A Phase I-II study of virus neutralizing antibodies against SARS-CoV-2. A focus on convalescent plasma and hyperimmune anti-SARS-CoV2 immunoglobulines

Published: 15-03-2021
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Primary Objective:• To create a population pharmacokinetic model of SARS-COV-2 neutralizing antibodies as present in ConvP.• To create a population pharmacokinetic model of SARS-COV-2 neutralizing antibodies as present in Nanogam*plusSecondary...

Ethical review	Approved WMO
Status	Completed
Health condition type	Immune disorders NEC
Study type	Interventional

Summary

ID

NL-OMON51004

Source
ToetsingOnline

Brief title
ConvP/COVig PK/PD study

Condition

- Immune disorders NEC
- 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, COVIG, plasma

Outcome measures

Primary outcome

Duration and titer of neutralization antibodies in serum of patients after

administration of different doses of convalescent plasma.

Duration and titer of neutralization antibodies in serum of patients after

administration of different doses of Nanogam plus.

Secondary outcome

- The incidence of COVID-19 during follow-up until antibody levels have become

undetectable

- Percentage of patients with adverse events after administration of

convalescent plasma

- Percentage of patients with adverse events after administration of

Nanogam*plus

Other study parameters (if applicable)

- Whenever a breakthrough infection is diagnosed, we will do everything

possible to collect the SARS-CoV-2 strain for sequencing in

order to identify new or emerging variants of concern (e.g. strain 501.V2 or

P.1 also known as the South-African or Brazilian variant) to evaluate

the virus neutralizing capacity of the ConvP or Nanogam*plus that the patient

received.

Study description

Background summary

Standard treatment for the novel coronavirus is admission in hospital or even ICU in case of common to severe disease. Even if we provide the most optimal care, 20% of all patients who were admitted to the hospital eventually die. Patients who have a weaker immune system have still higher risks. It is necessary to search for better treatment options for patients with COVID19. Antibodies from patients who have already recovered from the SARS-CoV-2 virus, are probably effective to help other patients clear the virus. By giving this treatment in the early phase of infection (before need of hospital admission), disease progression, admission and even death by COVID could be avoided. Antibodies are proteins made by our immune system if a patient is infected by a virus with purpose of fighting against the virus. These antibodies are found in the plasma. The immune system needs several days or weeks for production of these antibodieis. Patients who already have had the virus infection, will have those antibodies against SARS-CoV-2. Patients who are having early symptoms, normally don't have those antibodies. Patients with a weakened immune system do take longer for production of those antibodies, part of them never succeed in producing them.
In this study we will give plasma containing antibodies against the coronavirus coming from donors who already recovered from their infection or hyperimmune antibodies to patients with underlying weakened immune system.
Previous studies in Hongkong in 2003 showed that patients who suffered a SARS-CoV (1) virus recovered faster after administration of plasma coming from patients who had already recovered.

Study objective

Primary Objective:
• To create a population pharmacokinetic model of SARS-COV-2 neutralizing

antibodies as present in ConvP.
• To create a population pharmacokinetic model of SARS-COV-2 neutralizing antibodies as present in Nanogam*plus
Secondary Objective(s):
• To evaluate the protective potential against COVID-19 in B-cell depleted patients receiving Nanogam*plus or ConvP
• Evaluate the safety of ConvP and Nanogam*plus

Study design

Multi-center, open label, phase I-II prospective, non-randomized trial

Intervention

Infusion of convalescent plasma containing anti-SARS-CoV-2 antibodies (originatitng from donors with PCR-proven COVID-19 disease and recovered at least for 28 days).

OR

Infusion of Nanogam plus (hyperimmune antibodies) coming from donors with proven anti-SARS-CoV-2 antibodies.

Study burden and risks

Burden and risks are as followed:
- Half a day of admission in the hospital at the start of the study. After this, patients should come to the hospital approx. 12 times (1x for screening + blood sample + 1x for treatment and blood sample + 10x for blood samples)
- Burden of venapunction for blood samples and the risk of hematoma or pain around place of punction
- Very low risk of severe adverse effect after administration of plasma (TRALI or TACO)
- Very low risk of severe adverse effect after administration of Nanogam plus (TRALI, TACO)

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

* 18 years or older
* Informed consent
* B-cell depleted status because one of following:
o Prior B-cell depletion therapy (latest administration < 6 months prior to inclusion)
o Immunodeficiency requiring IVIG suppletion
* Wantai total Ig antibody optical density (OD) ratio of 2.0 or lower 2 weeks after complete vaccination against COVID-19

Exclusion criteria

* Symptoms of respiratory infection at time of inclusion
* Anti-SARS-CoV-2 antibodies prior to administration of study product > 2.0 OD (Wantai total Ig)
* Positive SARS-CoV-2 PCR
* Known previous history of transfusion-related acute lung injury
* Known IgA deficiency
* Liver cirrhosis
* Known hypersensitivity to human immunoglobulins
* Received anti-SARS-CoV-2 vaccination in the 2 weeks preceding screening or

baseline

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	17-05-2021
Enrollment:	104
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Nanogam
Generic name:	Immunoglobulins
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	15-03-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	29-03-2021
Application type:	First submission

Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	02-07-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-07-2021
Application type:	Amendment
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
EudraCT	EUCTR2021-000864-32-NL
CCMO	NL76798.078.21

Study results

Date completed:	19-03-2024
Results posted:	19-03-2024
Actual enrolment:	44

Summary results

Trial ended prematurely

First publication
19-03-2024