2019 euro PCR

Volume Management Through Direct Sodium Removal (DSR)

Ian Crosbie, CEO

Potential Conflicts of Interest

Speaker's name : Ian Crosbie

☑ I have the following potential conflicts of interest to declare:

CEO : Sequana Medical

Stock shareholder: Sequana Medical

Fluid Overload in Heart Failure

- Key clinical consequence of heart failure[1]
- One million HF hospitalisations / year in US[1]
  - 90% for fluid overload[1]
- ¾ admitted to emergency room
  - Average length of stay 5 – 6 days[2]
- 24% readmitted within 30 days and 50% within 6 months[3]
- $13 Billion annual cost of CHF related hospitalisations in US[2]

1: Costanzo et al., J. Am. Coll., 2007
2 Kilgore et al. (2017)
3: Ross et al. (2010)

Heart Failure: Can we do better than diuretics?

- Loop diuretics are standard therapy for prevention and treatment
  - Resistance is very common[1]
  - Directly cause neuro-hormonal activation, worsen renal function, and are associated with adverse outcomes[2]
- Long list of failed cardio-renal therapeutics has accumulated over the last decade
- Sodium and fluid removal by non-renal routes is an attractive alternative
  - Veno-Venous ultrafiltration has been explored
  - Low levels of interest in using peritoneal dialysis

1: Singh et al, J Card Fail 2014
2: Ellison et al, Cardiology 2001

Direct Sodium Removal (DSR)

- With a zero sodium solution, we should be able to get much more sodium removal with less volume than standard peritoneal dialysis fluid
- Lower volume of fluid allows for alternatives to the standard peritoneal dialysis catheter to get fluid in and out of peritoneum

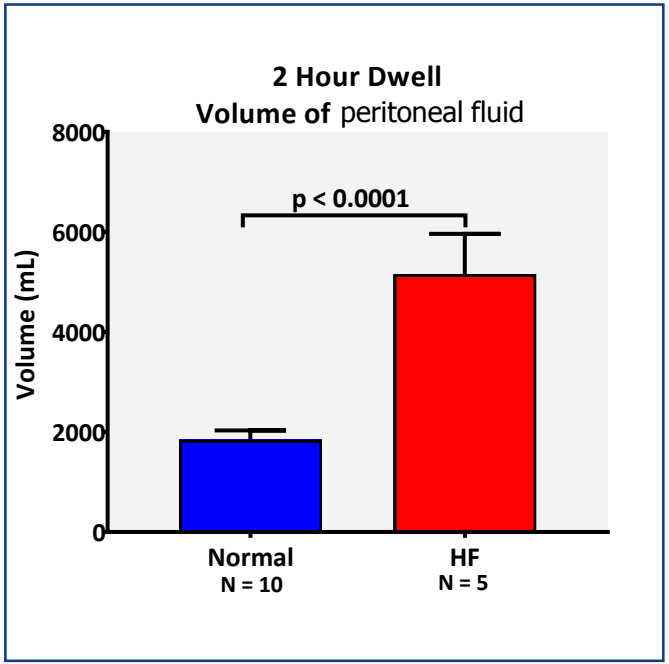
DSR – Pig proof of concept study

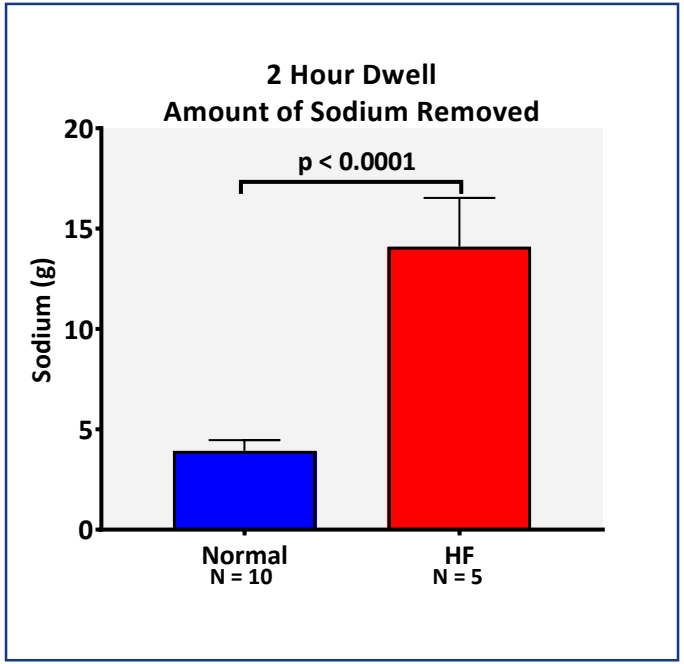
Yale

- Sodium-Free Infusate: 1 liter of 10% dextrose in water (“D10”)
- Dwell period: 2 hours

- 15 anesthetized 80kg pigs with peritoneal dialysis catheters implanted
  - 10 healthy pigs
  - 5 heart failure pigs
    - Experimental acute warm / wet heart failure; created by cardiac tamponade induced via pressurization of the pericardium

DSR – Pig proof of concept study





Yale

Plus no significant serum electrolyte impact

Presented HFSA 2018; Dr. Jeff Testani

DSR - first in human proof of concept

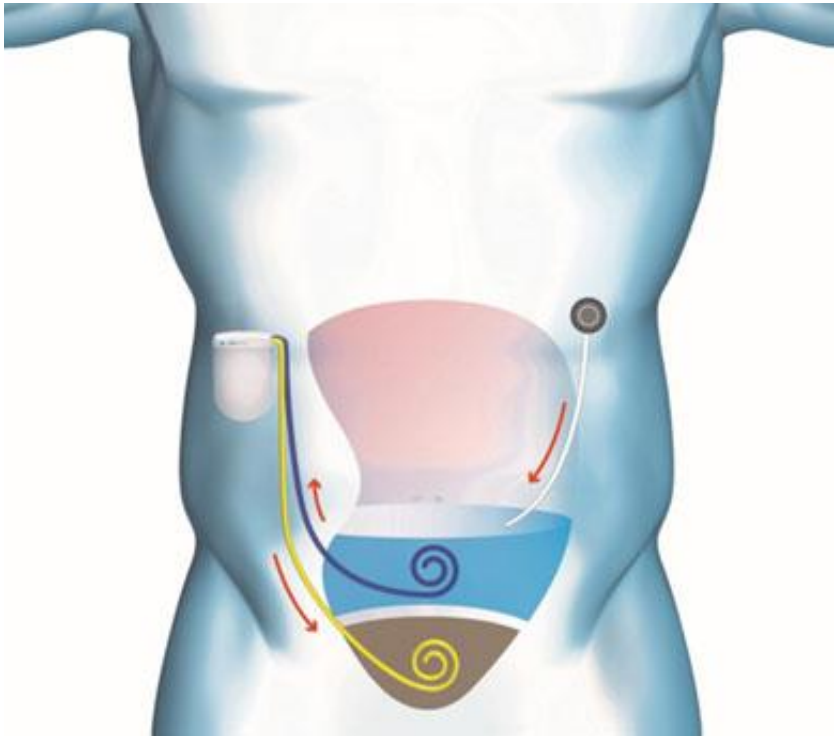
Yale

- Conducted by Dr. Jeff Testani, Yale University
- Up to 20 patients receiving PD
- Randomization to DSR Solution or standard PD solution, with crossover 1 week later
  - DSR Solution: Sodium-free 10% dextrose
  - Standard PD Solution: 4.25% dextrose standard PD solution (Dianeal, Baxter)
- One liter infused into the peritoneum and left to dwell for 2 hours
- **Primary endpoint**: Safety / Tolerability
  - Completion of 2-hour dwell without significant discomfort or AE
- **Secondary endpoint**: Efficacy
  - Difference in sodium removal between DSR and standard PD solution
  - Patient to patient variability
- Data to be presented as late breaking oral presentation at Heart Failure 2019

Study approved by Yale IRB and trial was registered on clinicaltrails.gov and with the FDA (NCT03801226; IND141103)

alfapump DSR: Fully implantable system

- Due to low volumes and long ultrafiltration time, fully implantable system possible
  - Fluid instilled through sub-q port
  - Removed from peritoneum by pump into bladder



Leverage proven alfapump technology

- Fully implanted, automatic, wirelessly charged, programmable smart alfapump
- Approved in EU for refractory ascites
  - Over 700 patient implants and over 400 hundred of patient-years of experience
- Pump can also:
  - Remove spontaneously generated peritoneal fluid
  - Report on changes in spontaneously produced fluid production
  - Continuously measure intra-abdominal pressure
- Both maintenance and bailout therapy can be delivered in addition to providing chronic monitoring information

DSR – A New Therapy for Volume Overload?

- Healthy & HF pig studies demonstrate DSR efficacy & safety
- First-in-man single dose DSR study will report shortly
- First-in-main repeated dose DSR study with implanted alfapump planned for next 12 months

- **alfa**pump DSR may provide a:
  - Convenient
  - Technically & clinically de-risked solution
  - For maintenance and bail-out therapy as well as patient monitoring
  - In heart failure patients with volume overload

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