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REMAP-CAP ITSC Chair  
International Trial Steering Committee REMAP-CAP  
Statistical Analysis Committee REMAP-CAP  
Global Project Management REMAP-CAP

September 22, 2023

Dear All,

The REMAP-CAP Data Safety Monitoring Board has reviewed the following documents:

1. The response document from the ITSC regarding inclusion of pediatric patients (received August 25, 2023) from the ITSC chair.
2. REMAP-CAP August Safety Analysis provided by ICNARC on August 31, 2023.

The analysis contained summaries for the following domains: Antibiotic Domain, Marcolide Domain, Corticosteroid Domain, Influenza Antiviral Domain, Anticoagulation Domain, Mechanical Ventilation Domain, Cysteamine Domain, the COVID-19 Immunoglobulin II Domain, and the COVID-19 Antiplatelet Domain. Data summaries for domains not included in the report include the endothelial domain in the PISOP Severe and PINSNP Severe states.

Following review of the documents listed above, the DSMB is recommending the following:

1. The DSMB conditionally approves enrolment for pediatric patients in the antiviral domain if the DSA is amended as proposed in formal communication documents to date.
2. The DSMB conditionally approves enrolment for pediatric patients in the corticosteroid domain with the following caveats:
  - a. The DSA is amended to point out that there is minimal safety data in children less than 3 months old on use of corticosteroids, or of corticosteroid courses longer than 3-5 days in young children.
  - b. The DSA must note the association of longer courses of steroids with neurologic harm in premature neonates.
  - c. The DSA should state the potential risks and potential benefits for corticosteroid use. The respective local IRB can decide the age cutoff to include for children.
  - d. The DSA needs to clearly outline any potential risks for very young infants in the event they have prolonged exposure to steroids.
3. Full DSMB approval for inclusion of the pediatric population in the antiviral and corticosteroid domains will be granted upon review of the aforementioned

contingencies in the respective DSA's. To facilitate timing of enrollment, the DSMB can review each DSA separately as it is updated.

4. The DSMB did not recognize any safety signals and recommends continuing enrolment of the reviewed domains.

We would like to recognize again the excellent work produced by ICNARC and thank them for their continued partnership. We would also like to thank the ITSC for their response to our queries regarding the inclusion of pediatric patients.

Your Sincerely,



Victoria G. Manax, MD  
Chair REMAP-CAP DSMB



Jason Connor, PhD  
Co-chair REMAP-CAP DSMB

Cc DSMB members, REMAP-CAP lead investigators, REMAP-CAP trial management, REMAP-CAP SAC, REMAP-CAP ITSC