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Trials

LETTER Open Access

The effect of prostacyclin (Iloprost) infusion at a dose of 1 ng/kg/min for 72 hours compared to placebo in mechanically ventilated patients with COVID-19: A structured summary of a study protocol for a randomized controlled trial

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Abstract

Objectives: To investigate the effect of continuous infusion of the potential endothelial cytoprotective agent prostacyclin (Iloprost) 1 ng/kg/min vs. placebo for 72 hours on pulmonary endotheliopathy in mechanically ventilated COVID-19 patients.

Trial design: A multicenter, randomized (1:1, active: placebo), blinded, parallel group exploratory trial

Participants: Inclusion criteria are: Adult patients (>18 years); Confirmed COVID-19 infection; Need for mechanical interventions; Endothelial biomarker soluble thrombomodulin >4ng/ml. Exclusion criteria: Withdrawal from active therapy; Pregnancy (non-pregnancy confirmed by patient being postmenopausal (age 60 or above) or having a negative urine- or plasma-hCG); Known hypersensitivity to iloprost or to any of the other ingredients; Previously included in this trial or a prostacyclin trial within 30 days; Consent cannot be obtained; Life-threatening bleeding defined by the treating physician; Known severe heart failure (NYHA class IV); Suspected acute coronary syndrome The study is conducted at five intensive care units in the Capital Region of Denmark at Rigshospitalet, Herlev Hospital, Hvidovre Hospital, Bispebjerg Hospital, Nordsjællands Hospital.

Intervention and comparator: The patients are randomized to 72-hours continuous infusion of either prostacyclin (Iloprost/Ilomedin) at a dose of 1 ng/kg/min or Placebo (normal saline).

Main outcomes: Primary endpoint: Days alive without mechanical ventilation in the intensive care units within 28 days

(Continued on next page)

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(Continued from previous page)

Randomisation: The randomisation sequence is performed in permuted blocks of variable sizes stratified for trial site using centralised, concealed allocation. The randomisation sequence is generated 1:1 (active/placebo) using the online randomisation software 'Sealed Envelope' (https://www.sealedenvelope.com/). Once generated the randomisation sequence is formatted and uploaded into Research Electronic Data Capture system (REDCap) to facilitate centralised, web-based allocation according to local written instruction.

Blinding (masking): The following are blinded: all clinicians, patients, investigators, and those assessing the outcomes including the statisticians.

Numbers to be randomised (sample size): Forty patients are planned to be randomized to each group, with a total sample size of 80 patients.

Trial Status: Protocol version 1.4 dated May 25, 2020. Recruitment is ongoing. The recruitment was started June 15, 2020 and the anticipated finish of recruitment is February 28, 2021 with 90 days follow up hereafter.

Trial registration: Trial registration at clinicaltrialregisters.eu; EudraCT no. 2020-001296-33 on 3 April 2020 and at ClinicalTrials.gov Identifier: NCT04420741 on 9 June 2020

Full protocol: The full protocol is attached as an additional file, accessible from the Trials website (Additional file 1).In the interest in expediting dissemination of this material, the familiar formatting has been eliminated; this Letter serves as a summary of the key elements of the full protocol.

Keywords: COVID-19, Randomised controlled trial, protocol, mechanical ventilation, endotheliopathy, thrombomodulin, prostacyclin

Supplementary information

Supplementary information accompanies this paper at https://doi.org/10.1186/s13063-020-04696-2.

Additional file 1. Full Study Protocol.

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Authors' contributions

PIJ is sponsor of the study and AP is the coordinating investigator. PSJ, KTK, NEC and MB are local study investigators. PIJ wrote this study summary and AP, PSJ, KTK, NEC, MB and JS read and approved it. The author(s) read and approved the final manuscript.

Funding

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Availability of data and materials

Not applicable.

Ethics approval and consent to participate

The study protocol has been approved by the Ethics Committees of the Capital Region of Denmark, reference no. VEK H-20026049 on June 12, 2020. I hereby certify that this trial has received ethical approval from the appropriate ethical committee as described above https://laegemiddelstyrelsen.dk/da/nyheder/temaer/ny-coronavirus-covid-19/~/media/F17E7272B4734EADA1FD0DA3EA082411.ashx.

Consent is obtained from a physician not involved in the study acting on the patients behalf before any trial related procedure are started as this is a trial in an acute setting and eligible patients for this trial will be temporarily incompetent due to acute severe illness and therefore not able to give informed consent. The Investigator will as soon as possible after inclusion of the patient obtain written consent from the patient or proxy consent from both a physician not involved in the study acting on the patient's behalf and next-of-kin. Patients, who, during the course of this trial, become able to give consent, will be asked to participate and give their consent even though a proxy consent is obtained.

Consent for publication

Not applicable.

Competing interests

PIJ is co-inventor on a patent for the biomarker thrombomodulin to identify critically ill patients with endotheliopathy and the use of prostacyclin as a therapy to combat this condition. The remaining authors declare that they have no competing interests

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