ECMO-free Trial: A Multicenter Pilot Feasibility Study

Background

- Decannulation from venovenous ECMO at the earliest and safest time would be expected to improve outcomes and reduce cost
- Daily assessments for readiness to liberate from therapies have demonstrated success in other realms of critical care
- Recent single-center studies demonstrated that a protocolized daily assessment of readiness for liberation from VV-ECMO was feasible
- Efficacy remains unclear

Aims

- Primary aim
  - Demonstrate the feasibility of a large, multi-center randomized controlled trial by conducting a multi-center pilot trial
- Secondary aim
  - To define and estimate the frequency of the primary efficacy, primary safety, and secondary outcomes of a future large, multi-center randomized controlled trial

3 centers; goal sample size 60 patients

Inclusion/Exclusion criteria

- Inclusion criteria
  - Patient is receiving VV-ECMO
  - Patient is located in a participating unit of an adult hospital
- Exclusion criteria
  - Patient is pregnant
  - Patient is a prisoner
  - Patient is < 18 years old
  - Participant is receiving ECMO as a bridge to transplant
  - Participant is receiving a hybrid configuration that includes an arterial cannula
  - Patient has received VV-ECMO for > 24 hours

Enrollment and Randomization

- Enrollment
  - At receipt of VV-ECMO (if cannulated in a participating unit of a participating center) or at the time of admission to the participating unit of the participating center (if cannulated at a non-participating unit or center)
- Randomization
  - 1:1 ratio to intervention or control group
  - Electronic though REDCap using permuted randomized blocks of two, four, and six

Study Interventions

- Study interventions
  - The ECMO-free protocol: protocol performed daily from enrollment until the first of death or decannulation; results recorded and shared with treatment team
  - Usual care: ECMO weaning and assessments of readiness for liberation at the discretion of treating clinicians
- Duration of study interventions
  - Randomization until the first of death or decannulation

Outcomes

- Primary efficacy outcome
  - 60-day ECMO-free days (EFDs = 60 minus the number of calendar days from randomization to final decannulation with patients who die before the first of day 60 or hospital discharge receiving “0” EFDs.)
- Primary safety outcome
  - Unsafe liberation; criteria met within 48 hours of decannulation
- Feasibility outcomes

The ECMO-free protocol

Patients randomized to the ECMO-free protocol group receive Phase 1 (Safety Screen) to Phase 3 (ECMO-free trial) as applicable

Patients randomized to the usual care group receive Phase 1 (Safety Screen) only

ECMO-free Protocol

Phase 1: Safety Screen

- Study personnel conduct screening daily between 6:00-10:00
- Patients fail safety screen for:
  - Sweep gas flow rate > 4lpm
  - Ventilator FiO2 > 60%
  - Presence of neuromuscular blockade
  - Presence of re-infusion cannula placed in an artery
  - Presence of intravenous pulmonary vasodilators for pulmonary hypertension
  - Neurologic or neuromuscular disease that precludes spontaneous breathing
  - High-dose vasopressors (>15 mcg/min norepinephrine or equivalent)
  - Oxygen saturation < 88%
  - Respiratory rate > 35 breaths per minute
  - Systolic blood pressure > 180 mmHg or < 90 mmHg
  - Evidence of respiratory distress characterized by nasal flaring, diaphoresis, and/or accessory muscle use
- If they fail the safety screen, they will be re-assessed the following day
- If they pass the safety screen, they will proceed to Phase 2

ECMO-free Protocol

Phase 2: Non-ECMO Respiratory Support Titration

- Non-ECMO FiO2 will be set at 60% (vent/NIPPV); for patients on other, high flow nasal cannula will be applied (if not already) and set to an FiO2 of 60% and a flow rate of 40lpm.
- Option to adjust mechanical ventilation with limits: Vt <8cc/kgs PBW and pplat ≤ 30cmH2O for volume-targeted modes or total inspiratory pressure ≤ 30cmH2O for pressure-targeted modes
- Patients fail phase 2 screening for :
  - SpO2 < 88%
  - Respiratory rate > 35 breaths per minute
  - Sustained increase or decrease in heart rate of > 20%
  - Systolic blood pressure > 180 mmHg or < 90 mmHg
  - Vasopressor requirements increase (defined as increase in 5 mcg/min of norepinephrine or equivalent)
  - Evidence of respiratory distress characterized by nasal flaring, diaphoresis, and/or accessory muscle use

ECMO-free Trial

Phase 3: ECMO-FREE Trial

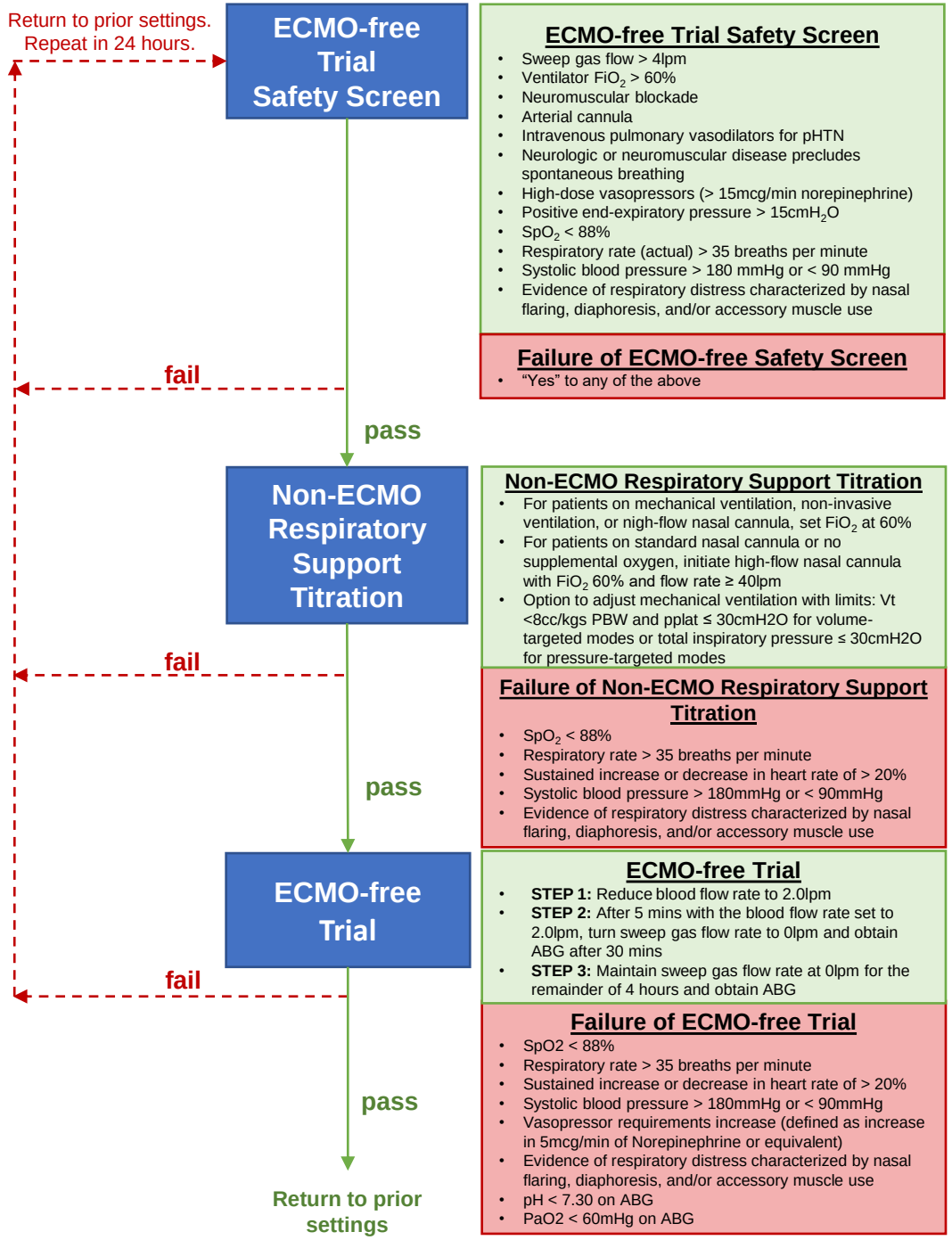
- For patients who successfully pass phase 2, an ECMO free trial will be initiated.
- Study personnel will remain at the bedside from the start of the ECMO-free trial to the first of failure or 30 minutes.

Step 1. Reduction of the blood flow rate to 2.0lpm

Step 2. Sweep gas flow turned to 0lpm

Step 3. Sweep gas flow rate is maintained at 0lpm for the remainder of 4 hours:

- Patients fail phase 3 and previous ECMO settings will be restored for:
  - SpO2 < 88%
  - Respiratory rate > 35 breaths per minute
  - Sustained increase or decrease in heart rate of > 20%
  - Systolic blood pressure > 180 mmHg or < 90 mmHg
  - Vasopressor requirements increase (defined as increase in 5 mcg/min of norepinephrine or equivalent)
  - Evidence of respiratory distress characterized by nasal flaring, diaphoresis, and/or accessory muscle use
  - pH < 7.30 on arterial blood gas
  - PaO2 < 60 mmHg on arterial blood gas
  - The treating clinician decides to reinstate sweep gas flow for a clinical or safety reason in the absence of other failure criteria
- Data (ABG, vital signs, respiratory physiology variables) are collected at 30 minutes and 4 hours, or when failure criteria are met if within 4 hours


Return to prior settings.
Repeat in 24 hours.
ECMO-free Trial Safety Screen
ECMO-free Trial Safety Screen
Sweep gas flow > 4lpm
Ventilator FiO2 > 60%
Neuromuscular blockade
Arterial cannula
Intravenous pulmonary vasodilators for pHTN
Neurologic or neuromuscular disease precludes spontaneous breathing
High-dose vasopressors (> 15mcg/min norepinephrine)
Positive end-expiratory pressure > 15cmH2O
SpO2 < 88%
Respiratory rate (actual) > 35 breaths per minute
Systolic blood pressure > 180 mmHg or < 90 mmHg
Evidence of respiratory distress characterized by nasal flaring, diaphoresis, and/or accessory muscle use
Failure of ECMO-free Safety Screen
"Yes" to any of the above
fail
pass
Non-ECMO Respiratory Support Titration
Non-ECMO Respiratory Support Titration
For patients on mechanical ventilation, non-invasive ventilation, or nigh-flow nasal cannula, set FiO2 at 60%
For patients on standard nasal cannula or no supplemental oxygen, initiate high-flow nasal cannula with FiO2 60% and flow rate ≥ 40lpm
Option to adjust mechanical ventilation with limits: Vt <8cc/kgs PBW and pplat ≤ 30cmH2O for volume-targeted modes or total inspiratory pressure ≤ 30cmH2O for pressure-targeted modes
fail
Failure of Non-ECMO Respiratory Support Titration
SpO2 < 88%
Respiratory rate > 35 breaths per minute
Sustained increase or decrease in heart rate of > 20%
Systolic blood pressure > 180mmHg or < 90mmHg
Evidence of respiratory distress characterized by nasal flaring, diaphoresis, and/or accessory muscle use
pass
ECMO-free Trial
ECMO-free Trial
STEP 1: Reduce blood flow rate to 2.0lpm
STEP 2: After 5 mins with the blood flow rate set to 2.0lpm, turn sweep gas flow rate to 0lpm and obtain ABG after 30 mins
STEP 3: Maintain sweep gas flow rate at 0lpm for the remainder of 4 hours and obtain ABG
fail
Failure of ECMO-free Trial
SpO2 < 88%
Respiratory rate > 35 breaths per minute
Sustained increase or decrease in heart rate of > 20%
Systolic blood pressure > 180mmHg or < 90mmHg
Vasopressor requirements increase (defined as increase in 5mcg/min of Norepinephrine or equivalent)
Evidence of respiratory distress characterized by nasal flaring, diaphoresis, and/or accessory muscle use
pH < 7.30 on ABG
PaO2 < 60mHg on ABG
pass
Return to prior settings