

Heart failure treatment: new drug update



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Since the publication of two key studies in 1987 and 1991, ACE inhibitors drugs (enalapril, lisinopril, ramipril and the other "prils") have been a standard drug treatment for patients with heart failure caused by dilated cardiomyopathy.

The drugs (their correct name is angiotensin-converting enzyme inhibitors) prevent the body from creating a hormone known as angiotensin II, which is overactive in heart failure. It has harmful long-term effects on the heart, blood vessels and kidneys.

The two other main treatments for heart failure – MRAs (mineralocorticoid receptor antagonists) such as eplerenone and spironolactone, and beta-blockers such as bisoprolol and carvedilol – act in a similar way to block other inappropriate actions of the body's hormonal and nervous systems.

What is often forgotten, though, is that potentially beneficial hormonal systems are also working in heart failure, although they may not be as active as they should be.

The heart also secretes the hormones A- and B-type natriuretic peptide, which circulate in the blood and are thought to have beneficial effects on the blood vessels and kidneys in heart failure. Other substances with similarly favourable actions are produced in the blood vessels and elsewhere.

For many years there have been attempts to develop treatments that boost the levels and actions of these helpful hormones. One approach has been to block the enzyme neprilysin, which breaks down several of these helpful substances.

By coupling a neprilysin inhibitor (sacubitril) with the ARB (angiotensin II receptor) valsartan, Novartis produced a drug (sacubitril-valsartan or LCZ696), which both blocks the harmful angiotensin system and boosts the helpful hormone levels (and possibly levels of other beneficial substances).

In a recent trial, called PARADIGM-HF, the new LCZ696 was compared with the ACE inhibitor enalapril. Treatment with LCZ696 led to significantly lower rates of death and hospital admission in patients with heart failure and a low left ventricular ejection fraction (a measure of the volume of blood pumped out of the heart with each beat).



Patients treated with LCZ696 were also less likely to report worsening of their heart failure symptoms, require other treatments for heart failure or need to attend a hospital's A&E department.

The positive effects of LCZ696 over enalapril were seen irrespective of the cause of heart failure, including in patients with dilated cardiomyopathy.

The trade-off for these benefits was an increased risk of hypotension (low blood pressure), which can cause symptoms such as dizziness, and a small increase in the risk of swelling to the body's tissues as you see in an allergic reaction or inflammation.

This usually appears as swelling of the face, lips or tongue and can rarely cause breathing difficulties (although this more severe type did not occur in any patient in the trial).

While the results of the PARADIGM-HF trial were statistically convincing and clinically important, patients studied were selected and LCZ696 may not be suitable for everybody.

Those taking part had an ejection fraction of 40 per cent or less, existing treatment with at least a moderate dose of an ACE inhibitor or an ARB, and a systolic blood pressure figure (the first number) of greater than 95.

This new evidence has to be reviewed by regulatory agencies in Europe and the USA before any decision about approval of LCZ696 for general use can be made. This review process is likely to take until this summer.

Drug granted accelerated assessment by European review body

A new drug found to cut heart failure deaths significantly may be available for use in the UK sooner than expected.

The drug, LCZ696, which research suggests can cut deaths by 20 per cent, has been granted accelerated assessment by a European review body.

Drug company Novartis say this means the Committee for Medicinal Products for Human Use's opinion will be given at day 150 from its initial meeting, two months earlier than normally happens.

The company says it is expecting to submit for marketing authorisation with the EU regulators early this year and if

approved, the drug could be authorised for use in the UK towards the end of this year.

NICE will then need to determine its use on the NHS, which could happen as soon as early 2016.

The drug helps improve blood flow in heart failure patients and researchers found it helped prevent the number of hospital admissions for heart failure.

The study was carried out by researchers from the University of Glasgow, the University of Texas Southwestern Medical Centre and Novartis, in collaboration with an international team of researchers from other universities and research institutes around the world.