REMAP-CAP
Randomized, Embedded, Multifactorial Adaptive Platform trial for Community-Acquired Pneumonia

REMAP-CAP: a platform trial for ICU patients with COVID-19

Background

Planning for REMAP-CAP commenced in 2011. The trial has been designed by clinicians who cared for patients and conducted research during the 2009 H1N1 pandemic.

REMAP-CAP is the combined output of the world's leading ICU trial networks that have enrolled tens of thousands of patients into trials and have extensive experience at the design and execution of clinical trials that enroll patients who are critically ill. As a consequence, REMAP-CAP is simple for sites to execute.

Objective

The objective is to generate evidence that can be applied to clinical practice during the pandemic, regarding the impact of multiple candidate interventions, to *reduce mortality* or *reduce the length of ICU admission* or both in critically ill patients with COVID-19 infection.

Designed for the pandemic

The trial has been recruiting (severe CAP) during the inter-pandemic period and was 'pre-designed' to adapt when a pandemic occurred. Sites, with ethics and other approvals, exist. The screening, recruitment, randomisation, intervention delivery systems, and data collection are working and practiced. Changes necessary for the pandemic have been approved or are submitted for approval. The platform recruits currently in more than 50 ICUs in 13 countries on 3 continents. Another 50 ICUs are in start-up. More countries and networks are being added. The trial does not require research staff for recruitment. The treating clinician enrols patients (5 minutes on web-site).

Designed to generate answers fast

The platform is a Bayesian Adaptive Platform Trial. It will generate answers to as many relevant questions, as fast as possible:

- Platform is multifactorial. This means each patient is randomised to multiple different combinations of treatment. It is 'multiple trials in one'.
- Frequent interim analyses- a question is concluded as soon as there is sufficient statistical confidence. Analyses can occur every week.
- Detects superiority, inferiority, or equivalence of interventions within the platform
- Additional interventions are added, as required, based on availability and external evidence

Current treatments

The platform will evaluate, on an open-label basis:

- Antiviral therapy (no antiviral / kaletra, hydroxychloroquine being added)
- Corticosteroid strategy (no steroid, fixed 7 days, only while in septic shock)
- Immune modulation (no modulator / interferon-beta / anakinra)

Where specified, the platform evaluates interactions, i.e. do steroids work only when an active antiviral is administered. In Australia, New Zealand, Canada, and in United States, platform is integrated and coordinated with planned pre-ICU trials.

Designed to improve outcome for participants

The platform applies 'Response Adaptive Randomisation'. After each interim analysis, the weighting of randomisation is varied so that the number of patients receiving each intervention is proportional to the probability of superiority of that intervention, i.e. if an intervention saves lives, more trial participants get that intervention.