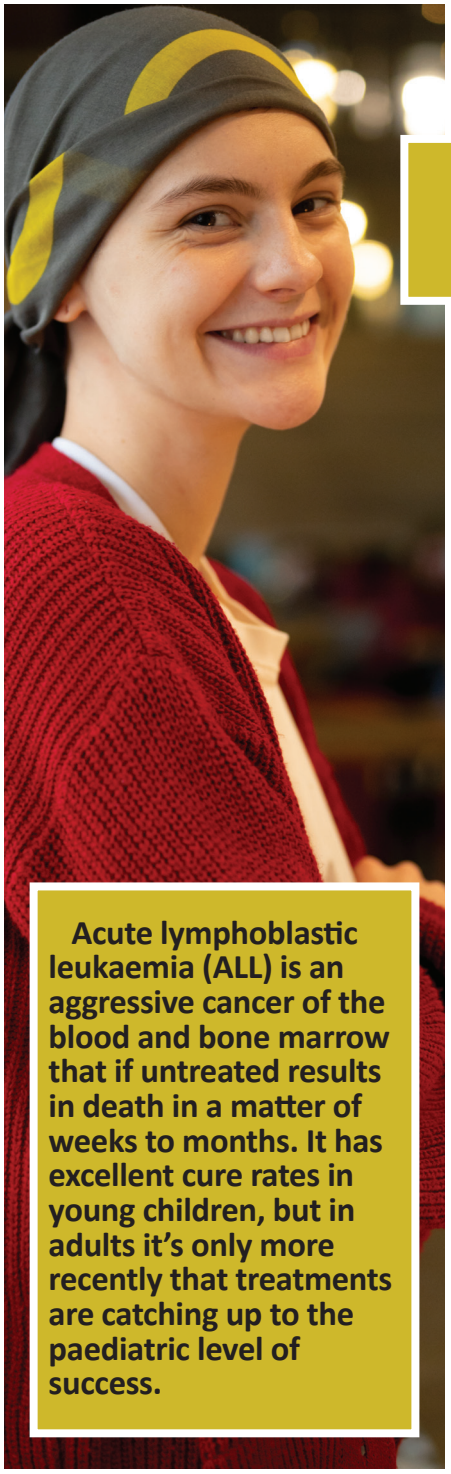
Is there new hope for acute lymphoblastic leukaemia patients?

Acute lymphoblastic leukaemia is at the forefront of immunotherapy. With these new and emerging treatments, substantially more effective therapies both upfront and at relapse are becoming a reality, both internationally and in SA.



Acute lymphoblastic leukaemia (ALL) is an aggressive cancer of the blood and bone marrow that if untreated results in death in a matter of weeks to months. It has excellent cure rates in young children, but in adults it's only more recently that treatments are catching up to the paediatric level of success.

HOW DOES ALL DEVELOP?

All the cells of the blood and immune system are made from stem cells in the bone marrow. When a cancer arises in the bone marrow in precursors of immune system cells (called lymphoblasts), ALL develops.

SYMPTOMS

Symptoms in ALL arise from the following actions of cancerous lymphoblasts:

- Grow out of control and displace normal blood production in the bone marrow. Therefore, normal blood counts fall, leading to: bleeding, fatigue, infections and bone pain (due to the overcrowding of the bone marrow).
- Spill out of the bone marrow and into the bloodstream where they travel to other organs (lymph nodes, liver, spleen and skin, among others) leading to enlargement and dysfunction of these organs.
- Don't mature into normal lymphocytes and therefore immune function is compromised. In addition, by taking over the bone marrow and lymph nodes they don't allow other immune cells to be made. As such, patients with ALL are very vulnerable to infections.

STANDARD TREATMENT

The standard approach involves intensive chemotherapy that is divided into induction phase, consolidation phase and maintenance phase. The goal of treatment is remission where the lymphoblasts can no longer be found in the blood or bone marrow, and bone marrow function returns to normal. Intensity of treatment is usually dictated by the age of patient and how fit they are to withstand such an aggressive approach.

STEM CELL TRANSPLANT

At diagnosis, all patients are assessed for stem cell transplant. Both the risk of the disease (high vs low risk) and the risk of transplant to the patient are evaluated. Importantly, a stem cell transplant can only be performed in patients who have responded well to chemotherapy (those in a complete remission).

During a stem cell transplant, the patient is subjected to high-dose radiotherapy and/or chemotherapy (conditioning) to destroy any remaining undetected leukaemia cells as well as their bone marrow and immune system. Then the bone marrow is re-populated with someone else's stem cells (allogeneic). These new stem cells don't have the same tendency to form leukaemia and will regrow a new blood and immune system.

IMMUNOTHERAPY

Although stem cell transplantation is a type of immunotherapy, it's untargeted and carries risk of serious complications. There has been a shift to more targeted and personalised treatments to kick-start the patient's own immune system to recognise and kill leukaemic cells. In ALL, the three main ways of doing this are:

1. **Monoclonal antibodies**
   These are engineered antibodies infused into the patient's. They are designed to attach to specific markers on the surface of the leukaemia cells which earmarks them for destruction by the patient's own immune system.
2. **BiTE (bispecific T-cell engager)**
   These are drugs that act as a bridge between the cancer cells and the patient's immune system. On one side of the bridge they attach to specific markers on the surface of the leukaemia cells, and on the other side of the bridge they attach to immune cells (T-cells) and activate them.
3. **CAR-T (chimeric antigen receptor T-cell therapy)**
   This involves removing the patient's own T-cells (immune cells) from their bloodstream, engineering them to recognise their leukaemia cells, growing them to make more of them, and then putting them back into the patient.

These technologies have shown huge promise in both trials and in clinical practice, although an ongoing challenge is the lack of affordability.

Monoclonal antibodies and BiTE medications are available in SA, but CAR-T cells are still in the process of being introduced. Currently only patients able to join an international clinical trial, or travel and self-fund treatment overseas can undergo CAR-T therapy.

To view references, visit *oncologybuddies.com*

MEET THE EXPERT

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