A randomized, double blinded clinical trial of convalescent plasma compared to standard plasma for treatment of hospitalized non-ICU patients with COVID-19 infections

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON23835

Source
Nationaal Trial Register

Brief title
COV-PLAS

Health condition

COVID-19

Sponsors and support

Primary sponsor: Leiden University Medical Center
Source(s) of monetary or material Support: none

Intervention

Outcome measures

Primary outcome

Ordinal outcome at day 14 of all cause mortality, mechanical ventilation, ICU admission and long duration of hospital stay (6 days or more), with less than 6 hospitalized days as reference category.

Secondary outcome

assessment of the primairy ordinal outcome at day 21, 28 and 56; combined outcome of death and ICU admission at day 14, 21, 28 and 56; duration of hospitalization in days; length of stay in ICU; and ICU mortality.
- The following safety parameters will be assessed during this trial: deterioration of respiratory, circulatory or otherwise the clinical status during transfusion; transfusion transmitted infections.
- The time until negative SARS-CoV-2 PCR (nasal/ pharyngeal swab)

Study description

Background summary

This is a randomized, prospective, multicenter, double blinded phase 2/3 trial comparing efficacy and safety of anti-SARS-CoV-2 convalescent plasma vs standard plasma in maximally 3 days hospitalized COVID-19 patients that are not at or bound to be referred to the ICU.

In the described context of possible benefits but still uncertain risks, we on purpose perform a double blinded phase 2/3 RCT to investigate both safety and effectivity of early in the disease course administrated convalescent plasma in patients with COVID-19. The latter patients are sick enough to warrant hospitalization but have not (yet) experienced overwhelming disease including a systemic inflammatory response, sepsis, and/or ARDS warranting ventilation and (eminent) ICU referral.

Study population:
This study will enrol adult patients with confirmed COVID-19 infection, who have been recently (not more than 3 days) hospitalized, but are not admitted to the ICU or expected to go to the ICU within 6 hours of first plasma administration.

Intervention:
Enrolled patients will either receive convalescent thawed fresh frozen plasma 1 unit (250-325 ml) (=treatment group) or standard thawed fresh frozen plasma 1 unit (250-325 ml) (=control group)

Study endpoints:
The estimated benefit in regard of the primary endpoint is a shift in the distribution of the scores towards less mortality, mechanical ventilation, ICU admission and shorter than the presently mean hospital stay (see figure). The primary endpoint will be analyzed using a Bayesian proportional odds model. Posterior probabilities will start to be computed after 20

patients have completed their follow-up and will be computed on regular basis afterwards. The endpoints can be summarized as following:
= Ordinal outcome of all cause mortality, mechanical ventilation, ICU admission and long duration of hospital stay (6 days or more), with less than 6 hospitalized days as reference category will be used for the primary outcome. The outcome will be primarily assessed at day 14.
- The following other efficacy parameters will be assessed as a secondary outcome: assessment of the primairy ordinal outcome at day 21, 28 and 56; combined outcome of death and ICU admission at day 14, 21, 28 and 56; duration of hospitalization in days; length of stay in ICU; and ICU mortality.
- The following safety parameters will be assessed during this trial: deterioration of respiratory, circulatory or otherwise the clinical status during transfusion; transfusion transmitted infections.
- The time until negative SARS-CoV-2 PCR (nasal/ pharyngeal swab)

Study objective

Convalescent plasma of ex-COVID-19 patients will improve outcome of recently admitted patients with active disease but not (yet) at ICU.

Study design

days 1,2,3,7,14,21,28,56

Intervention

Enrolled patients will either receive convalescent thawed fresh frozen plasma 1 unit (250-325 ml) (=treatment group) or standard thawed fresh frozen plasma 1 unit (250-325 ml) (=control group)

Contacts

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Eligibility criteria

Inclusion criteria

1. Maximal 3 days hospitalized at plasma infusion.
2. Age ≥ 18 years and ≤ 85 years
3. SARS-CoV-2 infection: confirmed by PCR (BAL, sputum, nasal and/or pharyngeal swap) not longer than 7 days before.
4. Symptoms not expected to lead to IC transfer within 6 hours of study plasma administration
5. Written informed consent including storing of specimen for future testing

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:

1. Accompanying diseases other than COVID-19 with an expected survival time of less than 6 months
2. Chronic severe pulmonary dysfunction like obstructive lung disease (COPD), Gold stage 4; severe emphysema; or lung fibrosis with usual interstitial pneumonia (IUP) pattern
3. Chronic heart failure NYHA >= 3 and/or pre-existing reduction of left ventricular ejection fraction to ≤ 30% for which among others e.g. strict fluid restriction is needed
4. Clinical diagnosis of circulatory overload for which active therapy (like increased doses of diuretics) is initiated
5. Clinical judgement of deterioration in oxygenation (e.g. more than 2 L increase in additonal O2 by nose tube), respiratory rates (e.g. more than 5 / min increase) in the 2 hours before the planned randomisation / plasma infusion
6. Signs of severe coagulopathy : thrombocytopenia by consumption (<100 x 10e9/l) or prolongation of the PT (+3 sec) , PTT (+ 5 sec)
7. Any history of severe adverse reactions to plasma proteins
8. Known deficiency of immunoglobulin A
9. Pregnancy
10. Breastfeeding women
11. Psychiatric or cognitive illness or recreational drug/alcohol use that in the opinion of the principal investigator, would affect subject safety and/or compliance

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-05-2020
Enrollment:	430
Type:	Anticipated

IPD sharing statement

Plan to share IPD: No

Ethics review

Positive opinion

Date:	13-05-2020
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

ID: 49946
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL8633
CCMO	NL73791.058.20
OMON	NL-OMON49946

Study results