

CLINICAL FLASHCARDS

Small Molecules VS CAR-T In CLL

The Life Science Feed

QUESTION

Before the advent of small molecules, chronic lymphocytic leukaemia (CLL) was primarily treated with

_____.

ANSWER

Chemoimmunotherapy

QUESTION

The FCR regimen for CLL consists of fludarabine, cyclophosphamide, and which anti-CD20 antibody?

ANSWER

Rituximab

QUESTION

Bruton's tyrosine kinase (BTK) is a critical node in which cellular signalling pathway?



ANSWER

The B cell receptor (BCR) signalling pathway

QUESTION

How does the small molecule ibrutinib inhibit the function of BTK?

ANSWER

It binds irreversibly to the BTK protein

QUESTION

Which 2013 clinical trial demonstrated the efficacy of ibrutinib in both previously treated and treatment-naïve CLL?

ANSWER

The RESONATE trial

QUESTION

Response to chemoimmunotherapy is typically poor in CLL patients exhibiting a deletion of which chromosome arm?



ANSWER

The 17p deletion

QUESTION

Patients with a mutation in which tumour suppressor gene generally show poor responses to traditional chemotherapy?

ANSWER

The TP53 gene

QUESTION

Identify the primary cardiovascular toxicity associated with ibrutinib therapy.

ANSWER

Atrial fibrillation

QUESTION

Beyond atrial fibrillation, which vascular condition is a common side effect of ibrutinib?

ANSWER

Hypertension

QUESTION

Resistance to continuous ibrutinib treatment often develops through which specific BTK mutation?

ANSWER

The C481S mutation

QUESTION

The ELEVATE-RR trial compared the safety and efficacy of ibrutinib against which second-generation BTK inhibitor?

ANSWER

Acalabrutinib

QUESTION

How did the efficacy of acalabrutinib compare to ibrutinib in the ELEVATE-RR trial?

ANSWER

It demonstrated non-inferior efficacy

QUESTION

Which second-generation BTK inhibitor demonstrated superior progression-free survival (PFS) against ibrutinib in the ALPINE trial?

ANSWER

Zanubrutinib

QUESTION

CLL cells depend on the overexpression of which anti-apoptotic protein for survival?

ANSWER

The BCL-2 protein

QUESTION

Venetoclax promotes the death of CLL cells through which pharmacological mechanism?

ANSWER

Restoration of apoptosis

QUESTION

The CLL14 trial established the use of venetoclax-obinutuzumab as a _____-duration regimen.

ANSWER

Fixed

QUESTION

For how many months are fit patients typically treated in a first-line venetoclax combination regimen?

ANSWER

12 months

QUESTION

The MURANO trial established the efficacy of venetoclax and rituximab in which CLL patient population?

ANSWER

Relapsed or refractory CLL patients

QUESTION

In haematology, what does the acronym MRD represent?

ANSWER

Measurable residual disease

QUESTION

What clinical status is achieved when residual leukaemia cells are below the threshold of clinical detection?

ANSWER

MRD-negativity

QUESTION

Achieving MRD-negativity with venetoclax is associated with a prolongation of which clinical outcome?

ANSWER

Progression-free survival

QUESTION

Approximately what percentage of first-line patients achieve MRD-negativity when using venetoclax combinations?

ANSWER

50–70 percent

QUESTION

Which clinical benefit allows CLL patients to live without daily oral medication following fixed-duration therapy?

ANSWER

The treatment-free period

QUESTION

The TRANSCEND CLL 004 trial evaluated which CAR-T product in relapsed/refractory CLL?

ANSWER

Lisocabtagene

QUESTION

The TRANSCEND CLL 004 trial reported a Complete Response (CR) rate of _____ percent.

ANSWER

18 percent

QUESTION

What is the approximate Overall Response Rate (ORR) for CAR-T in heavily pretreated CLL patients?

ANSWER

45 percent

QUESTION

Manufacturing CAR-T for CLL is challenging because patients often have profoundly dysfunctional _____.

ANSWER

T cells

QUESTION

Beyond T cell dysfunction, CAR-T efficacy in CLL is hindered by an immunosuppressive _____.

ANSWER

Tumour microenvironment

QUESTION

The 'leukapheresis-first' strategy involves collecting T cells at which stage of the disease?

ANSWER

Early in the disease course

QUESTION

Collecting T cells before starting BTK inhibitor therapy aims to improve the _____ of the final CAR-T product.

ANSWER

Manufacturing quality

QUESTION

What is the term for the transformation of CLL into an aggressive lymphoma, such as DLBCL?

ANSWER

Richter's transformation

QUESTION

Richter's transformation occurs in approximately _____ percent of CLL patients.

ANSWER

5 percent

QUESTION

Which aggressive lymphoma subtype is most commonly associated with Richter's transformation?

ANSWER

Diffuse large B cell lymphoma (DLBCL)

QUESTION

Which therapeutic antigen is targeted by CAR-T cells to treat Richter's transformation?



ANSWER

CD19

QUESTION

Ibrutinib shifts T cells from an exhausted phenotype toward which more active phenotype?

ANSWER

An effector phenotype

QUESTION

How does ibrutinib pre-treatment affect the anti-tumour function of CAR-T cells in preclinical models?



ANSWER

It improves CAR-T persistence and function

QUESTION

Which anti-CD20 antibody is paired with venetoclax in the CLL14 trial?



ANSWER

Obinutuzumab

QUESTION

Which anti-CD20 antibody is used alongside venetoclax in the MURANO trial?

ANSWER

Rituximab

QUESTION

Compared to ibrutinib, second-generation BTK inhibitors are designed to be more _____ to reduce off-target effects.

ANSWER

Selective

QUESTION

The ALPINE trial found that zanubrutinib resulted in lower rates of _____ compared to ibrutinib.

ANSWER

Atrial fibrillation

QUESTION

What finding from the CLL14 six-year update suggests long-term benefits of MRD-negativity?

ANSWER

Patients remain in remission years after completing therapy

QUESTION

How does the BCL-2 protein contribute to the survival of CLL cells?

ANSWER

It prevents the cells from undergoing programmed cell death

QUESTION

Patients in the TRANSCEND CLL 004 trial were required to have failed both BTK inhibitors and which other drug class?

ANSWER

BCL-2 inhibitors (venetoclax)

QUESTION

The immunomodulatory effects of BTK inhibitors are being studied as a potential way to enhance _____ therapy.

ANSWER

CAR-T

QUESTION

Prognosis for Richter's transformation is historically very poor when using _____ therapy.

ANSWER

Conventional

QUESTION

Which specific protein node in the BCR pathway does acalabrutinib target?



ANSWER

Bruton's tyrosine kinase (BTK)

QUESTION

The goal of 12 months of venetoclax therapy is to allow patients to enter a _____-free period.

ANSWER

Treatment

QUESTION

What was the primary efficacy outcome used to show zanubrutinib's superiority in the ALPINE trial?

ANSWER

Progression-free survival

QUESTION

In what year did ibrutinib first enter the CLL treatment landscape?

ANSWER

2013

QUESTION

Why is early T cell banking considered for CLL patients potentially needing CAR-T?

ANSWER

To ensure high-quality cells are collected before damage from disease or treatment