made in the past four years.**

Instruction to your Bank or Building Society to pay by Direct Debit

Name of Account Holder(s): ..... / .....

Bank/Building Society account number: ☐

Branch sort code: ☐

Name and full postal address of you Bank or Building Society: .....

.....

Instruction to your Bank or Building Society: Please pay Leukaemia Care from the account detailed in this instruction subject to the safeguards assured by the Direct Debit Guarantee. I understand that this instruction may remain with Leukaemia Care and, if so, details will be passed electronically to my Bank/Building Society.

Signature(s): ..... / .....

Date: ☐

This guarantee should be detached and retained by the payee.

The Direct Debit Guarantee

DIRECT Debit

This Guarantee is offered by all banks and building societies that accept instructions to pay Direct Debits.

The efficiency and security of the scheme is mentioned and protected by your own Bank or Building Society.

If the amounts to be paid or the payment dates change, Leukaemia Care will notify you 10 working days in advance of your account being debited or as otherwise agreed.

If an error is made by Leukaemia Care or your Bank or Building Society, you are guaranteed a full and immediate refund from your branch of the amount paid.

You can cancel a Direct Debit at any time by writing to your Bank or Building Society. Please also send a copy of your letter to us.

Leukaemia Care is the UK's leading leukaemia charity. For over 50 years, we have been dedicated to ensuring that everyone affected receives the best possible diagnosis, information, advice, treatment and support.

Every year, 10,000 people are diagnosed with leukaemia in the UK. 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

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

Company number: 11911752 (England and Wales).

Registered office address: One Birch Court, Blackpole East, Worcester, WR3 8SG

Leukaemia Care
YOUR Blood Cancer Charity

Trusted Information Creator
Patient Information Forum