



Dear REMAP-CAP investigators,

A lot has happened since you received our last newsletter. In this edition, we spotlight our collaboration with Critical Care Reviews. They hosted a free livestream of the IL-6ra results at the time of publication in the New England Journal of Medicine, a massive effort by the #CCR team. In addition to the results presentation and the excellent editorial by Tim Walsh, Derek Angus talked about the beauty of platform trials and Liz Lorenzi explained the Bayesian statistical framework. We also celebrated our women in science in various ways, we've added new sites to our growing family, and have added new domains and interventions to the trial.

You can follow us on social media to keep up with the latest REMAP-CAP news, and read all about it in this newsletter. These accomplishments were made because of you! Thank you for being part of our #remapcapfamily and for helping us find the best treatment for CAP and COVID-19.

Lennie Derde, European Coordinating Investigator

Like listening to a podcast? Find our podcast series in collaboration with Rob Mac Sweeney from Critical Care Reviews on **Spotify and iTunes**



IN THIS ISSUE:

- Recruitment update
- WE4YOU
- Welcome new sites
- Just published
- Announcements
- Featured domain - ACE2 RAS
- CCR Livestream

RECRUITMENT UPDATE

We are proud to announce that REMAP-CAP is currently (7th April 2021) active in **310** sites in **22** countries worldwide and a total of **6,781** unique patients have been included, of which **6,051** COVID-19 patients. These patients contributed to a total of **12,416** randomisations in the different domains.

Europe:

- **205** Active sites
- **5,096** Patient Inclusions
- **4,871** COVID-19 Patients
- **9,900** Randomizations

WE4YOU

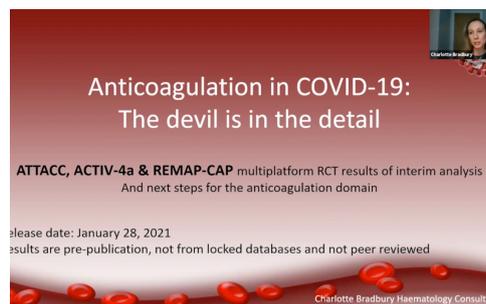
Every uneven week on Wednesday at 4 pm CEST, we have a webinar for all European REMAP-CAP sites. It's great to be connected in our region.

At each WE4YOU, we present different aspects of the trial. It can be about a new domain, new results, how we deliver the trial or an explanation of how the trial works. **The next WE4YOU about the new intervention Ivermectin takes place April 14th 2021.** Find below some recent examples. All previous webinars can be viewed on [here](#).

Convalescent plasma by Lise Estcourt



Anticoagulation in COVID-19 by Charlotte Bradbury



If there is any aspect you want to learn or talk about, let us know! Feel free to contact us directly at eu.remapcap@umcutrecht.nl

A BIG WELCOME

In the last months, we have welcomed **9 new European sites** to the family. We are excited about making a difference in the treatment of CAP and COVID-19 patients together. A big welcome to:

- CH de Mont de Marsan, France
- CH des Pays de Morlaix, France
- Cork University Hospital, Ireland
- Hôpital Nord Franche-Comté, Belfort, France
- Hôpital Simone Veil, Eaubonne, France
- Humanitas Research Hospital, Milan, Italy
- University Hospital Cologne, Germany
- University Hospital Waterford, Ireland
- Ziekenhuis Bernhoven, Netherlands

JUST PUBLISHED

Interleukin-6 Receptor Antagonists in Critically Ill Patients with Covid-19

Tocilizumab and Sarilumab reduce mortality by 8.5% in critically ill COVID-19 patients receiving organ support. Furthermore, the treatment improved recovery so that on average patients were able to be discharged from the ICU about 7 days earlier compared to patients who received no immune modulator.



The NEW ENGLAND
JOURNAL of MEDICINE

7 January 2021

New England Journal of Medicine

ANNOUNCEMENTS

We've finalised version 3.0 of the anticoagulation domain and the protocol for the new ivermectin arm in the COVID-19 Antiviral domain.

If you're interested to join (one of) these domains, let us know at eu.remapcap@umcutrecht.nl

We recently gave green light to the first Italian REMAP-CAP site, Humanitas Research Hospital in Milan. Welcome to PI Maurizio Cecconi and team. More Italian sites are joining the #remapcapfamily soon, and the first 6 patients have been recruited.



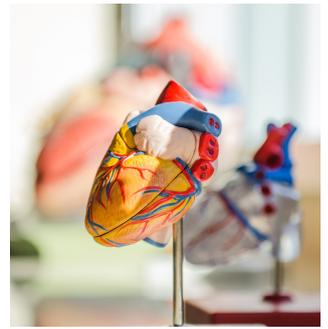
REMAP-CAP was featured in the Horizon Magazine of the European Commission on the study results of Tocilizumab and Sarilumab.



Lennie Derde discusses the use of Tocilizumab in targeting interleukin-6 and assesses its role in reducing the risk of invasive mechanical ventilation for critically ill patients with professor Daiana Stolz (ERS chair), in this ERS podcast.

FEATURED DOMAIN - COVID-19 ACE2 RAS DOMAIN

In COVID-19 patients, binding of the surface spike protein of SARS-CoV-2 to the ACE2 receptor of a host cell, and subsequent down-regulation of ACE2 expression may induce acute lung injury. Therefore, REMAP-CAP launched the ACE2RAS domain, in which we test the efficacy of reducing the alteration in the renin-angiotensin system (RAS) in response to SARS-CoV2-ACE2 binding compared to no treatment.



In this domain, COVID-19 patients are randomised to:

1. Angiotensin converting enzyme inhibitor (ACEi),
2. Angiotensin II receptor blocker (ARB)
3. ARB + DMX-200 or
4. No RAS inhibitor.

As ACEi/ARBs are well-known and widely available, these agents would provide an attractive treatment strategy for COVID-19 patients globally. Furthermore, pre-clinical studies suggest that concomitant inhibition of the AT1 and CCR2 receptor may reduce inflammation and possibly fibrosis in vasculopathy and inflammatory nephropathy models. Therefore, DMX-200, a chemokine receptor (CCR2) inhibitor, is used in addition to ARB treatment to attenuate excessive monocyte recruitment and mitigate associated injurious maladaptive sequelae of tissue inflammation and thrombosis. These treatments are not given as standard of care in COVID-19 patients but could be beneficial.

We are excited to further investigate the potential for benefit of RAS-modulation with ACEi/ARBs and DMX-200 for COVID-19 patients in REMAP-CAP. The first patient was included on the 16th of March 2021.

To learn more about the ACE2 RAS domain and to participate in this domain, please contact us at remapcap.org or eu.remapcap@umcutrecht.nl

Critical Care Reviews & REMAP-CAP Livestream



On 25-02-21, Critical Care Reviews hosted a dedicated 2.5 hour REMAP-CAP Expert Livestream.

Derek Angus (University of Pittsburgh, US) discussed the beauty of adaptive platform trials and why these are the future, followed by Liz Lorenzi (Berry Consultants, US) who clearly explained the Bayesian framework. The session ended with the Tocilizumab results discussed by Lennie Derde (UMC Utrecht, NL) and an independent editorial by Tim Walsh (Edinburgh, Scotland).

Click on the link, if you want to get up to speed with REMAP-CAP while learning more about adaptive platform trials and bayesian analyses.