Revolution in the treatment of chronic lymphoblastic leukaemia

Dr Phillipa Ashmore tells us how chronic lymphoblastic leukaemia (CLL) is now managed with increased emphasis on personalised and chemotherapy-free treatments.

CLL is the most common leukaemia in the western world. This blood/bone marrow cancer is most often seen in older patients, although younger patients can be affected, with a higher rate in men compared to women.

HOW DOES CLL DEVELOP?

The CLL cell is an immune system cell, called a B-lymphocyte, that becomes cancerous. This happens at a stage of development before the immune cell can make normal and healthy antibodies, resulting in a very dysfunctional immune cell that can slowly take over and suppress a person's normal blood and immune systems.

It's often detected incidentally as an increased white cell count on routine blood tests, although some patients are diagnosed later when symptoms have started to emerge.

SYMPTOMS OF CLL

Symptoms arise from three main disease processes:

1. **Lymph node and organ enlargement with CLL cells.**
   Patients may notice this as lumps in the neck, under the armpit, or in the groin. They may also notice discomfort or bloating in the abdomen, or a feeling of fullness after eating a small amount of food, despite being hungry. A rapid increase in the number of CLL cells can drain the patient's body, leading to loss of weight, and sometimes night sweats.
2. **Displacement of the healthy bone marrow by CLL cells.**
   This leads to dropping blood counts as production of healthy blood cells reduces in an overcrowded bone marrow. A low red cell count (anaemia) leads to fatigue, shortness of breath on exertion, and dizziness. A low white cell count (neutropenia) can predispose a patient to infections. A low platelet count (thrombocytopenia) can lead to increased bruising or bleeding from areas, such as the gums or nose.
3. **Immune dysregulation/autoimmune symptoms.**
   Because CLL cells are immune system cells, when they increase in number they can suppress healthy immune cell function leading to infections. They can also cause over activation of other aspects of the immune system, causing mistaken immune attack of healthy tissues.

STANDARD TREATMENT

Not all CLL needs treatment. This is because in some patients the CLL cells are dormant and never cause any of the problems listed. In these patients, there is no benefit to treatment as their disease doesn't cause any significant medical problems.

Only monitoring a cancer can be an emotionally difficult concept for both patient and treating doctor, but up to a third of CLL patients will never require treatment.

The standard approach to treating CLL patients who do need intervention has historically involved combinations of chemotherapy. In the last 20 years or so, there has been the addition of immune therapy to chemotherapy where the patient's own immune system is directed to kill the CLL cells.

An example of this, is a drug called rituximab which targets one of the markers on the CLL cell surface (CD20), labelling these cells for destruction by the patient's own healthy immune cells.

The type of chemotherapy paired with the immune therapy drug has depended on the fitness of the patient to withstand chemotherapy, bearing in mind that CLL tends to affect older patients who may well have other diseases. More aggressive regimes may be essentially curative, whereas less aggressive regimes may buy the patient treatment-free periods but with likely relapses down the line.

Now that there is an understanding of some of the changes that occur within the CLL cells themselves, different regimes can be selected over others, based on being able to predict which one will be more effective in an individual patient's CLL. This allows for personalising and refining the treatment choices further.

NOVEL THERAPIES

Two new drugs have revolutionised the landscape of CLL therapy over the last five to 10 years. They were developed to try and fill a real gap in effective therapy for aggressive versions of CLL, where the treatments mentioned above had little effect.

However, these novel treatments have slowly moved into first-line therapy for lower risk disease because they are so effective and offer significant advantages over chemotherapy. This is particularly, although not exclusively, true for the older CLL patient.

Both these drugs, venetoclax and ibrutinib, block signalling pathways within the CLL cell for a more targeted mechanism of cancer cell destruction compared to chemotherapy.

Venetoclax can be combined with more potent immune therapy than was previously available, which by all indications appears to offer a significant chance of cure in some patients.

Ibrutinib is used alone generally, as a chronic type of treatment which is a very effective way to control the disease long-term.

Both have the advantage of being in tablet/capsule form, which is of obvious benefit in maintaining quality of life for patients, and both are now available in South Africa.

These newer treatments have shown huge promise in both trials and in clinical practice, although with the frustrating challenge in the oncology arena of a significant financial burden.

EXCITING DEVELOPMENT

The changes in treatment options in CLL based on specific characteristics of the individual's CLL cells is an exciting development for both patients with this disease and doctors treating those patients. As with much of clinical haematology, this is a disease where a greater scientific understanding has led to improved and better tolerated treatment for patients, with the potential for cure. ■

MEET THE EXPERT

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