# Fluid management of Acute decompensated heart failure Subjects Treated with Reprieve Decongestion Management System (DMS) - FASTR Trial

Published: 19-03-2024
Last updated: 02-12-2024

The objective of this study is to prospectively compare decongestive therapy administered by the Reprieve DMS system to Optimal Diuretic Therapy (ODT) in the treatment of patients diagnosed with acute decompensated heart failure (ADHF). The main...

| | |
|---|---|
| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Heart failures |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON56708

**Source**
ToetsingOnline

**Brief title**
FASTR Trial

### Condition

- Heart failures

**Synonym**
Acute decompensated heart failure, heart failure

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Reprieve Cardiovascular, Inc.

**Source(s) of monetary or material Support:** Industry

## Intervention

**Keyword:** Congestive Heart Failure, Diuretics

## Outcome measures

### Primary outcome

The primary objective of this study is to compare Reprieve DMS to standard control therapy with respect to effective decongestion and acute kidney injury in ADHF patients.

The trial will employ co-primary endpoints, one for efficacy and one for safety. All study endpoints will be evaluated in two study cohorts (subjects with home dose of > 80 mg of furosemide equivalent and subjects with home dose of <80 mg of furosemide equivalent).

Primary efficacy endpoint is total urine sodium output at 24 hours post-treatment initiation.

Primary safety endpoint includes clinically significant acute kidney injury defined as KDIGO stage 2 or greater AKI [>= doubling of baseline serum creatinine or use of renal replacement therapy (RRT)], severe electrolyte abnormality (serum potassium <3.0 mEq/L, magnesium <1.3 mEq/L or sodium <135 mEq/L*), symptomatic hypotension or hypertensive emergency.

*For subjects enrolled with baseline sodium levels of <135 mEq/L, there needs to be drop of at least 5 mEq/L to be considered against primary safety endpoint.

### Secondary outcome

• Net fluid loss at end of randomized therapy.

• Time on IV loop diuretic Defined as the time from initiation of randomized therapy to last dose of IV loop diuretic administered for ADHF.

The assessment of all Device and Procedure related AEs and SAEs in the study population as determined by an Independent Clinical Events Committee (CEC), as outlined in the committee charter. It should be noted that episodes of hematuria associated with Foley catheter placement that can be adequately managed will not be included as a secondary safety endpoint, since this is an anticipated adverse event commonly associated with Foley placement.

## Study description

**Background summary**

This study will evaluate the safety, performance, and clinical utility of the Reprieve DMS device in comparison with *control* diuretic therapies. The Reprieve DMS ADHF study was developed based upon the initial conclusions drawn from the feasibility studies conducted outside the US (OUS).
The OUS feasibility studies provided the clinical experience to optimize the Reprieve DMS system algorithm to identify and efficiently deliver an individualized diuretic dose for each subject based upon their measured response. Using real time information from the minute-to-minute measurement of urine output, the system automatically identifies a target responsive diuretic dose by sequentially increasing the rate of diuretic infusion until the patient achieves a clinically significant rate of urine production or until a set limit of diuretic has been infused. The system then transitions to a continuous diuretic infusion rate based on a percentage of the amount of diuretic required to reach the target urine output rate. The subject also receives a personalized partial fluid/salt replacement of these urinary losses to ensure each subject has adequate intravascular volume and avoidance of activating renal sodium conserving pathways.

**Study objective**

The objective of this study is to prospectively compare decongestive therapy administered by the Reprieve DMS system to Optimal Diuretic Therapy (ODT) in

the treatment of patients diagnosed with acute decompensated heart failure (ADHF). The main objective is to determine if the Reprieve DMS can more efficiently decongest ADHF patients in comparison to Control Therapy.

**Study design**

A prospective, multicenter, randomized, controlled pilot trial (1:1) to compare the rate of decongestion for up to 72 hours with the Reprieve DMS compared to optimal diuretic therapy (ODT).

**Intervention**

DMS Therapy
a. DMS begins by administering IV furosemide to achieve the target urine rate of 525 ml/hr. using an exponentially increasing ramp dose until the target urine output rate is met or maximum IV furosemide dose (200 mg) is infused (*Dose Finding Phase*).
b. Once the target urine output rate is met, the IV furosemide infusion rate is reduced to an hourly infusion rate that is 20% of the total furosemide dose delivered during the Dose Finding Phase (minimum 4 mg/hr., maximum 40 mg/hr.) to maintain effective plasma concentration of furosemide and thus maintain the desired target urine output rate. (For example, if a total of 160 mg of furosemide was delivered during the Dose Finding Phase, the hourly infusion rate would be set to 32 mg/hr.).
c. The DMS provides a proportional saline replacement designed to maintain adequate intravascular volume and prevent activation of renal sodium retaining mechanisms. No saline is infused when the urine output rate is between 0 and 225 ml/hr. Urine output rate above this level triggers 100% IV saline replacement to match urine output between 225 ml/hr and 425 ml/hr. For urine output rates above 425 ml/hr to 1025 ml/hr., IV saline infusion is increased to add a 50% match of the urine output above 425 ml/hr up to 1025 ml/hr for a maximum infusion rate of 500 ml/hr. (Note: This saline infusion is adjusted based on the lab urine sodium entered into the system as described below).
d. Every time the urine collection bag is emptied, a sample should be sent to the laboratory for determination of sodium concentration. When the result is returned from the lab, the value will be entered into the DMS by a clinical staff member. The DMS will then calculate an *adjusted urine output rate*, and the treatment algorithm will use this rate to determine the saline infusion rate optimized for the patient*s urine sodium level. This process is repeated each time the urine bag is emptied.
e. If the urine output rate meets the criteria for sustained very high urine output rate, the DMS down-titrates the diuretic dose automatically.
f. If the patient*s urine output rate drops below the desired urine output rate for a sustained period, the DMS provides the investigator with the option to resume the diuretic IV furosemide Dose Finding Phase provided the previous Dose Finding Phase did not reach the maximum dose of 200 mg.

g. If the patient*s urine output rate remains low, the DMS provides the investigator with the option of administering additional adjunctive therapies (i.e., thiazide/thiazide like diuretics).

Note: Subjects receiving high dose oral loop diuretic at home (> 240 mg furosemide, 3 mg bumetanide, or 60 mg torsemide per 24 hours) must be administered an oral long half-life thiazide/thiazide like diuretic (10mg metolazone, 50mg chlorthalidone, 100mg HCTZ or equivalent) 2 to 12 hours prior to initiating Reprieve therapy.

Optimal Diuretic Therapy (ODT)
Consider best practices of optimal diuretic dosing such as those demonstrated in recent randomized trials (DOSE31, ADVOR32, CLOROTIC33). The Reprieve DMS can infuse a maximum dose of 1,120 mg/day of furosemide. It is recommended that subjects randomized to ODT should also not exceed maximum dose of 1,120 mg/day of furosemide.
Note: Consideration can be given to up-front use of oral long half- thiazide diuretic with appropriate adjustment of IV loop diuretic dose in patients receiving high dose loop diuretic prior to enrollment (> 240 mg furosemide, 3 mg bumetanide, or 60 mg torsemide per 24 hours).
Reprieve DMS, ODT Groups
As standard background therapy, all patients must receive 2 g daily sodium diet and a 2 L daily oral fluid intake restriction, in addition to strict fluid input and output recording and daily weights.

**Study burden and risks**

The risks associated with the use of peripheral IV catheter and Foley catheter with the Reprieve Decongestion Management System are expected to be similar to other procedure utilizing these catheters. There are also risks associated with over-hydration and under-hydration along with the risks associated with loop diuretic therapy for ADHF patients.
*Over-hydration* has a range of potential causes, including insufficient diuretic dosing, excess saline infusion, and hypotension/low intravascular volume. *Under-hydration* also has a range of potential causes, including excess diuretic dosing, insufficient saline infusion, and a rapid increase in diuresis. The risks of each are identified in more detail below:
Risks of under-hydration:
• Low urine production
• Symptomatic hypovolemia/hypotension
• Electrolytic Imbalance including hyponatremia and hypokalemia
• Abnormal laboratory values
• Dizziness and headaches
• Muscle cramps
• Ototoxicity
• Renal compromise/acute kidney injury
• Arrhythmia

Risk of over-hydration:
• Increased urination
• Symptomatic hypervolemia/hypertension
• Worsening pulmonary function
• Electrolytic imbalance
• Renal compromise
• Arrhythmia
General risks associated with Reprieve DMS:
• Allergic reaction/hypersensitivity to medication, or device materials
• Complications at IV/vascular catheter insertion sites, e.g., bruising, hematoma, pain, bleeding
• Device malfunction or breakage
• Extravasation/Infiltration at IV/vascular catheter insertion sites
• Infection (IV/vascular catheter insertion site or Foley catheter) or sepsis
• Injury or trauma to the bladder or urethra
• Hemorrhage or bleeding
• Embolism
• Fever
• Hematuria
• Hemodynamic compromise
• Myocardial infarction
• Pain/discomfort
• Pulmonary edema
• Worsening heart failure or low cardiac output
• Anemia
• Death
General risks associated with Study Participation:
• Increased risk of infection or blood loss due to increased blood draws

Complications may occur at any time during the procedure, post-procedure, or follow-up period. The above risks may require intervention to address the condition. There may also be other risks that are unforeseen at this time.

Blood tests can hurt or cause bruising. We take 40 ml of blood per visit. In total, an estimated 440 ml of blood will be taken from you during the entire study. This amount does not cause problems in adults.

Urine samples are taken for laboratory testing.
Hearing tests are administered by the patient using headphones and an iPad. Each hearing test takes approximately 2 minutes.

# Contacts

**Public**

Reprieve Cardiovascular, Inc.

Fortune Blvd 459
Milford, MA 01757
US
**Scientific**
Reprieve Cardiovascular, Inc.

Fortune Blvd 459
Milford, MA 01757
US

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

1. Hospitalized with a diagnosis of heart failure as defined by the presence of at least 1 symptom (dyspnea, orthopnea, or edema/swelling) AND 1 sign (peripheral edema, ascites, jugular venous distension).
2. >=10 lb (4.5 kg) above dry weight either by historical weights or as estimated by health care provider.
3. Prior use of outpatient oral loop diuretics within 30 days prior to admission.
4. Patients >= 18 years of age able to provide informed consent (or deferred consent) and comply with study procedures.

## Exclusion criteria

1. Inability to place Foley catheter or IV catheter or other urologic issues that would predispose the patient to a high rate of urogenital trauma or infection with catheter placement.

2. Hemodynamic instability as defined by any of the following: systolic blood pressure <90 mmHg, use of vasopressors, use of IV inotropes to treat hypotension (systolic blood pressure <90 mm Hg) or suspected/confirmed low cardiac output/shock, mechanical circulatory support, uncontrolled arrhythmias, active severe bleeding, or confirmed or suspected cardiogenic shock. Note: In the absence of the above conditions, use of inotropes to augment diuresis is permitted.
3. Dyspnea due primarily to non-cardiac causes (e.g., severe chronic obstructive pulmonary disease or pneumonia).
4. Acute infection with evidence of systemic involvement (e.g., clinically suspected infection with fever or elevated serum white blood cell count).
5. Estimated glomerular filtration rate (eGFR) < 20 ml/min/1.73m2 calculated using the MDRD equation or current use of renal replacement therapy (RRT).
6. Significant left ventricular outflow obstruction, uncorrected complex congenital heart disease, known severe stenotic valvular disease, infiltrative or constrictive cardiomyopathy, acute myocarditis, type 1 acute myocardial infarction requiring treatment (within previous week), or any other pathology that, in the opinion of the investigator, would make aggressive diuresis poorly tolerated.
7. Inability to follow instructions or comply with follow-up procedures.
8. Other concomitant disease or condition that investigator deems unsuitable for the study, including drug or alcohol abuse or psychiatric, behavioral or cognitive disorders, sufficient to interfere with the patient*s ability to understand and comply with the study instructions or follow-up procedures.
9. Severe electrolyte abnormalities (e.g., serum potassium <3.0 mEq/L, magnesium <1.3 mEq/L or sodium <125 mEq/l). Note: These are based on baseline/screening labs. Subjects whose electrolyte levels are repleted cannot be reassessed for inclusion in the trial.
10. Presence of active COVID-19 infection.
11. Enrollment in another interventional trial during the trial participation.
12. Inability to return for follow-up study visits.
13. Life expectancy less than 3 months.
14. Women who are pregnant. Pregnancy must be ruled out and the patient must make every effort not to become pregnant.

# Study design

## Design

| | |
|---|---|
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |

| | |
|---|---|
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Treatment |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 17-05-2024 |
| Enrollment: | 10 |
| Type: | Actual |

### Medical products/devices used

| | |
|---|---|
| Generic name: | Reprieve DMS |
| Registration: | No |

## Ethics review

Approved WMO

| | |
|---|---|
| Date: | 19-03-2024 |
| Application type: | First submission |
| Review commission: | METC Universitair Medisch Centrum Groningen (Groningen) |

## Study registrations

### Followed up by the following (possibly more current) registration

No registrations found.

### Other (possibly less up-to-date) registrations in this register

No registrations found.

## In other registers

| Register | ID |
| --- | --- |
| ClinicalTrials.gov | NCT05174312 |
| CCMO | NL84955.000.23 |