Chronic Eosinophilic Leukaemia (CEL)

A Guide for Patients

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

Being diagnosed with chronic eosinophilic leukaemia (CEL) can be a shock, particularly when you may never have heard of it. If you have questions about CEL – 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 personalised information, talk to your haematologist, clinical nurse specialist or hospital pharmacist.

This booklet was written by Isabelle Leach, Patient Information Writer at Leukaemia Care, and reviewed by Professor Claire Harrison.

Disclaimer: *As we are accredited by the Information Standard, all of our information has to adhere to a standardised process that ensures it is of the highest quality. Unfortunately, due to the rarity of CEL, we were unable to complete the production process which meant that this booklet cannot be formally accredited. However, we assure you that this information was created with the same values as that which is.*

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

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In this booklet

About Leukaemia Care

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

Our services

Helpline

Our helpline is available 9.00am - 10.00pm on weekdays and 9.00am - 12.30pm on Saturdays. If you need someone to talk to, call **08088 010 444**

Nurse service

We have two trained nurses on hand to answer your questions and offer advice and support, whether it be through emailing **nurse@leukaemiacare.org.uk**, over the phone on **08088 010 444** or via LiveChat.

Patient Information Booklets

We have a number of patient information booklets like this available to anyone who has been affected by a blood cancer. A full list of titles – both disease specific and general information titles – can be found on our website at **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**, as well as speak to one of our care advisers on our online support service, LiveChat (9am-5pm weekdays).

Campaigning and Advocacy

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

Patient magazine

Our free 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 CEL?

Eosinophils are a type of white blood cell that form part of the body's immune system. These have a protective immunity role against parasites and allergens.

In adults, more than 500 eosinophils per µl (microliter or 0.001 of 1 ml) of blood is known as eosinophilia. The normal count ranges between 50 and 500 eosinophils per µl of peripheral blood. Eosinophilia can occur in the blood (blood eosinophilia) or in tissues at the site of an infection or inflammation (tissue eosinophilia). Eosinophilia most often occurs in response to a parasitic infection, an allergic reaction or as a type of leukaemia, such as chronic eosinophilic leukaemia (CEL), NOS (not otherwise specified). NOS indicates there is no other cause involved.

A count of more than 1,500 eosinophils per µl of peripheral blood is associated with tissue damage and is called hyper-eosinophilia. Hyper-eosinophilic syndromes (HESs) are a group of rare illnesses characterised by a continued overproduction of eosinophils and is defined by a number of eosinophils of more than 1,500 cells per µl of blood for more than six months with associated organ damage attributable to the eosinophilia, but not explained by any obvious cause. Some people have a rare chromosome disorder. HES was first defined in 1975 by Chusid et al under the name of idiopathic HES to clarify the fact that the causes of most of the conditions were unknown.

CEL can be distinguished from HES by the presence of clonal molecular markers or significantly increased numbers of blasts cells. Clonal means that a group of identical eosinophil cells are multiplying in an unrestricted manner, and they are originating from immature cells in the bone marrow. Blasts is the name given to these immature bone marrow cells, which are often cancerous if present in large numbers (for more details, see section **How is CEL diagnosed?**).

Very rarely, CEL can be caused by a genetic mutation that

develops during a person's life due to environmental factors, smoking, and chemical/ radiation exposure. However, for most patients, no specific cause can be found. There is no known cause for chronic eosinophilic leukaemia. It has not been linked to a specific chromosome or genetic abnormality.

Studies on the prevalence of CEL are rare and reliable data on CEL is not available given past difficulties of distinguishing CEL from HES.

The severity of CEL and its potential associated mortality in patients is mainly due to either tissue damage, particularly thickening and scarring of the heart, or transformation to acute myeloid leukaemia (AML) in patients with high levels of blast cells.

Evidence from case reports indicates that CEL usually progresses slowly and may stay the same for many years. However, in some people, it may change quickly into acute myeloid leukaemia (AML).

At Leukaemia Care we have a freephone helpline service available for patients and carers who are affected by a blood cancer. We can provide emotional and practical support as well as medical advice. The telephone number of the helpline is **08088 010 444**.

What are the symptoms of CEL?

In around 10% of patients, CEL is diagnosed by chance in the early stages because the patient does not have any signs or symptoms. CEL may be found during a routine blood test.

Patients with CEL may experience the following symptoms or signs:

- Fever
- Itching
- Diarrhoea
- Night sweats
- Unexplained weight loss
- Unexplained fatigue or shortness of breath
- Cough
- Swollen lymph nodes (small swellings in the lymphatic system where lymph is filtered, and lymphocytes are formed. It is part of the immune system)
- Muscle pains (myalgias)
- Anaemia (low level of red blood cells and haemoglobin which is carried by the red blood cells)
- Thrombocytopenia (decrease in the level of platelets, which are small blood cells that help the body form clots to stop bleeding)
- Mucosal ulceration
- Endomyocardial fibrosis (fibrosing of the inside of the heart lining)
- Splenomegaly (enlarged spleen)

CEL is more common in men, with peak incidence at around 40 years of age. However, diagnosis is rare as this disease type can be excluded and requires exceptional skill to be confirmed.

How is CEL diagnosed?

The diagnosis of CEL is based on the presence of clonal cancerous proliferation of eosinophilic cells and the exclusion of other bone marrow cancers and blood disorders where eosinophilia is a feature.

Since both patients with HES and CEL will have more than 1,500 eosinophils per µl of peripheral blood and associated organ damage, the World Health Organisation (WHO) publishes the characteristics that will determine the diagnosis of CEL, NOS together with the risk stratification and management of eosinophilic disorders yearly. This document is updated with new research as it becomes available.

The WHO 2017 update of defined eosinophilic disorders gives the characteristics of an individual with CEL, NOS as:

1. Eosinophil count is greater than 1500 per µl of peripheral blood

2. The patient does not meet any of the WHO criteria for the following illnesses:

a. Chronic myeloid (bone marrow) leukaemia (CML): presence of BCR-ABL1 is positive for CML

b. Polycythaemia vera (proliferation of red blood cells)

c. Essential thrombocythemia (excess production of platelets leading to abnormal blood clotting)

d. Primary myelofibrosis (build-up of scar tissue in the bone marrow)

e. Chronic neutrophilic leukaemia (excess production of white cells called neutrophils)

f. Chronic myelomonocytic leukaemia (excess production of white cells called monocytes)

g. Atypical chronic myeloid leukaemia (unusual type of CML)

3. Genetic testing does not show:

How is CEL diagnosed? (cont.)

a. Any rearrangement disorder of the following genes:

- PDGFRa (platelet-derived growth factor receptor alpha)
- PDGFRb (platelet-derived growth factor receptor beta)
- FGFR1 (fibroblast growth factor receptor 1 is a protein involved in growth and proliferation of cells in the body and is commonly activated in human cancers)

b. The presence of any of the following fusion genes:

- PCM1-JAK2
- ETV6-JAK2
- BCR-JAK2

4. Both of these following are met:

a. The number of blast cells in the peripheral blood and the bone marrow is less than 20%

b. The following are absent:

- Abnormalities in the inv(16)(p13.1q22) and t(16;16)(p13;q22) genes
- Other diagnostic features of AML

5. Either of the following are met:

a. There is a clonal component to the cell genetics or an abnormality present in the molecular genetics

b. Blast cells are less than 2% in the peripheral blood or greater than 5% in the bone marrow

HES patients that have been revealed to have a deletion in chromosome 4, which fuses the FIP1 like-1 gene (FIP1L1) to the PDGFRA gene, leading to FIP1L1-PDGFRA rearrangement are now reclassified as having CEL because the FIP1L1-PDGFRA gene is considered a strong indicator of a clonal/cancerous disease. Possession of this clonal gene abnormality has been proposed as a new marker for CEL. More

importantly, patients with FIP1L1 PDGFRa have also been identified as responding extremely well to imatinib, which is an inhibitor of tyrosine kinase which works specifically on BCR-ABL, c-KIT, and PDGFRa. Tyrosine kinases are important components of the signalling and role determination in cell growth, cell differentiation, and cell death.

Diagnostic Tests

The diagnosis of CEL generally starts with a visit to your general practitioner, or if a routine blood test suggests there is abnormality with your blood.

Investigating a patient with HES is a priority, since the accurate detection of CEL can speed up the diagnosis and early initiation of treatment before involvement of heart fibrosis becomes established is paramount.

Initial diagnostic tests include:

- Complete blood cell counts to measure the number and quality of white blood cells, red blood cells and platelets.
- Blood chemistry tests to check that the liver, kidneys and spleen are normal in size and working properly.

If reactive/parasitic eosinophilia is unlikely, changes in cardiovascular and pulmonary (heart and lung) systems may be investigated. In the presence of cardiopulmonary disease, the following tests are needed:

- Chest X-ray
- Echocardiography (ultrasound to create an image of the heart)
- Pulmonary function test (series of tests to determine the severity of pulmonary impairment)
- Cardiac troponin T test (troponin T is a protein found in the cardiac muscles, which is released into the bloodstream when the heart is damaged)

How is CEL diagnosed? (cont.)

If the reactive causes for the eosinophilia are have been rejected or if a hematopoietic disease (disease of the bone marrow, spleen or lymph nodes) is suspected, analyses of the FIP1L1-PDGFRa, PDGFRb) and BCR/ABL gene rearrangements can be carried out.

To help confirm a diagnosis, the bone marrow may be examined for the following:

- Cell genetic abnormalities
- Karyotyping, which involves examination of the number and appearance of chromosomes to detect abnormalities.

The results of these tests will enable the oncologist to determine if the patient meets the WHO diagnostic criteria for CEL, NOS.

Risk of transformation in CEL

Because CEL is a rare disease, rates of acute transformation into acute leukaemia or into blast crisis are unknown. Case reports indicate that CEL usually progresses slowly and can remain the same for many years, but then transform rapidly into AML or blast crisis in some cases.

A series of case reports of patients diagnosed with CEL included 10 patients: 7 males and 3 females with a median age of 62 years. A total of 50% of patients has acute transformations after median of 20 months from diagnosis. There were four cases of secondary AML and one patient had T-cell lymphoblastic leukaemia/lymphoma.

How is CEL treated?

Given that chronic eosinophilic leukaemia is rare, current knowledge is that CEL develops differently in different people. It can be stable for many years and then quickly change into AML or other blood cancers. Similarly, it occurs mainly in middle age patients but can also present in young adolescents. As a result, there is no standard treatment plan for chronic eosinophilic leukaemia. Your physicians will create a treatment plan for you.

Chemotherapy and immunotherapy

Chemotherapy involves using drugs to prevent cancer cells from growing and dividing, which destroys the cancer cells overtime. Targeted therapy is a treatment that targets the specific genes or proteins of leukaemia cells, as in the case of imatinib. Imatinib prevents the tyrosine kinase enzymes from working and this can destroy the abnormal eosinophils by blocking the FIP1L1-PDGFRa gene. Therefore, it is more probable that imatinib will work for patients with this genetic mutation.

CEL patients who are FIP1L1-PDGFRa positive respond very well to treatment with low doses of imatinib (100 mg/day). In general, patients show good responses, achieving normal blood cell counts and most attain molecular remission (this is where there is no demonstrable FIP1L1-PDGFRa gene in the blood within 4 weeks of starting treatment). In selected cases, where no response is seen, or if some residual disease is present, the dose of imatinib may be increased to 400 mg/day.

For patients who do not have the FIP1L1 PDGFRa gene which responds to imatinib, the treatments which are used in other blood marrow cancers may be helpful. It is estimated that only approximately 10%–20% have the FIP1L1-PDGFRa gene. The goal of therapy is to prevent organ damage which is caused

How is CEL treated? (cont.)

by the eosinophilia.

- Although not a cure, hydroxycarbamide is an effective chemotherapy to control the eosinophilia. A typical starting dose is 500 to 1000 mg/day. It can also be used in combination with steroids to try and increase the response rate.
- Chemotherapy drugs such as vincristine, chlorambucil, cyclophosphamide, etoposide, cyclosporine, and 2-chlorodeoxyadenosine can be used as second line drugs, if hydroxycarbamide chemotherapy is not effective.
- If the therapies above have not yielded results, higher doses of imatinib for cases without the PDGFRα and PDGFRβ gene rearrangements may eventually produce a response, if only partial. But, even if a patient does not have this mutation, it is still possible that imatinib may work. For many patients, imatinib can improve blood counts and symptoms for many years, if the drug is taken on a regular basis.

Immunotherapy

Interferon-a (IFN-a), is a purified derivative from fractions of white blood cells from the blood, and is called immunotherapy as it is actually a natural part of your body's immune system. Immunotherapy helps to boost the body's natural immune system to fight the leukaemia.

IFN-a has shown reductions in white cell counts and reversed organ injury in patients with CEL. The use of IFN-a in CEL is partly based on its efficacy in CML. IFN-a is often used in CEL patients who do not respond to other therapies including steroids (prednisone) and hydroxycarbamide.

Stem cell transplant

Stem cell allogeneic transplantation (receipt of blood forming stem cells from a genetically similar, but not identical, donor) is used in patients with aggressive disease. A stem cell transplant may be

a treatment option for some people with chronic eosinophilic leukaemia. Most people with chronic eosinophilic leukaemia are older so they may not benefit from a stem cell transplant, but it may be suited for the younger patient.

Disease-free survival following stem cell transplantation ranges from eight months to five years. Although success has been described in several cases, the role of transplantation is not well established.

Supportive care and surgery

Supportive or palliative care is medical care that relieves symptoms without dealing with the cause of the condition.

Leukapheresis is a procedure in which the excess white blood cells are separated out from a sample of blood to help reduce the large numbers of eosinophils/white cells. However, it does not represent an effective maintenance therapy. Anticoagulants (which thin the blood) and anti-platelet agents (which prevent blood clotting) help patients avoid getting clots and embolisms caused by their eosinophilia.

A splenectomy, which is an operation to remove the spleen, that is also known to make white blood cells in addition to the bone marrow, may be recommended for some patients. As the spleen becomes enlarged with the high number of eosinophils, it causes severe abdominal pain for the patient. This not standard treatment, but can be a part of a palliative care treatment plan. A surgical oncologist who is a physician specialising in cancer surgery will usually perform this procedure.

Palliative cardiac surgery may prolong survival in patients with end-stage heart disease. Heart valve replacements or surgery on the heart muscle which is scarred can help recover heart function.

When making treatment plan decisions, patients are often encouraged to consider clinical

How is CEL treated? (cont.)

trials as an option they may give access to new treatments being investigated. Your physician can guide you in this decision.

Future therapies

Antibodies against interleukin-5 (IL-5) (mepolizumab), the IL-5 receptor (benralizumab), and CD52 (alemtuzumab), have been developed, but are still in the early research stages.

Follow-up

Follow-up after treatment is an important part of cancer care. Follow-up for chronic eosinophilic leukaemia is often shared among the cancer specialists (oncologists) or blood specialists (haematologists) and your family doctor. Your healthcare team will work with you to decide on follow-up care to meet your needs.

Glossary

Acute Leukaemia

Leukaemia is a cancer of the white blood cells. Acute leukaemia means it progresses rapidly and aggressively, and usually requires immediate treatment.

Acute Myeloid Leukaemia (AML)

Acute myeloid leukaemia is a type of blood cancer that starts from young white blood cells called granulocytes or monocytes in the bone marrow.

Anaemia

A medical condition in which the red blood cell count or haemoglobin is less than normal.

BCR-ABL gene

A fusion gene that is formed when the ABL gene on chromosome 9 and the BCR gene on chromosome 22 swap part of their DNA. The swap-over, or translocation, forms an abnormal fusion gene called BCR-ABL.

Bone marrow

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

Chemotherapy

A type of cancer treatment that uses one or more drugs with a powerful chemical to kill growing cancer cells.

Chronic Leukaemia

A type of blood cancer that affects the white blood cells. This tends to progress over many years.

Chronic Myeloid Leukaemia (CML)

A cancer that affects the blood and bone marrow defined by the presence of the BCR-ABL translocation.

Clinical trial

A highly regulated research study which assigns patients and non-patients to participate in the study to evaluate the efficacy of a drug or a combination of drugs.

Full Blood Count (FBC)

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

Leukaemia

A cancer of the blood with many different subtypes. Some forms are acute (develop quickly) and others are chronic (develop slowly). Leukaemia is an excess number of abnormal cells in the

Glossary

blood, usually white blood cells, which stop the bone marrow working properly.

Lymph node or lymph gland

An oval-shaped organ of the lymphatic system that catches viruses and bacteria. It contains white blood cells that fight infection.

Platelets

A disc-shaped element in the blood that assists in blood clotting. During normal blood clotting, the platelets clump together (aggregate).

Red blood cells

The blood cell that carries oxygen. Red cells contain haemoglobin, which permits them to transport oxygen (and carbon dioxide) around the body.

White blood cells

One of the cells the body makes to help fight infections. There are several types of white blood cells. The two most common types are the lymphocytes and neutrophils.

Tell us what you think!

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

Suitable for Android, iPhone 7 and above.

Useful contacts and further support

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

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

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

Leukaemia Care

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

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

Bloodwise

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

020 7504 2200
www.bloodwise.org.uk

Cancer Research UK

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

0808 800 4040
www.cancerresearchuk.org

Macmillan

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

0808 808 0000
www.macmillan.org.uk

Maggie's Centres

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

0300 123 1801
www.maggiescentres.org

Citizens Advice Bureau (CAB)

Offers advice on benefits and financial assistance.

08444 111 444
www.adviceguide.org.uk

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

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

Want to talk?

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

Office Line: **01905 755977**

www.leukaemiacare.org.uk

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