Convalescent Plasma Therapy from Recovered Patients to Treat COVID-19 Early in SARS-CoV-2 Disease

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Primary objectivesTo evaluate the efficacy, feasibility, viro-immunological kinetics and safety following the administration of ConvP as a therapy for outpatients diagnosed with COVID-19 at increased risk for an unfavourable clinical outcome and...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON49795

Source
ToetsingOnline

Brief title
CoV-Early

Condition

- Viral infectious disorders
- Respiratory tract infections

Synonym
corona virus, COVID-19, SARS-CoV-2

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: convalescent, COVID-19, plasma, SARS-CoV-2

Outcome measures

Primary outcome

• Highest disease status on the 5-point ordinal disease severity scale in the

28 days following transfusion of convP versus FFP.

Disease status is measured with a 5-point ordinal scale in which

1 = Fully recovered (no symptoms) within 7 days after transfusion

2 = Continued symptoms attributable to COVID-19 on day 7 after transfusion

3 = Admitted to hospital but no invasive ventilation needed

4 = Admitted to hospital and invasive ventilation needed

5 = Death

Secondary outcome

Evaluated in all patients:

• Number (%) of deaths in the 28 days following transfusion of convP versus FFP.

• Number (%) of hospital admissions in the 28 days following transfusion of

convP versus FFP

• Number (%) of ICU admissions in the 28 days following transfusion of convP

versus FFP

• Disease duration in days of symptoms in the 28 days following transfusion of

convP versus FFP

• Age and clinical frailty score stratified analysis of primary endpoint

following transfusion of convP versus FFP.

Evaluated in subgroups of patients:

• Change in functional decline in patients over 70 years between inclusion, day 28 and month 6 following transfusion of convP versus FFP

• Change in functional respiratory imaging, FVC and DLCOc, validated QoL questionnaires between day 28, month 3, 6 and 12 following transfusion of convP versus FFP

• Change in proportion of detectable SARS-CoV-2 RT-PCR results at day 3, 7, 14 and 28 following transfusion of convP versus FFP.

• Change in number (%) of anti-SARS-CoV-2 specific B-cell and CTL memory responses at d1, d14, d28, m3, m6, m12 followin transfusion of convP versus FFP

• Number (%) of patients who fulfill the in- and exclusion criteria, number (%) of patients asked to participate in the study, number (%) of patients who do and do not participate and reasons to decline participation.

• Cost-effectiveness of convP compared to FFP will be assessed by calculating the mean costs of the intervention in relation to the relative healthcare savings of convP compared to FFP.

Exploratory endpoints:

• Highest disease status on the 5-point ordinal disease severity scale in the 28 days following transfusion of convP versus FFP according to presence of neutralizing antibodies at baseline , symptom duration at baseline Change in proportion of detectable SARS-CoV-2 RT-PCR results at day 3, 7, 14 and 28 following transfusion according to the presence of neutralizing antibodies at

baseline

Study description

Background summary

An effective, readily available, and safe treatment that can reduce the duration, severity and mortality of COVID-19 is urgently needed. If effective in the outpatient settting, this therapy could also reduce the pressure on the health care system in the most affected regions.

Plasma from cured patients containing antibodies against SARS-COV-2 could be a treatment for COVID-19 but its efficacy has not yet been demonstrated.

The Concovid study in the Netherlands showed that most patients are already producing antibodies against SARS-COV-2 at the time of hospitalization. Giving convalescent plasma at the time of hospital admission is therefore probably too late.

The hypothesis being tested in this study is therefore that convalescent plasma therapy is an effective treatment when given for patients at increased risk for a more serious disease course when it is given early in the course of COVID-19.

Study objective

Primary objectives
To evaluate the efficacy, feasibility, viro-immunological kinetics and safety following the administration of ConvP as a therapy for outpatients diagnosed with COVID-19 at increased risk for an unfavourable clinical outcome and within 7 days after symptom onset.

Evaluated in all patients:
• To evaluate the impact of 300mL convP on mortality
• To evaluate the impact of 300mL convP on hospital admission
• To evaluate the impact of 300 mL convP on admission to ICU
• To evaluate the impact of 300mL convP on duration of symptoms
• To evaluate the impact of 300mL convP in relation to the age and clinical frailty of the patient

Evaluated in subgroups of patients:
• To evaluate the impact of 300 mL convP on functional decline in patients aged 70 or older
• To evaluate the impact of 300 mL convP on the pulmonary condition and daily functioning

• To evaluate the duration of viral shedding in patients with and without convp and according to the presence of neutralizing antibodies at baseline
• To evaluate the impact of convP on the primary outcome in patients with and without neutralizing antibodies at baseline
• To evaluate the kinetics of infection and development of cellular and humoral anti-SARS-CoV-2 immune responses including memory immunity development.
• To evaluate the difference in efficacy of convP in relation to the duration of symptoms at randomization
• To evaluate the feasibility of recruiting COVID-19 patients, administering convP and perform study follow-up in an outpatient setting
• To evaluate cost-effectiveness of convP in an outpatient setting compared to routine care
• To evaluate the duration of viral shedding in patients with and without convP and according to the presence of neutralizing antibodies at baseline

Study design

Fase III, dubbelblind randomized

Intervention

Patients will be randomized between the transfusion of 300mL of convP versus regular fresh frozen plasma (FFP).

Study burden and risks

Advantages of participating in this study can be; a lower risk of hospitalization and death.

Risks of participation are the possible side effects of plasma transfusion. These are transfusion reactions, transfusion-related lung damage (TRALI) and the transmission of (as yet unknown) communicable diseases. Precautions are taken against these risks

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• PCR-confirmed COVID-19
• Symptomatic (e.g but not limited to fatigue, fever, cough, dyspnoe, loss of taste or smell, diarrhea, falls or confusion)
• 70 years or older OR 50-69 years and 1 or more of the risk factors described in table 1

Table 1:
1. A/ Medical history
• Obesity with BMI 35 or higher
• Born as a male person
• History of cardiac or pulmonary disease (e.g. but not limited to atrial fibrillation, coronary artery disease, heart failure, COPD, asthma)
• History of neurological disease (e.g. a history of stroke or any other chronic debilitating neurological disease)
• Diabetes for which medical therapy is needed
• Chronic kidney disease with GFR <60 ml/min
• Reumatic disease (e.g. reumatoid arthritis, Systemic lupus erythematosus, psoriatric artritis)
• Immunodeficiency (e.g. organ or allogeneic transplantation, systemic immunosuppressive drugs)
• Cancer not in complete remission for >1 year (excluding baso -or spinocellular skin cancers)
• Untreated HIV and CD4 T-cells <200/microliter
• Chronic liver disease, liver cirrhosis

1. B/ Lab results (if available)
• CRP > 30
• SARS-CoV-2 RT-PCR Ct value <25

Exclusion criteria

• Life expectancy <28 days in the opinion of the treating physician
• Patient or legal representative is unable to provide written informed consent
• Symptomatic for 8 days or more
• Being admitted to the hospital at the informed consent procedure
• Known previous history of transfusion-related acute lung injury
• Known IgA deficiency

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	13-10-2020
Enrollment:	690
Type:	Actual

Ethics review

Approved WMO

Date:	25-09-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

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

No registrations found.

In other registers

Register	ID
CCMO	NL74972.078.20