Pirfenidone reduces scar tissue in patients with heart failure

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Patients with heart failure with preserved ejection fractionwho took the antifibrotic drug pirfenidone saw a significant reduction in a marker of heart muscles carring compared with patients who received a placebo,based on findings from an early-phase trial presented at the American College of Cardiology's 70th Annual Scientific Session.

"Observational data suggests that heart muscle scarring, or fibrosis,is an important disease process for heart failure prognosis," said Chris Miller, MD, a cardiologist and National Institute for Health Research Clinician Scientist at the University of Manchester and Manchester University NHS Foundation Trust andthe study's lead author. "With cardiac MRI, we were able to select a group of patients in whom fibrosis appears to be important and then reduce thats carring. While further investigationis needed, it suggests that fibrosis is an effective treatment target."

Heart failure means that the heart is no longer able to pump blood around the body properly, causing shortness of breath, swelling and fatigue.In about half of patients with heart failure, the forward pumping function of the heart, or ejection fraction,is normal. This is called heart failure with preserved ejection fraction, or HFpEF.While heart failure can involve multiple factors, scarring of the heart muscle is thought to be an important contributing factor in up to two-thirds of patients with HFpEF. This new trial suggests clinicians could one day use a personalized approach to prevent or reverse scarring in those individuals, thereby slowing the progression of heart failure, Miller said.

Pirfenidone is currently approved for treating adults with idiopathic lung fibrosis,or scarring in the lungs that makes it hard to breathe.While the mechanism of action has not been fully established,the drugis thought towork by inhibiting biological processes involved in scar formation. Preclinical studies suggest pirfenidone can both reduce scar tissue formation and reduce existing scarring in the heart.

Researchers enrolled patientswithheart failure, anejection fraction of 45% or higherand elevatednatriuretic peptides (markers of fluid retention).Eligible patients underwent cardiac MRI scanning.Those who hadevidence of scarring in the heart muscle, as indicated by an extracellular volume(a measurement of heart muscle scaring)of 27% or greater,wererandomly assigned to take pirfenidoneora placebo daily.In total,94 patientswere randomized, with 47 assigned to each treatment group.

At one year, patients underwent a second cardiac MRI tomeasurechange inheart muscleextracellular volume, the primary endpoint.Extracellular volumedeclined by 1.21% on average in patients who took pirfenidonecompared with those receiving placebo,a reduction Miller said was likely to be clinically significant.

"Based on the data we have from previous observational studies, this amount of change in fibrosiscould translate intoa significant reduction in death and hospitalization for heart failure,but further

work is neededtodeterminethis," Millersaid.

The study also found evidence that fluid retention, measured using natriuretic peptides,improved in patients who took pirfenidone compared to those receiving placebo.

"The associated reduction in natriuretic peptides provides support forheart scarring having a causal role in heart failure and being an efficacious therapeutic target,"Millersaid."Hopefully this work can lead to further development of therapeutics that target heart fibrosis and scarring, and a phase three trial to see if pirfenidone improves patient outcomes."

The most common adverse events were nausea, insomnia and rash.

More information: Pirfenidone In Heart Failure With Preserved Ejection Fraction, American College of Cardiology 70th Annual Scientific Session, May 17, 2021

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