

CLINICAL FLASHCARDS

How Four Drugs Beat Heart Failure

The Life Science Feed

QUESTION

What clinical definition is given for heart failure with reduced ejection fraction (HFrEF) in the context of the PARADIGM-HF trial?



ANSWER

An ejection fraction (EF) below 40 %.

QUESTION

Historically, what was the estimated five-year mortality rate for heart failure patients?



ANSWER

Approximately 50 %.

QUESTION

According to Sarah Mitchell, what is the total relative risk reduction in cardiovascular death when all four 'pillar' drug classes are combined?

ANSWER

A 70 % relative risk reduction compared to placebo.

QUESTION

Which historical heart failure medication improved symptoms but failed to improve overall survival?

ANSWER

Digoxin.

QUESTION

What specific drug class was introduced in the 1980s and 1990s as the first to actually reduce mortality in heart failure?

ANSWER

ACE inhibitors.

QUESTION

Beyond ACE inhibitors and beta-blockers, what was the third historical class added to target the neurohormonal axis?

ANSWER

Mineralocorticoid receptor antagonists (MRAs).

QUESTION

What does the abbreviation 'ARNi' represent in cardiology?

ANSWER

Angiotensin receptor-neprilysin inhibitor.

QUESTION

What were the two arms of the PARADIGM-HF (2014) trial for HFrEF patients?



ANSWER

Sacubitril-valsartan and enalapril.

QUESTION

In the PARADIGM-HF trial, what was the relative risk reduction for the primary endpoint of cardiovascular death or first hospitalisation?



ANSWER

A 20 % relative risk reduction.

QUESTION

What was the Number Needed to Treat (NNT) to prevent one death over three years in the PARADIGM-HF trial?

ANSWER

A value of 32.

QUESTION

What is the physiological function of the enzyme neprilysin?

ANSWER

It breaks down natriuretic peptides such as BNP and ANP.

QUESTION

How does neprilysin inhibition specifically benefit the heart?

ANSWER

It allows compensatory peptides to accumulate, promoting vasodilation and natriuresis.

QUESTION

Why must sacubitril be combined with an ARB rather than an ACE inhibitor?

ANSWER

The combination with an ACE inhibitor significantly increases the risk of angioedema.

QUESTION

What is the mandatory washout period required when switching a patient from an ACE inhibitor to an ARNi?

ANSWER

A 36-hour washout period.

QUESTION

For which medical condition were SGLT2 inhibitors originally developed?

ANSWER

Type 2 diabetes.

QUESTION

Which 2015 diabetes trial first highlighted the heart failure benefits of empagliflozin?

ANSWER

The EMPA-REG OUTCOME trial.

QUESTION

In the EMPA-REG OUTCOME trial, what was the relative risk reduction in hospitalisation for heart failure?

ANSWER

A 35 % relative risk reduction.

QUESTION

Which landmark 2019 trial established the benefit of dapagliflozin in HFrEF patients regardless of diabetes status?

ANSWER

The DAPA-HF trial.

QUESTION

Which landmark 2020 trial established the benefit of empagliflozin in HFrEF patients?

ANSWER

The EMPEROR-Reduced trial.

QUESTION

How do SGLT2 inhibitors affect the kidneys to reduce heart failure burden?

ANSWER

They block the SGLT2 transporter, causing glucose and sodium excretion in the urine.

QUESTION

According to current hypotheses, how might SGLT2 inhibitors improve myocardial fuel utilisation?

ANSWER

By shifting the myocardium toward ketone oxidation, which is more oxygen-efficient.

QUESTION

What are the four 'pillars' of quadruple therapy for HFrEF?

ANSWER

ARNi (or ACEi), beta-blockers, MRAs, and SGLT2 inhibitors.

QUESTION

Which specific beta-blockers are recommended for the quadruple therapy regimen?

ANSWER

Carvedilol, bisoprolol, or metoprolol succinate.

QUESTION

Name the two primary mineralocorticoid receptor antagonists (MRAs) used in heart failure management.

ANSWER

Spironolactone and eplerenone.

QUESTION

What are the two SGLT2 inhibitors specifically mentioned for HFrEF treatment?



ANSWER

Dapagliflozin and empagliflozin.

QUESTION

A 2021 analysis by Vaduganathan and colleagues projected what reduction in major events using full quadruple therapy versus placebo?

ANSWER

Approximately 73 % over two years.

QUESTION

According to Vaduganathan's modelling, what is the absolute risk reduction of quadruple therapy for major cardiac events?

ANSWER

Roughly 1 in 3 patients avoid a major event.

QUESTION

What term describes the clinical delay in updating a stable patient's medication to newer, evidence-based classes?

ANSWER

Clinical inertia.

QUESTION

What is the guideline recommendation level for SGLT2 inhibitors in HFrEF according to the ESC and AHA/ACC?

ANSWER

Class I, Level A.

QUESTION

Which trial provided evidence for rapid up-titration of all four pillars within two weeks of hospitalisation?

ANSWER

The STRONG-HF trial.

QUESTION

How has the approach to initiating heart failure medications shifted recently?

ANSWER

From slow sequential titration to rapid, simultaneous low-dose initiation.

QUESTION

What is the recommended target systolic blood pressure range during heart failure drug titration?

ANSWER

100 to 120 mmHg.

QUESTION

Which two lab parameters must be closely monitored when a patient is on an MRA?

ANSWER

Renal function and potassium levels.

QUESTION

How does the hypotension threshold for SGLT2 inhibitors compare to that of ARNi therapy?

ANSWER

The hypotension threshold for SGLT2 inhibitors is more forgiving (less restrictive).

QUESTION

The primary mechanism of SGLT2 inhibitors involves reducing cardiac preload through _____ and _____.

ANSWER

Osmotic diuresis; natriuresis.

QUESTION

Sacubitril-valsartan is the generic name for which common brand-name drug?

ANSWER

Entresto.

QUESTION

Why is it clinically significant that DAPA-HF and EMPEROR-Reduced enrolled patients without diabetes?

ANSWER

It proved the cardiac benefits of SGLT2 inhibitors are not solely metabolic/glucose-dependent.

QUESTION

Which heart failure drugs target the renin-angiotensin-aldosterone system (RAAS)?

ANSWER

ACE inhibitors, ARBs (within ARNi), and MRAs.

QUESTION

Which drug class specifically targets the sympathetic nervous system in heart failure?

ANSWER

Beta-blockers.

QUESTION

In HFrEF management, which drug class is considered the first 'plot twist' due to its origins in a different therapy area?

ANSWER

SGLT2 inhibitors.

QUESTION

What is the leading hypothesis regarding SGLT2 inhibitors and cardiac sodium-hydrogen exchangers?

ANSWER

They reduce intracellular sodium and calcium overload in the myocardium.

QUESTION

What was the historical five-year survival outlook for heart failure compared to most malignancies?

ANSWER

Heart failure survival was historically worse than most malignancies.

QUESTION

What are the common side effects of ARNi that can usually be managed with careful up-titration?

ANSWER

Dizziness and hypotension.

QUESTION

What is the estimated number of people living with heart failure in the United Kingdom?

ANSWER

Around 900,000 people.

QUESTION

What is the primary barrier to the implementation of ARNi in some healthcare systems?

ANSWER

Cost and access barriers.

QUESTION

How does the size of the clinical effect of SGLT2 inhibitors compare to ACE inhibitors?

ANSWER

It is comparable to adding an ACE inhibitor to a background of beta-blockade.

QUESTION

Which trial results were so striking that the study was stopped early in 2014?



ANSWER

The PARADIGM-HF trial.

QUESTION

Beyond diuresis, what anti-remodelling effects are hypothesized for SGLT2 inhibitors?

ANSWER

Anti-fibrotic and anti-inflammatory effects.

QUESTION

In the quadruple therapy model, which drug should be used if a patient cannot tolerate an ARNi?

ANSWER

An ACE inhibitor.

QUESTION

True or False: The benefits of quadruple therapy are only seen after years of titration.

ANSWER

False (STRONG-HF showed benefit with rapid titration within weeks).

QUESTION

Which compensatory hormones are increased by the use of sacubitril?

ANSWER

Natriuretic peptides (such as ANP and BNP).

QUESTION

Approximately how many people are affected by heart failure globally?



ANSWER

Over 60 million people.

QUESTION

What was the gold standard ACE inhibitor used as the comparator in the PARADIGM-HF trial?

ANSWER

Enalapril.

QUESTION

According to the podcast, what has been the 'single greatest advance' in HFrEF management history?

ANSWER

The four-pillar quadruple therapy.