CLINICAL FLASHCARDS

CAR-T Masterstroke Or Biological Chaos?

The Life Science Feed

QUESTION

Which two signals are required for a natural T cell to activate and kill a target cell?

ANSWER

Antigen recognition (Signal 1) and a co-stimulatory signal (Signal 2).

QUESTION

How does MHC downregulation allow cancer cells to evade the immune system?

ANSWER

It prevents T cells from recognising peptide fragments on the surface of the cancer cell.

QUESTION

What is the immune-suppressive effect of cancer cells expressing PD-L1?

ANSWER

It binds to PD-1 on T cells to suppress the immune response.

QUESTION

Which cells in the tumour microenvironment contribute to an immunosuppressive state alongside myeloid-derived suppressor cells?

ANSWER

Tregs (Regulatory T cells).

QUESTION

Why is CAR-T cell recognition considered independent of MHC presentation?

ANSWER

The synthetic receptor binds directly to the surface antigen on the cancer cell.

QUESTION

Which component of the CAR construct is responsible for binding the tumour antigen?

ANSWER

The extracellular domain (typically an scFv).

QUESTION

What does the acronym 'scFv' represent in CAR-T bioengineering?

ANSWER

Single-chain variable fragment.

QUESTION

From which immune molecule is an scFv usually derived?

ANSWER

An antibody.

QUESTION

What is the role of the intracellular signalling domains in a CAR?

ANSWER

They provide both the activation signal and the co-stimulatory signal within one receptor.

QUESTION

Which specific activation domain was used in first-generation CARs?

ANSWER

CD3-\zeta.

QUESTION

What structural addition differentiates second-generation CARs from first-generation CARs?

ANSWER

A co-stimulatory domain (such as CD28 or 4-1BB).

QUESTION

How do second-generation CARs compare to first-generation CARs regarding T cell persistence?

ANSWER

They show significantly improved persistence and anti-tumour activity.

QUESTION

Term: Autologous therapy.

ANSWER

Definition: A personalised treatment manufactured from the patient's own cells.

QUESTION

Which process is used to extract T cells from a patient's blood for CAR-T production?

ANSWER

Leukapheresis.

QUESTION

What tool is used to introduce the CAR gene into T cells during manufacturing?

ANSWER

A viral vector.

QUESTION

What is the typical duration of the CAR-T manufacturing process from collection to shipping?

ANSWER

2 to 5 weeks.

QUESTION

Why might a patient receive 'bridging treatment' during CAR-T manufacture?

ANSWER

To maintain control over the cancer while waiting for the engineered cells.

QUESTION

Why is CD19 a suitable target for treating B cell malignancies?

ANSWER

It is expressed on almost all B cell cancer cells but not on haematopoietic stem cells.

QUESTION

How does the absence of CD19 on haematopoietic stem cells benefit the patient long-term?

ANSWER

It allows the immune system to eventually regenerate healthy B cells from progenitors.

QUESTION

Which paediatric patient was the first to achieve complete remission using CD19-directed CAR-T?

ANSWER

Emily Whitehead.

QUESTION

In the ELIANA trial for paediatric ALL, what was the reported remission rate?

ANSWER

81 percent.

QUESTION

Which relapsed/refractory malignancy was treated in the JULIET trial?

ANSWER

Adult diffuse large B-cell lymphoma (DLBCL).

QUESTION

What was the complete response rate observed in the JULIET trial for DLBCL?

ANSWER

40 percent.

QUESTION

Which clinical trial demonstrated a 51 percent complete response rate for axicabtagene ciloleucel in DLBCL?

ANSWER

ZUMA-1.

QUESTION

What are the three primary inflammatory cytokines involved in the pathogenesis of Cytokine Release Syndrome (CRS)?

ANSWER

IL-6, IFN-\gamma, and IL-2.

QUESTION

Which symptoms characterise moderate-to-severe Cytokine Release Syndrome?

ANSWER

Fever, hypotension, and organ dysfunction.

QUESTION

What is the standard pharmacological agent used to treat CRS?

ANSWER

Tocilizumab.

QUESTION

By what mechanism does tocilizumab treat CRS?

ANSWER

It acts as an IL-6 receptor blocker.

QUESTION

What does the acronym 'ICANS' stand for?

ANSWER

Immune effector cell-associated neurotoxicity syndrome.

QUESTION

Which neurological symptom is often used to identify the onset of ICANS?

ANSWER

Word-finding difficulty (or encephalopathy/tremor).

QUESTION

What is the primary treatment for managing ICANS?

ANSWER

Corticosteroids.

QUESTION

What physiological event causes the blood-brain barrier disruption in ICANS?

ANSWER

Endothelial activation and cytokine-mediated disruption.

QUESTION

How does the expansion profile of 4-1BB CAR-T products differ from CD28 products?

ANSWER

They have a slower, more sustained expansion profile.

QUESTION

Why are 4-1BB co-stimulated CAR-T products associated with lower rates of ICANS?

ANSWER

They avoid the rapid, acute expansion seen with CD28 products.

QUESTION

Name one of the first two CAR-T products approved by the FDA in 2017.

ANSWER

Tisagenlecleucel (or axicabtagene ciloleucel).

QUESTION

The first-generation CARs lacked a _____ domain, leading to poor T cell persistence.

ANSWER

Co-stimulatory

QUESTION

What was the significance of the Bill Ludwig case in 2010?

ANSWER

It served as the proof of concept that launched the CAR-T revolution.

QUESTION

How does the CAR-T cell bypass the need for a co-stimulatory signal from the target cell?

ANSWER

The co-stimulatory domain is built directly into the synthetic CAR construct.

QUESTION

Which condition must be met for a CAR-T therapy to be safely administered to a patient?

ANSWER

It must be administered in a specialist centre with trained expertise.

QUESTION

What is the antigen-binding region of the CAR extracellular domain called?

ANSWER

The scFv (single-chain variable fragment).

QUESTION

What was the overall response rate (ORR) for adult DLBCL in the JULIET trial?

ANSWER

52 percent.

QUESTION

What was the overall response rate (ORR) for DLBCL in the ZUMA-1 trial?

ANSWER

72 percent.

QUESTION

Concept: Chimeric Antigen Receptor (CAR).

ANSWER

Definition: A synthetic receptor that allows T cells to recognise antigens without MHC presentation.

QUESTION

Which medication class is used for severe or tocilizumab-refractory CRS?

ANSWER

Corticosteroids.

QUESTION

What is the function of the transmembrane domain in the CAR structure?

ANSWER

It anchors the CAR to the T cell membrane.

QUESTION

Why is the CD19 protein nearly universal in B cell malignancies?

ANSWER

It is expressed across almost all stages of B cell development.

QUESTION

What dangerous complication can occur in the most severe cases of ICANS?

ANSWER

Cerebral oedema.

QUESTION

Which co-stimulatory domain is used in both tisagenlecleucel and lisocabtagene?

ANSWER

4-1BB.

QUESTION

What is the main practical limitation regarding the current manufacturing of autologous CAR-T?

ANSWER

The 2 to 5-week turnaround time for production.

QUESTION

How do CAR-T cells differ from natural T cells regarding antigen recognition?

ANSWER

They use an antibody-derived fragment instead of a T cell receptor.

QUESTION

What is the primary risk of targeting antigens shared between cancer and normal tissue?

ANSWER

Autoimmunity.