Pilot Study of Natriuretic Versus Standard Doses of Mineralocorticoid Receptor Antagonists in
Heart Failure and Loop Diuretic Resistance in Outpatients
NCT: 02585843
Date 8/30/2015

Study Endpoints
The primary endpoint for the study was defined as change in total body weight at day 7 of the study period. Multiple secondary endpoints from day 1 to 7 were assessed. These included a) changes in dyspnea assessment scores; Visual Analogue Scale and 7-Likert scale, b) signs of congestion (i.e. JVP, peripheral edema and respiratory rales), c) 6MWT, d) serum and urinary creatinine, sodium, potassium and plasma aldosterone and renin activity and biomarkers of congestion and neurohormonal activation, e) furosemide equivalent of treatment loop diuretics doses, e) hospitalization at 30-, 60- and 90-days.

Six-minute walk test was performed per American Thoracic Society guidelines, along with Borg scores for dyspnea and fatigue at day 1 and 7. Serum and urinary creatinine, potassium, and sodium, plasma aldosterone and renin activity, and pro-BNP were assessed at days 1 and 7. Other biomarkers of peripheral congestion (CD146), inflammation (interleukin-6, tumor necrosis factor-α, endothelin-1) oxidative stress (isoprostane) and endothelial activation (vascular cell adhesion molecule-1) were assessed at day 1 and 7 and analyzed by ELISA or LC-MS.

A data monitoring committee of two independent cardiologists was established to evaluate safety, with a pre-specified stopping rule for harm but not for efficacy. Safety endpoints included changes in serum creatinine levels, eGFR, and the incidence of hyperkalemia during the 7 day treatment period. Safety was assessed by tracking adverse events including new or worsening renal dysfunction, and hyperkalemia. Serious adverse events were defined as death and all-cause hospitalization.

Statistical Analysis
Statistical analyses were performed using SPSS version 23. Continuous variables are presented as mean $\pm$ SD (or median with IQR if not following normal distribution) and categorical variables were summarized as counts (percentages). The χ^2 test or Fisher's exact test (when cell counts were small) were used to compare categorical variables. Paired t-tests and the Wilcoxon rank sum test was used to compare continuous variables pre vs. post intervention within treatment arms. ANOVA was performed to compare continuous variables post-intervention. P< 0.05 considered statistically significant for all comparisons.