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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 34 (AM34)

I am submitting substantial amendment AM034 for the REMAP-CAP study.

Addition of releasing site information to section D9 of the MHRA CTA for licensed ascorbic acid

This involves changes to the MHRA CTA for the Ascorbic Acid stock for use within REMAP-CAP

Stock: 50ml vials of concentrate for solution for injection/infusion contains: 7,5g ascorbic acid

Addition of UK Releasing site: Alliance Healthcare; Unit 1, High View Road Ind Units, South Normanton, Derbyshire; DE55 2DT

Marketing Authorisation holder: Pascoe pharmazeutische Präparate GmbH

UK MA number: PL 14369/0009

Submission of associated SmPC

We are also formally submitting an amendment for the Pause of the ACE2/RAS domain within REMAP-CAP

On the 24th of February, 2022, we received correspondence from the REMAP-CAP Data Safety and Monitoring Board (DSMB) regarding the ACE2 Renin Angiotensin System (RAS) Domain.

The DSMB has raised concerns about the safety of ACE2 RAS domain interventions in severe state (critically ill) patients based on the most recent 2-monthly interim review of safety data. After reviewing the recommendations from the DSMB, REMAP-CAP has **stopped enrolment of critically ill patients into this domain**, which is currently in phase 2. We recommended that critically ill patients currently receiving an angiotensin converting enzyme (ACE) inhibitor or an angiotensin receptor blocker (ARB) – including in combination with DMX-200 – as part of the study protocol should have their study drug discontinued. Although the DSMB did not raise safety concerns for patients in the moderate state (noncritically ill), we believe that it is best to **temporarily pause enrolment of noncritically ill patients into this domain** to allow review of additional data prior to potentially resuming enrolment. Note that a fourth intervention in the domain, TRV-027, had not yet commenced recruitment.

The below documents are included in this submission:

MhraProductsForm_REMAP-CAP AM034 020322

Ascorbic Acid SmPC

REMAP-CAP AM034 Amendment_Tool_v1_6_LOCKED

Many Thanks
Farah

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