

ABOUT

HEART FAILURE



Heart failure is a chronic, progressive condition that develops when the pumping action of the heart is inadequate to meet the body's needs for blood and oxygen. The leading causes of heart failure are diseases that damage the heart muscle function, including coronary heart disease and high blood pressure.

The normal, healthy heart is a muscular organ that pumps blood continuously throughout the body. The right side of the heart pumps oxygen-depleted blood from the veins into the lungs. The left side of the heart pumps oxygen-rich blood from the lungs out through the arteries to the rest of the body. When the heart muscle contracts (called systole) blood is pumped out of the heart, and when the heart muscle relaxes (called diastole) blood enters the heart.

Heart failure can affect the right side of the heart only, or both sides of the heart. Right-side heart failure occurs when the heart can't pump enough blood to the lungs, resulting in fluid buildup in the feet, ankles, legs, liver, abdomen, and the veins in the neck. Left-side heart failure occurs when the heart can't pump enough oxygen-rich blood to the rest of the body, and as a consequence, blood may back up into the lungs. Both left and right-sided heart failure may occur together and can lead to shortness of breath and fatigue.¹

PREVALENCE OF HEART FAILURE

Almost 6 million people in the United States have heart failure¹, resulting in one million hospitalizations and almost 300,000 deaths each year². For people over 65, the incidence of heart failure approaches 10 per 1000.² The annual cost of heart failure to the U.S. health care system is estimated to be more than \$30 billion, which includes the cost of health care services, medications to treat heart failure and missed days of work.²

Heart failure is more common in:¹

- **People who are 65 years old or older.** Heart failure is the most common reason for hospital admittance among Medicare patients.
- **African Americans.** African Americans are more likely than people of other races to have heart failure and are more likely to have symptoms at a younger age, have more hospital visits due to heart failure, and eventually die from heart failure.

- **People who are overweight.** Being overweight increases your risk of heart disease and type 2 diabetes, which can lead to heart failure.
- **People who have had a heart attack.** Heart attacks can cause damage that weakens the heart.

SYMPTOMS OF HEART FAILURE

The most common symptoms of heart failure are shortness of breath, swelling in the ankles, feet, legs, abdomen, and veins in the neck, fatigue and persistent cough or wheezing.¹

All of these symptoms are the result of a build-up of fluid in the body or the poor delivery of blood to the tissues. As the heart muscle grows weaker, symptoms may get worse. In severe cases, patients may have shortness of breath even while lying flat. The build-up of fluid associated with worsening heart failure can also cause weight gain, frequent urination, and a cough that is aggravated at night and when lying down.¹

DIAGNOSING HEART FAILURE

Heart failure is diagnosed based on medical and family histories, a physical examination and test results. No single test can diagnose heart failure, so a physician may recommend one or more of the following tests and refer the patient to a cardiologist: electrocardiogram, chest X-ray, BNP blood test, echocardiography, Doppler ultrasound, Holter monitor, nuclear heart scan, cardiac catheterization, coronary angiography, stress test, cardiac MRI or thyroid function tests.¹

In order to determine the best course of therapy, physicians often assess the stage of heart failure according to the New York Heart Association (NYHA) Functional Classifications. This system relates symptoms to everyday activities and the patient's quality of life.³

NYHA FUNCTIONAL CLASSIFICATION⁴

CLASS	SYMPTOMS
Class I (Mild)	No limitation of physical activity. Ordinary physical activity does not cause undue fatigue, palpitation, or dyspnea (shortness of breath).
Class II (Mild)	Slight limitation of physical activity. Comfortable at rest, but ordinary physical activity results in fatigue, palpitation, or dyspnea.
Class III (Moderate)	Marked limitation of physical activity. Comfortable at rest, but less than ordinary activity causes fatigue, palpitation, or dyspnea.
Class IV (Severe)	Unable to carry out any physical activity without discomfort. Symptoms of cardiac insufficiency at rest. If any physical activity is undertaken, discomfort is increased.

PROGRESSION OF HEART FAILURE

Initially, the heart compensates by:

- Enlarging. When the heart enlarges, it can contract less vigorously and still pump the same amount of blood.
- Developing more muscle mass. The increase in muscle mass occurs because the contracting cells of the heart get bigger to allow the heart chamber to enlarge.
- Increasing heart rate. The pump works more often to help increase the heart's output.⁴

These temporary measures initially mask the problem. However, heart failure often worsens until these compensation mechanisms cannot address the diminished contractile function of the heart, and the patient may experience symptoms that prompt medical consultation. This explains why some people may not be aware of their condition until years after the heart muscle begins its decline.⁴



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References

1. National Heart, Lung and Blood Institute. Heart Failure. Available at: <https://www.nhlbi.nih.gov/health-topics/heart-failure>. Accessed December 6, 2018.
2. Mozaffarian D, et al Heart disease and stroke statistics-2016 update a report from the American Heart Association. *Circulation*. 2016.
3. American Heart Association. Classes of Heart Failure. Last revised May 31, 2017. <https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure/classes-of-heart-failure>. Accessed December 6, 2018.
4. American Heart Association. What is Heart Failure? Last revised May 31, 2017. <https://www.heart.org/en/health-topics/heart-failure/what-is-heart-failure>. Accessed December 6, 2018.
5. Krumholz, HM, et al. Patterns of hospital performance in acute myocardial infarction and heart failure 30-day mortality and readmission. *Circulation: Cardiovascular Quality and Outcomes*. 2009; 2(5), 407-413.

TREATING HEART FAILURE

The goals for heart failure treatment include treating the underlying cause such as coronary heart disease, high blood pressure or diabetes, reducing symptoms, preventing the heart failure from worsening and improving quality of life.¹

Currently, there is no cure to halt or reverse the progression of heart failure. However, treatments usually include lifestyle changes, medicines and ongoing care. If the heart failure is at a severe stage, medical procedures or surgery may be necessary. Heart failure patients often require multiple medications to treat different symptoms or contributing factors. Common medications to treat heart failure are diuretics, beta blockers, ACE inhibitors, aldosterone antagonists, digoxin, angiotensin receptor blockers and isosorbide dinitrate/hydralazine hydrochloride.¹

Despite currently available therapies, readmission rates for heart failure patients remain high. It is estimated that approximately 25% of patients admitted to the hospital for heart failure will be readmitted within 30 days.⁵ One in nine deaths has heart failure mentioned on the death certificate, and approximately 50% of people diagnosed with heart failure will die within 5 years.¹ The high morbidity and mortality in the setting of current therapies points to the need for novel therapeutics that offer further reductions in morbidity and mortality.

ABOUT OMECANTIV MECARBIL

Cytokinetics is developing *omecantiv mecarbil*, a novel, selective cardiac myosin activator for the potential treatment of heart failure with reduced ejection fraction (HFrEF) under a collaboration with Amgen, with funding and strategic support from Servier. *Omecantiv mecarbil* is designed to increase the duration of cardiac muscle contractility and improve cardiac muscle performance, potentially helping patients preserve cardiac function and quality of life, avoid hospitalizations, and decrease the risk of mortality due to heart failure.

Omecantiv mecarbil has been studied across eleven Phase 1 clinical trials, which enrolled over 300 healthy volunteers. More than 1,400 people with heart failure have been enrolled in seven Phase 2 clinical trials. *Omecantiv mecarbil* is the subject of a comprehensive Phase 3 clinical trials program comprised of GALACTIC-HF, a large, global cardiovascular outcomes study, and METEORIC-HF, designed to evaluate the effect of *omecantiv mecarbil* on exercise capacity.

Forward Looking Statements

This fact sheet contains forward-looking statements for purposes of the Private Securities Litigation Reform Act of 1995 (the "Act"). Cytokinetics disclaims any intent or obligation to update these forward-looking statements, and claims the protection of the Act's Safe Harbor for forward-looking statements. Examples of such statements include, but are not limited to, statements relating to Cytokinetics' and its partners' research and development activities, including the significance and utility of COSMIC-HF clinical trial results and the potential progression of *omecantiv mecarbil* to Phase 3 development; and the properties and potential benefits of Cytokinetics' drug candidates. Such statements are based on management's current expectations, but actual results may differ materially due to various risks and uncertainties, including, but not limited to: Cytokinetics' need for additional funding and such additional funding may not be available on acceptable terms, if at all; Amgen's decisions with respect to the design, initiation, conduct, timing and continuation of development activities for *omecantiv mecarbil*; potential difficulties or delays in the development, testing, regulatory approvals for trial commencement, progression or product sale or manufacturing, or production of Cytokinetics' drug candidates that could slow or prevent clinical development or product approval, including risks that current and past results of clinical trials or preclinical studies may not be indicative of future clinical trial results; patient enrollment for or conduct of clinical trials may be difficult or delayed; Cytokinetics' drug candidates may have adverse side effects or inadequate therapeutic efficacy; the U.S. Food and Drug Administration or foreign regulatory agencies may delay or limit Cytokinetics' or its partners' ability to conduct clinical trials, and Cytokinetics may be unable to obtain or maintain patent or trade secret protection for its intellectual property; Cytokinetics may incur unanticipated research and development and other costs or be unable to obtain additional financing necessary to conduct development of its products; standards of care may change, rendering Cytokinetics' drug candidates obsolete; and competitive products or alternative therapies may be developed by others for the treatment of indications Cytokinetics' drug candidates and potential drug candidates may target; and risks and uncertainties relating to the timing and receipt of payments from its partners, including milestones and royalties on future potential product sales under Cytokinetics' collaboration agreements with such partners. For further information regarding these and other risks related to Cytokinetics' business, investors should consult Cytokinetics' filings with the Securities and Exchange Commission. Forward-looking statements are not guarantees of future performance, and our actual results may differ materially from the forward-looking statements contained in this fact sheet. Any forward-looking statements that we make in this document speak only as of the date of this fact sheet.