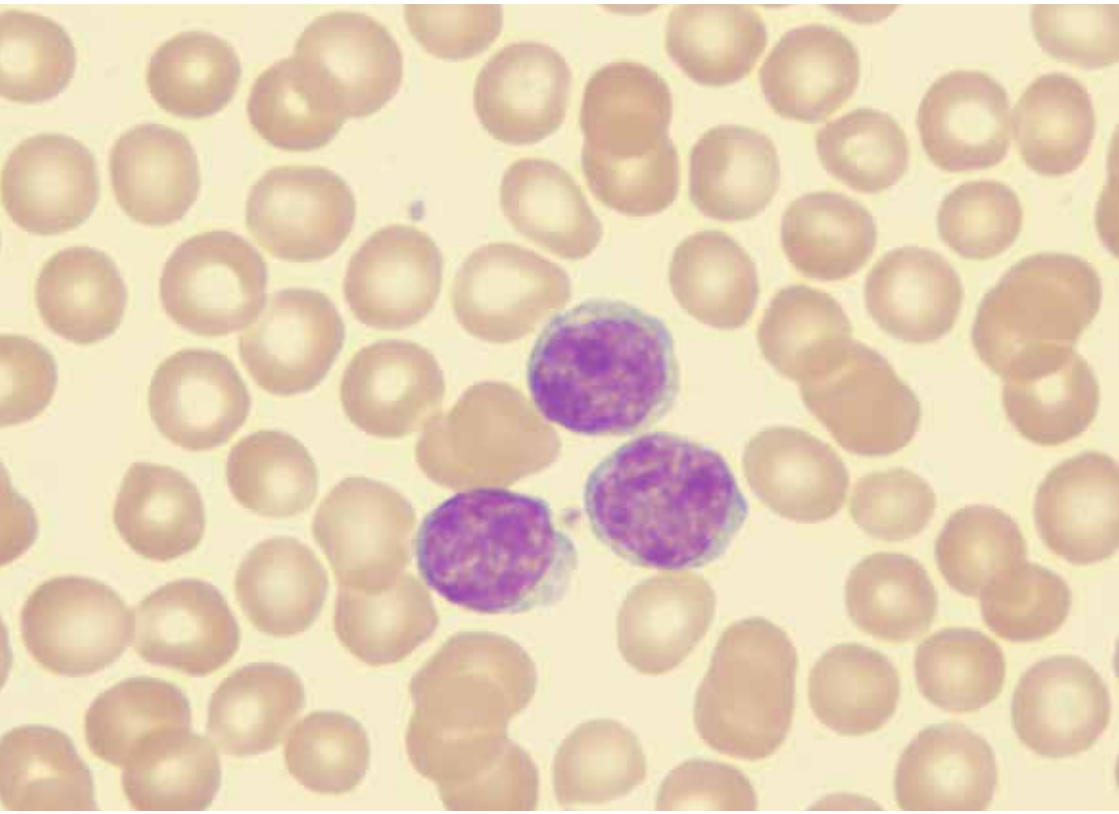
Nursing Matters

The Chronic Leukaemia edition

Winter 2018

www.leukaemiacare.org.uk



Cover image: Chronic lymphocytic leukemia (CLL), B-cell subtype

Leukaemia Care
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In this issue

Where has that year gone?

We can't believe it's December already. We hope that by the time you read this, your hospital should have received a few advent calendars from ourselves just as a little thank you for all the work you do.

While many people are winding down for Christmas, we're busy preparing for our next Nurse conference which is being held in March 2019 in London. It has a focus on Chronic leukaemias, looking at the hot topics in the field.

On the subject of hot topics, our Patient Advocacy Director Zack has been in San Diego for the American Society of Hematology conference and we've been filming about the information revealed at the conference, and we've got information in this edition on from page 6.

Have a wonderful Christmas and New Year - our next edition will be winging its way to you in the Spring.

Until next time,

Leukaemia Care team

P.S. Have you signed up for the free e-learning? It's RCN accredited for 10 hours of CPD. Find out more on page 16.

Acute leukaemia buddy service to launch

Due to the success of our CLL buddy scheme, we are delighted to be launching a buddy scheme aimed at patients affected by AML.

Our buddy scheme is in place to match patients that have had similar experiences so they can be supported, or support others.

Those who wish to become "buddies" are given a mobile phone to make phone calls, but some patients prefer to be contacted by email. Anybody signed up to the scheme will be assisted by the co-ordinator, Kay Drew.

We are also collating data for a potential carer buddy scheme.

To find out more, contact Kay Drew on 01905 755977 or email Kay.Drew@leukaemiacare.org.uk

Edinburgh Fatigue patient conference 2019

Places are now available for our fatigue patient conference which will be taking place in Edinburgh in March 2019.

The conference is lead by Dr Anne Johnson, an expert in cancer-related fatigue and offers practical tips and information as to managing life with fatigue.

Although the conference is aimed at patients, health care professionals are welcome to attend to help improve their clinical knowledge.

To find out more, go to the Leukaemia Care website or ring 01905 755977.

Drug approval news

Liposomal cytarabine and daunorubicin approved by NICE

The National Institute of Health and Care Excellence (NICE) have recommended the use of liposomal cytarabine with daunorubicin to treat previously untreated therapy-related AML and AML with myelodysplastic changes.

The brand name for this treatment is Vyxeos and it is manufactured by Jazz Pharmaceuticals.

Liposomal cytarabine is a chemotherapy drug, which works by imitating a part of DNA called cytidine, and so cells replace the cytidine with the cytarabine in their DNA. The presence of cytarabine in place of cytidine then stops the cell from being able to replicate the DNA and causes the cell to die. Cytarabine is already used to treat AML, but Vyxeos is different in that the cytarabine is encased in droplets of fat molecules called liposomes. It is thought that doing this may make the cytarabine work better and last longer in the body, hence why it is has been proposed as an alternative treatment to standard cytarabine. Both kinds of cytarabine are delivered with daunorubicin, which also

Keep up with the latest news and patient stories at www.leukaemiacare.org.uk

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Many thanks to these following people and for their contributions:
Fiona Heath, Nickey Bate, Jo Peplow, Nicole Scully, Charlotte Martin

works by preventing DNA from replicating, but it does this in a different way to cytarabine. It is called an intercalator, meaning it sits in gaps in the DNA, stopping enzymes in the cell from copying or fixing the DNA. Again, this leads to the death of the cells. It is targeted at the leukaemia cells by being delivered into the bloodstream. AML patients undergo several stages of the chemotherapy to induce and sustain remission; NICE have approved liposomal cytarabine and daunorubicin for both induction (the first stage) and consolidation (subsequent stages) chemotherapy.

The decision was made following a clinical trial called Study 301, which was run in the USA and Canada. The trial was conducted in adults aged between 60 and 75 years, who had "high risk" AML and which had not yet been treated. High-risk AML included patients who had AML as a result of treatment for other cancers (known as therapy-related AML) or AML with myelodysplastic changes. These types of AML a can be difficult to treat; for example, therapy-related AML has arisen as a result of other chemotherapy, so one must choose chemotherapy options to which the leukaemia cells will not already be resistant. Patients receiving liposomal cytarabine with daunorubicin had an increased overall survival time of 9 months versus just under 6 months for the comparison group of patients, who were receiving non-liposomal cytarabine with daunorubicin.

NICE has also concluded that the treatment is within the reasonable cost per quality-adjusted life year (QALY); this is a measure of cost-effectiveness, where treatments are decided for approval based on how much they cost in order to give patients one extra year of life.

"A diagnosis of acute myeloid leukaemia can have a huge emotional impact on the lives of patients, as well as their family and friends," said Zack Pemberton-Whiteley, Patient Advocacy Director at Leukaemia Care. "We welcome the decision to recommend this treatment for adults with high-risk AML. Leukaemia Care has been working with NICE to enable patients to access this important new treatment, where options have been previously limited."

For regular updates on drug approvals, head to the news section on the Leukaemia Care website:

www.leukaemiacare.org.uk

If you have any questions about accessing treatments, speak to the advocacy team on advocacy@leukaemiacare.org.uk or ring the office on 01905 755977.

Drug approval news

Axicabtegene ciloleucel approved by NICE

The National Institute for Health and Care Excellence (NICE) has approved the use of axicabtagene ciloleucel (brand name Yescarta) to be funded for use on the NHS in England. It will be available for patients with diffuse large B-cell lymphoma (DLBCL) and primary mestinal B-cell lymphoma (PMBL), after they have tried two other systemic therapies. Yescarta is a brand of chimeric antigen receptor (CAR) T-cell therapy, is manufactured by Kite Pharma.

Yescarta will be funded through the Cancer Drugs Fund (CDF), as NICE decided the evidence that Yescarta was better than other available drugs was not yet strong enough. Clinical trials assess drugs by determining if they have any benefit over drugs currently used for the particular disease; the current drug chosen for comparison is called the comparator. It was difficult to find a comparator for Yescarta because there are few other options available to these patients who have already tried two therapies; they have exhausted most options already. The CDF allows the NHS to get a funding agreement whilst more data on the effectiveness of the drug is gathered, and so patients can access the drug immediately while this happens.

Lymphoma is a type of cancer involving the lymphatic system, which is system of vessels that run through your body in a similar way to the veins and arteries of your blood. Lymph (the liquid in the lymphatic system) carries cells of the immune system around the body and there are certain areas where immune

cells can gather and complete their development; these are called lymph nodes. Lymphoma occurs when abnormal immune cells collect in lymph nodes (sometime other areas too like the liver, spleen or bones), stopping the lymph nodes from working properly.

DLBCL is a type of lymphoma where abnormally large B-cells accumulate, stopping the lymph node for working normally. PMBL is a rare type of DLBCL that affects mainly young adults. In this type of lymphoma, the B-cells start accumulating in the chest under the breastbone or sternum; one symptom is can fluid on the lungs, caused by the pressure of the cells gathering in the wrong place. More information on the types of lymphoma affected by this announcement can be found here: https://lymphoma-action.org.uk/types-lymphoma-non-hodgkin-lymphoma/diffuse-large-b-cell-lymphoma#PMBL.

CAR-T therapy, also called adoptive cell therapy, is a type of immunotherapy, meaning parts of the immune system are used as a treatment. Immunotherapy usually uses parts of the immune system made in other animals or in a laboratory, such as antibodies. CAR-T cell therapy is brand new and innovative, involving harvesting of the patient's own immune cells from their body to be used in the treatment. The cells taken are then edited to be more effective at fighting the cancerous cells, then returned to the patient's blood to start fighting the cells. There can be some severe side effects, but the treatment is approved here for use where lymphoma patients have tried other therapies, which may have less severe side effects, but they have not worked.

Our Patient Advocacy Director, Zack Pemberton Whiteley, said "The potential of CAR-T therapy is promising, with the potential to cure lymphoma patients who have exhausted most alternative treatments. We are glad that NICE has chosen to enter Yescarta into the cancer drugs fund so patients are able to access this important new treatment as soon as possible."

The first brand of CAR-T therapy to be approved was Tisageneleucel-T (Kymriah, manufactured by Novartis), which NICE and NHS England confirmed earlier this year. You can see our response to the decision on Kymriah here: https://www.leukaemiacare.org.uk/support-and-information/latest-from-leukaemia-care/news/leukaemia-care-response-to-nhs-england-car-t-announcement/.

Updates from ASH (American Society of Hematology)

In this video, Deborah Sims, CLL patient and advocate from Melbourne, Australia interviews Dr Brian Wierda and Dr Barbara Eichorst about CLL developments that were discussed at the conference.

More data has been presented at ASH from the Ibrutinib and Venetoclax trial and this data has matured, featuring patients that had received the combination for a longer period of time.

Much of this discussion centres around the hot-topic of MRD or minimal residual disease. MRD stands for minimal, or measurable, residual disease.

Using the most sensitive methods of detection, clinicians are now able to detect 1 leukaemia cell within 100,000 healthy cells. This is minimal residual disease (MRD), the presence of very small but still measurable numbers of leukaemia cells.

MRD negativity (no detectable cells) has not previously been the end goal of CLL treatment, however, it is looking increasingly important with the introduction of novel agents and combination therapies. Clinical trials have been demonstrating that patients are significantly more likely to achieve MRD negativity than with current standard treatments. This is of importance as MRD negativity is associated with longer remission and survival. To watch this video in full, head to the Leukaemia Care YouTube channel here.

In this video, Deborah Sims interviews Professor Pete Hillmen about what he was going to be speaking about at the conference.

One of the key topics for discussion was targeted therapy in CLL patients that had relapsed, looking at ibrutinib and how the drug can be well utilised. Professor Hillman also discusses using combination therapies to drive the disease into a state where it cannot be detected.

Over 1,000 CLL abstracts were published at ASH. Interesting data has emerged from the MURANO trial, the first phase 3 randomised trial combining Venetoclax and Rituximab. It showed previously that the combination was better than chemotherapy in relapsed disease, and also that most patients with a combination achieve an MRD negative deep remission.

Watch the full video on our YouTube channel.

Further reading:

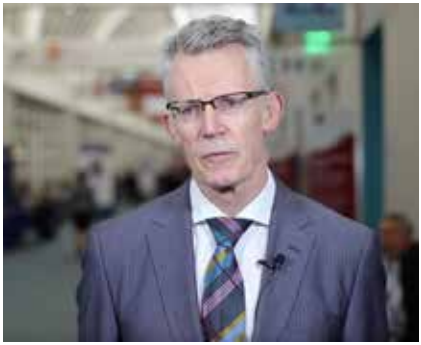
The ASH website is full of content and updates from this years conference.

The ASH website can be found here.

You can also read updates from conference delegates by searching the hashtag #ASH18

Other video resources have been made available via VJHemOnc.

CLL update



In this video, Dr. John Seymour talks about three emerging themes, the importance of depth of remission, time-limited therapy and limiting drug exposure to avoid resistance via combination therapy. Dr Seymour also discusses venetoclax and its key role in combination therapy as a promising way forward.

In a second video which is also on the Leukaemia Care YouTube channel, Dr. Seymour discusses what CLL patients can hope for in the future.

Watch video 1 here.

Watch video 2 here.

In this video, Dr. Piers Blombury talks about the upfront treatment of CLL with chemotherapy, and how novel agents are now looking potentially as good or even better than FCR.

Data was also presented at ASH demonstrating patients showing deep responses and being able to come off therapy for periods of time.

Watch Dr. Blombury's video on YouTube here.

AML update

We were delighted to catch up with Professor Mary Frances McMullin at ASH. She spoke to us about trial data being presented at the conference. Mutations being key in prognostic diagnosis of AML patients was also a key topic at the meeting, and she also discusses this.

You can watch all the videos recorded by Professor McMullin on our ASH playlist here.

New treatments in AML were discussed widely at ASH 2018. In these videos, Dr. Manos Nikolousis discusses how molecular profiling can match patients to the newer, emerging treatments.

Trials have taken place for patients with relapsed or refractory AML and Dr. Nikolousis discusses this in a further clip.

Also discussed is the future of AML treatment with the emerging options for patients with the disease. Watch his videos in full here.

Acute Complications of Allogeneic Transplant

Article Two: Pulmonary, Gastrointestinal and Renal Acute Complications

This article gives an overview of pulmonary, gastrointestinal and renal acute complications of allogeneic bone marrow transplants. It is vital that nurses are aware of these complications to enable them to provide effective care to patients undergoing stem cell transplants.

Pulmonary Complications

Pulmonary complications, including pulmonary infections may account for 40%-65% of acute transplant related toxicities. Factors that may predispose transplant recipients to non-infectious pulmonary toxicities are:

- Conditioning chemotherapy regimen
- Severe GVHD
- Pre-existing pulmonary disease
- Thoracic radiation/total body irradiation
- Methotrexate use for GVHD prophylaxis
- Older age
- Type of underlying malignancy

Pleural Effusions

Fluid overload is the primary cause of non-infectious pleural effusions, followed by high dose chemotherapy and recurrent malignancy. Other contributing factors may include congestive heart failure produced by myocardial ischemia, dysrhythmias, or severe myopericarditis. Dyspnoea, cough, weight gain,

tachypnoea and hypoxemia are all indications of this complication. Supportive oxygen therapy along with prompt administration of diuretics and accurate monitoring of intake and output are important nursing actions.

Pulmonary Embolism

As with any medical treatment, the risk of pulmonary embolism, although uncommon in transplant patients, exists because of thrombocytopenia and should be monitored with each nursing assessment. Central venous catheters and transplant conditioning along with immobility may predispose patients to venous thrombosis. Treatment typically involves anticoagulants, which can be difficult to manage for transplant patients.

Diffuse Alveolar Haemorrhage

Diffuse alveolar haemorrhage was once seen at the onset of engraftment in almost 20% of transplant recipients, but the incidence has decreased over time. Affected patients exhibit sudden onset of dyspnoea, non-productive cough, fever and progressive hypoxemia. Treatment includes platelet transfusion, respiratory support and high-dose corticosteroids.

Idiopathic Pneumonia Syndrome

Specific to transplant recipients, idiopathic pneumonia (IPS) is a syndrome involving interstitial pneumonitis and alveolar injury for which no infectious or non-infectious aetiology can be identified. Symptoms include dyspnoea, hypoxemia, non-productive cough and non-localised infiltrates on chest x-ray. There is no specific therapy proven effective for IPS so treatment is therefore, primarily supportive.

Gastrointestinal Complications

Patients undergoing allogeneic stem cell transplantation commonly experience gastrointestinal toxicities. The earliest gastrointestinal complications are anorexia, nausea, vomiting and diarrhoea related to the high dose chemotherapy and radiotherapy conditioning regimens.

Mucositis

After chemotherapy induced nausea and vomiting, mucositis is the next most common transplant associated gastrointestinal side effect, occurring in 36% to 89% of patients, and corresponding to the period of neutropenia. Nursing assessment is an integral part of mucositis management. Detailed assessments and early interventions that prevent trauma and pain are the most important factors for the prevention and treatment of severe mucositis and infection.

Malnutrition

Transplant patients may have a sub optimal nutritional status

prior to conditioning, which is then exacerbated by anorexia, taste alteration, xerostomia, mucositis, nausea, vomiting and diarrhoea and other effects from the transplant conditioning and accompanying medications.

Daily weights, fluid balance, calorie calculations, and serum protein and albumin levels are some of the parameters used to evaluate nutritional status.

Research about the effectiveness of neutropenic diets for the reduction of infection is inconclusive and there is no one, standardised neutropenic diet. Some transplant centres still use strict neutropenic diets whilst others follow a modified regular diet that avoids high-risk foods. Options for patients who are unable to eat include IV hydration, total parenteral nutrition and enteral feeding.

Typhilitis

Typhilitis, also known as neutropenic or necrotising enterocolitis, is an acute toxicity characterised by transmural inflammation of the small and large bowel, neutropenia, and mucositis. The exact cause is unknown, but alteration in gut flora and mucosal integrity related to transplant conditioning, steroid, and antibiotic use may be contributing factors. Early recognition is important:

Symptoms include:

- Intermittent or constant lower quadrant abdominal pain
- May mimic appendicitis
- Fever
- Watery or bloody diarrhoea
- Nausea/vomiting
- Abdominal distention

Treatment options range from aggressive medical management with antibiotics and supportive care to surgical intervention.

Gastrointestinal bleeding

Gastrointestinal bleeding has an incidence of 7% - 18% in allogeneic transplant recipients.

The most common aetiologies include:

- Acute GVHD
- Regimen related mucositis or enterocolitis
- Viral infection
- Veno-occlusive disease / sinusoidal syndrome
- Gastric antal vascular ectasia (GAVE)
- Peptic ulcer disease (rare)

Treatment is usually supportive, generally including administration of a proton pump inhibitor, close observation, and monitoring laboratory values with correction of coagulopathy as indicated.

Renal Complications

Transplant patients are at risk for a variety of nephrotoxicities in the initial phase of transplantation. Early recognition of risk factors, careful nursing assessment and monitoring of fluid balance, weight, serum electrolytes and creatinine may help prevent or minimise renal injury. Treatment options range from identifying and removing the source of the injury to critical care involving renal replacement therapies.

Acute Tubular Necrosis

Acute tubular necrosis is acute renal failure resulting from ischemia or nephrotoxic injury to the tubular epithelial cells. In transplant patients this can be precipitated by exposure to nephrotoxic drugs or a decrease in renal perfusion resulting from regimen-related side effects causing dehydration and hypotension.

This is a list of common nephrotoxic drugs:

- Aminoglycosides
- Foscarnet
- Ifosfamide
- Melphalan
- Carboplatin
- Cisplatin
- Methotrexate
- Cyclophosphamide
- Tacrolimus
- Ganciclovir
- Acyclovir

Acute Renal Failure

Transplant recipients may develop acute renal failure, defined as a doubling of baseline serum creatine, due to multiple aetiologies in the first one to three weeks after transplantation.

These include:

- Hypotension
- Dehydration
- Tumour lysis syndrome
- Haemolysis
- Marrow infusion toxicity
- Sepsis
- Multi-organ system failure
- VOD/SOS
- Drug side effects (calcineurin inhibitors, aminoglycosides, amphotericin B, ganciclovir)

Treatment of acute renal failure is preferable, and more likely if conditions resulting in hypotension and electrolyte imbalance are avoided, or quickly identified and corrected. Pre-transplant evaluation of renal function is done

to identify existing impairment and nephrotoxic medications should be avoided if possible or administered with pre-medication or hydration that may help reduce the impact on renal function.

Haemorrhagic Cystitis

Haemorrhagic cystitis is recognised in transplant patients who have urinary symptoms that include haematuria, dysuria, frequency and urgency. In the early transplant period, transplant patients may develop haemorrhagic cystitis as a side effect of high dose cyclophosphamide, ifosfamide, etoposide, busulfan, or radiation used in the conditioning regimen. Vigorous hyperhydration, diuresis and administration of mesna are used as a preventative measure.

It is vital for nurses to have a deep understanding of these acute post-transplant complications and to be able to recognise and identify their signs and symptoms. If not recognised and treated effectively, these complications can lead to significant morbidity and mortality.

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Free E-Learning available

Image: A screenshot from the new Leukaemia Care nurse academy

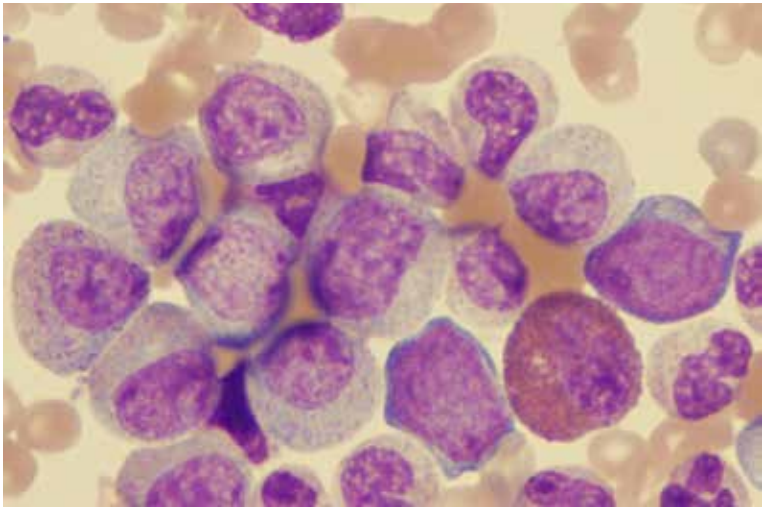
Our online e-learning academy is now open and is free for all healthcare professionals.

The online nurse academy is aimed at haematology CNS' or aspiring CNS' - it may also be useful for junior doctors within the field.

We're delighted that the online platform has been accredited for **10 hours** CPD points by the Royal College of Nurses (RCN) and nurses and health care professionals can take the course free of charge.

Every nurse that successfully completes the academy will be issued with the relevant certificates as well as a Leukaemia Care Nurse Academy fob watch.

To join the e-learning platform, please go to https://www.leukaemiacare.org.uk/support-and-information/for-healthcare-professionals/nurse-academy-e-learning/ and fill out the form. Enquiries on the platform are typically answered within three working days.



Chronic Leukaemia overview

Ahead of our Chronic Leukaemia conference in March 2019, we're looking at chronic leukaemias in-depth in this edition of Nursing Matters.

Chronic myeloid leukaemia (CML)

Chronic myeloid leukaemia is characterised by increased proliferation of the myeloid cell line without the loss of differentiation. In the natural history of the condition, the disease progresses through three general phases:

- chronic stable phase (CML-CP)
- accelerated phase (CML-AP)
- blast phase (CML-BP).

The WHO20 and European LeukemiaNet22 suggest differing diagnostic criteria for these different phases; in modern practice, this includes the response to tyrosine kinase inhibition therapy. The recognition of these different phases of disease is important as they relate to greatly differing responses to treatment, and may suggest the need for more aggressive treatment, such as stem cell transplantation.

Chronic lymphocytic leukaemia

Chronic lymphocytic leukaemia can be subtyped on the basis of its staging classification, which is similar to lymphoma staging.

There are two main stages:

- asymptomatic early-stage disease
- symptomatic or advanced-stage disease.

CLL and the indolent lymphoma, small lymphocytic lymphoma, are considered by the WHO classification scheme to be the same disease in different clinical phases.

Epidemiology

Chronic myeloid leukaemia

The number of new cases of chronic myeloid leukaemia (CML) was 1.8 per 100 000 men and women per year in the USA and there were 750 new cases in the UK in 2014.

The incidence of CML increases with age with the median age of diagnosis being 64 years. There is a predominance in males: in the UK, 1 in 840 men and 1 in 1180 women will be diagnosed with CML during their lifetime.

Since the discovery of tyrosine kinase inhibitors, the survival rates with this leukaemia have increased dramatically. The 5-year relative survival rate increased from 17% in 1975 to 64% in 2009.

Chronic lymphocytic leukaemia

The number of new cases of chronic lymphocytic leukaemia (CLL) was 4.7 per 100 000 men and women per year in the USA between 2010 and 2014, and there were 3500 new cases in the UK in 2014.

The incidence of CLL increases with age, and the median age of diagnosis is 70 years. However, because of the indolent nature of this leukaemia, the 5-year survival rate is about 83%.

There is a slight predominance of white male patients. There also appears to be an increased risk of developing CLL and other lymphoid malignancies in patients with relatives who have CLL; there is an 8.5-fold risk of developing CLL if a relative also has CLL.

Aetiology and risk factors

Recurrent genetic mutations.

Like most cancers, the main risk factor for AML, CML and CLL is age, and so with an ageing population the prevalence of these conditions increases. Despite the presence of certain aetiological factors, the major reason for the development of most leukaemias is the accumulation of genetic mutations as a person ages. Many different gene mutations can lead to leukaemia. Both AML and B-cell ALL can be subtyped on the basis

of recurrent genetic mutations. CML is one of the few cancers in which most cases are caused by a single, specific genetic mutation: chromosome translocation t(9;22), a cytogenetic abnormality known as the Philadelphia chromosome.

Key points – epidemiology, aetiology and risk factors

- Acute myeloid leukaemia (AML) is the most common acute leukaemia in adults.
- Age is the main risk factor for AML, chronic myeloid leukaemia (CML) and chronic lymphocytic leukaemia (CLL); the prevalence of these leukaemias increases with age.
- Acute lymphoblastic leukaemia (ALL) most commonly affects younger people; over 50% of patients with ALL are under 20 years of age.
- The main risk factor for AML, CML and CLL is the accumulation of recurrent genetic mutations over time.
- Predisposing conditions such as myelodysplastic syndrome and monoclonal B-cell lymphocytosis increase the risk of AML and CLL, respectively.

Picture: Dr Timothy Hughes discusses TFR on the Leukaemia Care YouTube channel

Treatment Free Remission in CML

TKI's revolutionised treatment for chronic myeloid leukaemia patients - here we give an overview of Treatment Free Remission (TFR).

How well do the TKIs work?

The TKIs have provided a huge improvement in the treatment of CML. In 1975, about 1 in 5 patients with CML survived for 5 years.

In 2009, two-thirds of patients survived for 5 years. Now, over 80% of patients survive for more than 10 years.

Patients are advised to take TKIs long term, and many patients with CML now have a normal life expectancy when taking TKIs.

Which TKI is right for patients?

Response to TKI treatment will be monitored by regular blood tests, which include measuring levels of the BCR–ABL gene in the blood. Patients with lower levels of the BCR–ABL gene have a better response to treatment.

For patients on imatinib therapy, if the levels of the BCR-ABL gene are greater than 10% after three months of treatment, they will receive more frequent blood tests between three and six months. If the levels are still above 10% at six months, other TKI's may be tried.

This approach also applies to patients on second-generation

TKIs. Switching therapy has not been shown to have any negative effect on the final outcome, compared to staying on the same treatment.

What is treatment-free remission (TFR)?

It has become clear in clinical trials that treatment with imatinib can achieve what is known as a 'deep molecular response'. This means that the BCR–ABL gene is no longer detected in the blood.

About half of all patients who received imatinib as their first treatment for CML in the stable or chronic phase have been able to stop taking imatinib altogether without the CML relapsing(i.e. getting worse again). This is known as treatment-free remission (TFR) because the CML stays in remission without any treatment. In the European STOP TKI study, about half of all patients who stopped taking imatinib had not relapsed after two years.

When is a patient considered to be in treatment-free remission?

Patients who have a deep molecular response are considered to be eligible to attempt TFR and can stop taking the TKI. This means that levels of the BCR–ABL gene in the blood are below a certain level for at least two years whilst taking imatinib.

Patients who stop taking their TKI require close monitoring to ensure their CML is under control.

At the moment, scientists are working out the level of BCR–ABL that can remain in the blood for TFR to be possible, and new tests are being developed. Scientists are also trying to identify factors that might predict who can stop taking TKIs and remain in TFR.

Treatment-free remission is currently only considered for patients who are taking part in clinical trials or involved in a registry, because doctors need to closely monitor what is happening. The data collected in these trials is important to help doctors work out how best to use the TKIs.

What are the risks associated with treatment-free remission?

Stopping TKIs involves weighing up the benefits and risks. Some patients may want to stop treatment with TKIs because they have side effects that affect their quality of life. However, other patients may accept the side effects of continuing withTKI treatment because this gives them confidence that the CML will not recur.

The key risk of TFR is that CML recurs. For example, in the STOP

TKI study, some patients had a relapse of CML more than 30 months after stopping TKIs. So far it appears that a molecular response can be achieved again if the same TKI, or a different TKI, is started again but this is not guaranteed.

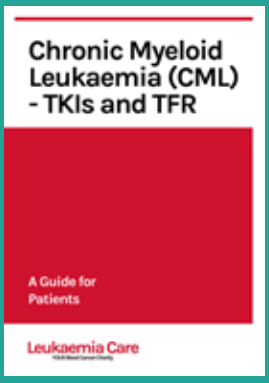
Doctors do not yet know what happens if a second TFR is achieved, or if TFR is achieved with a TKI other than imatinib. This will be explored in more clinical trials.

Individual patients need to consider the risks and benefits of stopping or continuing with a TKI and to discuss this with their doctor.

Is treatment-free remission a cure?

A deep molecular response indicates no or very low levels of BCR–ABL, which could be considered to be a cure. However, there is always the possibility that the disease will recur (relapse), although this becomes less likely the longer the TFR goes on for.

Information for this article has been taken from our booklet "CML TKI's and Treatment Free Remission".



Future treatments in CML

What is ABL-001?

In addition to the T315I mutation, other very rare mutations of the BCR-ABL gene have now been found. None of the TKI therapies work in the patients who have these rare mutations. Researchers are therefore continuing to develop more safe and effective medicines for Ph+ CML.

Asciminib (ABL001) is a new medicine being developed for the treatment of Ph+ CML.

What is asciminib (ABL001)?

Asciminib inhibits the BCR-ABL protein, but in a different way from the TKIs. Instead of blocking the protein, it makes it change shape, disabling it so that it no longer works.

The first-, second- and third-generation TKIs do not work in some patients, or they stop working because of changes (mutations) that develop in the BCR–ABL gene. Because asciminib works in a different way, it is expected to work when the TKIs don't.

Early studies in the laboratory have shown that asciminib, when used together with nilotinib, got rid of cancer cells in the long term and prevented them from coming back. If this same effect is seen in patients, this combination of medicines has the potential to cure CML completely. This will need to be explored in clinical trials.

Who can have asciminib (ABL001)?

ABL001 is currently being tested in clinical trials involving patients

with Ph+ CML who have already had treatment with at least two different TKIs, or in patients with the T315I mutation who have received one TKI therapy.

Asciminib is being tested as a therapy on its own, and in combination with imatinib, nilotinib and dasatinib.

Asciminib is also being tested in patients with Ph+ ALL.

Is asciminib (ABL001) available in the UK?

ABL001 is still in clinical trials. It cannot be prescribed by a haematologist However, patients may be able to take part in a clinical trial.

So far, clinical trials have produced a recommended dose for asciminib therapy on its own for patients with Ph+ CML who do not have the T315I mutation.

Specific doses are being studied in patients with the T315I mutation.

A study of asciminib–imatinib combination therapy is now planned in patients who have not responded well to initial imatinib therapy.

A study to compare asciminib therapy and bosutinib therapy is also planned.

Leukaemia Care
Nurse Academy

Chronic leukaemia - From Diagnosis to Treatment

DATE
1st March 2019

VENUE
Millennium Hotel London
Knightsbridge, 17 Sloane St,
Knightsbridge, London SW1X 9NU

9:00am - 9:30am	Registration and refreshments
9:30am - 9:35am	Introduction to the day
9:35am - 10:15am	Overview of CLL, past and present - Professor Chris Fegan, Professor of Haematology, University Hospital Wales
10:15am - 11:15am	Treating CLL Ben Kennedy, Consultant Haematologist
11:15pm - 11:30am	Break
11:30am - 12:30pm	Richter's tranformation & Progressive CLL - Niamh Appleby, HEE/GE Genomic Medicine Fellow
12:30pm - 1:30pm	Lunch
1:30pm - 2:10pm	Overview of CML, past and present TBC
2:10pm - 2:40pm	Treatment free remission - a patient's perspective - Nigel Deekes, Patient Representative
2:40pm - 2:55pm	Break
2:55pm - 3:35pm	Diagnostic/next generation sequencing in CML Jamshid Khorashad, Head of Pathology, Imperial Hospital
3:35pm - 4:05pm	Compliance with treatment and CML TBC
4:05pm - 4:10pm	Closing remarks

Timings are subject to change.

To book, head to www.leukaemiacare.org.uk or call the team on 01905 755977