CLINICAL FLASHCARDS

CAR-T Therapy Versus Bispecific Antibodies

The Life Science Feed

QUESTION

What is the primary logistical limitation regarding the manufacturing time for autologous CAR-T therapy?

ANSWER

It takes several weeks to manufacture the cells from the patient's own T cells.

QUESTION

Why is the requirement for a 'living patient' a challenge for current autologous CAR-T therapies?

ANSWER

Patients must be stable enough to survive the multi-week manufacturing wait time.

QUESTION

In what type of medical facilities is access to autologous CAR-T therapy currently concentrated?

ANSWER

A small number of specialist centres globally.

QUESTION

Term: Allogeneic CAR-T

ANSWER

Definition: 'Off-the-shelf' CAR-T therapy manufactured in large batches using T cells from healthy donors.

QUESTION

How does allogeneic CAR-T therapy achieve a significant reduction in cost compared to autologous therapy?

ANSWER

Multiple doses can be manufactured from a single donor collection.

QUESTION

What complication arises in allogeneic CAR-T when donor T cells recognise and attack the recipient's tissues?

ANSWER

Graft-versus-host disease (GvHD).

QUESTION

What is the purpose of using CRISPR or TALEN gene editing in the production of allogeneic CAR-T cells?

ANSWER

To knock out the T cell receptor (TCR) and prevent graft-versus-host disease (GvHD).

QUESTION

What immunological challenge results in allogeneic CAR-T cells having a shorter duration of persistence than autologous ones?

ANSWER

Host-versus-graft rejection by the recipient's immune system.

QUESTION

How does a lymphodepletion conditioning regimen assist in allogeneic CAR-T therapy?

ANSWER

It helps prevent the recipient's immune system from immediately eliminating the foreign donor cells.

QUESTION

What strategy is being investigated to compensate for the shorter persistence of allogeneic CAR-T cells in patients?

ANSWER

Administering multiple doses (re-dosing) of the product.

QUESTION

ALLO-501 is an allogeneic CAR-T product directed against which specific antigen?

ANSWER

CD19.

QUESTION

In which disease state has ALLO-501 demonstrated response rates comparable to autologous products in early trials?

ANSWER

Relapsed/refractory diffuse large B-cell lymphoma (DLBCL).

QUESTION

What is the fundamental mechanism of 'in vivo' CAR-T engineering?

ANSWER

Delivering gene engineering directly to T cells while they are still inside the patient's body.

QUESTION

Which two delivery vehicles are primarily used to transport CAR genes to circulating T cells in vivo?

ANSWER

Viral vectors or lipid nanoparticles.

QUESTION

What is the main logistical advantage of in vivo CAR-T therapy regarding manufacturing?

ANSWER

It eliminates the need for complex, specialised laboratory manufacturing facilities.

QUESTION

What is the primary technical challenge regarding the specificity of in vivo CAR-T gene delivery?

ANSWER

Ensuring the CAR gene is delivered to T cells specifically and not other cell types.

QUESTION

Name two biotech companies mentioned as being in early clinical development for in vivo CAR-T platforms.

ANSWER

Beam Therapeutics and Umoja Biopharma.

QUESTION

A bispecific antibody redirects T cells by simultaneously binding a tumour antigen and which T cell marker?

ANSWER

CD3.

QUESTION

How do bispecific antibodies physically facilitate cancer cell death?

ANSWER

By linking the T cell to the cancer cell, redirecting the T cell to kill the target.

QUESTION

What is the primary manufacturing advantage of bispecific antibodies over CAR-T therapies?

ANSWER

They are conventional antibodies that can be manufactured at scale and stored off-the-shelf.

QUESTION

Where are bispecific antibodies typically stored and dispensed in a hospital setting?

ANSWER

The hospital pharmacy.

QUESTION

Which BCMA \times CD3 bispecific antibody was investigated in the MajesTEC-1 trial?

ANSWER

Teclistamab.

QUESTION

What overall response rate (ORR) was observed for teclistamab in patients with triple-class refractory myeloma?

ANSWER

63%.

QUESTION

In the MajesTEC-1 trial, what percentage of myeloma patients achieved a complete remission (CR)?

ANSWER

39%.

QUESTION

Elranatamab is a bispecific antibody targeting which two antigens?

ANSWER

BCMA \times CD3.

QUESTION

Which trial reported a 61% overall response rate for elranatamab in myeloma treatment?

ANSWER

MagnetisMM-3.

QUESTION

Talquetamab is a bispecific antibody that targets which specific antigen in myeloma?

ANSWER

GPRC5D.

QUESTION

What overall response rate (ORR) was reported for talquetamab in the MonumenTAL-1 trial?

ANSWER

73%.

QUESTION

Mosunetuzumab is a bispecific antibody targeting which two markers?

ANSWER

CD20 \times CD3.

QUESTION

For which indication did mosunetuzumab receive approval following the CELESTIMO trial?

ANSWER

Relapsed/refractory follicular lymphoma.

QUESTION

Name the two CD20 \times CD3 bispecific antibodies showing significant activity in relapsed DLBCL.

ANSWER

Glofitamab and epcoritamab.

QUESTION

In terms of dosing frequency, how do bispecific antibodies differ from autologous CAR-T?

ANSWER

Bispecifics require continuous weekly or biweekly dosing rather than a one-time infusion.

QUESTION

Which therapy type is generally associated with deeper and more durable remissions in responding patients?

ANSWER

CAR-T therapy.

QUESTION

Why might a clinician choose a bispecific antibody over CAR-T for a patient needing a rapid response?

ANSWER

Bispecifics are immediately available 'off-the-shelf' without a manufacturing wait.

QUESTION

The trial CARTITUDE-6 is a direct comparison between cilta-cel and which other regimen?

ANSWER

Pomalidomide combination.

QUESTION

How do Natural Killer (NK) cells identify target cells independently of antigen presentation?

ANSWER

Through innate activating receptors that recognise stressed, infected, or transformed cells.

QUESTION

What is the primary advantage of CAR-modified NK cells regarding allogeneic compatibility?

ANSWER

NK cells do not cause graft-versus-host disease (GvHD).

QUESTION

What is the typical toxicity profile of CAR-NK cells compared to traditional T cell CARs?

ANSWER

A potentially less severe profile with lower risks of CRS and neurotoxicity.

QUESTION

The landmark 2020 NEJM paper from MD Anderson evaluated CAR-NK cells targeting which antigen?

ANSWER

CD19.

QUESTION

What response rate was observed in the MD Anderson CAR-NK trial for relapsed/refractory B cell malignancies?

ANSWER

73%.

QUESTION

Which common CAR-T side effects were notably absent in all patients during the MD Anderson CAR-NK trial?

ANSWER

CRS, ICANS, and HLH.

QUESTION

What is the predicted role of bispecific antibodies in myeloma and lymphoma treatment by 2030?

ANSWER

They are expected to become the standard first choice due to their convenience and accessibility.

QUESTION

When is in vivo CAR-T gene delivery expected to potentially achieve clinical approval?

ANSWER

Before 2030.

QUESTION

What is identified as the final major challenge for transformative blood cancer therapies like CAR-T?

ANSWER

Ensuring equitable access for patients in all health systems globally.

QUESTION

In the context of lymphoma trials, what was the reported CR rate for mosunetuzumab in relapsed follicular lymphoma?

ANSWER

37%.

QUESTION

Which antigen is targeted by the myeloma-focused bispecific antibody talquetamab?

ANSWER

GPRC5D.

QUESTION

How does the 're-dosing' strategy potentially address the exhaustion of allogeneic CAR-T cells?

ANSWER

It allows for the infusion of a fresh batch of cells once the initial product is rejected or exhausted.

QUESTION

Which bispecific antibody targets BCMA and was tested in the MagnetisMM-3 trial?

ANSWER

Elranatamab.

QUESTION

What is the primary difference in peak toxicity between CAR-T and bispecific antibodies?

ANSWER

CAR-T has higher peak toxicity requiring hospitalisation, while bispecifics typically have lower peak toxicity.

QUESTION

What does the term 'off-the-shelf' imply regarding the availability of a therapy?

ANSWER

The product is pre-manufactured, frozen, and immediately available for patient use.

QUESTION

Which specific T cell marker is targeted by the second binding domain of most bispecific antibodies?

ANSWER

CD3.

QUESTION

What is the primary benefit of allogeneic CAR-T for patients with 'poor quality' T cells?

ANSWER

It eliminates the risk of product failure by using high-quality cells from a healthy donor.

QUESTION

What is the predicted future state of autologous CAR-T manufacturing within five years?

ANSWER

It is expected to become more efficient with faster manufacturing and better product quality.

QUESTION

The redirecting of T cells to kill cancer cells without gene engineering is the hallmark of _____.

ANSWER

Bispecific antibodies.

QUESTION

Which trial focused on the use of mosunetuzumab for follicular lymphoma?

ANSWER

CELESTIMO.

QUESTION

In allogeneic CAR-T, the knockout of _____ is required to ensure the donor cells do not attack the recipient.

ANSWER

The T cell receptor (TCR).

QUESTION

What does the term 'triple-class refractory' refer to in the context of myeloma patients?

ANSWER

Patients whose cancer has stopped responding to the three main classes of myeloma drugs.

QUESTION

What is the primary target cell for in vivo CAR-T gene delivery inside the body?

ANSWER

Circulating T cells.

QUESTION

Which haematological malignancy was targeted in the MajesTEC-1 and MonumenTAL-1 trials?

ANSWER

Multiple Myeloma.

QUESTION

What major patient-centric goal is achieved by transitioning from autologous to allogeneic CAR-T?

ANSWER

The elimination of manufacturing delays, allowing for immediate treatment.