## **Overview of Study Design**

#### **Study Population**

### Inclusion Criteria

- Acute renal failure clinically consistent with a diagnosis of ATN defined as
- clinical setting of acute ischemic or nephrotoxic injury and
- oliguria (average urine output < 20 mL/hr) for > 24 hours; or an increase in serum creatinine of ≥2.0 mg/dL (≥1.5 mg/dL in females) over a period of ≤ 4 days
- •Plan for renal replacement therapy by clinical team
- •Receiving care in a critical care unit
- •One non-renal organ failure (SOFA organ system score ≥ 2) or sepsis
- •Age ≥ 18 years
- Patient/surrogate willing to provide informed consent

#### Exclusion Criteria

- Premorbid serum creatinine > 2 mg/dL (> 1.5 mg/dL in females)
- Acute renal failure clinically believed to be due to an etiology other than ATN
- More than 72 hours since meeting both of the following:
- -fulfillment of definition of ARF
- -BUN > 100 mg/dL
- > 1 hemodialysis treatment or > 24 hours of CRRT
- Prior kidney transplant
- Pregnancy
- Prisoner
- Weight > 128.5 kg
- Non-candidacy for renal replacement therapy
- Moribund state
- Patient not expected to survive 28-days because of an irreversible chronic medical condition
- Comfort-measures only status
- Participation in a concurrent interventional study
- Patient/surrogate refusal
- · Physician refusal

#### Randomization

- 1:1 randomization to treatment arms
- Stratification of randomization by:
  - site
  - oliguria
- SOFA cardiovascular score (0-2 vs 3-4)

#### Sample Size

•582 patients per group

#### Study Sites

- •18 VA Sites (9 patients/year)
- •9 Non-VA sites (28 patients per year)

## **Study Duration**

- •3-years enrollment
- •60 days maximum primary follow-up

# **Overview of Study Design (continued)**

## Randomization

### **Intensive Management Strategy**

### If hemodynamically stable

•Intermittent hemodialysis 6-times per week (target delivered spKt/V ~ 1.2-1.4/treatment)

## If hemodynamically unstable

- •Continuous venovenous hemodiafiltration at 35 mL/kg/hour; or
- •Sustained low-efficiency dialysis, 6-times per week (target delivered Kt/V ~ 1.2-1.4/treatment)

### **Conventional Management Strategy**

### If hemodynamically stable

•Intermittent hemodialysis 3-times per week (target delivered spKt/V ~ 1.2-1.4/treatment)

## If hemodynamically unstable

- •Continuous venovenous hemodiafiltration at 20 mL/kg/hour; or
- •Sustained low-efficiency dialysis, 3-times per week (target delivered Kt/V ~ 1.2-1.4/treatment)

#### **End-Points**

## Primary Endpoint

•60-day all cause mortality

### Secondary Endpoints

- •Hospital mortality
- •1-year mortality
- •Recovery of renal function by day 28

#### Tertiary Endpoints

- •Duration of renal support
- •ICU length-of-stay
- •Hospital length-of-stay
- •Discharge to "home" off of dialysis by day-60
- •SOFA Organ Failure Scores at days 1-14, 21and 28

### **Economic Analysis**

- •Renal replacement therapy-specific cost of care
- •Global cost of care
- •Incremental cost-effectiveness