



# JACC

## Heart Failure

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#### MINI-FOCUS ISSUE: PULMONARY HYPERTENSION

#### Effect of Macitentan on Hospitalizations: Results From the SERAPHIN Trial

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Richard N. Channick, Marion Delcroix, Hossein-Ardeschir Ghofrani, Elke Hunsche, Pavel Jansa, Franck-Olivier Le Brun, Sanjay Mehta, Tomás Pulido, Lewis J. Rubin, B.K.S. Sastry, Gérald Simonneau, Olivier Sitbon, Rogério Souza, Adam Torbicki, Nazzareno Galiè

In the global SERAPHIN (Study with an Endothelin Receptor Antagonist in Pulmonary arterial Hypertension to Improve cliNical outcome) trial, 742 pulmonary arterial hypertension (PAH) patients were randomized to receive placebo or 3 or 10 mg of macitentan. Compared with placebo, 3 mg and 10 mg of macitentan reduced the risk of all-cause hospitalization by 18.9% ( $p = 0.1208$ ) and 32.3% ( $p = 0.0051$ ), respectively, and the rate of all-cause hospitalization by 20.5% ( $p = 0.0378$ ) and 33.1% ( $p = 0.0005$ ), respectively. For PAH-related hospitalization, macitentan at 3 mg and 10 mg reduced the risk of PAH-related hospitalization by 42.7% ( $p = 0.0015$ ) and 51.6% ( $p < 0.0001$ ), respectively, and the rate of PAH-related hospitalization by 44.5% ( $p = 0.0004$ ) and 49.8% ( $p < 0.0001$ ), respectively. Risks of non-PAH-related hospitalization were similar between treatments. Macitentan 10 mg significantly reduced the risk and rate of hospitalization in PAH patients.

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#### The Diastolic Pulmonary Gradient Does Not Predict Survival in Patients With Pulmonary Hypertension Due to Left Heart Disease

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Emmanouil Tampakakis, Peter J. Leary, Van N. Selby, Teresa De Marco, Thomas P. Cappola, G. Michael Felker, Stuart D. Russell, Edward K. Kasper, Ryan J. Tedford

Patients with combined post- and pre-capillary pulmonary hypertension due to left heart disease (PH-LHD) have worse prognosis than those with passive pulmonary hypertension. The transpulmonary gradient (TPG) and pulmonary vascular resistance (PVR) have been used to identify high-risk patients with PH-LHD. The diastolic pulmonary gradient (DPG) has been suggested as a better marker. This study evaluated if DPG predicts survival in PH-LHD by studying retrospectively 1,236 patients followed for a mean time of 4.4 years. The relationships between DPG, TPG, or PVR and survival were evaluated. DPG was not associated with mortality in PH-LHD whereas TPG and PVR predicted death.

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#### EDITORIAL COMMENT

#### Characterization of Pulmonary Hypertension in Heart Failure Using the Diastolic Pressure Gradient: Limitations of a Solitary Measurement

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Neal A. Chatterjee, Gregory D. Lewis

CME

JACC: Heart Failure CME is available online. Go to <http://heartfailure.onlinejacc.org> to participate.

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**CLINICAL RESEARCH****Safety and Tolerability of Omecamtiv Mecarbil During Exercise in Patients With Ischemic Cardiomyopathy and Angina**

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Barry H. Greenberg, Willis Chou, Khalil G. Saikali, Rafael Escandón, Jacqueline H. Lee, Michael M. Chen, Tatyana Treshkur, Irakli Megreladze, Scott M. Wasserman, Paul Eisenberg, Fady I. Malik, Andrew A. Wolff, Tamaz Shaburishvili

Omecamtiv mecarbil is a novel, direct cardiac myosin activator that increases cardiac contractility, and it may become an important therapy for heart failure patients with systolic dysfunction. In this double-blind, randomized, placebo-controlled study, omecamtiv mecarbil was well tolerated and did not seem to increase the likelihood of myocardial ischemia during exercise in patients with ischemic cardiomyopathy and angina.

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**Effects of Left Ventricular Assist Device Support on Biomarkers of Cardiovascular Stress, Fibrosis, Fluid Homeostasis, Inflammation, and Renal Injury** CME

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Tariq Ahmad, Teresa Wang, Emily C. O'Brien, Marc D. Samsky, John A. Pura, Yuliya Lokhnygina, Joseph G. Rogers, Adrian F. Hernandez, Damian Craig, Dawn E. Bowles, Carmelo A. Milano, Svati H. Shah, James L. Januzzi, G. Michael Felker, Chetan B. Patel

Left ventricular assist device (LVAD) therapy mechanically unloads the failing heart and may result in reversal of certain aspects of the end-stage heart failure phenotype. However, serial changes in biomarkers of myocardial stress, fibrosis, inflammation, fluid homeostasis, and renal injury in this setting are unknown. This study measured plasma levels of amino-terminal pro B type natriuretic peptide (NT-proBNP), galectin-3, ST2, copeptin, growth differentiation factor (GDF)-15, C-reactive protein (CRP), and neutrophil gelatinase-associated lipocalin (NGAL) from 37 individuals prior to continuous flow LVAD implantation and a median of 136 (interquartile range: 94 to 180 days) days after implantation. Our primary finding was that although heart failure biomarkers decreased substantially with long-term LVAD use, they each remained significantly elevated. This suggests the need for further investigations to evaluate whether this continued molecular dysfunction might be modifiable further. Our findings imply that more targeted therapeutic interventions after LVAD placement may be required to increase rates of myocardial recovery.

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