Reviewer’s report

Title: Anticoagulation in critically ill patients on mechanical ventilation suffering from COVID-19 disease, The ANTI-CO trial: A structured summary of a study protocol for a randomised controlled trial

Version: 0 Date: 13 Aug 2020

Reviewer: Kirsty Loudon

Reviewer's report:

Review #4
The summary is now comprehensive and well written, conforming to the COVID-19 study protocol structured summary template.

Review #3
Thank you for amending the wording in the letter regarding consent and writing an addendum to the protocol regarding deferred consent to clarify procedures and ensure the letter and the protocol match.
I have made a very minor change so edited himself to themself so gender neutral. I trust this is acceptable.

Review #2
ETHICS APPROVAL AND CONSENT TO PARTICIPATE
There is a mismatch between the information in the protocol and the letter summary on consent processes which urgently needs to be addressed.

In the PROTOCOL, you mention that written informed consent will be obtained from the patient/or family member if the patient is not able to give consent. This is consistent with principle 28 of the Declaration of Helsinki. However, the Trials journal is bound by ICMJE "Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly work in Medical Journals" (http://www.icmje.org/). I note the attached IRB ethical approval for the study but it would thus be helpful if the authors could cite the relevant legislation and explain how it has authority in the conduct of research involving incapable patients.
In the SUMMARY you state: "If this person is not available a deferred consent is taken, which needs later confirmation by the participant or the legal representative."

There is, however, an issue with deferred consent mentioned in the letter. Principle 30 of the Declaration of Helsinki states that Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research group. In such circumstances the physician must seek informed consent from the legally authorised representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent PROVIDED THAT THE SPECIFIC REASONS FOR INVOLVING SUBJECTS WITH A CONDITION THAT RENDERS THEM
UNABLE TO GIVE INFORMED CONSENT HAVE BEEN STATED IN THE RESEARCH PROTOCOL AND THE STUDY HAS BEEN APPROVED BY A RESEARCH ETHICS COMMITTEE. Consent to remain in the research must be obtained as soon as possible from the subject or a legally authorised representative.

Trials requires both documents, the summary and protocol, to have identical information to avoid confusion. Please revise the summary and protocol to ensure there is consistent information. IF there is deferred consent, your research protocol should state the specific reasons for involving patients with COVID-19 who are unable to give consent - currently there is no mention of deferred consent. I note that your research ethics committee has given approval. Please state that consent to remain in the research will be obtained as soon as possible from the subject or a legally authorised representative. And as mentioned above: please cite the relevant legislation (that authorised your research) and explain how it has authority in the conduct of research involving incapable patients.

Review #1
Thank you for submitting a summary to Trials to publish alongside your trial protocol. This is a well written, comprehensive structured abstract for a protocol for a randomized controlled trial to explore the use of anticoagulation in seriously ill patients suffering from COVID-19 disease.

I had a few comments detailed below.

TITLE: I have added information to define the population being studied: "seriously ill patients on mechanical ventilation."

OBJECTIVES: The wording was changed in acknowledgement of clinical equipoise in assessing bivalirudin and routine anticoagulant treatment. Please check this is okay.

TRIAL DESIGN: "parallel group, superiority, randomized (1:1 allocation ratio) has been added to describe the RCT - please confirm the RCT is superiority design to show bivalirudin is superior not equivalent to routine anticoagulant treatment.

PARTICIPANTS: Some additional information about settings has been inserted - Hamad Medical Corporation-ICU in Qatar. Also minor edits of wording has been undertaken. Have you specific criteria ie WHO or PCR test to confirm COVID-19 diagnosis?

INTERVENTION AND COMPARATOR: Abbreviations have been spelt out as first time used and some editing of wording has been done - please check okay.

RANDOMISATION: "using a 1:1 allocation ratio" has been inserted. This was based on sample size information. Please edit if incorrect.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE: "If this person is not available a deferred consent is taken, which needs later confirmation by the participant or the legal representative." Please insert local legislation if possible as my colleague requested.
FUNDING: Standard wording has been inserted regarding the independence of the trialists from the funder.

AUTHORS' CONTRIBUTIONS: This has been edited. Please check okay.

I have no further comments.

Thank you!

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