New Medications in the Treatment of Acute Decompensated Heart Failure

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Abstract

Acute decompensated heart failure is a sudden worsening of heart failure symptoms, typically resulting in peripheral edema and dyspnea as a result of pulmonary congestion. Acute decompensated heart failure is responsible for over 1 million hospitalizations every year. Current pharmacologic therapy is limited in its options. Despite an improved survival rate, statistic still suggests that about 50% of patients die within 5 years of diagnosis. New pharmacologic agents aim to improve efficacy by targeting previously unexplored physiological pathways.

Keywords

investigational drugs, formulary management/P&T, cardiovascular, drug information

Epidemiology

The lifetime risk for developing heart failure in a patient over 40 years of age is 20% with the risk increasing as age increases.¹ Almost 5 million people in the United States have heart failure, with a higher prevalence in men than women.² Heart failure is responsible for over 1 million hospitalizations annually, with 80% of these hospitalizations caused by acute decompensation.³ As of 2013, the readmission rate of patients hospitalized with acute decompensated heart failure was 25%.¹ The total annual cost for heart failure was \$30.7 billion in 2012 and is predicted to increase to \$69.7 billion by 2030.²

Current Treatment

Current pharmacologic therapy for acute decompensated heart failure involves correcting volume status using loop diuretics and decreasing increased filling pressures and afterload with vasodilators. Oxygen therapy is added to treat respiratory distress, respiratory acidosis, and/or hypoxia.¹ In addition, maintenance medications are typically reviewed and adjusted. Continuation or adjustment of maintenance medications such as an angiotensin-converting enzyme (ACE) inhibitor, an angiotensin receptor blocker (ARB), or an angiotensin receptor blocker neprilysin inhibitor (ARNI), plus a beta blocker, mineralocorticoid receptor antagonist, and a loop diuretic depends on the patient's hemodynamic and renal status.¹

Despite these medications showing symptomatic improvement and prolonging survival, the patient's health-related quality of life is not always improved by medications alone.²

A worsening of renal function in patients with acute decompensated heart failure has been seen in 25% to 33% of patients. Patients can progress to diuretic resistance and require the use of ultrafiltration for fluid removal.⁴ In addition, the 5-year mortality rate for patients with heart failure remains high. About 50% of patients die within 5 years of diagnosis.²

New Treatment Options

Several new medications are in development for acute decompensated heart failure, with a few showing promising results (Table 1). RT-100 is a gene therapy that increases expression of adenylyl cyclase type 6 to improve ejection fraction. The drug has demonstrated promising results in a phase II trial.⁵ RT-100 is unique, in that a single dose was able to improve ejection fraction at 12 weeks by about 8.2 ejection fraction units.⁵ A 12-month, phase III trial is planned to measure the effect of a single intracoronary injection of RT-100 on cardiovascular events. Urocortin analogues, such as stresscopin, act on corticotropin-releasing hormone receptors, which results in increased cardiac output, vasodilation, and reduces peripheral vascular resistance.⁶ Serelaxin is a peptide hormone stimulant that has shown mixed results in its phase III trials but could be beneficial in managing

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Table 1. New Treatment Options.

Generic name	Sponsor	Drug class	Comments
Ad5.hAC6 (RT-100)	Renova Therapeutics	Gene therapy	In a 56-patient, phase II trial, a single dose of RT-100 increased left ventricular peak and ejection fraction compared with placebo at 4 weeks. Ejection fraction remained elevated after 12 weeks in patients with nonischemic HF, but not ischemic HF. There was no difference in treadmill walking times between RT-100 and placebo. ⁵
Omecamtiv mecarbil	Amgen, Cytokinetics	Myosin activator	In a 606 ADHF patient, phase II trial, an intravenous infusion of omecamtiv mecarbil did not improve dyspnea compared with placebo, but a subgroup analysis suggested a possible decrease with the highest dose. ⁷ Omecamtiv mecarbil is also being developed as an oral treatment for stable HF. A recent 448-patient, phase II trial suggested the drug improved cardiac function and ventricular remodeling. ⁸
Serelaxin	Novartis	Relaxin	In a 1161 patient, phase III trial, serelaxin improved dyspnea after the first 24 hours through day 5 and decreased CV death and all-cause death at 6 months. ⁹ Novartis announced that in a 6600-patient, phase III trial, serelaxin was no different than placebo in preventing further decompensation over the first 5 days or in reducing CV death at 6-months.
Stresscopin (RT-400)	Renova Therapeutics	Urocortin hormone	In a 62-patient, phase II trial, stresscopin increased the cardiac index and decreased systemic vascular resistance compared with placebo in stable HF patients with a left ventricular ejection fraction of 35% or less. ¹⁰
Ularitide	Cardiorentis AG	Natriuretic peptide	In a phase III, 2157 ADHF patient trial, ularitide did not improve HF symptoms during the first 48 hours or decrease CV death at 15 months compared with placebo. ¹¹

Note. Information adapted from the Prescribe Right Pharmaceutical Pipeline Tracker database.¹² ADHF = acute decompensated heart failure; HF = heart failure; CV = cardiovascular.

dyspnea. Ularitide, a urodilatin analogue, is a vasodilator that has not shown a benefit for acute decompensated heart failure. Omecamtiv mecarbil is a cardiac myosin activator that increases stroke volume. While omecamtiv mecarbil has not shown a benefit in acute decompensated heart failure, the drug may have potential for chronic heart failure.

Authors' Note

Information is summarized from selected materials; additional information may be available from other sources. Due to the preapproval nature of the information, non-peer-reviewed data may be utilized. The information provided is meant to provide a way to assess the development status of a new drug and should not be used in making patient care decisions.

Declaration of Conflicting Interests

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