Bispecific Antibodies: A New Frontier in Haematologic Malignancies

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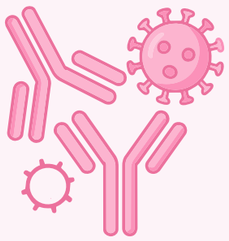
What are Bispecific Antibodies?

A bispecific antibody is a specially engineered antibody that can recognize **two different molecular targets simultaneously**.



Bispecific antibodies bring immune cells directly into contact with diseased cells, for example by simultaneously binding a **tumour-associated antigen and CD3 on T cells**, or by blocking two disease pathways with a single therapeutic molecule.

Unlike CAR-T cell therapy, **bispecific antibodies** can be administered directly and do not require T cell collection. Administration can be done **subcutaneously or intravenously**.[1]

Common tumour antigen targets[1,2]

Common diseases treated

BCMA	RMM
GCRP5D	RMM
FcRH5	RMM
CD19	B-ALL, DLCL, FL
CD20	DLBCL, FL, MCL

How are Bispecific Antibodies Shaping Haematologic Cancer Care?

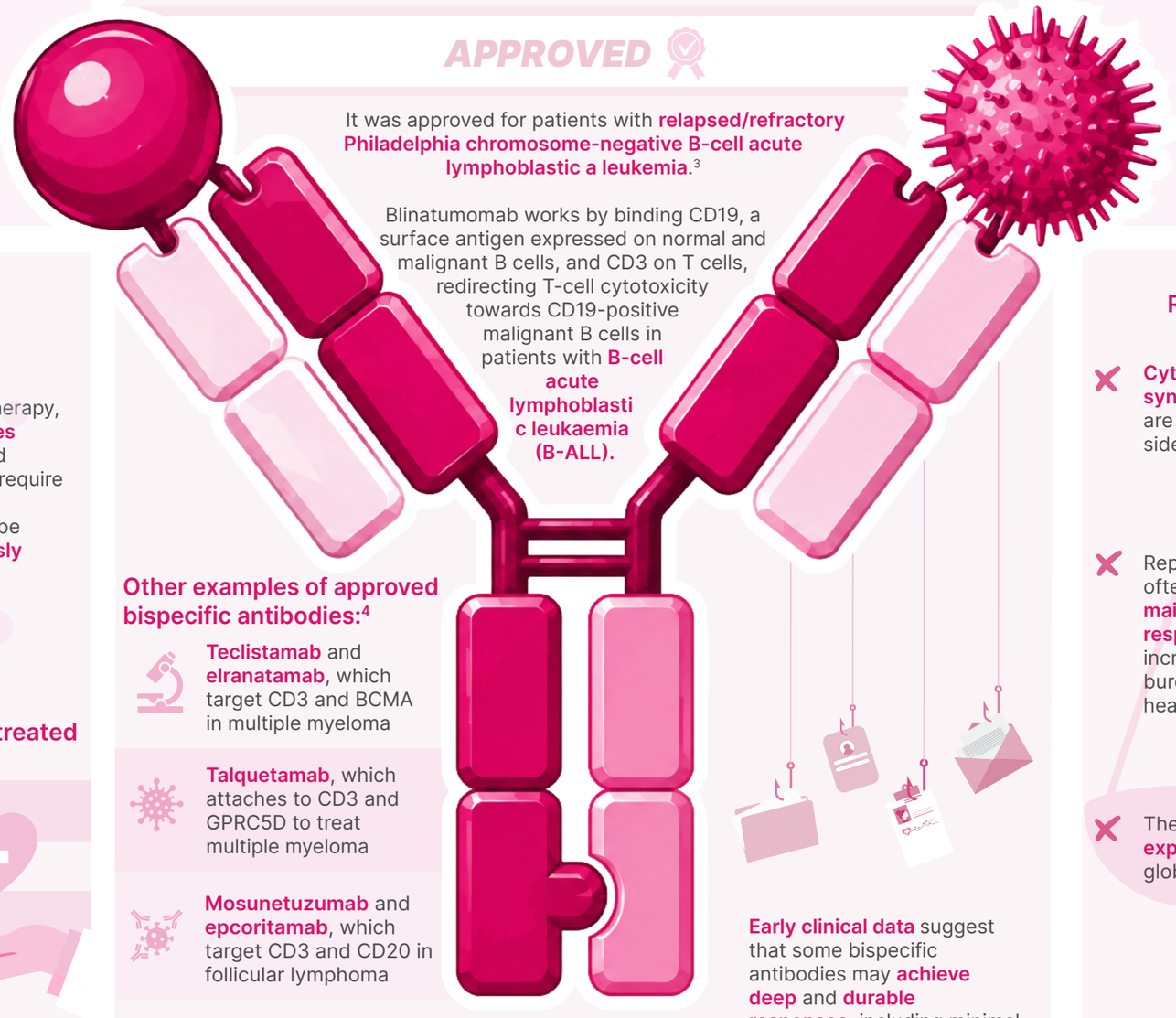
2017

In 2017, blinatumomab was the first bispecific antibody to receive FDA approval for a haematological malignancy.

APPROVED

It was approved for patients with **relapsed/refractory Philadelphia chromosome-negative B-cell acute lymphoblastic a leukemia**.[3]

Blinatumomab works by binding CD19, a surface antigen expressed on normal and malignant B cells, and CD3 on T cells, redirecting T-cell cytotoxicity towards CD19-positive malignant B cells in patients with **B-cell acute lymphoblastic leukaemia (B-ALL).**



Other examples of approved bispecific antibodies:[4]

Teclistamab and **elranatamab**, which target CD3 and BCMA in multiple myeloma

Talquetamab, which attaches to CD3 and GPRC5D to treat multiple myeloma

Mosunetuzumab and **epcoritamab**, which target CD3 and CD20 in follicular lymphoma

Epcoritamab and **glofitamab** also target CD3 and CD20 to treat diffuse large B cell lymphoma

Early clinical data suggest that some bispecific antibodies may **achieve deep** and **durable responses**, including minimal residual disease negativity in selected patients.

Future Directions

Next-generation bispecific antibodies are being engineered with extended half-lives and reduced cytokine release profiles to improve safety and dosing convenience.[5]

Research is ongoing to **identify predictive biomarkers** that may help stratify patients most likely to benefit from bispecific antibody therapy.[5]

Risks

- ✗ **Cytokine-release syndrome** and **ICANS** are reported side effects.[4]
- ✗ Repeated dosing is often required to **maintain therapeutic response**, which may increase treatment burden for patients and healthcare systems.
- ✗ The treatments can be **expensive** with uneven global availability.

Benefits

- ✓ Bispecifics are off-the-shelf, meaning they are pre-manufactured, stored, and **immediately available for use**, unlike CAR-T, where a patient's T cells must be collected, genetically engineered, and reinfused.
- ✓ Bispecific antibodies can be **administered** to a **broader** patient **population.**
- ✓ The two arms **increase specificity** compared to monoclonal antibodies, reducing off-target toxicity.[2]

Abbreviations:
B-ALL: B-cell acute lymphoblastic leukaemia; BCMA: B-cell maturation antigen; CD: cluster of differentiation; DLBCL: diffuse large B-cell lymphoma; FcRH5: Fc receptor-homolog 5; FL: follicular lymphoma; GCRP5D: G protein-coupled receptor class C group 5; ICANS: immune effector cell-associated neurotoxicity syndrome; MC: mantle cell lymphoma; RMM: relapsed/refractory multiple myeloma.

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