
B-cell Acute Lymphoblastic Leukaemia (ALL)

**A Guide for
Patients**

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

Being diagnosed with B-cell acute lymphoblastic leukaemia (ALL) can be a shock, particularly when you may never have heard of it. If you have questions about B-cell ALL – what causes it, who it affects, how it affects your body, what symptoms to expect and likely treatments – this booklet covers the basics for you.

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

Booklet compiled by our Patient Information Writer Isabelle Leach and peer reviewed by Dr Prem Mahendra, Consultant Haematologist at University Hospital Birmingham. Thank you to patient reviewer Gary Bowman for all your helpful insight.

If you would like any information on the sources used for this booklet, please email communications@leukaemiacare.org.uk for a list of references.

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About Leukaemia Care

Leukaemia Care is a national charity dedicated to ensuring that people affected by blood cancer have access to the right information, advice and support.

Our services

Helpline

Our helpline is available weekdays 8:30am - 5:30pm and 7:00pm - 10:00pm on Thursdays and Fridays. 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@leukaemicare.org.uk or over the phone on **08088 010 444**.

Patient Information Booklets

We have a number of patient information booklets like this available to anyone who has been affected by a blood cancer. A full list of titles – both disease specific and general information titles – can be found on our website at www.leukaemicare.org.uk.

leukaemicare.org.uk/support-and-information/help-and-resources/information-booklets/

Support Groups

Our nationwide support groups are a chance to meet and talk to other people who are going through a similar experience. For more information about a support group local to your area, go to www.leukaemicare.org.uk/support-and-information/support-for-you/find-a-support-group/

Buddy Support

We offer one-to-one phone support with volunteers who have had blood cancer themselves or been affected by it in some way. You can speak to someone who knows what you are going through. For more information on how to get a buddy call **08088 010 444** or email

support@leukaemiacare.org.uk

Online Forum

Our online forum, **www.healthunlocked.com/leukaemia-care**, is a place for people to ask questions anonymously or to join in the discussion with other people in a similar situation.

Patient and carer conferences

Our nationwide conferences provide an opportunity to ask questions and listen to patient speakers and medical professionals who can provide valuable information and support.

Website

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

Campaigning and Advocacy

Leukaemia Care is involved in

campaigning for patient well-being, NHS funding and drug and treatment availability. If you would like an update on any of the work we are currently doing or want to know how to get involved, email **advocacy@leukaemiacare.org.uk**

Patient magazine

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

What is B-cell ALL?

Acute lymphoblastic leukaemia (ALL) is a blood cancer where high numbers of abnormal, immature lymphocytes called blasts start over-multiplying in the bone marrow. Lymphocytes are white blood cells involved in the immune response. There are three types of lymphocytes:

1. B-lymphocytes (B-cells):

Formed in the bone marrow, B-cells produce antibodies that immobilise and label the bacteria, viruses, and toxins which invade the body.

2. T-lymphocytes (T-cells):

Formed in the thymus gland behind the sternum, T-cells destroy the invading organisms that have been labelled by the B-cells, as well as any cells that have become cancerous.

3. Natural killer lymphocytes (NK-cells): Formed in the bone marrow, lymph nodes, spleen, tonsils, and thymus, NK-cells attack viruses and all types of cancer cells. NK cells are unique because they recognise cells under attack without

needing antibodies to label them and therefore produce a much faster immune reaction.

Approximately 85% of patients with ALL are children under 15 years of age and the remaining 15% of ALL cases are adults, mainly aged over 50 years.

In children with ALL:

- 80% to 85% of ALL consists of early B-cells (also called precursor B-cell)
- 15% are early T-cells
- Approximately 2% are mature B-cells

In adults with ALL:

- 75% of cases are early B-cells
- 25% are malignant early T-cells

According to the 2016 World Health Organisation Classification of Tumours of Haematopoietic and Lymphoid Tissues, B-cell acute lymphoblastic leukaemia (B-cell ALL) is a subtype of ALL that begins in the bone marrow when the immature blast cells

proliferate (multiply rapidly) rather than developing normally into B-cell lymphocytes.

In B-cell ALL, there is widespread bone marrow and blood involvement. If the condition occurs only as a body mass lesion, with no or little involvement of the marrow or blood, the term lymphoma is used, i.e. B-cell lymphoma. If patients present with a mass lesion and involvement in the marrow, the distinction between leukaemia and lymphoma is not made.

Who is affected by B-cell ALL?

B-cell ALL is mainly a children's disease, with approximately 75% of cases being children aged <6 years. However, while the majority of B-cell ALL cases occur in children <15 years of age, a second peak of incidence is seen in people around 40 years of age.

The worldwide estimated annual incidence of B-cell ALL is 1 to 4.75 cases per 100 000 of the population and is slightly higher

in males than females.

What causes B-cell ALL?

There is no specific proportion of blasts (cancerous B-cells) required in the bone marrow or blood for a diagnosis of B-cell ALL. However, it is generally agreed that the diagnosis should be avoided if there are not 20% of blasts or more present.

The exact cause of B-cell ALL is not known. However, research suggests that factors such as lifestyle, genetic disorders or chromosome abnormalities may play a role in developing B-cell ALL.

Pesticides, magnetic exposure and an overstimulation of the immune response during the first years of life are thought to be related to the increase in B-cell ALL. Also, children with Down's syndrome and other genetic disorders are more likely to develop B-cell ALL.

In children with B-cell ALL, there are chromosomal abnormalities

What is B-cell ALL? (cont.)

associated with B-cell ALL which include changes in the patient's number of chromosomes and translocations of the chromosomes. A translocation is the transfer of one part of a chromosome to another part of the same or a different chromosome, resulting in rearrangement of the genes.

The most common changes in chromosome numbers are:

- **Hyperdiploidy:** Having more than the normal 46 chromosomes or 23 pairs
- **Hypodiploidy:** Having less than the normal 46 chromosomes
- **Trisomy of chromosomes 4, 10 or 21 as in Down's syndrome:** Having three versions of a chromosome instead of the normal pair of chromosomes.
- **Intrachromosomal amplification of chromosome 21 (iAMP21):** Multiple copies of the RUNX1 gene on chromosome 21

The four most common translocations are:

1. t(4;11) MLL-AF4

2. t(9;22) BCR-ABL1
3. BCR-ABL1-like
4. t(12;21) ETV6-RUNX1

Adults with ALL tend to have a greater number of high-risk chromosome abnormalities with poor outcomes and a lower incidence of genetic abnormalities which have a good prognosis. The most common chromosome abnormalities in adults are:

- **t(9;22)(q34;q11.2), also known as the Philadelphia chromosome:** This genetic abnormality is a fusion of a portion of chromosome 9 on chromosome 22.
- **BCR-ABL1-like:** This chromosome abnormality is similar to the t(9;22) BCR-ABL1 translocation but crucially it lacks the BCR-ABL1.



Symptoms of B-cell ALL

As the bone marrow is involved in all cases of B-cell ALL, the majority of patients present with consequences of bone marrow depression, such as reduced levels of red blood cells, neutrophils (white blood cells involved in fighting infection) and platelets (one of the types of blood cells which help to stop bleeding). Involvement of B-cell ALL outside the bone marrow is common, with the central nervous system (CNS - brain and spinal cord), spleen, liver, and lymph nodes being the organs commonly implicated.

Common signs and symptoms of patients with B-cell ALL are:

- Anaemia
- Loss of appetite
- Fever
- Fatigue
- Bruising/bleeding
- Swollen or painful abdomen due to enlarged spleen and liver
- Bone and joint pain
- Recurring infections

CNS involvement in patients with B-cell ALL occurs in 5-8% of

patients. In adult patients, CNS involvement is more common in patients who have relapsed. Patients are said to have relapsed when they initially respond to leukaemia treatment, but after six months or more, response stops. This is also sometimes called a recurrence.



Prognosis of B-cell ALL

Prognosis for B-cell ALL in children is generally good, but it is not as favourable in adults. Five-year survival for patients with B-cell ALL is greater than 90% in children, but only 40% to 50% in adults and elderly patients, respectively.

The overall complete remission rate in children is >95% and 60-85% in adults. Some 15 to 20% of children with B-cell ALL will relapse, after which they have a less favourable prognosis. For adults with B-cell ALL, the relapse rate is approximately 50%, and a poor prognosis is expected with a median survival of invariably less than six months after relapse.

More intensive therapy for patients can improve cure rates, and in younger adults, there is some evidence that treatment with the more intensive children's regimens is associated with better outcome.

Prognostic factors

Chromosome abnormalities linked to good and poor prognoses

Depending on patients' chromosome abnormalities, a good and poor prognosis can be predicted.

Chromosome abnormalities linked to a good prognosis are:

- Hyperdiploidy: Having more than the normal number of 46 chromosomes (23 pairs)
- Chromosomes 4 and 10 trisomy as in Down's syndrome. Prognosis is very good with this chromosome abnormality
- t(12;21) ETV6-RUNX1

Chromosome abnormalities linked to a poor prognosis are:

- Hypodiploidy
- t(4;11) MLL-AF4
- t(9;22) BCR-ABL1 - Philadelphia chromosome
- BCR-ABL1-like
- iAMP21

Poor prognostic factors

The following factors are associated with a poor prognosis:

- Age <1 year and >65 years
- Presence of CNS involvement at diagnosis
- High initial white blood cell count
- Slow response to initial treatment
- Presence of minimal residual disease after treatment.
Minimal residual disease is a measure of the presence of leukaemia at a molecular level rather than at a cellular level. It can be measured using flow cytometry.

Positive prognostic factors

Prognosis for patients is related to the speed with which they achieve complete remission. Overall survival for patients achieving complete remission within four weeks of treatment therapy has been shown to be longer than patients whose

complete remission takes longer.

Diagnosis of B-cell ALL

As with most types of leukaemia, the diagnosis of B-cell ALL is usually achieved with a bone marrow biopsy, which shows the number and types of the cancerous B-cells in the bone marrow. There are no specific levels of blasts required in the peripheral blood or bone marrow to make a diagnosis of B-cell ALL; however, as previously mentioned, there is a general agreement that 20% or more of blasts should be present in order to make a diagnosis.

To make a diagnosis of B-cell ALL, the following tests are needed:

Blood laboratory tests

A full blood count which shows the number of red blood cells, white blood cells and platelets is done. Inclusion of a differential count, which will provide additional details of the different type of white blood cells, is useful. In patients with B-cell ALL, levels of red blood cells, neutrophils and platelets are typically reduced as the bone marrow is busy making cancerous B-cell lymphoblasts. In contrast, the total level of white

blood cells will be increased because of the increased numbers of cancerous B-cells.

Peripheral blood smear and bone marrow aspiration and biopsy

A sample of blood is smeared and viewed under a microscope to count different circulating blood cells and to see whether the cells look normal. Similarly, the cells from the bone marrow biopsy are also examined under the microscope.

The bone marrow aspiration procedure removes a liquid marrow sample and the biopsy removes a small amount of bone filled with marrow. Medication is normally given to numb the area when taking a biopsy.

Examination of the bone marrow liquid sample and biopsy can determine the percentage of B-cells in the bone marrow and any abnormalities of the B-cells. The appearance of the cancerous B-cells in the bone marrow is indistinguishable from T-cells, therefore the microscopic

appearance is not diagnostic and should only be used as part of the series of diagnostic tests.

Cerebrospinal fluid examination

To check the spread of cancerous B-cells in the central nervous system (CNS), a sample of cerebrospinal fluid, obtained by a lumbar puncture, is the most reliable test as it enables examination of the B-cells with flow cytometry.

Flow cytometry is a technique that processes either blood, bone marrow fluid or tissue by adding specific antibodies that have been labelled with fluorescent markers. These antibodies will bind to corresponding antigens on the white blood cells. The cells are suspended in a solution and passed through a flow cytometer that shines multiple laser beams causing deflection or absorption of the laser light. According to the light changes, the various physical properties of the individual cells are analysed. The flow cytometer can rapidly measure the size and

internal cellular structures of thousands of cells, and assess the characteristics of the fluorescent antigen-antibody complexes present.

To check the spread of cancerous B-cells in the CNS, magnetic resonance imaging is superior to computed tomography; however, it is known to miss a sizeable number of cases (called false negatives), and so should not be used as a diagnostic tool.

Immunophenotyping

The process of immunophenotyping helps analyse the types of antigens or markers on the surface of the cancer cells based on the antibodies in the patient's blood. According to which antibodies are present, it is possible to identify the type of leukaemia.

ALL is characterised by negative staining with myeloperoxidase, and the presence of immature lymphoblast cells which can be confirmed by the presence of terminal deoxynucleotidyl transferase, an enzyme involved in creating DNA molecules. In

Diagnosis of B-cell ALL (cont.)

the case of mature lymphoid cells, testing for terminal deoxynucleotidyl transferase is always negative.

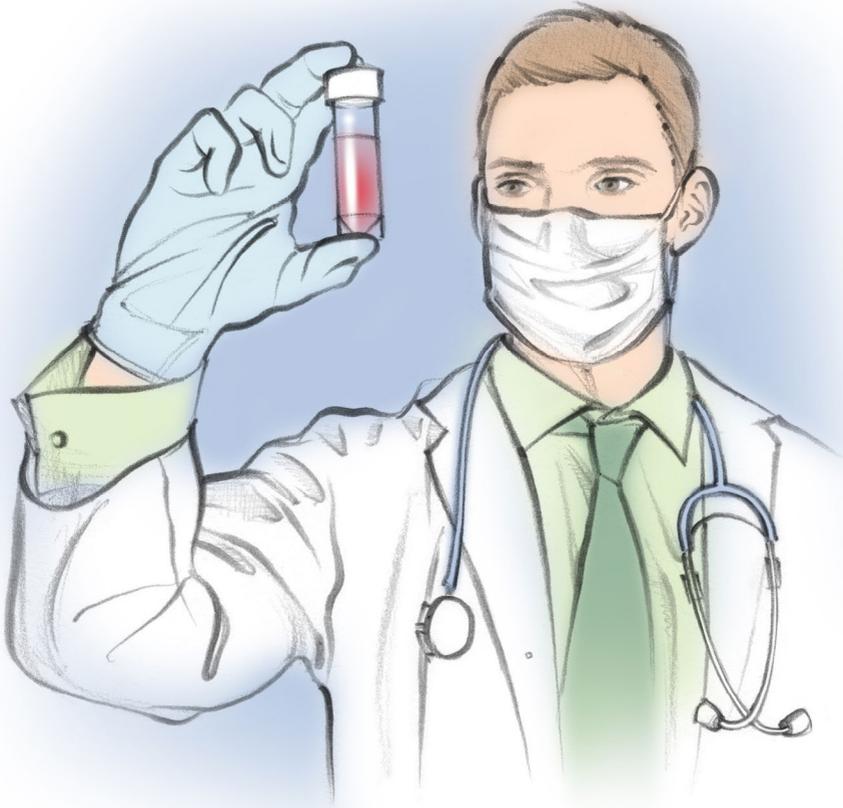
In nearly all patients with B-cell ALL, CD19 can be demonstrated by flow cytometry. In addition, the cancerous B-cells are almost always positive for the B-cell markers cCD79a and cCD22. Despite none of these markers being diagnostic on their own, their combined presence will support the diagnosis.

Chromosomal analysis

Chromosomal analysis involves analysing the bone marrow or blood cells to identify any changes in the number and size of chromosomes within cells that might have led to the development of B-cell ALL. Chromosome abnormalities are seen in the majority of patients with B-cell ALL. These are either an increase/decrease in chromosome numbers or chromosomal translocations.

The diagnosis of B-cell ALL is therefore based on the comprehensive review of the

patient's symptoms, microscopic examination of blood, blood marrow aspirate/tissue, cerebrospinal fluid, and most importantly, the findings from the immunophenotyping and chromosome analysis.



Treating B-cell ALL

The ideal outcome of treatment for patients with B-cell ALL is to achieve complete remission with induction chemotherapy, followed by a bone marrow transplant or maintenance treatment, dependent on which is in the best interest of the patient.

Complete remission is said to have occurred when the following conditions have been met:

- Blood cell counts return to normal
- Flow cytometry has been used to detect that minimal residual disease has been achieved (that is, the number of leukaemia cells being detected at a molecular level)
- There are no cancerous B-cells anywhere else in the body

Currently, approximately 90% of children with B-cell ALL and 40% of adult patients will recover from B-cell ALL. This recent improvement in recovery rates is a result of specific therapies which have developed following a better understanding of the chromosome abnormalities involved in leukaemia and the use of stem cell transplantation.

The different treatment phases for ALL are as follows:

- **Induction therapy:** The aim of this phase is to kill all or the majority of the cancerous B-cells in the blood and bone marrow and to restore normal blood cell production which has been disrupted by the presence of the cancerous B-cells.
- **Consolidation therapy:** In this phase, any remaining leukaemia in the body, such as in the brain or spinal cord, is ideally destroyed.
- **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).
- **Preventive therapy for the CNS (sometimes called intrathecal chemotherapy):** During any of the treatment phases, additional treatment to kill cancerous B-cells located in the CNS may be given. The chemotherapy drugs are often injected directly into the fluid that covers the spinal cord.
- **Maintenance therapy:** This

ongoing phase is intended to prevent any cancerous B-cells from multiplying again. Lower doses of therapy are often given for years.

The types of treatment that patients with B-cell ALL will receive may include:

Chemotherapy

Chemotherapy drugs either kill the cancerous B-cells or stop them from dividing. Chemotherapy is commonly used as induction therapy, but can also be used as consolidation and maintenance therapies.

Children

For children with B-cell ALL, chemotherapy regimens used as induction therapy commonly include one to two cycles of an anthracycline, vincristine, prednisone and asparaginase. An anthracycline is a drug that was originally used as an antibiotic, but was subsequently found to be an effective anti-cancer drug. Examples of anthracyclines are daunorubicin or doxorubicin.

Children who achieve remission can progress to

consolidation treatment with either an allogeneic stem cell transplantation (SCT) or repeated cycles of combination chemotherapy administered over six or eight months. Preventive CNS therapy should be an essential element of the treatment of ALL in children and needs starting as early as possible. Low-dose maintenance chemotherapy with daily 6-mercaptopurine and weekly dosing of oral methotrexate is generally given for a period of two to three years. This is often combined with monthly doses of corticosteroids and vincristine during the first year. It is crucial that the 6-mercaptopurine treatment is maintained to prevent the chances of relapse.

Younger adults

For younger adults (15-50 years) who are Philadelphia chromosome-negative and are eligible, allogeneic SCT during their first complete remission is an established cure for ALL. In a large review of patients with ALL, matched sibling donor allogeneic SCT for patients aged 15 years and over has been shown to reduce the risk of disease relapse and

Treating B-cell ALL (cont.)

improve overall survival.

Some studies have shown that young adults treated with similar chemotherapy regimens that are used in children have a better outcome.

Adults

For patients aged between 25 and 65 years or between 19 and 65 years who have the Philadelphia chromosome, the UKALL14 regimen is used as first-line treatment. This involves patients with B-cell ALL being treated with rituximab as well as standard chemotherapy. For some, they may be treated with a newer form of chemotherapy drug called pegylated asparaginase instead, or could be offered a stem cell transplant.

Older adults

Older adults (aged >65 years) with ALL have lower complete response rates, higher relapse rate, and poorer survival compared with younger patients. They experience more side effects with ALL treatments and often find the intensive chemotherapy and subsequent allogeneic SCT quite

hard to tolerate.

Older adults also tend to have a poorer prognosis because of factors which relate to their chromosomal abnormalities, and the fact they may have other illnesses as well, such as heart, lung and kidney disease. Older patients are more likely to have Philadelphia chromosome positive ALL which is linked to a poor prognosis. The incidence of Philadelphia chromosome positive in adults is around 25%; however, it rises to >50% among patients >55 years. Philadelphia chromosome positive ALL occurs in only 5% of patients <20 years and 33% in patients <40 years. Nevertheless, some older patients can achieve long-term survival when treated with intensive therapies.

Treatments for B-cell ALL in adults are adapted for the older patient. Modifying the doses or eliminating some of the drugs to make the regimen more tolerable, the routine use of a tyrosine kinase inhibitor which is effective against Philadelphia chromosome positive ALL, and early referral for

reduced-intensity ASCT are all helpful.

Maintenance

The benefit of maintenance therapy for patients with ALL has been investigated in a number of studies. In a recent study where maintenance therapy was not given to some of the patients, the patients who received maintenance therapy had significantly higher remission rates and overall survival rates compared with patients who did not receive maintenance therapy. When undergoing maintenance therapy, patients can usually return to a relatively normal lifestyle with limited restrictions.

Targeted therapy

Targeted therapy is treatment with drugs that attack specific abnormalities present in cancer cells that allow them to grow and thrive. These drugs do not simultaneously harm healthy cells the way conventional chemotherapy drugs do. Targeted therapy may be used during or after chemotherapy.

Examples of targeted therapy are adding a tyrosine kinase inhibitor for patients with Philadelphia chromosome positive ALL, or rituximab for patients with CD20-positive ALL to their UKALL14 regimen. Tyrosine kinase inhibitors have been shown to be especially effective against Philadelphia chromosome positive ALL because they target the faulty Philadelphia chromosome.

These types of targeted therapy have resulted in substantial improvements in overall survival for patients.

Stem cell transplantation

SCT can be used as consolidation therapy in patients who have a high risk of relapse, or for treating relapse when it occurs. SCT helps patients re-establish a healthy bone marrow. Patients receiving a SCT are given high doses of chemotherapy or radiation to destroy any cancerous B-cells. The recipient's bone marrow is then replaced by compatible bone

Treating B-cell ALL (cont.)

marrow. There are two types of SCT:

- 1. Allogeneic stem cell transplantation (Allogeneic SCT)** - In an allogeneic SCT, stem cells from a matching donor, which must be HLA compatible, are transplanted into the patient. A sibling is likely to be a good match; however, a parent or child will only be a haploidentical match. Donors who are not relations may be found through national bone marrow registries. Allogeneic transplantation is generally considered in younger patients.
- 2. Autologous stem cell transplantation (ASCT)** - This is where healthy stem cells are taken from the patient themselves before they start chemotherapy. However, this type of stem cell transplant is not normally done in ALL patients due to the rapid progression of the disease.

Radiation therapy

Radiation therapy may be used if cancer cells have spread to the

CNS. It consists of irradiation of the brain and spinal cord. High doses of X-rays or proton beams are used to kill the cancer cells.

Radiation is the oldest form of CNS prophylaxis and is now generally combined with either intrathecal or intravenous chemotherapy to prolong survival. Chemotherapy is injected directly into the spinal fluid through the intrathecal space, usually during a lumbar puncture. In patients at low risk of CNS involvement, it can be replaced with intrathecal or intravenous methotrexate.

Radiation may be associated with late side effects such as secondary cancers, hormone related diseases and damage to the nervous system.

New targeted therapies

Because nearly all patients with B-cell ALL have the antibody to CD19 protein on the cancerous B-cells, CD19 is an attractive target for immunotherapy drugs. Similarly, for patients with B-cell ALL positive for the Philadelphia chromosome, drugs that target cells containing this chromosome

abnormality, like the tyrosine kinase inhibitors, are useful.

Current new targeted therapies which are being investigated are:

- **Inotuzumab ozogamicin:** Inotuzumab ozogamicin (Besponsa™, Wyeth Pharmaceuticals) is a humanised monoclonal antibody against the CD22 protein (inotuzumab), which has been linked to a toxic compound called ozogamicin. Inotuzumab ozogamicin has been approved in the UK for the treatment of patients with relapsed or refractory CD22-positive B-cell precursor ALL.
- **Blinatumomab:** Blinatumomab (Blincyto®, Amgen) is a bi-specific monoclonal antibody which contains two protein binding sites (CD3 and CD19), and whose actions result in the selective disintegration of tumour cells. On 19 June 2018, the European Medicines Agency granted blinatumomab full approval for Philadelphia chromosome-negative relapsed or refractory B-cell precursor ALL. Blinatumomab has also

been approved by NICE.

- **Ponatinib:** Ponatinib (Iclusig®, ARIAD Pharma Ltd) is a third-generation tyrosine kinase inhibitor which has a strong anticancer effect in Philadelphia chromosome-positive ALL. Ponatinib is active against all tyrosine kinase inhibitor mutations including the cross-resistant BCR-ABL(T315I) mutation, which is particularly challenging to treat. It has been approved in Europe since July 2013 for the treatment of patients with Philadelphia chromosome-positive ALL resistant/intolerant to tyrosine kinase inhibitors, or patients with the T315I mutation.
- **Chimeric antigen receptor T-cell (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.

CAR T-cell therapy was developed to target a protein on the surface

Treating B-cell ALL (cont.)

of the B-cell called CD19. This protein is on the surface of nearly all B-cells.

CAR T-cells have been particularly effective against cancers derived from B-cells such as ALL and chronic lymphocytic leukaemia. Anti-CD19 CAR T-cell therapies have achieved remission in up to 90% of patients with B-cell ALL.

In Europe, the anti-CD19 CAR T-cell drug tisagenlecleucel (Kymriah®, Novartis) was authorised in September 2018 by the European Medicines Agency for the treatment of children and young adults up to 25 years of age whose cancer did not respond to previous treatment, has come back two or more times, or has come back after a transplant of stem cells. This essentially covers relapsed or refractory B-cell ALL. It is already recommended by NICE for the same indication.



Seeing your doctor

Your symptoms

Whatever symptoms you or your child have, make sure you write a list of all of them to share with the doctor as they may be important to the treatment.

Your appointment

Arranging an appointment with the GP will be one of the first things you will need to do when you start to notice symptoms. Pick a time convenient for you that you know you will be able to attend.

Your preparation

It is important to know exactly what you would like to ask the doctor. Make a list of your questions and leave spaces for the answers so you can write them down when you see the doctor. This way you can go into the appointment ready and prepared.

Examples of questions to ask the doctor:

- What tests will be needed?
- What will the tests show?

- How long will it take to get the results back?
- How common is my or my child's condition?
- What sort of treatment will I or my child need?
- How long will the treatment last?
- How will we know if the treatment has worked?
- What will the side effects be?
- Are there any foods or medications that need to be avoided?
- Will I be able to go back to work?
- Where can I get help with claiming benefits and grants?
- Where can I get help dealing with my feelings?

Talking to your doctor

Be honest with the doctor; they have seen and heard everything before, so there is no need to feel embarrassed about anything. If you saw the healthcare team before seeing the doctor, be sure to share with your doctor

everything your healthcare team told you about your or your child's condition, the blood tests that were performed, and the next steps in your or your child's B-cell ALL journey. Ask also if any intensive treatment or palliative care will be needed.

Your support

If it helps, take a family member or friend in with you for support. Some people take a pen and paper in to make notes, and repeat back to their doctor everything they have been told to ensure that they are on the same page, and that nothing has been missed or forgotten.

The next steps

Always ensure that you leave the GP surgery, or the hospital, having shared everything you know about your or your child's condition, with all of your questions answered, and knowing exactly what the next steps are, whether it is more tests, further treatment or palliative care. You can ask for a summary letter of the consultation to have everything in writing. Your doctor will generally

send a letter like this to your GP.

Furthermore, be sure to access all of the other support available to you or your child as this may be able to help you with your feelings towards the diagnosis and treatment.

Telling your family

Planning who to tell

Telling your family and friends that you or your child has been diagnosed with B-cell ALL can be difficult.

You may want to create a list of people you want to tell, starting with close family and friends, and then extending it beyond, from your colleagues at work to friends in your neighbourhood.

Planning what to say

It is important to know what you want to say and exactly how much you want people to know. Being clear in your mind about that before speaking to anyone will make this a much smoother experience. Know the story that you want to tell, the diagnosis, the prognosis, the next treatment steps, and what you expect will happen physically and emotionally. Be sure to speak to people in an environment where both of you can hear each other clearly and where there are likely to be no interruptions.

How to say it

Using a conciliatory tone will help keep both yourself and the other person calm. Deliver what you have to say slowly, calmly, concisely, and sentence by sentence to allow the other person time to take in the information. Be sincere, and hold their hands if you need to.

You can use the following sentences to help you articulate what you need to say:

- "This is going to be difficult, but I need to tell you something."
- "I've had some bad news but there's a good chance that everything will be okay after treatment."
- "You know I or my child have been feeling unwell for a while. Some tests have been done and they've found out what's wrong."

How to respond

Naturally people will feel sad and concerned for you. Everyone deals with this type of news in their own way, from shock and silence, to questions and support. Invariably,

people respond positively, which in turn means you will respond back positively.

Accepting help

Sometimes people feel guilty if they or their child gets cancer, that it's their fault, and that they will be a burden on those around them. This is where your loved ones come in, so make sure you do ask for and accept offers to help and support you. Do not try to cope on your own. If they offer to help, tell them that you will get in touch when you need them.

Repeating yourself to different people can become burdensome. Your network of family and friends can help you out by telling those beyond them about your current situation. You can receive help from us on how to deal with breaking the news to your family and friends. You can visit **www.leukaemiacare.org.uk**, or call **08088 010 444**, to find out more.

Managing your emotions

Being told that you or your child has cancer may be difficult for you to deal with.

You may have a positive demeanour, which will obviously be helpful to you during the next steps in the management of the condition. However, you may experience a range of emotions, including uncertainty, isolation, anxiety, anger, sadness and depression. Understanding each emotion and developing ways that help you deal with them will help you move forward with your life.

Uncertainty

You may think "What happens next?". You may be unsure about yours or your child's health and what the future holds for you. You may or may not have had meetings with the healthcare team to discuss the next steps. Once you have a clear path set out in front of you, you will be able to develop a clearer picture of where you are headed. Gaining a sensible balance between being vigilant about symptoms and carrying on with your life will help ease any anxieties. Help, care, kindness and

support will be available to you from the healthcare team, and you will have access to counsellors and therapists if and when you need it.

Isolation

If you or your child has received a diagnosis of B-cell ALL, you may feel alone.

Alternatively, you may feel dealing with your or your child's cancer allows you to be around those closest to you. Being around those closest to you, such as your family and friends, can be positive and negative.

Let them know what you do and don't want to do, how you do and don't wish for you or your child to be treated, and what you do and don't feel comfortable talking about. Sometimes, it is difficult for your family, friends and colleagues to understand what you are feeling and going through. Being clear will help create the kind of positive, supportive, and caring environment that will help as you move forward with your life.

Anxiety

Being fearful of the unknown, especially when we are feeling threatened, is natural. You may experience an increased heart rate, rapid breathing, and muscle tension. These things help us to face a danger or run away. These changes in you are part of the 'fight or flight' response. Any feeling of discomfort, pain or even another appointment with your healthcare team may elicit such responses, and give you sleepless nights or feelings of worry. This is completely natural.

Such reflexes and responses will ease over time with the building of daily routines and planning things for the future, which will help you to cope with the physical effects of anxiety. Cognitive behavioural therapy can help you deal with your worrying thoughts.

Anger

Feeling angry after your or your child's diagnosis is natural and normal. You may be angry with yourself, with the healthcare team or with family and friends. You may display your anger

as impatience, irritability and frustration with people and things that would not normally bother you.

Understanding exactly what is making you angry will help you deal with your feelings effectively. In addition, setting yourself or your child achievable but demanding goals will help reduce the anger and impatience, especially with each passing success. Don't forget to congratulate yourself or your child for each successfully completed task, however small.

Physical exercise is a great way to release your anger and frustrations, and channel energy positively with no negative impact on the body. Talking about feelings and letting them out, will also help stop you or your child lashing out at people and keep things calm.

Sadness and depression

You may feel a sense of loss, and how safe you felt. You may also feel that your or your child's

Managing your emotions (cont.)

illness is a heavy burden on those around you. You might be feeling low, which is a natural effect of your situation and the illness, treatment and recovery process. However, if this low mood persists for more than several weeks, and you feel hopeless, and lose interest and pleasure with things in life, then you may have depression.

Your first steps should be to speak to your loved ones around you about your mood and state of mind, and then contact your GP. You may lift the way you feel by engaging in activities that you were enjoying before the diagnosis and connecting back with your life. Only do as much as you can, and try and talk about your thoughts and feelings. This will help lighten your burden and put things into perspective. If you have made any acquaintances or friends in the same position as you, talk to them over coffee as they will understand what you are facing.

Self-confidence

Being forced to adjust from your

daily routine during the visits to the hospital for treatment can take its toll. This interruption of your life can impact on how you feel about your appearance and how you feel emotionally. In turn, this can knock your self-confidence and self-esteem. Your feelings of relief, hope and optimism have just been replaced with their polar opposites.

You can gradually build your self-confidence and self-esteem back up by engaging in the activities you did before the diagnosis, and socialising with family, friends, and those in the same position as you. This will help create a supportive atmosphere to get you back to your old self.

Mindfulness and relaxation

Simple practices from mindfulness and relaxation techniques can help you calm the mind, release tension and ease any pain.

- Put yourself in a relaxing environment, sitting or lying down comfortably.

- Loosen your clothing so you can move more freely.
- Calmly breathe in through your nose, and out through your mouth, developing a steady natural rhythm, focusing on your chest and abdomen as you do so.
- Visualise that you are inhaling positivity and exhaling negativity.

By taking some time out of your day to do these exercises, you can help quieten your mind and remove the stress of coming to terms with your diagnosis, so you feel calmer and more relaxed.

Survivorship

Someone who is living with or is beyond a cancer diagnosis can be considered a cancer survivor. If your child has B-cell ALL, you may experience this process on their behalf as they may be too young to know.

Survivorship can be defined as:

"...cover[ing] the physical, psychosocial and economic issues of cancer, from diagnosis until the end of life. It focuses on the health and life of a person with cancer beyond the diagnosis and treatment phases. Survivorship includes issues related to the ability to get health care and follow-up treatment, late effects of treatment, secondary cancers and quality of life. Family members, friends and caregivers are also part of the survivorship experience."

When living with cancer, you or your child will face new challenges to cope with from physical to psychological and social ones. Survivorship aims to provide personalised care based on improving yours or your child's health, wellbeing, quality of life, and your confidence and motivation, to help you manage. Survivorship also focuses on

your or your child's health and life with cancer after the end of treatment until the end of life. At this point, your routine of meeting frequently with your healthcare professionals also ends, so you may feel a mixture of emotions from relief to fear, anxiety and uncertainty about the future. You may wonder how you will slot back into your life after coming through the treatment period.

Your survivorship pathway began at the point when you or your child was diagnosed with B-cell ALL. By this point, you will have been starting to receive support for work, finance, and personal relationships through to managing pain, fatigue and making positive lifestyle changes, such as starting a healthy diet and gentle exercising.

Your individual needs will be identified and addressed, including:

- Dealing with the emotional impact of receiving a B-cell ALL diagnosis which may have created feelings of uncertainty, fears of recurrence and difficulties in planning for the future. These will be discussed with you to develop your or your

child's individualised care plan with support from social care staff and therapists, as you need it.

- Improving your quality of life through efficient and co-ordinated care during treatment, with effective communication within the treatment team, and a positive attitude.
 - Taking care of any comorbidities – that is, other medical conditions and diseases – and offering cancer rehabilitation based on your or your child's clinical needs as assessed by informed professionals and ensuring compliance with the National Cancer Rehabilitation Pathways and Rehabilitation Peer Review requirements.
 - Providing you with a treatment summary from the diagnosis of your or your child's condition to the end of treatment. This would include any ongoing medication and noting possible symptoms that may occur in the future. You would also be provided details of who to contact in addition to your GP for any concerns you may have.
- Preparing you fully for the impact of your or your child's B-cell ALL and treatment, the physical and physiological side effects of treatments and the psychological impact of B-cell ALL in general. You will be provided physical equipment and taught about various coping strategies to adapt to yours or your child's new situation.
 - Supporting you with advice for social and financial difficulties, including caring responsibilities, your inability to participate in social activities, any debt and financial worries from not being able to work, and perhaps the need to return to work before you feel ready.
 - Receiving health and nutrition advice from a nutritionist on following a healthy and balanced diet to help improve your or your child's general health and wellbeing. The World Cancer Research Fund published a report for cancer survivors which suggests that even small dietary and lifestyle changes can produce large health benefits.

Palliative care

Palliative care, also known as supportive care, involves a holistic or "whole person" approach, which includes the management of pain and symptoms as well as psychological, social and spiritual support for you or your child and your loved ones.

Palliative care aims to reduce the symptoms, control the B-cell ALL, extend survival, and give you or your child and your loved ones the best quality of life possible. Your doctor will discuss the options with you in detail before you decide the next steps.

Who provides palliative care?

Palliative care will be provided by a team of health and social care professionals trained in palliative medicine who will coordinate the care.

These professionals can include your GP, hospital doctors and nurses, community nurses, hospice staff and counsellors, social care staff, physiotherapists, occupational therapists, complementary therapists, and

religious leaders, if you would like this. The palliative care services may be provided by the NHS, local council or a charity. You or your child may receive day-to-day care at your home and at the hospital.

What is the clinical course?

You or your child will have a number of treatments and be prone to frequent infections because of the B-cell ALL and the impact of the treatments. The therapy may continue because of potential remission and/or useful palliation.

Various pains and other clinical complications can occur such as:

- **Bone pain:** Radiotherapy and/or oral steroids, and sometimes non-steroidal anti-inflammatory drugs (NSAIDs), may be used, although these are used with caution because they can interfere with the immune system and kidney function.
- **Bone marrow failure:** Blood and platelet transfusions are provided to prevent and fight recurrent infections and

bleeding episodes.

- **Oral problems:** Analgesic mouth washes and topical ointments may help with ulceration. Chewing gum and mouth washes have been shown to help with dry mouth, tooth decay and oral thrush.
- **Night sweats and fever:** These can place a heavy burden on carers because of so many changes of night clothes and bedding.
- **Pathological fractures:** Orthopaedic intervention and subsequent radiotherapy, with consideration given to prophylactic pinning of long bones and/or radiotherapy to prevent fracture will be performed. This will reduce the likelihood of complex pain syndromes developing.
- **Spinal cord compression:** Immediate high single daily dose oral steroids will be given.
- **Back pain from wedge and crush fractures of the vertebrae of the spinal column:** Treatments can include

analgesics, antidepressants and/or anticonvulsant medication used in tandem with opioids.

- **Hypercalcaemia:** Treatment is usually with intravenous hydration and intravenous bisphosphonates.
- **Loss of appetite:** Low-dose steroids may temporarily boost the appetite, while small, frequent and appetising meals and supplement drinks will also help.

End of life care

When does end of life care begin?

If the treatment hasn't worked and you or your child is going through palliative care, end of life care may be offered. End of life care begins when it is needed and may last a few days, months or years.

What does end of life care involve?

End of life care is support for people who are in the last few months or years of their life. The aim is to help patients enjoy a good quality of life until they die, and to die with dignity. The professionals looking after you or your child will ask you about your wishes and preferences on how to be cared for and put these into action. They will also provide support to your family, carers and loved ones. You will be able to decide where you or your child will receive end of life care, be it at home or in a care home, hospice or hospital. The same will be true of where you or your child would like to die. Wherever this is, you will receive high quality end of life

care.

Who provides end of life care?

A team of health and social care professionals may be involved in the end of life care, including hospital doctors and nurses, your GP, community nurses, hospice staff and counsellors, social care staff, physiotherapists, occupational therapists or complementary therapists, and religious leaders, if you would like this. If you or your child are being cared for at home or in a care home, your GP will have overall responsibility for your care with the support from community nurses, along with your family and friends.

What choices do I have in terms of end of life care?

Deciding where you or your child want to die can be a difficult choice to make. Working out what you and your loved ones want, together with seeing what services are available can help to make the decision a little easier.

- **Staying at home:** A place of familiarity, surrounded by loved ones, may be something that will be reassuring. External care professionals will be able to visit your home to make sure the symptoms are looked after.
- **Hospices:** These are specialised in looking after those with life-limiting illnesses and those who are coming to the end of their life, hospices are staffed with care professionals who are able to keep an eye on you or your child, make sure that symptoms are controlled and offer a number of services to make the stay as comfortable as possible. For more information on the care that they can provide, go to <https://www.hospiceuk.org/>
- **Residential care/nursing homes:** If you think that your or your child's stay may be a few months or more, then a residential care home may be more suitable than a hospice. These can be private or run by a charity or the local council so be sure to check if there are any fees.
- **Hospitals:** Although you or your child may be used to staying in a hospital ward, the care routine cannot always be tailored to patients' specific needs. Pressures on the NHS mean that you or your child's stay will only be as long as strictly required. As soon as the condition requiring hospital admission has been resolved, you or your child will need to go back to where you have been staying. However, a number of specialists will be available to help look after specific problems, and a number of hospitals also have a designated palliative care team for patients who require them.

Whatever your choice, speak with your GP or healthcare team who will be able to help you put everything into place.

Glossary

Allogeneic stem cell transplant

A transplant of stem cells from a matching donor.

Anaemia

A condition where the number of red blood cells, which contain haemoglobin and transport oxygen to body cells, are reduced. This may be due to a lack of iron, leukaemia, or sickle cell disease.

Antibody

A large Y-shaped protein produced by B-cell lymphocytes in response to a specific antigen, such as a bacteria, virus, or a foreign substance in the blood. The antibodies neutralize the bacteria and viruses.

Antigen

A toxin or other foreign substance which induces an immune response in the body, especially the production of antibodies.

Autologous stem cell transplant (ASCT)

A transplant of stem cells derived from part of the same individual.

Bone marrow failure

The term used when the bone marrow is unable keep up with the body's need for white and red blood cells and platelets.

Body mass lesions

An abnormal growth of cells in the body which can appear as a lump.

Central nervous system (CNS)

Part of the nervous system which includes the brain and spinal cord.

Chromosomes

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

Cytogenetic

Relating to the study of inheritance in connection with the structure and function of chromosomes.

Cytoplasm

A jelly-like fluid that houses all the constituents required for survival and reproduction of the cell.

Fatigue

Tiredness and weakness rendering the patient unable to work or perform usual activities.

Genes

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

Haploidentical match

A modality of allogeneic transplantation where the donor is a relative of the patient, but the HLA compatibility is not ideal for transplantation purposes.

HLA compatible

The degree of similarity between the HLA of the donor and patient.

Human Leukocyte Antigen (HLA)

A unique protein signature expressed on the surface of most cells in the body of every person.

Hyperdiploidy

Having more than the normal 46 number of chromosomes (23 pairs).

Hypodiploidy

Having less than the normal 46 number of chromosomes.

Lymph nodes

Components of the lymphatic system (part of the body's immune system) that contain lymphocytes which produce antibodies and macrophages to digest dead cells. Lymph nodes are swollen with cell fragments in the event of infection or cancer. They are located mainly in the neck, armpit and groin.

Nucleoli

The small dense spherical structure in the nucleus of a cell.

Philadelphia chromosome

The Philadelphia chromosome (BCR-ABL) is the most common genetic abnormality associated with adult ALL and has a very poor prognosis for both children and adults. It only occurs in 3 to 5% of patients with ALL, but less than 40% of them are cured with intensive chemotherapy.

Platelets

One of the types of blood cells

Glossary (cont.)

which help to stop bleeding.

Prognosis

An indication of how well a patient is expected to respond to treatment based on their individual characteristics at the time of diagnosis or other timepoints in the disease.

Radiation treatment

Cancer treatment that uses high doses of radiation to kill cancer cells and shrink tumours.

Refractory leukaemia

Leukaemia for 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.

Relapsed leukaemia

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

Translocation

In genetics, translocation is the transfer of one part of a chromosome to another part of the same or a different chromosome, resulting in rearrangement of the genes.

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.leukaemicare.org.uk
support@leukaemicare.org.uk

Bloodwise

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

020 7504 2200
www.bloodwise.org.uk

Cancer Research UK

Cancer Research UK is a leading charity dedicated to cancer research.

0808 800 4040
www.cancerresearchuk.org

Macmillan

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

0808 808 0000
www.macmillan.org.uk

Maggie's Centres

Maggie's offers free practical, emotional and social support to people with cancer and their families and friends.

0300 123 1801
www.maggiescentres.org

Citizens Advice Bureau (CAB)

Offers advice on benefits and financial assistance.

08444 111 444
www.adviceguide.org.uk

Leukaemia Care is a national charity dedicated to providing information, advice and support to anyone affected by a blood cancer.

Around 34,000 new cases of blood cancer are diagnosed in the UK each year. We are here to support you, whether you're a patient, carer or family member.

Want to talk?

Helpline: **08088 010 444**

(free from landlines and all major mobile networks)

Office Line: **01905 755977**

www.leukaemiacare.org.uk

support@leukaemiacare.org.uk

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Registered charity
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Leukaemia Care
YOUR Blood Cancer Charity

