Effects of pirfenidone on scar size and ventricular remodeling after myocardial infarction: a preclinical study

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Background: An intense fibrotic response after myocardial infarction (MI) may lead to scar expansion and left ventricular (LV) remodeling, increasing the risk for ventricular arrhythmias and heart failure. Pirfenidone is a drug currently approved for the treatment of idiopathic pulmonary fibrosis, and reduces LV fibrosis in patients with heart failure and preserved ejection fraction. We aimed to characterize the different profiles or protein expression in the infarct zone in rats receiving or not receiving pirfenidone on top of standard therapy for MI.

Methods: Male Wistar rats were randomized to: sham procedure (group 1; n=13), reperfused MI induced by surgical ligation of the left anterior descending artery (LAD) for 45 minutes (group 2; n=17), reperfused MI plus standard therapy (aspirin, angiotensin-converting enzyme inhibitor, beta-blocker, and also mineralocorticoid receptor antagonist [MRA]) (group 3; n=17), reperfused MI plus pirfenidone alone (group 4; n=17), reperfused MI plus standard therapy and pirfenidone (group 5; n=17). Rats surviving LAD ligation and reperfusion underwent cardiac magnetic resonance (CMR) after 72 hours and 30 days from MI, and were sacrificed the day after the second CMR exam. The primary endpoint was the change in late gadolinium enhancement (LGE) mass as a percentage of LV mass.

Results: Forty-six rats survived until the second CMR. Percent changes in LV end-diastolic and end-systolic volume (p=0.370 and 0.423, respectively), ejection fraction (p=0.236) and mass (p=0.815) did not differ significantly between rats on pirfenidone plus standard therapy compared with those receiving standard therapy alone. The decrease in LGE mass was significantly greater in rats on pirfenidone plus standard therapy vs. those on standard therapy alone: -22.0% (interquartile range, -37.1 to -5.7, range -51.1 to +37.5) vs. +1.9% (-7.7 to +12.5, range -19.8 to +56.5), p=0.029.

Conclusions: Pirfenidone had additive effects to standard therapy for MI (including an MRA) in reducing LV fibrosis in a rat model of reperfused MI, while it did not further improve LV function, volumes or mass.