

Lung drug hope for heart failure patients

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An early phase trial of a drug currently used to treat lung fibrosis has shown it may also help patients who suffer from a common form of heart failure.

Trialed by University of Manchester and Manchester University NHS



Foundation Trust doctors and scientists, in conjunction with Liverpool Clinical Trials Centre, pirfenidone could offer a much-needed viable treatment for heart failure with preserved ejection fraction (HFpEF).

But larger scale trials are needed to confirm the findings for the drug, produced by Roche Products Limited, before it can be licensed for use in the NHS.

The study, funded by the National Institute for Health Research, is published in *Nature Medicine* today.

Heart failure means that the <u>heart</u> is no longer able to pump blood around the body properly, causing shortness of breath, swelling and extreme fatigue.

Around a million people in the UK live with heart failure, and many more are at risk of developing it.

Just under a third of 55-year-olds will develop heart failure, and 2 to 3 of every 10 people diagnosed die within a year.

In about half of patients with heart failure, the forward pumping function of the heart is normal. This is called heart failure with preserved ejection fraction, or HFpEF.

While a number of processes lead to heart failure, <u>scarring</u>—or fibrosis—of the heart muscle is thought to be an important mechanism in around half to two-thirds of patients with HFpEF and is associated with adverse outcomes.

Dr. Chris Miller, National Institute for Health Research Clinician Scientist at The University of Manchester and Consultant Cardiologist at Manchester University NHS Foundation Trust led the study.



He said: "Heart failure is as devastating an illness as some of the most common cancers, however its profile its much lower and <u>treatment</u> options for HFpEF are very limited.

"Using cardiac MRI, we were able to select patients in whom heart scarring is important. Pirfenidone then reduced that scarring."

Pirfenidone works by inhibiting the biological processes involved in <u>scar</u> <u>formation</u>.

The study enrolled patients with heart failure, normal forward pumping function of the heart and evidence of fluid retention.

Eligible patients had cardiac MRI scanning, and those who had evidence of heart scarring, as indicated by a measurement called 'extracellular volume', were randomly assigned to take pirfenidone or a placebo daily. 94 patients were randomized, with 47 assigned to each treatment group.

At one year, patients underwent a second cardiac MRI to measure change in heart scarring. Extracellular volume declined by 1.21% on average in patients who took pirfenidone compared with those receiving placebo.

"Based on data from previous studies, this amount of reduction in heart scarring could translate into a substantial reduction in rates of death and admission to hospital for heart failure, however larger trials are needed to determine this," said Dr. Miller.

Fluid retention, measured using a blood test called NT-proBNP, also improved in patients taking pirfenidone compared to those receiving placebo.

Dr. Miller added: "Though further investigation is required, the



associated improvement in fluid retention provides support for heart scarring having a causal role in heart failure and being an effective treatment target".

The most common side effects were nausea, insomnia and rash, which are similar to that which lung patients can experience when taking Pirfenidone.

Dr. Miller said: "These findings are exciting and suggest that <u>pirfenidone</u> could benefit patients with this condition, however further trials are required."

The paper "Pirfenidone in heart failure with preserved ejection fraction: a randomized phase 2 trial" is published in *Nature Medicine*.

More information: Gavin A. Lewis et al, Pirfenidone in heart failure with preserved ejection fraction: a randomized phase 2 trial, *Nature Medicine* (2021). DOI: 10.1038/s41591-021-01452-0

Provided by University of Manchester

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