

EXPAND-ECLS Domain

Protocol summary for Protocol v3.0 08-Apr-2025

Primary Outcome:	<p>The primary outcome of this pilot study is feasibility, which includes 3 components;</p> <ol style="list-style-type: none">1. Successful patient recruitment defined as enrolment of 100 AHRF patients from sites over 2 years2. Adherence to protocol defined as >80% of patients having <20% of monitored values determined to be major protocol deviations3. Success for lack of crossovers defined as <10% of crossovers between groups (when not allowed by protocol) in either direction
Eligible Platform Defined Patient States:	<p>This domain includes patients in the following platform defined state:</p> <ol style="list-style-type: none">1. Intubated patients, not on ECLS, with low normalized respiratory elastance (<2.5 cm H₂O/(mL/kg predicted body weight))2. Intubated patients, not on ECLS, with high normalized respiratory system elastance (≥2.5 cm H₂O/(mL/kg predicted body weight))
Domain Design:	<p>An interventional, open-label, randomized, multi-site feasibility study .</p>
Duration:	<p>2 years of accrual and 6 month follow-up for a total study duration of approximately 2.5 years</p>
Planned Total Sample Size:	<p>Approximately 100 evaluable patients will be randomized in this domain protocol.</p>
Intervention:	<p>Participants will be randomized to the control arm and applicable intervention(s) available. Each site will randomize patients into the control arm, and at least one intervention arm:</p> <ol style="list-style-type: none">1. Ultra-protective ventilation facilitated by an ECMO device (ULTIMATE)2. VV ECMO-facilitated strategy of earlier awakening, extubation and rehabilitation (PROACTIVE)3. Control Arm: conventional lung-protective ventilation (LPV).
Inclusion/Exclusion Criteria:	<p>Patients will be eligible for randomization in this domain if they meet PRACTICAL platform eligibility criteria as well as ULTIMATE specific eligibility criteria.</p>

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	<p>PRACTICAL Inclusion Criteria:</p> <ol style="list-style-type: none">1. Acute hypoxemic respiratory failure meeting all of the following criteria;<ul style="list-style-type: none">○ New or worsening respiratory symptoms developing within 2 weeks prior to the onset of need for oxygen or respiratory support,○ Receiving any of the following types of oxygen or respiratory support for at least 4 hours prior to the time of randomization; supplemental oxygen at 10 L/min or higher, high flow nasal oxygen (at any flow rate), invasive ventilator support, extra-corporeal life support (ECLS), or non-invasive ventilator support,○ Minimum $FiO_2 \geq 0.40$ (for venturi mask, high flow nasal cannula, or invasive or non-invasive ventilation) or oxygen flow rate ≥ 10 L/min on face mask for at least 4 hours at the time of evaluation for eligibility unless already on extra-corporeal life support.2. Age ≥ 18 years <p>PRACTICAL Exclusion Criteria:</p> <ol style="list-style-type: none">1. Hypoxemia is primarily attributable to acute heart failure or fluid overload.2. Hypoxemia is primarily attributable to pulmonary embolism.3. Hypoxemia is primarily attributable to status asthmaticus.4. Extubation is planned or anticipated on the day of screening.5. ICU discharge is planned or anticipated on the day of screening.6. The patient is moribund and deemed unlikely to survive past 24 hours (as determined by the clinical team).7. The patient is being transitioned to a fully palliative philosophy of care. <p>Domain Inclusion Criteria</p>
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	<ol style="list-style-type: none">1. Receiving invasive mechanical ventilation for ≤ 72 hours.2. Moderate-severe hypoxemic respiratory failure with a $\text{PaO}_2/\text{FiO}_2 \leq 150$ mmHg for at least 6 hours. <p>Domain Exclusion Criteria:</p> <ol style="list-style-type: none">1. Patients over 70 years of age.2. Currently receiving any form of ECLS (e.g., Venovenous, venoarterial, or hybrid configuration).3. Chronic hypercapnic respiratory failure defined as $\text{PaCO}_2 > 60$ mmHg in the outpatient setting.4. Home mechanical ventilation (non-invasive ventilation or via tracheotomy) except for CPAP/BiPAP used solely for sleep-disordered breathing.5. Actual body weight exceeding 1 kg per centimeter of height.6. More than 48 hours have passed since meeting inclusion criteria.7. Severe hypoxemia with $\text{PaO}_2/\text{FiO}_2 < 80$ mmHg for > 6 hours at time of screening.8. Severe hypercapnic respiratory failure with $\text{pH} < 7.25$ and $\text{PaCO}_2 > 60$ mmHg for > 6 hours at time of screening.9. Expected mechanical ventilation duration < 48 hours at time of screening.10. Confirmed diffuse alveolar hemorrhage from vasculitis.11. Contraindications to limited anticoagulation (e.g., active GI bleeding, bleeding diathesis).12. Previous hypersensitivity/anaphylactic reaction to heparin or heparin-induced thrombocytopenia13. Neurologic conditions at risk for or undergoing treatment for intracranial hypertension14. Underlying illness with life expectancy < 1 year15. Pregnancy (due to unknown effects of PaCO_2 changes on placental blood flow)16. Respiratory failure known or suspected to be caused by COVID-19.
Statistical Analysis:	A target sample size of 100 AHRF patients will be randomized over a period of 2 years. This timeline will determine feasibility, as well as test the validity of our eligibility criteria, ventilation protocols, and study procedures. Descriptive statistical analyses and an intention-to-treat principle will be employed for the pilot phase of the trial.