

KOL event with Dr. Jeffrey Testani — Friday, December 11th, 2020

The challenge of diuretic resistance in the management of heart failure patients and the potential for alfapump DSR therapy



KEY OPINION LEADER - DR. JEFFREY TESTANI

Associate Professor of Medicine and Director of Heart Failure Research at Yale University School of Medicine.

KEY LEARNINGS, PRESENTED BY DR. TESTANI

Fluid overload is the primary cause of heart failure symptoms, hospitalisation, and quite possibly mortality

The majority of patients showing up to the hospital have too much fluid. Removal of fluid seems to be increasingly important to keep patients alive. Loop diuretics are the standard treatment for these patients but they have dose dependent adverse effects and patients rapidly develop resistance.

“Congestion is really a big part of the disease... and not just a nuisance symptom”

So why is there so much diuretic resistance?

The problem with diuretic resistance is that the kidneys are doing exactly what they were designed for, which is to keep the right amount of sodium and fluid in the body. In most patients, diuretics block sodium reabsorption locally but sodium is pumped back by the kidney downstream because it thinks the body is

dehydrated. All novel therapies have failed because they are too distal in the sodium avidity pathway and the kidneys outsmart them.

“We talk about fluid overload, but it’s really all about the sodium.”

Targeting sodium removal rather than fluid is key

The peritoneum is an alternative membrane that can be used for fluid and solute removal, just like in peritoneal dialysis. With Direct Sodium Removal or DSR, a sodium-free peritoneal solution is used to effectively remove the sodium. The alfapump DSR combines this DSR concept with the alfapump to use it in a chronic multi-dose setting.

“Diuretic resistance is nearly ubiquitous.”

RED DESERT INTERIM RESULTS, PRESENTED BY DR. TESTANI

KEY OBJECTIVE

Demonstrate if repeated dose alfapump DSR therapy can replace diuretics and maintain euvolemia in heart failure patients



MAIN FINDINGS FROM FIRST 5 PATIENTS WHO HAVE COMPLETED THE STUDY

- ✓ Repeated dose alfapump DSR is well tolerated
- ✓ Majority of patients lost weight and had reduction in natriuretic peptide levels
- ✓ Loop diuretic response actually normalized in the majority of patients by the end of the study
- ✓ Improved global sodium avidity of the patient
- Despite volume loss all signs point toward improved renal function which is the opposite of what we see with diuretics
- Most patients were not requiring full dose DSR by the end of therapy
- Improvement in diuretic response durable for months in many patients

Overall these preliminary findings provide optimism that alfapump DSR therapy is fundamentally improving the cardio-renal substrate of the patient.

“Use of alfapump DSR really reversed the diuretic resistance essentially to normal levels, giving a lot of optimism that this therapy could be a real game changer in the space.”

“Most patients were not requiring full dose DSR by end of therapy as the kidney had woken up and was doing a much better job of removing sodium on its own.”



Replay available on our [website](#)