Chronic Lymphocytic Leukaemia (CLL) - Starting Active Treatment

A Guide for Patients

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

Being diagnosed with chronic lymphocytic leukaemia (CLL) and having to start active treatment can be a shock, particularly if you were previously on Watch and Wait. If you have any questions – including when to start active treatment and likely treatments – this booklet covers the basics for you.

For more specialised, tailored advice, speak to your GP or medical team.

This booklet has been compiled by our Patient Information Writer Isabelle Leach and peer reviewed by Helen Knight, CLL Clinical Nurse Specialist and Professor Chris Fegan from University Hospital Wales as well as our Patient Advocacy Manager Charlotte Martin and Patient Advocacy Healthcare Liaison Officer Nick York. We are also grateful to Lisa Henley-Durcan, Michael Albero, Ryan Chappell, Paul Walmsley, Geoffrey Brown and Lionel Levy for their contributions as patient reviewers.

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

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In this booklet

About Leukaemia Care

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

Our services

Helpline

Our helpline is available 8:30am – 5:00pm Monday - Friday and 7:00pm – 10:00pm on Thursdays and Fridays. If you need someone to talk to, call **08088 010 444**.

Alternatively, you can send a message via WhatsApp on **07500068065** on weekdays 9:00am – 5:00pm.

Nurse service

We have two trained nurses on hand to answer your questions and offer advice and support, whether it be through emailing **nurse@leukaemiacare.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.leukaemiacare.org.uk/support-and-information/help-and-resources/information-booklets/**

Support Groups

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

Buddy Support

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

Online Forum

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

Patient and carer conferences

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

Website

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

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

What is chronic lymphocytic leukaemia?

Chronic lymphocytic leukaemia (CLL) is a cancer of the B-lymphocyte cells (B-cells). Lymphocytes are a type of white blood cell. They are fundamental to the immune response and fighting off infection. B-cells produce antibodies that seek out and immobilise the bacteria, viruses, and toxins which invade the body.

In CLL, the B-cells in the bone marrow start multiplying abnormally. This leads to large numbers of small, immature lymphocyte cells, which are unable to fight infection. Their presence prevents the bone marrow from producing healthy blood cells of all types. The diagnosis of CLL requires the presence of 5x109/L of B-cells or more in the blood, for at least three months.

CLL is the most common form of leukaemia in adults. In the United Kingdom, around five to six out of every 100,000 people are diagnosed with it every year. It affects nearly twice as many men as women, and the average age at diagnosis is 72 years.

CLL normally progresses slowly over months and years, although 30% of people diagnosed with CLL will never require any treatment. In some cases, the disease can progress more rapidly.

For more information on CLL, read our dedicated booklet. You can download it from the website **www.leukaemiacare.org.uk** or order a copy via the helpline on **08088 010 444.**

Chromosomal abnormalities

An important aspect of CLL is the presence of chromosomal abnormalities found in patients. They can have a direct impact on the choice of treatment, should you require it, and prognosis. The type of chromosomal abnormality you have will hint at your response to treatments and the likelihood of this response.

Abnormalities in a patient's chromosomes and genes which are associated with a poor response are:

- Deletion of the chromosome region 17p (17p deletion)
- TP53 tumour suppressor gene (TP53) mutation or deletion contained within chromosome 17
- No mutation in the immunoglobulin heavy chain variable region (IGHV) gene (unmutated IGHV gene)

All patients should be tested for TP53 deletion/mutation and 17p deletion prior to starting treatment. Your IGHV mutation status should also be investigated.

Why change from Watch and Wait to active treatment?

With other types of leukaemia, early treatment is advisable, but this is not true for CLL. The clinical course of CLL can be variable. Some CLL patients are free of symptoms and remain well for years. Others experience symptoms quite rapidly after their diagnosis and require immediate treatment.

For patients who do not have any symptoms and those with mild symptoms or disease progression, the Watch and Wait approach is the current standard of care. Your haematologist will decide when your symptoms or disease progression will require treatment. Watch and Wait is also sometimes called active monitoring. The rationale for this approach is based on the fact that there is no treatment available to cure CLL. It is more a question of managing your CLL with the treatments available for you to lead the best life possible.

The main reasons for Watch and Wait are:

- Some patients can live with CLL having minimal impact on their life expectancy. For some, this means that treatment isn't necessary to aid survival.
- First-line treatments can have side effects with the possibility of treatment-related complications.

For these reasons, the British Society for Haematology, the International Workshop on Chronic Lymphocytic Leukaemia and the European Society for Medical Oncology recommend no treatment for CLL patients who do not have any symptoms.

The initiation of active treatment will be decided upon by your haematologist who will weigh up the benefit of controlling your symptoms and the potential of drug side effects.

Finding out you need to start treatment may be overwhelming to hear, and you may experience a wide range of emotions. There are a number of places that you can seek support from:

- Caregivers and loved ones can be there for you at home. They can also attend hospital appointments with you. Having someone else there to take in all the information can help things seem less vast.
- You may be assigned a clinical nurse specialist. They will be there to assist you with your treatment pathway. They can be a great source of medical and supportive information relating to your CLL.
- Charities and organisations, including Leukaemia Care, offer a number of services that aim to offer some comfort. You can call our helpline on **08088 010 444** to speak to a nurse or a trained member of our Patient Services team. Sometimes, speaking to someone you don't know or who isn't directly involved in your situation can be useful. For a full list of our other services, you can ask about this on our helpline, or find more information on our website **www.leukaemiacare.org.uk**.
- It is also important to form a positive working relationship with your consultant. This should be based on good patient-doctor communication. You should feel comfortable to seek as much information from them as you would like, but also be able to question something if it doesn't feel quite right. Having this type of working relationship with them will help you to feel supported.

When should treatment be started?

Your medical team will determine when to start your treatment, as your symptoms worsen or tests reveal there is disease progression. This is based on:

- The stage of your disease
- How quickly your disease is progressing
- Your age
- Your general health
- Chromosome and gene analysis

Regular blood tests will be performed to help with treatment decisions and to monitor that any treatment you have is working as it should. These blood tests will also help to indicate what stage your CLL is at.

In the UK, the Binet clinical staging system is used to describe the area of the body where the CLL is located, the number and size of lymph nodes and the extent to which the CLL is affecting the blood count.

The Binet clinical staging system of CLL is used to predict how quickly the cancer may grow and how to keep track of it. The potential risks and benefits of a particular treatment need to be fully assessed in each individual patient by an experienced CLL clinician and discussed at the multidisciplinary team meeting.

Risk group	Clinical features
Stage A	No cytopenia (reduction in the number of all mature blood cells) and less than 3 enlarged lymphoid organs* involved
Stage B	No cytopenia and 3 or more enlarged sites lymphoid organs* involved
Stage C	Cytopenia present and anaemia: low haemoglobin level and/or low platelet count

*There are five sites for lymphoid organs: lymph nodes in neck, armpit or groin, the spleen and the liver.

While some patients in Binet stage B or C may benefit from the initiation of treatment, some of these patients (in particular Binet stage B) can be monitored without therapy until they have evidence for progressive or symptomatic disease, known as "active disease".

The indications for treatment of CLL patients are outlined in the 2018 International Working Group CLL criteria to assist haematologists with deciding the right time to start treatment. At least one of the following criteria should be met:

- Weight loss of more than 10% in previous six months
- Extreme fatigue
- Fever 38°C or higher for two or more weeks without evidence of infection
- Night sweats for longer than one month
- Progressive bone marrow failure
- Auto-immune anaemia or thrombocytopenia not responding to glucocorticoids
- Progressive or symptomatic enlargement of the spleen
- Massive or symptomatic enlargement of lymph nodes
- Progressive lymphocytosis (a high level of lymphocytes). This is defined by an increase of more than 50% in two months or a doubling time of less than six months

Being told you need active treatment after a period of Watch and Wait can be a shock and difficult to cope with. Advice on how to live with CLL and the emotional impact is available in our dedicated booklet. Go to our website to download a copy **www.leukaemiacare.org.uk** or call the helpline to order a copy on **08088 010 444.**

Sometimes it can be useful to hear about the experiences of others in a similar situation. It can be reassuring to know you are not alone. Here are two patients'

When should treatment be started? (cont.)

stories which may help you cope with your situation and pick up tips on how to manage.

Paul was only 38 when he was diagnosed with CLL and he was placed on Watch and Wait for four years until his symptoms appeared. Despite several rounds of chemo-immunotherapy, treatment was unsuccessful. He was then scheduled for a bone marrow transplant. While this was a difficult process, eight years after his transplant, he remains positive and is now in excellent health. In 2019 he completed a half marathon and plans to do more. He recounts how he dealt with each step of his journey.

http://bit.ly/PaulWalmsley

Geoffrey was diagnosed in February 2016 during a routine medical. After two years on Watch and Wait, he developed symptoms rapidly and was taken into hospital. Because he was shown to have a TP53 deletion/ mutation, he was treated with one of the new targeted B-cell drugs, ibrutinib. Following 18 months of oral treatment with ibrutinib at home, he is back to his normal self.

http://bit.ly/GeoffreyBrown

What are the options for treatment after Watch and Wait?

The aim of treatment for patients with CLL is to treat any symptoms until they are resolved. The majority of patients with CLL will not require treatment at the time of the diagnosis. They may eventually require treatment during their lifetime. However, a recent study showed that only 43.6% of patients needed treatment.

The main treatment for CLL is chemo-immunotherapy which consists of chemotherapy to which a targeted immunotherapy drug has been added.

Immunotherapies used in the treatment of CLL include:

- CD20 monoclonal antibodies such as rituximab and obinutuzumab
- Ibrutinib, a Bruton tyrosine kinase inhibitor
- Idelalisib, a phosphatidylinositol 3-kinase inhibitor
- Venetoclax, a B-cell lymphoma-2 inhibitor

Ibrutinib and venetoclax may be used alone or in combination with a monoclonal antibody. Idelalisib is used only in combination with rituximab.

First-line treatments for CLL are:

- A combination of fludarabine, cyclophosphamide and rituximab (FCR)
- A combination of bendamustine and rituximab (BR)
- Chlorambucil combined with the CD20 monoclonal antibodies rituximab or obinutuzumab
- Ibrutinib alone in adults who have at least one prior therapy or who have a 17p deletion or TP53 mutation and in whom chemo-immunotherapy is unsuitable
- Idelalisib combined with rituximab in untreated adults with a 17p deletion or TP53 mutation or in treated adults who have relapsed within 24 months

Chlorambucil is an alkylating chemotherapy. It damages the DNA of the leukaemia cells to prevent them from duplicating. Monoclonal antibodies are man-made antibodies created from genetically identical immune cells. They all bind to the same protein which is commonly found on the leukaemia cells (for example, the protein CD20).

One of the differences between treatments is how long they are given for. Chemo-immunotherapy is typically given for a limited time of six months. Targeted drugs can be given continuously until the CLL progresses or unacceptable side effects occur. Your treatment plan will be decided by your doctor, so it is best to speak with them regarding timeframes.

Future treatment options

The combination of venetoclax and obinutuzumab has been approved by the European Medicines Agency (EMA) for the treatment of adult patients with previously untreated CLL. The combination of venetoclax and obinutuzumab is being appraised by the National Institute of Health and Care Excellence (NICE) and a decision on recommendation is expected in October 2020.

Acalabrutinib is a Bruton tyrosine kinase inhibitor that has had an orphan designation since 2016. In July 2020, it was recommended for approval by the European Union for the following indications:

- Alone or in combination with obinutuzumab for the treatment of adult patients with previously untreated CLL
- Alone for the treatment of adult patients with CLL who have received at least one prior therapy

It is being made available through an early access scheme to National Health Service patients with indications for first-line treatment. It is also being appraised by NICE for the use of patients with untreated and treated CLL.

Characteristics of these chemo-immunotherapies and new targeted immunotherapies are summarised below.

What are the options for treatment after Watch and Wait? (cont.)

Fludarabine, cyclophosphamide and rituximab (FCR)

FCR is the first-line treatment for patients with previously untreated CLL without the TP53 deletion/mutation. It is especially for patients who are younger and fitter.

CLL is predominantly seen in elderly patients, who may also have other diseases and decreased organ and bone marrow function. Treatments need customising to the patient's level of fitness, because of the potential impact on their quality of life.

Reduced dose FCR regimens can be used in elderly patients (over the age of 65 years) who are known to suffer from severe side effects with FCR. However, a better treatment regimen for these patients may be BR. Alternatively, chlorambucil combined with an anti-CD20 monoclonal antibody may be given.

Method of administration

The FCR combination is normally given every 28 days for six cycles together with a treatment for the prevention of infections. Rituximab is given as an infusion, while fludarabine and cyclophosphamide are given as oral tablets.

Side effects

The most common side effects seen in large studies of patients treated with FCR are:

- Low levels of neutrophils (white blood cells involved in fighting inflammation and infection)
- Infection risk
- Bruising and bleeding (low levels of platelets)
- Anaemia (low number of red blood cells)
- Nausea
- Bladder irritation
- Diarrhoea
- Fatigue

Secondary cancers have also been reported in long-term follow-up of patients who have received FCR. However, the risk is 2.38 times greater than for the general population.

Bendamustine and rituximab (BR)

The BR combination is an established first-line treatment for those who cannot tolerate FCR. This includes frail, elderly patients and patients with kidney disease. It is less intensive than FCR, while still being effective for the treatment of CLL.

Method of administration

The BR regimen is given by intravenous infusion on two consecutive days every 28 days. It is given with preventative treatment for infections.

Side effects

Side effects commonly reported with BR include:

- Low neutrophil count
- Low platelet count (type of blood cells which help to stop bleeding)
- Anaemia
- Fatigue
- Nausea and vomiting
- Rashes or hives
- Severe infections

Chlorambucil and a monoclonal antibody

Chlorambucil is a chemotherapy that disrupts the cell's DNA to prevent it from growing and multiplying. It has low levels of side effects, is inexpensive and convenient to administer as it can be given orally.

When combined with an anti-CD20 monoclonal antibody, such as rituximab or obinutuzumab, chlorambucil makes a very useful treatment for elderly or unfit patients.

The combination of chlorambucil with obinutuzumab has been shown to be superior to the combination of chlorambucil with rituximab both in terms of response to treatment and survival rates.

Method of administration

Chlorambucil is administered

What are the options for treatment after Watch and Wait? (cont.)

for seven to ten days of a 28-day cycle. This is usually for six cycles alongside the monoclonal antibodies which are also administered for six cycles. Chlorambucil is available as a tablet for daily oral administration on an empty stomach. The monoclonal antibodies are infused intravenously.

Side effects

Side effects seen with combination of chlorambucil and anti-CD20 monoclonal antibody include:

- Infusion-related reactions
- Low levels of neutrophils
- Infections

Obinutuzumab

Obinutuzumab (brand name Gazyvaro, Roche Pharma AG) is a type 2 monoclonal antibody. It targets areas of the CD20 protein on the leukaemia B-cells.

Obinutuzumab in combination with chlorambucil is indicated for the treatment of adult patients with previously untreated CLL, who are elderly or unfit and unsuitable for treatment with FCR.

Obinutuzumab is approved on the condition that bendamustine-based therapy is not suitable.

Method of administration

Obinutuzumab is administered intravenously on days one, two, eight and 15 of the first 28-day cycle, and day one of the following five cycles. Chlorambucil is administered orally on an empty stomach on day one of each cycle.

Side effects

Side effects commonly reported with obinutuzumab include:

- Low levels of neutrophils
- Low levels of platelets
- Feeling weak
- Diarrhoea and/or constipation
- Fever
- Headaches
- Back and/or joint pain

Idelalisib

Idelalisib (brand name: Zydelig, Gilead Sciences) is an inhibitor of the phosphatidylinositol 3-kinase (PI3K) delta enzyme. This enzyme is present on normal B-cells, but particularly on the leukaemia B-cells as well. Idelalisib blocks several signalling pathways required to maintain the B-cells.

Idelalisib has been shown to significantly improve survival in patients with relapsed CLL.

Idelalisib combined with the anti-CD20 monoclonal antibody rituximab is currently indicated for:

- The treatment of adult CLL patients who have received at least one prior therapy and relapsed within 24 months.
- First-line treatment in the presence of 17p deletion in patients who are not eligible for any other therapies.

Idelalisib is approved by NICE for these indications.

Idelalisib is also effective in patients with high-risk features. It is able to control CLL in difficult-to-treat patients better than many of the currently approved therapies.

Method of administration

Idelalisib is available as an oral drug. The starting dose is 150mg twice daily. The dosage is then adjusted as often as needed in line with the amount of side effects experienced. Treatment should be given until your CLL progresses or you experience unacceptable toxicity.

Side effects

The most common side effects are:

- Low levels of neutrophils
- Infections
- Lymphocytosis (an increase in lymphocyte count)
- Diarrhoea
- Colitis (inflammation of the colon)
- Liver damage
- Rashes
- Fever
- Pneumonitis

What are the options for treatment after Watch and Wait? (cont.)

Ibrutinib

Ibrutinib (brand name: Imbruvica, Janssen-Cilag) is a Bruton tyrosine kinase inhibitor. Bruton tyrosine kinase is an abnormal protein kinase present in leukaemia B-cells. It is essential for their survival.

Ibrutinib disrupts the specific signalling pathways for B-cells. It therefore prevents their development, maturation and survival. Inhibitors of Bruton tyrosine kinase have shown excellent efficacy for B-cell cancers.

In the treatment of CLL, ibrutinib is currently indicated:

- As a single agent or in combination with obinutuzumab for the treatment of adult patients with previously untreated CLL.
- As a single agent or in combination with BR for the treatment of adult patients with CLL who have received at least one prior therapy.

Ibrutinib is approved by NICE for these indications.

Ibrutinib given alone is the treatment of choice for patients with CLL who:

- Do not respond to chemo-immunotherapy
- Have relapsed a relatively short time after chemo-immunotherapy

Ibrutinib is effective in patients with CLL and high-risk features such as 17p deletion or TP53 deletion/mutation.

Method of administration

Ibrutinib is available as a tablet for oral administration. Ibrutinib is given daily until you experience unacceptable side effects or your CLL progresses.

Side effects

The most common side effects reported in patients treated with ibrutinib include:

- Low levels of neutrophils and platelets
- Fever
- Nausea
- Diarrhoea
- Rash
- Bruising
- Bone and/or joint pain
- Pneumonia
- Cardiac problems (such as abnormal heart rhythms or high blood pressure)
- Problems with your eyes

Venetoclax

Venetoclax (brand name: Venclyxto from AbbVie/Roche) is a selective B-cell lymphoma 2 (BCL-2) inhibitor. Venetoclax inhibits the action of the BCL-2 protein. This protein regulates the natural death of cells, particularly the leukaemia B-cells. In CLL and other blood cancers, the BCL-2 protein builds up and stops the leukaemia cells from dying naturally. By binding to BCL-2, venetoclax restores the natural death cycle of CLL leukaemia cells.

Venetoclax has been shown to have anticancer activity in patients with CLL. This includes those who have been previously treated numerous times, or those with a 17p deletion. Venetoclax is also effective for CLL patients whose treatment with ibrutinib has not been successful.

Venetoclax alone is indicated for adult CLL patients who:

- Are unsuitable for, or have failed treatment with, a B-cell receptor inhibitor and have a 17p deletion or TP53 loss/inactivation.
- Have not been successful with treatment. This includes using both chemo-immunotherapy and a B-cell receptor inhibitor.

When combined with rituximab, venetoclax is indicated for the treatment of adult CLL patients who have received at least one prior therapy.

Venetoclax is approved by NICE for these indications.

Method of administration

Venetoclax is available in tablet form and is given orally. The film-coated tablets should be swallowed whole with water at roughly the same time each day. Ideally, it should be taken at the same time as food. The tablets should not be broken, crushed or

What are the options for treatment after Watch and Wait? (cont.)

chewed before swallowing.

For the first five weeks, your dose of venetoclax is gradually increased until it reaches the full standard dose. Venetoclax is administered daily until progression of your CLL or unacceptable side effects occur.

Side effects

Common side effects reported with venetoclax include:

- Low number of neutrophils with fever
- Diarrhoea or constipation
- Nausea/vomiting
- Feeling tired
- Anaemia
- Urinary tract infections
- Chest infections
- Pneumonia
- High levels of phosphate (a naturally occurring body salt)
- Sepsis (severe infection in the blood)

A serious side effect that can occur with venetoclax is tumour lysis syndrome. The rapid destruction of large numbers of white blood cells can increase the levels of uric acid in the blood. This may cause damage to the kidneys, heart or liver. This damage is known as tumour lysis syndrome.

The risk of tumour lysis syndrome is greater with:

- An extremely rapid destruction of leukaemia cells
- Pre-existing poor kidney function
- Any other serious diseases

The schedule for venetoclax is designed to reduce the number of leukaemia cells killed in a short period of time.

What is my prognosis once I have started active treatment?

Currently, there is still no treatment available to cure CLL. However, since the introduction of the new targeted B-cell treatments, which can be used alone or with current chemo-immunotherapies, the prognosis for patients with CLL has greatly improved.

Research into the genetics of CLL has enabled patients to be divided into different risk groups. This helps to determine the most appropriate treatment and allows for more accurate assessment of your prognosis.

Between 50% and 70% of patients with CLL will have a good outcome. Of these, around 30% of patients will have a chronic clinical course and they may not require any treatment at all.

As mentioned previously, chromosomal abnormalities associated with poorer outcomes in patients treated with chemo-immunotherapy are:

- 17p deletion, seen in 5% to 8% of new CLL patients.
- Nearly 80% of patients with the 17p deletion chromosome abnormality will have an inactivated TP53 gene.
- TP53 gene deletion/mutation, present in 4.5% of CLL patients.
- Unmutated IGHV gene – The IGHV gene is not mutated in slightly less than 50% of patients.

Loss/inactivation of the TP53 gene and 17p deletion are the most reliable indications for the prognosis of patients.

The new targeted therapies have markedly altered the management of patients with CLL. They have improved response rates and survival without progression of the CLL. This is particularly the case for patients with the 17p deletion or TP53 deletion/mutation, who are considered high-risk.

The efficacy of the new targeted treatments in these subgroups emphasises the need for all patients to be tested for the presence of del (17p) or TP53 deletion/mutation before any course of treatment.

The status of the IGHV gene mutation can indicate the differing clinical courses of CLL that patients will experience.

What are the options for treatment after Watch and Wait? (cont.)

Patients with a mutated IGHV gene tend to have the subtype of CLL which is slow to progress and has little symptoms. These patients have a better prognosis and greater overall survival.

Patients with an unmutated IGHV gene tend to have the more aggressive subtype of CLL with a poorer prognosis and lower overall survival.

The status of the IGHV gene mainly impacts on the duration of complete remission and overall survival. Patients who have an unmutated IGHV gene treated with chemo-immunotherapy tend to have a shorter overall survival.

Richter syndrome

Richter syndrome is the development of an aggressive lymphoma in patients with CLL. It is also called Richter transformation. Richter syndrome occurs in 2% to 10% of all patients with CLL during the course of their disease, amounting to a transformation rate of 0.5% to 1% per year.

In patients with CLL who have Richter syndrome, the breakdown of lymphomas is as follows:

- Approximately 90% of cases develop diffuse large B-cell lymphoma

For further details on Richter syndrome, read our dedicated booklet. You can download it from our website **www.leukaemiacare.org.uk.**

- The remaining 10% develop Hodgkin's lymphoma

Allogeneic stem cell transplant

An allogeneic stem cell transplant is considered as an option for certain CLL patients. However, it does have several risks including the possibility of rejection and increased infections. Also, it is only suitable for patients who are able to withstand the intensity of this treatment due to the risk of death.

An allogeneic stem cell transplant is considered as a treatment option for patients with CLL who:

- Have failed chemo-immunotherapy and B-cell receptor inhibitor therapy, irrespective of the status of the TP53 gene.
- Possess the TP53 gene deletion/mutation and have not responded or lost response to B-cell receptor inhibitor therapy.
- Are eligible patients with Richter syndrome.

New emerging treatments

As well as the recent approved treatments, a number of promising new drugs are in clinical trials. These include:

- Second-generation Bruton tyrosine kinase inhibitors such as acalabrutinib and tirabrutinib
- PI3K delta inhibitors such as duvelisib

CAR T-cell therapy (tisagenlecleucel) is approved for acute lymphoblastic leukaemia and some lymphomas. It is also being tested for relapsed CLL. CAR T-cell therapy is a new treatment involving the patients' own immune cells. They are genetically modified outside of the body to recognise leukaemia cells. They are then re-infused into the patient to attack the leukaemia B-cells.

These new treatments are being studied in the hope of producing longer remissions or even a cure for CLL.

Glossary

Allogeneic Stem Cell Transplant

The transplant of stem cells from a matching donor.

Anaemia

A condition where the number of red blood cells are reduced. Red blood cells contain haemoglobin and transport oxygen to body cells. 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. The antibodies neutralise the bacteria and viruses.

Antigen

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

Bone Marrow

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

Bone Marrow Failure

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

Chemotherapy

Drugs that work in different ways to stop the growth of cancer cells, either by killing the cells or by stopping them from dividing.

Chemo-immunotherapy

Chemotherapy to which an immunotherapy drug has been added.

Complete Remission

Complete remission has occurred when:

- Blood cell counts have returned to normal
- Less than 5% of abnormal, leukaemia cells are still present in the bone marrow

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.

Chronic Lymphocytic Leukaemia (CLL)

A leukaemia in which the B-lymphocytes in the bone marrow start multiplying excessively. This leads to large numbers of small, mature lymphocyte cells which are unable to fight infection. Their presence prevents the bone marrow from producing healthy blood cells of all types.

Cytopenia

The reduction in the number of all the mature blood cells produced by the bone marrow.

DNA (deoxyribonucleic acid)

A thread-like chain of amino acids found in the nucleus of each cell in the body. It carries genetic instructions used in the growth, development and functioning of the individual's cells.

Fatigue

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

First-line Treatment

A treatment regimen that is generally accepted by the medical establishment for initial treatment of a given type of cancer.

Immunoglobulin Heavy Chain Variable (IGHV) Gene

Another name for antibody, immunoglobulins consist of two identical heavy chains and two identical light chains. These are used for immobilising the antigen (bacteria or virus). Each chain has a constant and variable region. The IGHV gene is responsible for generating antibodies used by the immune response.

Genes

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

Leukaemia

A group of cancers that usually begin in the bone marrow and result in high numbers of abnormal blood cells. These cells are not fully developed and are called blasts or leukaemia cells. Depending on the type of blood cell involved, there are different types of leukaemia. This includes being acute (develops quickly) or

Glossary (cont.)

chronic (develops slowly).

Lymph Nodes

Components of the lymphatic system (part of the body's immune system) that contain lymphocytes. These 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 spleen but also in the neck, armpit and groin.

Lymphocytes

Lymphocytes are a type of white blood cell that are vitally important to the immune response. There are three types of lymphocytes: B-cells, T-cells and natural killer (NK)-cells. B-cells produce antibodies that seek out invading organisms. T-cells destroy the organisms that have been labelled by the B-cells, as well as internal cells that have become cancerous. NK-cells attack cancer cells and viruses.

Lymphocytosis

An increase in lymphocyte cell count.

Lymphoid

Relates to lymphocytes.

Monoclonal Antibody

Man-made antibodies created from identical cloned immune cells. They all bind to the same protein commonly found on the leukaemia cells.

Neutrophils

The white blood cells involved in fighting inflammation and infection. They are specifically useful in fighting bacterial infections.

Platelets

One of the types of blood cell which helps to stop bleeding.

Prognosis

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

Protein Kinase Inhibitor

Protein kinase inhibitors block the protein kinase enzymes that are involved with cell growth. This prevents the growth of the cancer cells.

Red Blood Cells

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

Refractory Condition

A condition for which treatment does not result in a remission. However, the condition may be stable.

Relapse

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

Richter Syndrome

Also called Richter transformation, this is the development of an aggressive lymphoma in patients with CLL.

Secondary Cancers

A second primary cancer often appears, if at all, after a number of years. This can be following chemotherapy or radiation treatment for a previous primary cancer. Secondary cancer is not an occurrence or spread of the primary cancer in another part of the body. That is called a metastatic cancer. Secondary cancers are often other blood cancers, lung cancer and skin cancers.

Sepsis

An infection in the blood that can cause septic shock.

Spleen

The largest organ of the lymphatic system whose function is to help rid the body of toxins, waste and other unwanted materials. The spleen is located under the ribs on the left of the abdomen.

Stem Cell

The most basic cell in the body that has the ability to develop into any of the body's specialised cell types, from muscle cells to brain cells. What makes stem cells reproduce uncontrollably is thought to be linked to chromosome abnormalities.

Stem Cell Transplant

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

Glossary (cont.)

Targeted Therapy

Drugs that specifically interrupt the leukaemia cells from growing in the body. These drugs do not simultaneously harm healthy cells the way conventional chemotherapy drugs do.

Thrombocytopenia

Low levels of platelets, which are small blood cells that help the body form clots to prevent or stop bleeding.

Toxicity

Harmful effect.

Tumour Lysis Syndrome

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

Tyrosine Kinase Receptors

Receptors present in the membranes of all of the body's cells which can be activated by the enzyme tyrosine kinase. It functions as an 'on' or 'off' switch in many cellular functions.

Uric Acid

The product of the metabolic breakdown of purine nucleotides which are the chemical building blocks of DNA. Uric acid is a normal component of urine.

White Blood Cells

A type of cell found in the blood and bone marrow, along with red blood cells and platelets. The main role of white blood cells is creating an immune response against both infections and foreign bodies. There are several different types of white blood cells, and each has a different role. The granulocytes, so called because they contain small granules in their cells, include neutrophils (protect against bacterial infections and inflammation), eosinophils (protect against parasites and allergens) and basophils (create the inflammatory reactions during an immune response). The other group of white blood cells include lymphocytes (recognise bacteria, viruses and toxins, to which they produce antibodies) and monocytes (clear infection products from the body).

Useful contacts and further support

There are a number of helpful sources to support you during your diagnosis, treatment and beyond, including:

- Your haematologist and healthcare team
- Your family and friends
- Your psychologist (ask your haematologist or CNS for a referral)
- Reliable online sources, such as Leukaemia Care
- Charitable organisations

There are a number of organisations, including ourselves, who provide expert advice and information.

Leukaemia Care

We are a charity dedicated to supporting anyone affected by the diagnosis of any blood cancer. We provide emotional support through a range of support services including a helpline, patient and carer conferences, support group, informative website, one-to-one buddy service and high-quality patient information. We also have a nurse on our help line for any medical queries relating to your diagnosis.

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

Blood Cancer UK

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

0808 2080 888
www.bloodcancer.org.uk

Cancer Research UK

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

0808 800 4040
www.cancerresearchuk.org

Macmillan

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

0808 808 0000
www.macmillan.org.uk

Maggie's Centres

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

0300 123 1801
www.maggiescentres.org

Citizens Advice Bureau (CAB)

Offers advice on benefits and financial assistance.

08444 111 444
www.adviceguide.org.uk

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

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

Want to talk?

Helpline: **08088 010 444**
(free from landlines and all major mobile networks)

Office Line: **01905 755977**

www.leukaemiacare.org.uk

support@leukaemiacare.org.uk

Leukaemia Care,
One Birch Court,
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Leukaemia Care is registered as a charity in England and Wales (no.1183890) and Scotland (no. SC049802).
Company number: 11911752.
Registered office address: One Birch Court, Blackpole East, Worcester, WR3 8SG

Leukaemia Care
YOUR Blood Cancer Charity