

LETTER

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“Early transfusion of convalescent plasma in older patients with COVID-19 to prevent disease progression: A structured summary of a study protocol for a randomised controlled trial”

Luciana Teofili^{1*} , Raffaele Landolfi¹, Antonella Cingolani¹, Andrea Antinori², Jacopo Vecchiet³, Maurizio Sanguinetti¹, Antonio Gasbarrini¹, Tina Pasciuto¹, Nicoletta Orlando¹ and Silvia Lamonica¹

Abstract

Objectives: The primary objective is to demonstrate that COVID-19 convalescent plasma (CCP) prevents progression to severe pneumonia in elderly COVID-19 pneumonia patients with chronic comorbidities. Secondary objectives are to demonstrate that CCP decreases the viral load in nasopharyngeal swabs and increases the anti-SARS-CoV-2 antibody titre in recipients.

Trial design: This is a randomized, open-label, parallel group, phase II/III study with a superiority framework. The trial starts with a screening phase II designed with two-tailed $\alpha=0.2$. In case of positive results, the trial will proceed in a formally comparative phase III ($\alpha=0.05$).

Participants: Adult patients with confirmed or suspected COVID-19 who are at risk according to CDC definition are eligible. Inclusion criteria are all the following: age ≥ 65 ; pneumonia at CT scan; $\text{PaO}_2/\text{FiO}_2 \geq 300$ mmHg; presence of one or more comorbidities; signed informed consent. Exclusion criteria are one of the following: age < 65 ; $\text{PaO}_2/\text{FiO}_2 < 300$ mmHg; pending cardiopulmonary arrest; refusal to blood product transfusions; severe IgA deficiency; any life-threatening comorbidity or any other medical condition which, in the opinion of the investigator, makes the patient unsuitable for inclusion. The trial is being conducted at three reference COVID-19 centres in the middle of Italy.

Intervention and comparator: Intervention: COVID-19 Convalescent Plasma (CCP) in addition to standard therapy. Patients receive three doses (200 ml/day on 3 consecutive days) of ABO matched CCP. Comparator: Standard therapy

Main outcomes: A. Primary outcome for Phase II: Proportion of patients without progression in severity of pulmonary disease, defined as worsening of 2 points in the ordinal scale of WHO by day 14.

B. Primary outcome for Phase III: Proportion of patients without progression in severity of pulmonary disease, defined as worsening of 2 points in the ordinal scale of WHO by day 14.

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* Correspondence: luciana.teofili@unicatt.it

¹Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy
Full list of author information is available at the end of the article



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Secondary outcomes for Phase III: Decreased viral load on nasopharyngeal swab at days 6, 9 and 14; Decreased viremia at days 6 and 9; Increased antibody titer against SARS-CoV2 at days 30 and 60; Proportion of patients with negative of SARS-CoV2 nasopharyngeal swab at day 30; Length of hospital stay; Mortality rate at day 28; Total plasma related adverse event (day 60); Total non-plasma related adverse events (day 60); Severe adverse events (SAE) (day 60).

Randomisation: Treatment allocation is randomized with a ratio 1:1 in both phase II and phase III. Randomization sequences will be generated at Fondazione Policlinico Gemelli IRCCS through the RedCap web application. Randomized stratification is performed according to age (under/over 80 years), and sex.

Blinding (masking): None, this is an open-label trial.

Numbers to be randomised (sample size): Phase II: 114 patients (57 per arm).

Phase III: 182 patients (91 per arm)

Trial Status: The trial recruitment started on May 27, 2020. The anticipated date of recruitment completion is April 30, 2021. The protocol version is 2 (May 10, 2020).

Trial registration: The trial has been registered on ClinicalTrials.gov (May 5, 2020). The Identifier number is [NCT04374526](https://clinicaltrials.gov/ct2/show/study/NCT04374526)

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, elderly, comorbidities

Supplementary information

Supplementary information accompanies this paper at <https://doi.org/10.1186/s13063-020-04821-1>.

Additional file 1: Full study protocol

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Authors' contributions

LT, RL, AC, AA, JV, MS, AG: study conception and design; protocol writing. TP, NO and SL: data management and study monitoring. All authors contributed to refinement of the study protocol and approved the final manuscript.

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Availability of data and materials

Authors can access data through the REDCap web platform. Data will be available from the authors on reasonable request. Please address the requests to: luciana.teofili@unicatt.it; antonella.cingolani@unicatt.it; raffaele.landolfi@unicatt.it

Ethics approval and consent to participate

The ethics committee of Fondazione Policlinico A. Gemelli IRCCS approved the study (Prot. N. 0020131/20, May 13, 2020). We certify that this trial has received ethical approval from the appropriate ethical committee as described above. The participants will be adequately informed in clear, simple and understandable words of the technical terms used and will be invited to provide oral or written informed consent. The participants will be provided with a description of the general aims of the research, the methodology and procedures used, the indication of any benefits or possible risks and adverse effects. In addition to consent to participate in the study, all patients should give consent to receive blood products. The consent can be expressed orally if two different witnesses state that the patient was properly informed and fully understood study aim and procedures, and sign the consent.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

Author details

¹Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy. ²Istituto Nazionale Malattie Infettive Lazzaro Spallanzani IRCCS, Rome, Italy. ³Presidio Ospedaliero S.S. Annunziata, ASL Lanciano -Vasto-Chieti, Università di Chieti, Chieti, Italy.

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