Background

- Heart failure with reduced ejection fraction (HFrEF) is a progressive disease that is the leading cause of hospitalizations and ultimately death.
- Close to 6 million adults in the United States have heart failure, and ~50% die within 5 years of diagnosis.
- Five factors demarcate the clinical course of heart failure: class II–IV symptoms, New York Heart Association class, clinical status, and left ventricular ejection fraction.
- Current therapies aim to improve exercise capacity by increasing coronary blood flow and directly activating the enzymatic domain of the cardiac myosin heavy activator that increases cardiac contractility by selectively and independently force generators, independent of calcium concentration.
- The presence of afferent fibers on exercise capacity in patients with HFrEF.
- A new class of medications for chronic HFrEF aims to directly improve myocardial contractility, as there is a critical need for agents that improve cardiac performance with a favorable safety profile.
- Omecamtiv mecarbil is a novel small molecule classified as a cardiac myosin activator that increases cardiac contractility by selectively and directly activating the enzymatic domain of the cardiac myosin heavy activator, thus producing state with a higher number of myosin molecules able to bind actin and generate force when systole starts.

Key Inclusion Criteria

- Male or female, ≥ 18 years of age
- History of chronic HF, defined as requiring continuous treatment with medications for HF for ≥ 3 months within the previous 6 months
- New York Heart Association class ≥ II
- Overall ambulatory status of patients with HFrEF receiving standard of care (SoC)

Key Exclusion Criteria

- Use of canes for stability while ambulating is acceptable if the subject is deemed capable of device-assisted mobility.
- Participants with persistent atrial fibrillation and no history of conversion to sinus rhythm within the previous 6 months, direct-current (DC) cardioversion, or episodes of decompensated HF that require assistance to walk or use of mobility assistive devices such as motorized devices, wheelchairs, or scooters.
- Participants with persistent atrial fibrillation and no history of conversion to sinus rhythm within the previous 6 months, direct-current (DC) cardioversion, or episodes of decompensated HF that require assistance to walk or use of mobility assistive devices such as motorized devices, wheelchairs, or scooters.

Study Design

- METEORIC-HF is a Phase 3, randomized, placebo-controlled, double-blind, parallel group, multinational, multicenter study for oral treatment in patients with HFrEF.
- The study aims to enroll 2370 patients in 30 clinical sites across nine countries in North America and Europe for 20 weeks of treatment with follow-up at Week 24, providing 90% power to detect a change in peak VO2 with a two-sided type I error of 0.05.
- Randomization will be stratified based on the RER on the baseline CPT.

Study Participants

- 75% of patients will be categorized as HFrEF receiving standard of care (SoC), standard of care; W, week.

Trial Overview

- Placebo + SoC requires assistance to walk or use of mobility assistive devices such as motorized devices, wheelchairs, or scooters.
- Both treatment arms are in conjunction with SoC treatment for HF.
- Invasive procedures will be administered only if used, or restricted and conditions, and must be swallowed white.
- The study is being conducted by Cytokinetics, Inc. with funding and strategic support from Servier.

Disclosures

- Questions related to the study can be directed to Andrew LeGrice. Cytokinetics, Inc. and Servier have a financial relationship by virtue of their collaborative development of omecamtiv mecarbil.
- Andrew LeGrice, PhD, has received research support from Applied Therapeutics, AstraZeneca, Cyclerion, Cytokinetics, EBR Systems, Medtronic, Merck, Novartis, scPharma, and Windtree Biotechnology Inc.
- Edward R. Packer, MD, has received research support from Abbott, AstraZeneca, Bayer, Boehringer Ingelheim, BMS, Medtronic, Servier, and Vifor; has received research funding and consulting fees from Amgen and Cytokinetics, with funding and strategic support from Servier.

Additional Information

- This study is being conducted by Cytokinetics, Inc. with funding and strategic support from Servier.
- Additional information can be found at www.clinicaltrials.gov (NCT02717186), NCT02666474, NCT02616586, NCT02616759, NCT02616989, and NCT02617016.