Bispecific antibodies (see diagram below) and BiTE® therapies (not shown on diagram) bind targets on the surface of cancer cells (e.g. CD20 on malignant B-cells or FcRH5 on myeloma cells) and immune cells (e.g. CD3 on T-cells or CD16A on natural killer cells) simultaneously. Upon binding, immune cells are redirected to cancer cells for T-cell-mediated destruction of cancer cells via the release of cytotoxic granules.

T-cell engaging therapies in blood cancer

Novel immune-engaging treatments are being investigated in blood cancers. These include bispecific antibodies, bispecific T-cell engagers (BiTE®s), and chimeric antigen receptor (CAR) T-cell therapies. What are these therapies, how do they work, and how do they differ from one another?

Mechanism of action

A. Bispecific antibodies

- Mechanism of action: Engage the immune system by redirecting immune cells to cancer cells
- Structure: Monoclonal antibodies engineered to recognize and bind to two different targets, on two different cells (i.e. cancer cells and immune cells), simultaneously. Include an Fc region as part of their structure that enhances its ability to generate an appropriate immune response when bound to its targets.
- Access/production: Being investigated in leukaemias, lymphomas and myelomas as ‘off-the-shelf’ treatments. They are designed to recruit a patient’s existing T-cells to attack cancer cells, and therefore do not require cell collection or genetic engineering. This could be important for patients who need to be treated quickly.
- Mechanism of action: Improve the ability of T-cells to recognize and kill cancer cells.

B. BiTE® therapy

- Mechanism of action: Engage the immune system by redirecting immune cells to cancer cells
- Structure: T-cells with chimeric antigen receptors on their surface.
- Access/production: Multistep process across several weeks (see figure).

C. CAR T therapy

- Mechanism of action: Engage the immune system by redirecting immune cells to cancer cells
- Structure: Fusion proteins, made up of two antibody fragments that target T-cells and tumour cells, connected by a peptide linker.
- Access/production: CAR T-cell therapy

References