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

19th December, 2020

Dear REMAP-CAP sites,

**RE: Therapeutic Anticoagulation Domain in Severe State**

I am writing to inform you of decisions that have been made by the REMAP-CAP international trial steering committee (ITSC) in response to communication from the Data Safety Monitoring Board (DSMB).

After reviewing the results of interim analyses and safety reports, the REMAP-CAP DSMB have notified the ITSC that the therapeutic anticoagulation intervention has reached a prespecified threshold for futility for patients in the Severe State (admitted to an Intensive Care Unit and receiving one or more qualifying organ failure supports). At the same time, the DSMB also indicated concerns regarding the overall safety of therapeutic anticoagulation for patients in the Severe State. The unanimous recommendation of the DSMB was that this domain be closed for randomisation, to patients in the Severe State. This recommendation has been accepted by the ITSC. This has been implemented within the REMAP-CAP eligibility system at all sites. This is occurring as a 'pause' pending additional analyses which are being undertaken urgently.

For current patients who are enrolled in the anticoagulation domain in the Severe State and have been assigned therapeutic anticoagulation, the recommendation of the ITSC is for the treating clinician to cease therapeutic anticoagulation, as soon as practicable, unless the patient has developed a co-existing accepted indication for therapeutic anticoagulation.

The DSMB recommended that patients in the Moderate State continue to be enrolled and randomised in the therapeutic anticoagulation domain. This recommendation has also been accepted by the ITSC and the domain remains available for randomisation of patients in the Moderate State. The protocol, for Moderate Patients, specifies a period of treatment for patients assigned to therapeutic anticoagulation, irrespective of the progression of illness severity. The DSMB have made no recommendation to modify the protocol and, at this time, patients enrolled in Moderate State should continue their treatment assignment as specified in the trial protocol.

We will work to analyse and report these findings as soon as possible and request that sites make this information available only to relevant clinical staff.

On behalf of the REMAP-CAP ITSC I would like to thank the DSMB and the Statistical Advisory Committee for their vital work in ensuring the safety of patients enrolled in REMAP-CAP. I would also like to sincerely thank all investigators, research coordinators, participants and their families who continue to support REMAP-CAP and the generation of evidence for the treatment of COVID-19.

If you have any questions about any of the above, please don't hesitate to contact me.

Sincerely,

Professor Steve Webb
Chair,
REMAP-CAP International Trial Steering Committee

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