

30<sup>th</sup> November, 2023

Dear REMAP-CAP site investigators and research staff,

**RE: REMAP-CAP Anticoagulation and Antiplatelet Domains**

We are writing to inform you of a decision that has been made by the REMAP-CAP International Trial Steering Committee (ITSC) to close recruitment to the Anticoagulation and Antiplatelet Domains of REMAP-CAP.

To date, over 1,300 critically ill participants have been randomized to the second iteration of the Anticoagulation Domain, without having reached a pre-defined statistical trigger. Due to declining case numbers of critically ill patients with COVID-19, recruitment to this domain has substantially slowed. In this context, consideration has been given to the operational futility of this domain.

A series of statistical simulations have been conducted by the REMAP-CAP statisticians at Berry Consultants, and suggest that this domain is likely to be sitting at an indeterminate point between statistical triggers for superiority and futility. It is estimated that continued recruitment at the current rate is unlikely to substantially increase the likelihood of reaching a statistical trigger.

In light of these simulations and the low likelihood of reaching a statistical trigger with continued recruitment to this domain, it is therefore considered that continuing recruitment to this domain is operationally futile. The DSMB has regularly monitored this domain for safety, and no safety concerns have been communicated to the ITSC.

The Antiplatelet Domain was reopened in April 2022, and to date only 10 participants have been randomized to this domain globally. It was therefore considered that continuation of this domain is also operationally futile.

In the aim of making data regarding the optimal treatment for COVID-19 available to the public while it still has relevance for clinical care, the REMAP-CAP ITSC has made the decision to close recruitment and disseminate the results of these domains. This decision has the support of the REMAP-CAP DSMB.

We recommend that for participants who have been allocated to an intervention within these domains, administration of allocated interventions should be continued as per the Domain-Specific Appendices.

Updates will be forthcoming when available. We thank you sincerely for your participation in the Anticoagulation and Antiplatelet Domains, and REMAP-CAP overall, as we continue to evaluate optimal treatment for CAP and COVID-19. We look forward to sharing the results of these domains with you, and the public, as soon as they are available.

Sincerely,



Srinivas Murthy

Chair, REMAP-CAP International Trial Steering Committee



Ryan Zarychanski

Co-Chair, Anticoagulation Domain Specific Working Group



Charlotte Bradbury

Co-Chair, Anticoagulation Domain Specific Working Group

Chair, Antiplatelet Domain Specific Working Group