
Chronic Myelomonocytic Leukaemia (CMML)

A Guide for
Patients

Leukaemia Care
YOUR Blood Cancer Charity

Introduction

Being diagnosed with chronic myelomonocytic leukaemia (CMML) can be a shock, particularly when you may have never heard of it before, and may even have had no obvious symptoms. If you have questions about CMML – 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.

You'll also find useful advice about how to get the best from your haematologist, as well as practical advice on how to help important people in your life understand such a rare condition. For more information, talk to your haematologist, clinical nurse specialist or hospital pharmacist.

This booklet was originally compiled by Ken Campbell and

the rewrite was put together by Lisa Lovelidge. This booklet has then been updated by our Patient Information Writer, Isabelle Leach. The booklet has been peer reviewed by Dr Steve Knapper and Mary Frances McMullin. We are also grateful to Adrian Thomas, Mike Wilson and John Stredwick, our patient reviewers, for their valuable contributions.

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

In this booklet

Introduction	2
In this booklet	3
About Leukaemia Care	4
What is chronic myelomonocytic leukaemia?	6
Symptoms of CMML	12
How is CMML diagnosed?	14
Treating CMML	18
Seeing your doctor	26
Telling your family	28
Managing your emotions	30
Survivorship	33
Palliative care	35
End of life care	37
Glossary	39
Useful contacts and further support	43

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

What is chronic myelomonocytic leukaemia?

Chronic myelomonocytic leukaemia (CMML) is a rare type of leukaemia characterised by increased levels of monocyte white blood cells, as well as features from the myelodysplastic syndromes (MDS) and myeloproliferative neoplasms (MPNs).

Monocytes are large white blood cells, derived from the myeloid stem cells in the bone marrow. They are part of the immune system and their main function is to fight off bacteria, viruses and fungi. Monocytes secrete chemical messengers, which recruit additional immune cells to the site of an infection. This enables the immune system to make antibodies to the organisms.

In addition, monocytes proliferate in response to infection and transform themselves into scavenger macrophages which ingest the inactivated foreign organisms, as well as any remaining infected tissue.

MDS are a group of cancers where bone marrow cells of all

types reproduce uncontrollably and have abnormal (dysplastic) changes. MDS are characterised by a poorly functioning bone marrow and a likelihood of progression to acute myeloid leukaemia (AML).

MPNs are a group of chronic disorders in which the myeloid stem cells in the bone marrow make too many abnormal red blood cells, white blood cells, or platelets. These abnormal cells do not function properly.

The main MPNs are:

- Chronic myeloid leukaemia (CML)
- Essential thrombocythaemia (ET)
- Polycythaemia vera (PV)
- Primary Myelofibrosis (MF)

Some MPNs are also likely to transform into AML.

If you would like more information on AML, MDS, CML, ET, PV or MF, you can download our dedicated booklets from our website www.leukaemicare.org.uk. Alternatively, you can order hard copies by calling the helpline on **08088 010 444** or emailing support@leukaemicare.org.uk.

Origin of chronic myelomonocytic leukaemia

In the bone marrow, more than a trillion new blood cells are produced every day to replace those that are worn out. Blood stem cells may become myeloid stem cells or lymphoid stem cells. They then transform themselves and mature into the blood cells that can be seen in the blood.

Myeloid stem cells can become any of the following types of mature blood cells:

1. Red blood cells that carry oxygen and other substances to all tissues of the body.
2. Platelets that form blood clots to stop bleeding.
3. White blood cells that fight infection and disease.

A lymphoid stem cell becomes one of three types of lymphocytes, which are also white blood cells:

1. B-lymphocytes (B-cells) make antibodies to help fight infection.
2. T-lymphocytes (T-cells) help B-lymphocytes make the antibodies for fighting infection.
3. Natural killer cells (NK-cells) attack cancer cells and viruses.

Monocytes are therefore derived from myeloid stem cells.

Granulocyte/macrophage colony stimulating factor (GM-CSF) is a growth factor that contributes in promoting myeloid cell development, maturation and survival, including monocytes.

What is chronic myelomonocytic leukaemia? (cont.)

Despite having overlapping features with both MDS and MPNs, such as the overproduction of blood cells and the potential transformation to AML, CMML is still a distinct condition of its own. CMML is biologically different to MDS.

Who is affected by CMML?

CMML can occur at any age, but it is most commonly seen in older adults, with a median age at diagnosis of 71 years. There is a slight male predominance with CMML, especially in older patients.

Although the exact incidence of CMML is not known, it is estimated to be less than one case per 100,000 per year.

The percentage of CMML cases are slightly greater in white, non-Hispanic, Asian and Pacific islanders compared with Black and Hispanic individuals.

CMML in children is known as juvenile myelomonocytic leukaemia (JMML) and is a different disease.

If you would like more information on JMML, you can download our booklet from our website www.leukaemicare.org.uk. Alternatively, you can order hard copies by calling the helpline on **08088 010 444** or emailing support@leukaemicare.org.uk.

What causes CMML?

The exact cause of CMML is not known. However, it cannot be caught from someone or passed onto your children.

Known risk factors that increase the chances of getting CMML include:

- Old age (60 years or older)
- Being male
- Being exposed to certain chemicals at work or in the environment
- Past treatment with anticancer drugs and radiation

- Having certain chromosome abnormalities and gene mutations

The origins of the CMML cells have been linked with the myeloid stem cells in the bone marrow. Bone marrow stem cells have the ability to develop into any type of blood cell. However, what makes the excessive reproduction of these monocytes derived from the myeloid stem cells is thought to be linked to genetic abnormalities.

Chromosome abnormalities and gene mutations

Chromosome abnormalities and gene mutations in total have been identified in approximately 90% of all adults with CMML, and are thought to be the source of CMML.

Chromosome abnormalities

In patients with CMML, chromosomal abnormalities specifically are seen in approximately 30% of patients.

Chromosome abnormalities that are frequently seen in the CMML

blast cells of patients include:

- Trisomy 8 (an extra chromosome 8)
- Deletion of parts of chromosome 7
- The loss of the Y chromosome

Gene mutations

Gene mutations specifically are identified in more than 80% of patients. CMML is known to be associated with a large number of mutations. Patients with CMML have a combination of recurrent mutations in approximately 40 genes.

The most frequently mutated genes in patients with CMML are:

- *TET2* (Ten-Eleven Translocation-2), present in 40% to 60% of patients
- *ASXL1* (Additional Sex comb-like 1), present in 30% to 60% of patients
- *SRSF2* (Serine and arginine Rich Splicing Factor 2), present in 30% to 50% of patients
- *RAS* (Rat Sarcoma) genes, seen

What is chronic myelomonocytic leukaemia? (cont.)

in around 30% of patients

Therapy-related CMML

Another cause of CMML, which accounts for about 10% of CMML cases, is thought to be receiving previous cancer treatment for a different cancer. This is known as therapy-related CMML. Therapy-related CMML is common after chemotherapy or radiation therapy. In comparison to CMML, therapy-related CMML patients have more complicated chromosome abnormalities and gene mutations.

Therapy-related CMML is treated in the same way as other cases but does not respond as well to treatment.



Symptoms of CMML

In CMML patients, the immature, abnormal cells (also called blast cells) take over the bone marrow and prevent it making enough normal blood cells. Although the marrow is producing more cells than normal, many of these are abnormal and do not mature into working blood cells.

Therefore, patients have lower levels of normal, working numbers of red blood cells (leading to anaemia), white blood cells (predisposing to infection) and platelets (leading to bleeding). These changes are responsible for some of the symptoms of CMML.

The most common symptoms of CMML are:

- Fatigue
- Anaemia
- Breathlessness
- Bruising and unusual bleeding
- Loss of appetite and weight loss
- Frequent, persistent infections
- Sweating

It is uncommon to see effects of CMML outside the bone marrow; however, they may be in organs such as the spleen, liver, skin, and lymph nodes. This can result in the following symptoms:

- Itching of the skin
- Bone pain
- Muscle pain
- Enlarged lymph nodes
- Fluid around the lungs (pleural effusion)
- Enlarged spleen/liver (the enlargement may cause abdominal discomfort and, because the spleen lies next to the stomach, this enlargement may cause a feeling of early fullness when eating)



How is CMML diagnosed?

For the majority of patients, a diagnosis of CMML can be made on the basis of a full blood count with a blood film and examination of a bone marrow sample.

However, chromosome analysis and immunophenotyping are always carried out additionally to confirm the diagnosis, and to identify specific cases of CMML which are difficult to diagnose. They can also be useful in helping to rule out similar conditions and other types of leukaemia.

Full blood count and a blood film (examination under the microscope)

Using the patient's blood sample, a full count of the number of red blood cells, white blood cells and platelets is carried out, including a breakdown of the different white blood cell types to determine which are involved.

For patients with CMML, this will show an increase in monocyte cells which appear abnormal in the blood film.

Bone marrow sample

A sample of bone marrow is taken from the hip bone, generally under local anaesthesia, and examined

to determine the number and type of cells present and if they are developing normally. Examination of a bone marrow sample is the most important test for diagnosing CMML. It will show an increased number of abnormal monocyte cells.

Chromosome analysis

By identifying the abnormalities in the chromosomes and genes of patients with CMML, it is possible to not only establish the diagnosis, but also it assists in the classification of CMML and the risk.

Immunophenotyping

Immunophenotyping is a process which helps to calculate the proportion of abnormal CMML blast cells relative to normal cells. This is required to determine the diagnosis. In the laboratory, specific antibodies to the antigens on the CMML blast cells are developed and tagged with fluorescent markers.

When mixed with the patient's blood sample, the antibodies attach themselves to the antigens on the CMML blast cells. The sample is then processed using

a flow cytometer which rapidly counts both the number of cells with the tagged antibodies attached to the leukaemia cells and the normal cells.

Diagnosis of CMML

The 2016 World Health Organisation (WHO) requirements in order to make a diagnosis of CMML include:

- Persistent increase (for at least three months) in high levels of monocytes equal or greater than $1.0 \times 10^9/l$, and a monocyte count greater than 10% of the white blood cells count.
- Exclusion of the following conditions: other leukaemias with the Philadelphia chromosome fusion gene BCR-ABL1, classical MPN disorders or all other blood cancer that have increased levels of monocytes as a main feature.
- CMML blast cells of up to 19% in either the blood or bone marrow, and exclusion of all other features of AML.

Three months or more of persistent increase in levels of blood monocytes is an

important criteria which helps to differentiate CMML from an increase of monocytes resulting from an infection. In the case of an infection, the increase in monocytes returns to normal when the infection clears up.

The Philadelphia chromosome fusion gene *BCR-ABL1* is an abnormal fusion gene due to a swapping over of sections of DNA between chromosome 9 (*ABL1*) and 11 (*BCR*). This gene causes the overproduction of myeloid cells. Having *BCR-ABL1* means a patient is likely to have CML, which is a different type of leukaemia and is treated differently to CMML.

If the percentage of CMML blasts is 20% or more of the white blood cells in the blood or bone marrow, then a diagnosis of acute myeloid leukaemia (AML), which is a more aggressive form of leukaemia, should be made.

Chromosome abnormalities and gene mutations

As previously mentioned, patients with CMML have several chromosome abnormalities

How is CMML diagnosed? (cont.)

and numerous gene mutations. Identification of those most commonly seen in patients with CMML is useful in confirming a diagnosis.

While not particularly common in CMML, several other gene mutations are significant in patients with CMML as they contribute in confirming the diagnosis and establishing a prognosis. These gene mutations include:

- *SETBP1* (SET binding protein) mutation, present in 8.9% of patients
- *RUNX1* (Runt-related transcription factor 1) gene, present in 7.9% of patients

Although only present in 4% of CMML patients, a mutation in the *PDGFR* (Platelet Derived Growth Factor Receptor) gene indicates a rare sub-type of CMML that has a very good chance of responding well to drugs called tyrosine kinase inhibitors. These drugs have been used for some years to treat CML and can be effective in CMML patients with the *PDGFR* abnormality.

In addition to confirming the diagnosis, especially if there is question of whether a patient might have a different illness, chromosome and mutation analyses can help classify CMML patients and determine their risk.

Classification of CMML

Three types of CMML have been recently described in the new WHO classification:

CMML Type	% of blasts in blood	% of blasts in bone marrow	Rate of progression to AML
CMML-0	Less than 2%	Less than 5%	18.5%
CMML-1	2-4%	5-9%	26.9%
CMML-2	5-19%	10-19% Auer rods present	42.3%

The classification is largely based on the percentage of CMML blast cells in the blood and bone marrow. The latest anticipated rate of transformation to AML for CMML patients is also included.

The percentage of CMML blast cells in the blood and bone marrow are higher for each type of CMML. In addition, Auer rods, which are elongated needles made from granular material that form in the cytoplasm of blast cells, are present in CMML-2. Auer rods are also seen in the blast cells of patients with MDS and AML.

Risk classification

The CMML Prognostic Scoring System (CPSS) was developed using four factors to stratify how well CMML patients were likely to respond to standard treatment.

The four factors are:

1. WHO CMML classification
2. White blood cell count (whether it is lower or greater than $13 \times 10^9/l$)
3. Presence of certain gene abnormalities
4. A need for red blood cell transfusion

Using a point allocation system, the CPSS enables patients to be allocated a risk group: low,

intermediate-1, intermediate-2 and high. The system was developed and validated using international data.

This CPSS has since been updated to include gene mutations which have been shown to be important in determining the prognosis for CMML patients. Details of the updated scoring can be found in the prognosis section of this booklet, starting on page 23.

Treating CMML

Overview of treatment

For most patients, CMML is treatable, but, as yet, it cannot be cured. However, it must be noted that many patients can lead a normal, good quality life while managing their CMML. This includes patients who might not need any active treatment and are under an approach called watch and wait, or active monitoring.

Once they have symptoms and need treatment, most patients with CMML are treated with chemotherapy, the most commonly used being hydroxycarbamide (sometimes referred to as hydroxyurea) and hypomethylating agents such as azacitidine. These drugs prevent DNA synthesis of proteins needed for growth of the CMML blast cells.

Patients may also receive treatment known as supportive treatment or palliative care. This helps to deal with complications from having low blood cell levels. It can involve red blood cell and platelet transfusions, and antibiotics to prevent and treat infections.

If you would like more information on stem cell transplants, including side effects, you can download our dedicated booklets from our website www.leukaemiacare.org.uk. Alternatively, you can order hard copies by emailing our Patient Services team at support@leukaemiacare.org.uk or by calling the helpline on **08088 010 444**.

Watch and wait (also known as active monitoring)

If you do not have any symptoms when you are first diagnosed with CMML and you have no high-risk factors, your haematologist may suggest a watch and wait approach. Also referred to, sometimes more favourably, as active monitoring, this usually involves regular check-ups and blood counts, as well as your haematologist advising you on

ways to live a healthy lifestyle. If symptoms develop or the disease progresses, you may then start a suitable treatment.

The European Haematology Association recommends the watch and wait approach for CMML patients who do not have an excess of abnormal bone marrow blasts and whose levels of any blood cells are low.

If you would like more information on watch and wait, you can download our booklet from our website www.leukaemiacare.org.uk. Alternatively, you can order a hard copy by emailing the Patient Services at support@leukaemiacare.org.uk or calling the helpline on **08088 010 444**.

Chemotherapy

Although chemotherapy will not cure your CMML, it will help control your blood counts and disease and improve your quality of life. Chemotherapy is the use

of drugs that work in different ways to stop the growth of cancer cells, either by killing the cells or by stopping them dividing. It is usually quite effective in helping to control CMML.

There are three groups of chemotherapy drugs that are used in treatment of CMML which are:

- Hydroxycarbamide
- Hypomethylating agents such as azacitidine
- Conventional chemotherapy such as cytarabine

Hydroxycarbamide

Hydroxycarbamide is used when a patient's CMML has mainly myeloproliferative features, which means that the main problem is an excess production of CMML blast cells.

Hydroxycarbamide is a drug that inhibits an enzyme called ribonucleotide reductase which prevents DNA making the protein needed by CMML blast cells to multiply. Low-risk CMML patients with myeloproliferative characteristics show good

Treating CMML (cont.)

results when managed with hydroxycarbamide.

In patients with all types of CMML, hydroxycarbamide achieves a response in 60% of patients, which is why it remains the treatment of choice for CMML patients who require cell reduction.

Hypomethylating agents

Hypomethylating agents are best suited for CMML patients with myelodysplastic features, where the main problem is the production of abnormal blood cells that do not mature or work correctly. Hypomethylating agents, such as azacitidine and decitabine, work by inhibiting the DNA methyltransferase enzyme, which prevents DNA from producing the proteins required for the normal development of CMML. This leads to a reduction of the growth of these cells.

Azacitidine is approved to treat non-proliferative CMML-2 in the UK, whereas both are approved for CMML in the US because no clinical trials of decitabine with CMML-2 patients were available in Europe.

Azacitidine and decitabine have shown overall response rates in 40% to 70% of patients with all types of CMML.

Conventional chemotherapy

In the 2008 WHO classification of myeloid neoplasms, CMML was categorised as an MDS/MPN. Consequently, patients with CMML were treated with the same conventional chemotherapies as MDS/MPNs. These chemotherapies, including cytarabine, etoposide and topotecan showed poor response rates and severe side effects in patients with CMML. Administering lower doses of chemotherapy helped reduce the serious side effects.

Conventional chemotherapies have only moderate success in CMML, with often only 30% to 40% of patients showing complete response, which lasts for a few months.

Conventional chemotherapies are generally only used in young and otherwise healthy patients with CMML. It can be an option for some elderly patients with advanced CMML; however, careful

monitoring is required, and chemotherapy should be reduced or stopped for a short time, if any serious side effects do occur.

Stem cell transplants (SCTs)

Since chemotherapies cannot cure patients with CMML, SCTs are seen as the only potential cure, but the patients must be young and relatively fit to withstand the procedure. A SCT involves giving strong chemotherapy to kill off the cells in the bone marrow to prepare it for the transplant (also called conditioning) of healthy stem cells from a matched donor. The SCT helps re-establish a healthy bone marrow.

There is currently no evidence as to when is the best time for a SCT in CMML; however, expert recommendation based on clinical practice advises that a SCT should be performed in patients with CMML-2 or high-risk CMML.

There are two types of SCTs that can be performed:

- 1. Myeloablative transplant**
 - For this transplant, which

is better suited for fitter or younger patients, very strong doses of chemotherapy and radiotherapy are used. This has the advantage of minimising the risk of the CMML returning (also known as a relapse), and may even cure the CMML. However, the high doses of chemotherapy and radiotherapy are very toxic.

- 2. Reduced intensity conditioning transplant** - If a patient is well enough to have a transplant, but not fit enough for a myeloablative transplant, a procedure called reduced intensity conditioning (RIC) transplant may be done. In a RIC transplant, lower doses of chemotherapy are administered before the transplant, which means that it is less dangerous, but there may be a higher chance of relapse.

For CMML-2 patients who have more than 10% of bone marrow blasts, treatment with hypomethylating agents prior to reduced intensity conditioning and the SCT is recommended as it has shown a decrease in the

Treating CMML (cont.)

incidence of relapse.

Relapse rates of up to 30% have been described in patients with CMML following treatment with SCTs. Complications of SCTs include mortality not related to the CMML and graft-versus-host disease, where the transplanted cells start attacking the recipient of the donated cells.

If you are being considered for a stem cell transplant, your haematologist will explain in detail what this will involve, and the possible risks and benefits.

Supportive treatment

Supportive treatment does not include active treatment, but it is given to maintain or improve the patient's quality of life. It concentrates on treating any symptoms or complications that arise from the lack of normal blood cells which are features of CMML. The supportive care delivered will be adapted to the number of normal blood cells that are present in your blood.

Treatments for CMML, especially chemotherapies, destroy the CMML blast cells, but also most

of the normal bone marrow cells. In patients with low-risk CMML and MDS features, anaemia can be treated with erythropoiesis stimulating agents to increase the production of red blood cells. For patients with proliferative features, administration of hydroxycarbamide remains the standard of care by preventing the multiplication of CMML blast cells which invade the bone marrow.

Blood transfusions may be needed if treatment with erythropoietin is unsuccessful, and platelet transfusions should be given if the platelet count level becomes too low. Chemotherapy treatment destroys CMML blast cells, but also most of normal bone marrow cells; therefore, patients may need antibiotics if they develop infections.

New treatments and treatments on the horizon

Decitabine is not approved for CMML-2 without myeloproliferative features in the UK because there have been no clinical trials. A large clinical trial of decitabine (with or without

hydroxycarbamide) which is being compared with hydroxycarbamide alone is due to be finished in October 2021. It is expected that decitabine will then gain approval for CMML-2 patients in the UK.

An early clinical trial with the drug ruxolitinib has shown efficacy in patients with CMML. Ruxolitinib is an inhibitor of the JAK2 (Janus Kinase 2) gene which instructs cells to make proteins that promotes the growth and division of cells. Further trials with ruxolitinib are planned.

Research is being conducted into a combination of drugs in patients with CMML. A recent trial of patients with MDS/MPNs of which 50% fulfilled criteria for CMML found that the combination of ruxolitinib and azacitidine achieved an overall response in 57% of patients and was well-tolerated. Patients with unclassified MDS/MPNs have a better median survival compared to CMML patients. Further clinical trials are required with the combination of ruxolitinib and azacitidine in CMML patients.

New hypomethylating agents such as guadecitabine are being

tested in patients with CMML, but early results show they may not be any more effective than azacitidine or decitabine although their oral formulation will be much more convenient for patients.

Your doctor may suggest you consider taking part in a trial of one of the new drugs. If this is the case, you will be given full information and a chance to ask questions. If you decide not to take part in a trial, you will receive the best available treatment.

What is the prognosis of CMML?

Stratifying CMML patients, according to their prognostic factors, enables haematologists to make decisions about the best type and intensity of treatments for patients. For example, treatment for the less high-risk CMML patients focuses on improving symptoms and increasing quality of life for patients. Also, stem cell transplants are currently indicated for younger or fitter patients, particularly those with high-risk factors.

Treating CMML (cont.)

CMML patients often have mutations in approximately 40 genes, some of which are associated with a poorer prognosis such as *ASXL1*, *NRAS*, *RUNX1* and *SETBP1*. Provision of these mutations are incorporated into the new CMML-specific prognostic scoring systems.

As with the original CPSS, the new mutation-updated CPSS (CPSS-Mol) uses a point allocation system for the following four clinical factors to determine patient prognosis for overall survival time and incidence of patients progressing to AML.

These four factors are:

1. Genetic risk group
2. If the white blood cell count is equal to or greater than $13 \times 10^9/L$
3. If the percentage of bone marrow blasts is equal to or greater than 5%
4. If there is a need for red blood cell transfusions

The genetic risk score is then calculated using the original CPSS genetic score and the presence

of mutations for the *ASXL1*, *RUNX1*, *NRAS* and *SETBP1* genes.

Some people may want to know the survival statistics for patients with their type of cancer, whilst others may not find that useful or may not want to know. By using patients' individual CPSS-Mol scores, they can be assigned to one of our risk groups: low, intermediate-1, intermediate-2 and high risk. The prognosis in each of these risk groups, in terms of a median overall survival rate and a four-year incidence of progressing to AML, is shown by risk group below:

Risk group	CPSS-Mol	Median overall	4-year incidence of progression to AML
Low	0	Still ongoing	0
Intermediate-1	1	64 months	3%
Intermediate-2	2-3	37 months	21%
High	4-5	18 months	48%

Other prognostic factors

If when being treated with hypomethylating agents, patients still exhibit the following clinical signs, their survival rate is reduced:

- WBC count greater than $13 \times 10^9/l$
- Enlarged spleen that can be felt on clinical examination
- Greater than 10% of CMML blasts in the bone marrow

A significantly worse overall median survival is seen in patients with treatment-related CMML (13 months) compared with patients whose CMML is not related to past treatment (20 months). Patients with treatment-related CMML are more likely to have higher-risk chromosomal abnormalities and gene mutations due to past treatment with chemotherapy and radiation.

CMML progresses to AML in approximately 15% to 20% of patients over three to five years. This change from CMML to AML is called a transformation or progression.

Seeing your doctor

Your symptoms

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

Your appointment

Arranging an appointment with your 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 your 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 this condition?
- What sort of treatment will be needed?
- How long will the treatment last?
- How will I know if the treatment has worked?
- What will the side effects be?
- Are there any food 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 your doctors; they have seen and heard everything before, so there is no need to feel embarrassed about anything. If you saw your healthcare team before seeing your doctor, be sure to share with your doctor everything your healthcare team told you about your condition, the blood tests that were performed,

and the next steps. 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 the 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 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 what is happening 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 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 get 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 telling 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 have 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 your health and what the future holds for you. You may or may not have had meetings with your 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 your symptoms and carrying on with your life will help ease any anxieties. Help, care, kindness and support will be available to you from your healthcare team, and you will have access to

counsellors and therapists when you need it.

Isolation

If you have received a diagnosis of CMML, you may feel alone.

Alternatively, you may feel dealing with your cancer allows you to be around those closest to you. Being around 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 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 at the cancer 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 achievable, but demanding, goals will help reduce the anger and impatience, especially with each passing success. Don’t forget to

congratulate yourself 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, letting them out, will also help stop you lashing out at people and keep things calm.

Sadness and depression

You may feel a sense of loss of how safe you felt. You may also feel that your 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

Managing your emotions (cont.)

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 exactly 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, sat 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.

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 will face new challenges to cope with from physical to psychological and social ones. Survivorship aims to provide personalised care based on improving your health, wellbeing, quality of life, and your confidence and motivation, to help you manage. Survivorship also focuses on your 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 were diagnosed with CMML. 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 CMML 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 an individualised care plan with support from social care staff

Survivorship (cont.)

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 a cancer rehabilitation based on your 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 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 the treatment, the physical and physiological side effects of treatments and the psychological impact of CMML in general. You will be provided physical equipment, and taught about various coping strategies to adapt to your 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 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

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 and your loved ones.

Palliative care aims to reduce the symptoms, control the CMML, extend survival, and give you 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 may receive day-to-day care at your home and at the hospital.

What is the clinical course?

You will have a number of treatments, and be prone to frequent infections because of the CMML 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 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

Palliative care (cont.)

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, dental caries 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 are 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 will ask 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 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 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 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 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

End of life care (cont.)

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, 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 stay may be a few months or more, then a nursing 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 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 your stay will only be as long as strictly required. As soon as the condition requiring hospital admission has been resolved, you will need to go back to your home or nursing home. 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

Acute myeloid leukaemia (AML)

Rapid and aggressive cancer of the myeloid cells in the bone marrow.

Amino acids

Organic molecules which are the building blocks for making proteins.

Anaemia

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

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 neutralise the bacteria and viruses.

Antigen

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

Blast cells (blasts)

Immature cells found in the bone marrow which are not fully

developed. In humans, up to 5% of the cells found in the bone marrow are blast cells. Patients with leukaemia have a high number of immature, abnormal cells called blasts cells.

Bone marrow

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

Chemotherapy

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

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 myeloid leukaemia

Leukaemia in which the myeloid cells start multiplying in the bone marrow leading to large numbers of abnormal, immature myeloid cells called blasts, which prevent the bone marrow from producing enough healthy blood cells of all types.

Glossary (cont.)

DNA (deoxyribonucleic acid)

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

Eosinophil

Type of white blood cell which has a protective immunity role against parasites and allergens.

Essential thrombocythaemia

Increased production in the bone marrow of the platelets by the megakaryocytes, which are the platelet-forming cells. The condition leads to abnormal blood clotting or bleeding.

Erythropoiesis stimulating agents

Drugs which stimulate the bone marrow to make red blood cells.

Flow cytometry

Technology used to analyse the physical and chemical characteristics of particles in a fluid as it passes through at least one laser. A flow cytometer can rapidly measure the size and structures of thousands of cells.

Granulocytes

Group of white blood cells, which

have granular bodies in their cytoplasm. They include the neutrophils, eosinophils and basophils white blood cells, all of which protect the body from bacteria, allergens and inflammation.

Immunophenotyping

Process that uses antibodies to identify cells based on the types of antigens or markers on the surface of the cells. This process is used to diagnose specific types of leukaemia or lymphoma.

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 with varying characteristics, such as acute (develop quickly) or chronic (develop slowly).

Lymphoid

Relates to lymphocyte white blood cells.

Monocyte

White blood cell that attacks invading organisms and helps

combat infections.

Myelofibrosis (Primary)

Reactive and reversible process which occurs with many cancerous and non-cancerous diseases of the bone marrow.

Myeloid

Relates to bone marrow.

Myeloid cell

Cell originating in the bone marrow which will eventually become the following white blood cells: neutrophils, monocytes (present in the blood), macrophages (present in different tissues), basophils, and eosinophils. Myeloid cells can also develop into red blood cells and platelets.

Philadelphia chromosome, also called Breakpoint Cluster Region-Abelson Murine Leukaemia Viral proto-oncogene 1 (BCR-ABL1)

Abnormal chromosome fusion gene due to a swapping over and fusion of sections of DNA between chromosomes 9 (ABL1) and 22 (BCR), resulting in a new fusion gene BCR-ABL1. This gene causes overproduction of myeloid

cells. It is found in all patients with chronic myeloid leukaemia and some patients with acute lymphoblastic leukaemia.

Platelets

One of the types of blood cells which help to stop bleeding.

Polycythaemia vera

Chronic increased production of red blood cells, white blood cells and platelets in the bone marrow. When the increased production is only of the red blood cells, the condition is erythrocytosis.

Red blood cells

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

Relapse

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

Secondary cancers

Second primary cancer that often appears after a number of years following chemotherapy or radiation treatment for a previous

Glossary (cont.)

different primary cancer.

Spleen

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.

Steroids (also called corticosteroids)

Man-made versions of the hormones normally produced by the adrenal glands; two small glands found above the kidneys. Steroids reduce inflammation (redness and swelling) and the activity of the immune system. Steroids are used for inflammatory conditions such as asthma and eczema and autoimmune diseases such as rheumatoid arthritis.

Tyrosine kinase inhibitors

Drugs that inhibit the tyrosine kinase enzyme which controls the function of a cell. Tyrosine kinase inhibitors can switch 'off' tyrosine kinase enzymes that are permanently active due to a mutation.

White blood cells

White blood cells are one of the

types of cells found in the blood and bone marrow, along with red blood cells and platelets. White blood cells create an immune response against both infectious disease and foreign invaders. Granulocyte white blood cells include the neutrophils (protect against bacterial infections and inflammation), eosinophils (protect against parasites and allergens) and basophils (create the inflammatory reactions during an immune response). Other white blood cells include the lymphocytes (recognise bacteria, viruses and toxins, to which they produce antibodies) and monocytes (clear infection products from the body).

Y chromosome

One of the two sex chromosomes in humans, the other being the X chromosome. Men have a Y and X chromosome and women have two X chromosomes. Therefore, men determine the sex of the offspring, since it is the presence or absence of Y chromosome that determines if the offspring are male (XY) or female (XX).

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

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.leukaemicare.org.uk

support@leukaemicare.org.uk

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

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

Leukaemia Care
YOUR Blood Cancer Charity