PRACTICAL Platform Trial Summary

Updated: 13Nov2023

Platform of Randomized Adaptive Clinical Trials in Acute Hypoxemic Respiratory Failure: the PRACTICAL Adaptive Platform Trial

Overview

PRACTICAL is a Bayesian adaptive randomized platform trial studying new interventions to improve outcomes for patients with acute hypoxemic respiratory failure (AHRF). The Platform Lead Investigators are Dr. Ewan Goligher and Dr. Eddy Fan (University of Toronto). Access the study website here: https://practicalplatform.org/

Platform Structure

The platform evaluates interventions within several different states of AHRF. Current states are:

Non-intubated state: Patients receiving non-invasive oxygen or ventilation support

Low elastance state: Intubated patients, not on extracorporeal life support (ECLS), with low normalized respiratory system elastance (≤2.5 cm H_2O/(mL/kg PBW))

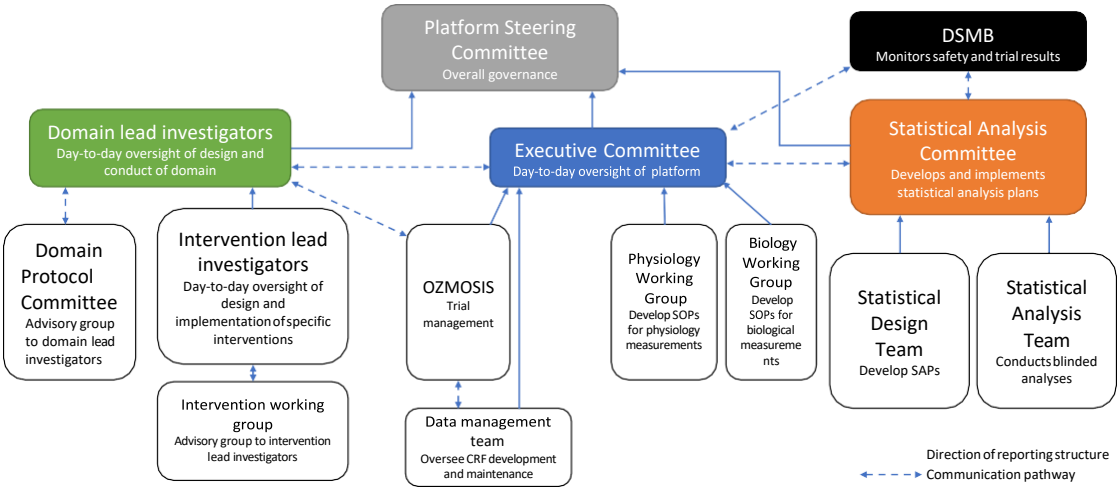
High elastance state: Intubated patients, not on ECLS, with high normalized respiratory system elastance (>2.5 cm H_2O/(mL/kg PBW))

ECLS state: Patients receiving extracorporeal life support

Interventions will be studied at various phases of investigation, including pilot and feasibility trials, preliminary trial of physiological and biological effect, and definitive trials evaluating treatment effect on patient-centered outcomes. The platform is designed to function as a "pipeline" to facilitate seamless and efficient evaluation of novel clinical strategies from preliminary proof-of-concept trials to full scale definitive clinical trials. Each study within the platform is called a domain.

Platform Governance

PRACTICAL is governed by a Platform Steering Committee (PSC) involving investigators with experience in trial design and clinical investigation in respiratory failure and critical illness from multiple institutions in Canada and internationally. Day-to-day operations are overseen by an Executive Committee (EC) that includes the chair of the Statistical Analysis Committee (SAC) and the clinical trial management team (Ozmosis Research Inc.). Each domain is overseen by Domain Lead Investigators with an advisory Domain Protocol Committee (DPC) providing input on the individual domain. Domains with multiple interventions or comparisons may have intervention lead investigators and intervention working groups as needed.



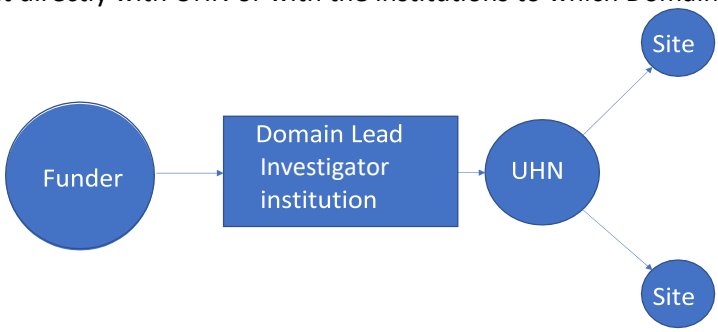
Platform Funding

Currently, the platform is funded primarily through peer-reviewed grants supporting specific interventions within domains. Domain Lead Investigators are primarily responsible for ensuring funding for interventions studied in the

domain, and funding applications will be led by domain lead investigators or intervention lead investigators, with funding held at their home institution.

Platform Network

University Health Network (UHN) is the sponsoring institution for the trial. All sites participating in the network will contract with UHN. Domain Lead Investigators will contract with UHN to disseminate funds to the platform network, and data and samples will flow back to the Domain Lead Investigators through the same contractual agreement. Funders can contract directly with UHN or with the institutions to which Domain Lead Investigators belong.



Platform Logistics

Data collection will be operationalized through registry-based mechanisms (where possible) or through a case report form with domain-specific data requirements. Clinical trial management, data coordination and monitoring will be provided by Ozmosis Research Inc., a full-service clinical trials management company with extensive experience in clinical trials.

Statistical Design

Platform conclusions will be based on regular adaptive interim analyses of trial results computed from Bayesian statistical models according to pre-specified stopping rules based on posterior probabilities of superiority, inferiority, and futility. These probabilities will be computed independently for each state as separate hierarchies in a single overarching Bayesian hierarchical model.

The platform design facilitates evaluation of interactions between interventions in different domains. Pre-specified rules may guide determination of whether to graduate intervention from preliminary evaluation to definitive clinical trials.

Simpler statistical designs may be specified for preliminary phase studies.

Site Participation

Sites can define their participation in the platform with the following options:

- Participation in registry-based data collection or trial-specific case report form
- Selection of domains
- Selection of specific interventions of interest within domains

Platform Adjacent Trials

Despite the various advantages of platform trials, there can be some obstacles to platform trial participation for certain proposed trials. These obstacles include differences in target population, and requirements vis-à-vis trial sponsorship and regulation (particularly for industry trials). These trials may still be eligible for platform adjacent status, which constitutes a partnership between a new clinical trial and the existing platform, where the new clinical trial is not conducted under the platform master protocol, but varying degrees of platform collaboration and cooperation are implemented to facilitate conduct of the platform-adjacent trial.

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Current Domain Snapshot

Name	Intervention(s)	Primary Research Purpose/Question(s)	AHRF States Included	Status
ULTIMATE	Ultra-protective ventilation facilitated by CO2 removal through VV ECMO	*Feasibility stage:* What is the feasibility of recruiting 72 patients over 1 year of active enrollment? What is the rate of participant recruitment and are there any barriers to recruitment?	- High elastance	**Actively Recruiting**
PROACTIVE	VV ECMO facilitated strategy of earlier awakening, extubation and rehabilitation	*Feasibility stage:* What is the feasibility of recruiting 60 patients over 2 year of active enrollment? Is there a high level of protocol adherence and lack of cross-overs? Could patients be awake, extubated, and able to participate in rehabilitation by study Day 7?	- Low elastance	Protocol Development
IMV Strategies	Driving pressure limited ventilation, lung/diaphragm protective ventilation & sedation	What is the invasive mechanical ventilation (IMV) strategy that most effectively improves patient outcomes in patients intubated for AHRF?	- Low elastance - High elastance - ECLS	**Actively Recruiting**
CORT-E2	Corticosteroids	Will early corticosteroids improve survival in patients with non-COVID acute respiratory failure and, will extending corticosteroids improve survival in those with acute respiratory failure who are still requiring invasive or non-invasive respiratory support at day 10?	- Non-intubated - Low elastance - High elastance - ECLS	**Actively Recruiting**
ESCAPE	N/A – Observational Study	Identify phenotypes across immunocompromised patients with AHRF using clinical characteristics and biomarkers.	- Non-intubated - Low elastance - High elastance - ECLS	Protocol Development