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29/06/21
Re: Study Title: Randomized, Embedded, Multi-factorial, Adaptive Platform Trial for community - Acquired Pneumonia
REC reference: 18/lo/0660
EudraCT number: 2015-002340-14
IRAS project ID: 237150

Substantial amendment 27 (AM027) Expedited Approval
Dear MHRA submission team,
I am submitting substantial amendment AM027 for the REMAP-CAP study to the MHRA for review.

AM027 involves:
The addition of the DMX-200 intervention (ACE2/RAS domain) to the Participant information sheets as well as the addition of DMX-200 documentation

ACE2 RAS domain
The addition of the ACE2 / RAS domain specific appendix was part of AM025.
Within the current ACE2 RAS domain specific appendix there is the DMX-200 intervention, a chemokine receptor-2 (CCR2) inhibitor that can be used in combination with an ARB.
DMX-200 is a novel drug that will be supplied as a clinical trial IMP with clinical trial labelling.
This intervention is now being added as part of AM026.

I have also made the below changes to the MHRA CTA.
We added 1 IMP product to the MHRA CTA:
DMX-200

The below documents have been submitted:
237150_AM026_Locked
DIL2501 REMAP CAP label Proof english & dutch 20210505
DMX-200 ARDS IB v4 SIGNED
DMX-200 ARDS IB v4.0 track changes
DMX-200 COVID-19 IMPD v2.0 April 2021
DMX-200_REMAP_CAP_label_proof_Part_2_sign_of 20210506
Grant Agreement-101003589-RECoVER_FE
IRASEudractExport
MhraProductsForm AM026
MIA_Fisher_DE_BW_01_MIA_2021_0022_DE+ EN

QP Declaration REMAP CAP_27May2021
Site GMP Certificate FDA EU and Registration Database Reference 2020 Signed

As requested an RSI section has been added to the IB.

I would also like to inform you of the closure of the REMAP-CAP Antiplatelet domain.
On the 22nd of June 2021 the REMAP-CAP International Trial Steering Committee (ITSC) received correspondence from the REMAP-CAP DSMB notifying us of Platform Conclusions arising from an adaptive analysis.

This adaptive analysis revealed that for patients with COVID-19 who are receiving organ support in an ICU, antiplatelet therapy, either with aspirin or P2Y12 inhibitor (which were found to be equivalent), was ineffective when compared to no antiplatelet therapy (OR = 0.99 [95% CrI 0.82 – 1.19], probability of OR < 1.2 = 98%). The unanimous recommendation of the DSMB was that this domain be closed for patients with severe COVID-19 (i.e. patients receiving organ support in an ICU). This recommendation has been accepted by the ITSC.

In addition, in light of the recent publication of results from the RECOVERY trial, which found that treatment with aspirin did not improve 28-day mortality, the REMAP-CAP ITSC have decided to also close the Antiplatelet Domain to patients with moderate COVID-19 (i.e. hospitalised patients not receiving organ support in an ICU). These data are reflective of high-quality evidence from a large randomised trial, which further suggest that antiplatelet therapy is not associated with improved outcomes for patients with COVID-19.

Many Thanks
Farah

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

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