Randomised, Embedded, Multi-factorial, Adaptive Platform for Community-Acquired Pneumonia

WELCOME TO THE SECOND EDITION OF THE REMAP-CAP PANDEMIC NEWSLETTER

THANK YOU

The REMAP-CAP team would like to extend a SINCERE and BIG thank you to EVERYONE for their commitment to the REMAP-CAP study.

Thanks to YOUR hard work, the UK now has:

- 142 (48%) of the 296 sites open globally
- 4243 (67%) of the 6290 patients recruited globally
- 4163 (76%) of the 5488 COVID-19 patients recruited globally

ACTIVE PANDEMIC TREATMENT DOMAINS

Active both on the ward and ICU
- Antiplatelet

Active on ICU only
- Immune Modulation
- Vitamin C (central supplies available soon)
- Simvastatin

UPDATED AND NEW DOMAINS COMING SOON

Updated domains
- Anticoagulation
- Immune Modulation

New domain
- ACE-2 Renin-Angiotensin System
SUMMARY OF REMAP-CAP RESULTS

**Corticosteroid domain:**

REMAP-CAP has helped establish corticosteroids as standard care for critically ill patients with COVID-19. The results of the REMAP-CAP steroid domain, evaluating hydrocortisone, were published in JAMA on 2 September 2020, alongside a meta-analysis of corticosteroids. Subsequently, the World Health Organisation (WHO) issued new guidance recommending the use of systemic corticosteroids in critically ill patients with COVID-19. An updated COVID-19 Therapeutic Alert for corticosteroids was issued on 3 September 2020.

**Immune Modulation domain:**

REMAP-CAP established, for the first time, that Interleukin-6 inhibitors (sarilumab and tocilizumab) reduce mortality and time in ICU for critically ill patients with COVID-19. Preliminary results were published as a pre-print on 7 January 2021. A Therapeutic Alert interim position statement for Tocilizumab and Therapeutic Alert for Interleukin-6 inhibitors for critically ill patients with COVID-19 pneumonia (adults) were issued on 25 November 2020 and 1 February 2021, respectively.

**Antiviral domain:**

REMAP-CAP established that Kaletra (lopinavir/ritonavir) provided no benefit for critically ill patients with COVID-19.

**Immunoglobulin domain:**

REMAP-CAP established that treatment with convalescent plasma treatment provided no benefit for the general critically ill population with COVID-19.

**Therapeutic anticoagulation domain:**

Statements on the effect of therapeutic anticoagulation were released from the REMAP-CAP trial on 23 December 2020 and from ATTACC, ACTIV-4a & REMAP-CAP Multiplatform RCT on moderately sick hospitalised patients on 28 January 2021. For critically ill patients with COVID-19 (receiving organ support) therapeutic-dose heparin, compared with standard of care, was found to be futile with high probability of inferiority/harm. In contrast, in hospitalised patients (not receiving organ support) therapeutic-dose heparin treatment was beneficial. A therapeutic alert and summary on heparin anticoagulation for patients admitted to hospital with COVID-19 were issued on 23 December 2020 and 8 February 2021, respectively.

These results show the evidence you are generating in REMAP-CAP is already being used to guide treatment decisions and improve outcomes for patients with COVID-19.
REMAP-CAP Covid-19 Milestones

CAS: Central Alerting System
DSA: Domain Specific Appendix
RA: Regulatory Approval

Antiviral & Immune Modulation DSA RA
27-Apr-20
Therapeutic Anticoagulation (ICU) DSA RA
27-Mar-20
Therapeutic Anticoagulation (Ward) and Vitamin C DSA RA
15-Jul-20
Corticosteroid Publications
02-Sep-20
Antiplatelet (ICU) DSA RA
12-Oct-20
Immune Modulation CAS
25-Nov-20
Immune Modulation Pre-Print Publication
28-Jan-21
Multiplatform RCT Anticoagulation Results

Immunoglobulin DSA RA
22-Apr-20
23-May-20
Immunoglobulin Press Release
07-Jan-21
08-Feb-21
01-Feb-21
11-Jan-21
19-Nov-20
23-Dec-20
27-Apr-20
22-Apr-20
09-Jan-20
03-Aug-20
03-Sep-20
Corticosteroid DSA RA
Corticosteroid CAS
Anticoagulation CAS (& Press Release)
Urgent Safety Measure: Closed randomisation to Hydroxychloroquine - Antiviral Domain
Corticosteroid DSA RA
09-Jan-20

WEB LINKS

Corticosteroid domain:
02 Sep 2020 Effect of Hydrocortisone on Mortality and Organ Support in Patients With Severe COVID-19: The REMAP-CAP COVID-19 Corticosteroid Domain Randomized Clinical Trial
02 Sep 2020 Association Between Administration of Systemic Corticosteroids and Mortality Among Critically Ill Patients With COVID-19: A Meta-analysis | Critical Care Medicine | JAMA | JAMA Network
02 Sep 2020 Editorial: Corticosteroids in COVID-19 ARDS - Evidence and Hope During the Pandemic
03 Sep 2020 Covid-19 Therapeutic Alert: Corticosteroids in the treatment of suspected or confirmed COVID-19

Immune Modulation domain:
19 Nov 2020 Arthritis drug effective in treating sickest Covid-19 patients
25 Nov 2020 Publication of an interim position statement: Tocilizumab for patients admitted to ICU with COVID-19 pneumonia (adults)
07 Jan 2020 Arthritis drugs may reduce mortality and time in ICU for sickest ICU patients
07 Jan 2020 Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19 – Preliminary report
01 Feb 2021 Interleukin-6 inhibitors (tocilizumab and sarilumab) for critically ill patients with COVID-19 pneumonia (adults)

Antiviral domain:
19 Nov 2020 Arthritis drug effective in treating sickest Covid-19 patients (Reports Kaletra ineffective)

Immunoglobulin domain:
11 Jan 2021 Blood plasma treatment has limited effect for the sickest Covid-19 patients

Anticoagulation domain:
23 Dec 2020 Statement from REMAP-CAP Trial on Blood Thinners in Covid-19 Patients
23 Dec 2020 Therapeutic Anticoagulation (Heparin) in the Management of Severe COVID-19 (SARS-CoV-2 Positive) Patients
28 Jan 2021 ATTACC, ACTIV-4a & REMAP-CAP multiplatform RCT - Results of interim analysis
08 Feb 2020 Heparin anticoagulation in patients admitted to hospital with Covid-19
DATA ENTRY

Please ensure that data are entered in a timely and accurate manner so that we can analyse and publish data using the most complete and accurate dataset.

General missing pages reports will continue to be sent bi-weekly basis. Urgent form-specific query reports will be sent when we are approaching scheduled data analysis.

RECENT SPINNAKER UPDATES

A question has been added to the baseline form to collect the patient’s vaccination status prior to this acute illness (Yes/No/Unknown).

- For patients randomised before the vaccination program began, the answer will default to "No"
- For patients randomised since the vaccination program began, but before the addition of this field, it will default to "unknown".
- It is not necessary for sites to retrospectively update this information.

The "<" and ">" options for physiological and laboratory variables have been removed. If a laboratory has not reported a specific value and has instead reported that the value is beyond a certain threshold (i.e. >999) then the site should enter the threshold value (i.e. 999). No action is required by sites for data previously entered.

CO-ENROLMENT WITH REMAP-CAP

The following co-enrolment agreements are in place with the REMAP-CAP study:

ACCORD, ADAPT-Sepsis, ARCADIA, ARREST, ASICS, BALANCE, BLING III, cEEG SE STUDY, COVRAS, COVSurf, COVEMERALD, EFFORT, EMPRESS, GenOMICC, INHALE, INNATE, INNATE IMMUNITY IN CRITICAL ILLNESS, INTENT, ISARIC, LUCID, PASS, Patch, Plasma-Lyte 148® vs Saline study, PROMEDIC, PRONTO, REACTOR, REALIST, RECOVERY, SUDDICU, START-AKI, STOP-COVID, STRESS-L, SUDDICU, TEAM-ICU, VACIRIS, VITAMINS Trial, XARELTO.
CELEBRATE YOUR SUCCESS

So much has been achieved by the UK REMAP-CAP sites over the past year. THANK YOU EVERYONE for your continued SUPPORT. The evidence you are generating is already improving care for patients with COVID-19.

We look forward to the time when we can celebrate your success together.

WE4YOU SEMINARS

The next WE4YOU seminar ‘Convalescent Plasma’ is scheduled for Wednesday 17th February 2021 at 15:00 GMT.

Please click the link below to join the webinar:

https://us02web.zoom.us/j/82888442003?pwd=TEtwTC91RVBPUGkrNGNQQ3Y5R2c5QT09

Webinar ID: 828 8844 2003; Passcode: 632964

Recordings of previous Webinars can be accessed here:

https://www.remapcap.org/site-education

NIHR Urgent Public Health Studies Research Workforce Participation Certificate

The COVID Consenting Initiative will present anyone who has consented participants to UPH studies with a certificate which can be included in their continuing professional development (CPD) portfolios.

Please sign up and log into NIHR Learn to download the certificate.

The NIHR Learn Platform link is: https://learn.nihr.ac.uk/course/view.php?id=808

If there are any difficulties, please contact: covid19application@nihr.ac.uk.