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Date: 22 May 2020

Full Title:	mulTi-Arm Therapeutic study in pre-ICu patients admitted with Covid-19 – Repurposed Drugs
Short Title:	TACTIC-R
EUDRACT Number:	2020-001354-22
IRAS Number:	282213
REC Reference:	20/EE/0135

Dear Sir/Madam,

I am writing to submit a substantial amendment to the documentation listed below for the above-named trial.

The TACTIC-R trial protocol has been amended to reflect the following changes:

- Clarification on the primary outcome measure
- Correction of units for Cockcroft-Gault formula since they were misrepresented with the units for eGFR, in the previous protocol version.
- Reference to mechanical ventilation has also been modified to invasive mechanical ventilation throughout the protocol for further clarification.
- Addition of the option of venous endothelial cell collection as an exploratory biomarker, due to the emerging evidence of an endotheliitis in COVID-19 infections. This may drive the organ dysfunction and clotting, and may be amenable to immunomodulatory therapy. This will not add to the amount of blood taken.
- Clarification that adverse events will only be recorded in the medical notes and not in the trial data collection tools. This has been done to facilitate the workload on the wards when dealing with the number of adverse events experienced by COVID-19 patients.

A number of minor administrative updates and corrections have been also made throughout the protocol.

In response to feedback from the patients screened, over the last week, for TACTIC-R, we have also drafted a shortened version of the Patient Information Sheet. Patients reported that the existing Participant Information Sheet was too long and detailed, given that they are unwell and that relatives/friends are unable to accompany, and directly support, them. A shortened PIS will facilitate the consent process. The original full-length PIS will be available on the web. We note that is the strategy used in the RECOVERY trial, which has now recruited approximately 10,000 subjects.

As part of this amendment we are submitting a new PIS which details endothelial cell collection.

We would also like to add some new sites to this trial and change PIs at two existing participating sites.

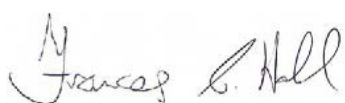
Please find enclosed the following documentation in support of our application for review

Document	Version	Date
Cover letter	n/a	22May2020
Notice of substantial amendment form	n/a	20May2020
TACTIC-R Protocol tracked and clean	2.0	20May2020
TACTIC-R PIS ICF Endothelial Cell Collection	1.0	20May2020
TACTIC-R Short PIS ICF	1.0	20May2020
Sponsor Authorisation e-mail	n/a	22May 2020

Please do not hesitate to contact us should you require further information.

I look forward to hearing from you in due course.

Many thanks.



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