EUPHRATES PMX STUDY

PI: Michael Seneff Enrollment goal: 6 subjects

This phase III, multi-center device study will compare the safety and efficacy of the PMX cartridge, based on 28-day mortality, in subjects with septic shock who have high levels of endotoxin* and are treated with standard medical care plus use of the PMX cartridge, versus subjects who receive standard medical care alone.

*Endotoxin level determined by the screening blood test which requires consent and is performed by study staff. Patients with endotoxin activity levels (EAA) below 0.6 units are not eligible for enrollment.

Inclusion Criteria:

1. Age ≥18 years of age
2. Hypotension requiring vasopressor support: Requirement for at least one of the vasopressors listed below, at the dose shown below, for *at least* 2 continuous hours and no more than 30 hours*
    a. Norepinephrine > 0.05mcg/kg/min
    b. Dopamine > 10 mcg/kg/min
    c. Phenylephrine > 0.4 mcg/kg/min
    d. Epinephrine > 0.05 mcg/kg/min
    e. Vasopressin > 0.03 units/min
    f. Vasopressin (any dose) in combination with another vasopressor listed above
3. The subject must have received intravenous fluid resuscitation of a minimum of 30mL/kg administered within 24 hours of eligibility
4. Documented or suspected infection defined as definitive or empiric intravenous antibiotic administration
5. Endotoxin Activity Assay ≥ 0.60 EAA units
6. Evidence of at least 1 of the following criteria for new onset organ dysfunction that is considered to be due to the acute illness

a. Requirement for positive pressure ventilation via an endotracheal tube or tracheostomy tube
b. Thrombocytopenia defined as acute onset of platelet count < 150,000 μ/L or a reduction of 50% from prior known levels
c. Acute oliguria defined as urine output < 0.5 ml/kg/hr for at least 6 hours despite adequate fluid resuscitation

Exclusion Criteria:

1. Inability to obtain an informed consent from the subject, family member or an authorized surrogate.
2. Lack of commitment for full medical support
3. Inability to achieve or maintain a minimum mean arterial pressure (MAP) of ≥ 65mmHg despite vasopressor therapy and fluid resuscitation
4. Subject has end stage renal disease and requires chronic dialysis

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5. There is clinical support for non-septic shock such as
a. Acute pulmonary embolus
b. Transfusion reaction
c. Severe congestive heart failure (e.g. NYHA Class IV)
6. Subject has had chest compressions as part of CPR this hospitalization without immediate return to communicative state
7. Subject has had an acute myocardial infarction (AMI) within the past 4 weeks
8. Subject has uncontrolled hemorrhage (acute blood loss requiring > 3 UPC in the past 24 hours)
9. Major trauma within 36 hours of screening
10. Subject has severe granulocytopenia (leukocyte count less than 500 cells/mm3) or severe thrombocytopenia (platelet count less than 30,000 cells/mm3)
11. HIV infection in association with a last known or suspected CD4 count of <50/mm3
12. Subject's baseline state is non-communicative
13. Subject has sustained extensive third-degree burns within the past 7 days
14. Body weight < 35 kg (77 pounds)
15. Known hypersensitivity to polymyxin B
16. Subject has known sensitivity or allergy to heparin or has a history of heparin associated thrombocytopenia (H.I.T.)
17. Subject is currently enrolled in an investigational drug or device trial
18. Subject has been previously enrolled in the current trial
19. Any other condition, that in the opinion of the investigator, would preclude the subject from being a suitable candidate for enrollment, such as end stage chronic illness with no reasonable expectation of survival to hospital discharge

Study procedures: Subjects will be randomized to active treatment or placebo and will receive 2 treatments of 1.5-2 hours over a 24 hour period in the ICU; data collection and multiple blood samples.

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