

## **Major Kidney Clinical Research Studies and Projects Inventory\***

### **Acute Renal Failure Trial Network (ATN) Study**

#### **1. Administrative Data**

(a) Name of study/research project and acronym:

Intensive vs. Conventional Renal Support in Acute Renal Failure (VA CSP#530)  
to be known as the **Acute Renal Failure Trial Network Study (ATN Study)**

(b) Type of study/research project (randomized clinical trial, epidemiological study, database, etc.):

Randomized clinical trial

(c) Funding status (currently funded, study/project completed):

Funded jointly by VA Cooperative Studies Program and NIDDK

(d) Recruitment status (recruitment completed, currently recruiting):

To begin recruitment in ~6months

(e) For studies/project currently recruiting, indicate total sample size/ number currently enrolled, anticipated period of recruitment:

Total sample size: 1,184 patients  
Recruitment: 3 years

(f) Data coordinating center principal investigator contact information (mailing address, phone, fax, e-mail address):

*Principal Investigator/Study Chairman:*

Paul M. Palevsky, M.D.  
Renal Section (111F-U)  
VA Pittsburgh Healthcare System  
University Drive Division  
Pittsburgh, PA 15240  
*Phone:* 412-688-6000, x5932  
*Fax:* 412-688-6908  
*Pager:* 412-644-9334  
*E-mail:* [palevsky@pitt.edu](mailto:palevsky@pitt.edu)

(g) Number of recruiting sites, list of principal investigators at recruiting sites and contact information as in (f) above:

Study sites currently being identified. There will be 24 VA-funded sites and 7 NIH-funded sites

(h) List of principal investigators at central laboratories/facilities (identify type of central facility) and contact information as in (f) and (g) above

N/A

(i) Roster of Data and Safety Monitoring Board/Scientific Advisory Committee or other oversight committee(s):

DSMB currently being formed

(j) Private-sector support (type of support, e.g., financial, donation of drugs/placebo, etc.):

Pending requests for support from industry for donation of or reduced price for supplies.

## 2. Study Design

(a) Objective:

To determine if a strategy of intensive renal support decreases 60-day, all-cause mortality in critically ill patients with acute renal failure as compared to conventional management of renal replacement therapy.

(b) Study design:

Multi-center, prospective, randomized, parallel group trial

(c) Major inclusion criteria:

- Acute renal failure clinically consistent with a diagnosis of ATN defined as clinical setting of acute ischemic or nephrotoxic injury and (2) oliguria (urine output <20 mL/hr) for >24 hrs; or an increase in serum creatinine of  $\geq 2.0$  mg/dL ( $\geq 1.5$  mg/dL in females) over a period of  $\leq 4$  days
- Plan for renal replacement therapy by clinical team

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- Receiving care in a critical care unit
- One non-renal organ failure (SOFA organ system score  $\geq 2$ ) or sepsis (ACCP/SCCM Consensus Conference definition)
- Age  $\geq 18$  years
- Patient/surrogate willing to provide informed consent

(d) Major exclusion criteria:

- Baseline 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
  - pre-renal azotemia
  - obstructive uropathy
  - allergic interstitial nephritis
  - acute or rapidly progressive glomerulonephritis
  - vasculitis
  - HUS/TTP
  - malignant hypertension
  - scleroderma renal crisis
  - atheroembolic disease
  - functional or surgical nephrectomy
  - hepatorenal syndrome
  - cyclosporin or tacrolimus nephrotoxicity
- 1 hemodialysis treatment or  $>24$  hours of CRRT
- Prior kidney transplant
- Pregnancy
- Prisoner
- Weight  $>120$  kg
- Non-candidacy for renal replacement therapy
- Moribund state
- Patient not expected to survive 28-days because of an irreversible medical condition
- Comfort-measures only status

- Participation in a concurrent interventional study
- Patient/surrogate refusal

(e) Description of the intervention(s)

*Intensive Management Strategy:*

- If hemodynamically stable (SOFA Cardiovascular score 0-2): Intermittent hemodialysis 6-times per week (target delivered spKt/V ~ 1.2/treatment)
- If hemodynamically unstable (SOFA Cardiovascular score 3-4): Continuous venovenous hemodiafiltration at 35 mL/kg/hour; or sustained low-efficiency dialysis, 6-times per week (target delivered Kt/V ~ 1.2/treatment)

*Conventional Management Strategy:*

- If hemodynamically stable (SOFA Cardiovascular score 0-2): Intermittent hemodialysis 3-times per week (target delivered spKt/V ~ 1.2/treatment)
- If hemodynamically unstable (SOFA Cardiovascular score 3-4): Continuous venovenous hemodiafiltration at 20 mL/kg/hour; or sustained low-efficiency dialysis, 3-times per week (target delivered Kt/V ~ 1.2/treatment)

(f) Baseline/eligibility visit schedule (number of visits, major assessments):

In-patient study

(g) Follow-up contact schedule (frequency, type of visit/phone, in-clinic, major assessments):

In-patient follow-up for up to 28-days with 60-day and 1-year follow-up as inpatient or by telephone/mail as outpatient

(h) Primary outcome, secondary outcomes:

*Primary Endpoint*

- 60-day all cause mortality

*Secondary Endpoints:*

- Hospital mortality
- 1-year mortality

- Recovery of renal function by day 28

(i) Brief summary of power estimates used to justify sample size/duration, including critical assumptions (i.e., effect-size estimates, estimated event rates, or rate of change in outcome measure):

Assuming a 60-day, all-cause mortality of 55% in the conventional-management arm the sample size of 1,184 patients (592 in each arm) will provide 90% power to detect a reduction in mortality to 45% (absolute reduction of 10%) with  $\alpha=0.05$  and assuming a drop-out rate of 10%.

(j) Web site:

Not yet functional

### 3. Data and Biological Sample Resources

(a) Biological samples collected in ongoing studies/research projects (specify the type of sample, e.g., blood, urine, etc., the amount, and the point in the study when samples were collected, e.g., baseline visit #1, baseline visit #2, follow-up visit #1; specify months after randomization/study entry):

There is currently no plan for banked biological samples.

(b) Biological samples currently in storage from completed trials (grid showing sample collection time, type of sample, amount, and number of study participants sample was collected from, and physical location of where the samples are stored):

N/A

(c) Brief summary of typical informed consent provisions (template informed consent form acceptable), including major variables in participant consents, if applicable (e.g., “use for other studies or not”, “allow genetic studies or not”). Does consent include use of samples in other studies that are not part of the main study?

N/A

(d) Data collected (grid of data collection by time/clinic visit with specificity on the type of information collected, e.g., quality of life with SF-MOS 36, measurement of kidney function by GFR, serum creatinine measurement, etc.):

General Data Collection						
	Screening	Baseline	Study Days 1-14,	Day 28	Day 60	1-Year

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			<b>21, 28</b>			
<b>Screening Evaluation</b>	<b>X</b>					
<b>Baseline Serum Creatinine</b>						
<b>Etiology of ARF</b>						
<b>Duration of ARF</b>						
<b>History</b>		<b>X</b>				
<b>Physical Examination</b>		<b>X</b>				
<b>Charlson Score</b>		<b>X</b>				
<b>Laboratory Assessment</b>						
<b>CBC</b>		<b>X</b>	<b>X</b>			
<b>Comprehensive Chemistry Panel</b>		<b>X</b>				
<b>Basic Chemistry Panel</b>			<b>X</b>			
<b>Hemodynamic Assessment</b>		<b>X</b>	<b>X</b>			
<b>Pressors</b>		<b>X</b>	<b>X</b>			
<b>24-Hour Urine Volume</b>	<b>X</b>	<b>X</b>	<b>X</b>			
<b>SOFA Score</b>	<b>X</b>	<b>X</b>	<b>X</b>			
<b>APACHE II Score</b>		<b>X</b>				
<b>CCF ARF Score</b>		<b>X</b>				
<b>SIRS Score</b>		<b>X</b>	<b>X</b>			
<b>Nutrition Management</b>		<b>X</b>	<b>X</b>			
<b>Medication Usage</b>			<b>Days 7 &amp; 28</b>			
<b>Renal Replacement Therapy Data</b>			<b>All treatment days</b>			
<b>Assessment of Renal Function</b>				<b>X</b>		
<b>Survival Status</b>				<b>X</b>	<b>X</b>	<b>X</b>
<b>ICU LOS</b>				<b>X</b>	<b>X</b>	
<b>Hospital LOS</b>				<b>X</b>	<b>X</b>	
<b>Economic and Utility Data (HUI)</b>					<b>X</b>	<b>X</b>

(e) Any provisions for distributing resources outside of the study? What is the sharing plan?

Not yet established

#### 4. Ancillary Studies

(a) Process and contact person (name, address, phone, fax, and e-mail address) for application to perform ancillary studies:

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Study Chairman's Office (Paul M. Palevsky, M.D.) – see above

(b) List of ancillary studies approved, completed and ongoing (including source of funding and amount):

None yet approved

**5. List of Publications and Presentations (full citations, also note manuscripts in progress)**

N/A

**\*Cooperative Agreement, Contract, and Selected Investigator-Initiated NIDDK-Supported Studies**

### 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 (urine output < 20 mL/hr) for > 24 hours; or an increase in serum creatinine of  $\geq 2.0$  mg/dL ( $\geq 1.5$  mg/dL in females) over a period of  $\leq 4$  days
- Plan for renal replacement therapy by clinical team
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#### ***Exclusion Criteria***

- Baseline serum creatinine > 2 mg/dL (> 1.5 mg/dL in females)
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  - obstructive uropathy
  - allergic interstitial nephritis
  - acute or rapidly progressive glomerulonephritis
  - vasculitis
  - HUS/TTP
  - malignant hypertension
  - scleroderma renal crisis
  - atheroembolic disease
  - functional or surgical nephrectomy
  - hepatorenal syndrome
  - cyclosporin or tacrolimus nephrotoxicity
- > 1 hemodialysis treatment or > 24 hours of CRRT
- Prior kidney transplant
- Pregnancy
- Prisoner
- Weight > 120 kg
- Non-candidacy for renal replacement therapy
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- Patient not expected to survive 28-days because of an irreversible medical condition
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- Participation in a concurrent interventional study
- Patient/surrogate refusal

### Enrollment Window

Enrollment must occur within 48 hours of first meeting any of the following criteria for initiation of renal replacement therapy:

- BUN  $\geq 60$  mg/dL
- Volume overload
- Persistent hyperkalemia ( $K^+ > 6.2$  mEq/L or the presence of ECG changes)
- Severe metabolic acidosis (pH < 7.20 or  $tCO_2 < 15$  mEq/L)
- Uremic signs or symptoms

No more than one hemodialysis treatment or 24 hours of CRRT may be provided prior to enrollment

#### ***Sample Size***

- 582 patients per group

#### ***Study Sites***

- 24 VA Sites (8-10 patients/year)
- 7 Non-VA sites (25-30 patients per year)

#### ***Study Duration***

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

#### **Randomization**

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

