Combining 3 Diuretic Drugs for Heart Failure Patients

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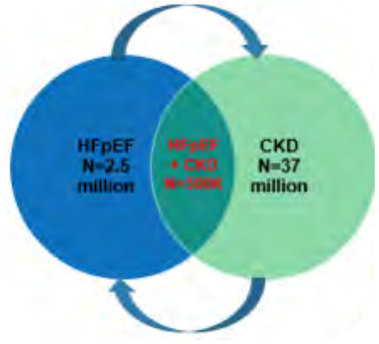
SUMMARY STATEMENT

Testing the efficacy and safety of combining low doses of three drugs – bumetanide, eplerenone and dapagliflozin – into a single pill in a pilot trial of 60 heart failure patients at high risk of hospitalization

DISEASE/CONDITION

Heart failure with preserved ejection fraction (HFpEF) and chronic kidney disease (CKD) are conditions that commonly coexist, and they place a major burden on patients and the healthcare system. Because HFpEF/CKD co-existence is high, this is a major public health concern.

Patients with HFpEF and CKD experience significant morbidity and mortality and have a poor health-related quality of life that is worse than most metastatic cancer diagnoses. Affected individuals are at significantly increased risks of hospitalizations and mortality.



CURRENT TREATMENT

Currently, there are no FDA approved treatment options for HFpEF.

Treatment is limited to the management of congestion through diuretics, and this approach has several limitations:

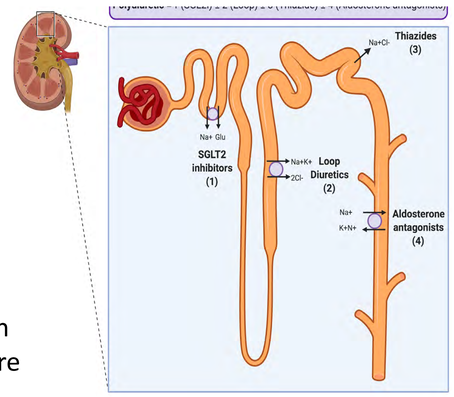
- Diuretic resistance
- Worsening renal function
- Inadequate decongestion leading to poor quality of life and recurrent hospitalizations.

PROPOSED TREATMENT

Utilizing a novel polydiuretic therapy in patients with heart failure with preserved ejection fraction (HFpEF) and chronic kidney disease (CKD) by repurposing three FDA-approved diuretic medications into a single combination pill.

The key driver for hospitalization of patients with HFpEF and CKD is congestion, the accumulation of extra fluid. Low-dose polydiuretic therapy is a promising strategy to more safely and easily improve decongestion, symptoms, and renal and cardiovascular outcomes with comorbid HFpEF and CKD.

Low-dose combination therapy has already been demonstrated to be safe and effective in the prevention of atherosclerotic cardiovascular disease. Bumetanide is currently FDA-approved to treat heart failure, liver disease, and kidney disease. Dapagliflozin is approved to treat diabetes and heart failure, and eplerenone is approved for high blood pressure and heart failure.



These medications are each currently recommended for HFpEF/CKD by clinical practice guidelines but have not been studied in this unique combination that may safely and more efficaciously provide symptom relief and decongestion. Combining these drugs into one pill may also improve adherence and lower adverse renal outcomes.

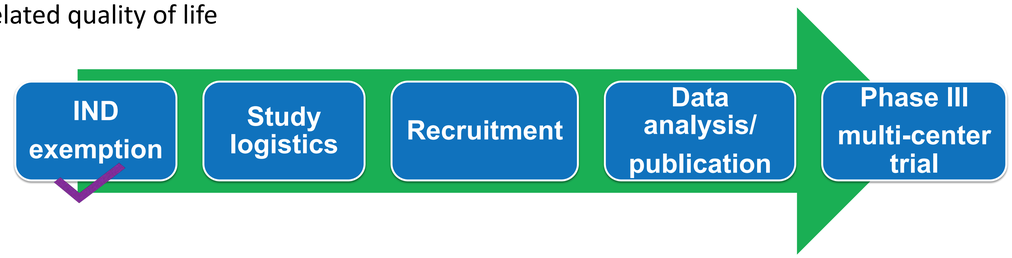
PROJECT

The proposed proof-of-concept randomized, double-blinded trial will compare the effectiveness of low-dose triple polydiuretic therapy compared to placebo in reducing congestion and improving fluid balance.

The trial will enroll approximately 5 participants per month for a total of 30 patients to undergo the low-dose triple polydiuretic therapy, and another 30 patients to undergo placebo/standard-of-care.

Specific Aims

- To observe the efficacy and safety of the treatment
- To test whether the treatment will lead to stable or improved renal function and better health-related quality of life



Results could provide the basis for a larger, multi-center Phase II/III trial examining low-dose triple polydiuretic therapy in patients with HFpEF and CKD with the long-term goal of changing current diuretic paradigms to improve quality and length of life for these patients.

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