Convalescent Antibody-Mediated Treatment of COVID-19 Infections in Patients with B-cell dysfunction, a Randomized Trial (COVID-Compromise Study).

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There have been reports of a more serious course of COVID-19 infections in patients with a reduced immune system, such as patients with congenital immune disorders, (haematological) malignancies or patients taking medications that suppress the...

Ethical review	Approved WMO
Status	Suspended
Health condition type	White blood cell disorders
Study type	Interventional

Summary

ID

NL-OMON51203

Source
ToetsingOnline

Brief title
COVID-Compromise Study

Condition

- White blood cell disorders
- Immunodeficiency syndromes
- Viral infectious disorders

Synonym
b-cell dysfunction

Research involving

Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: COVID-19, ICP, Nanogam

Outcome measures

Primary outcome

The endpoint of this study is a severe course of disease, which is defined

until day 28 after randomization:

* Start of adjunctive ventilator support (HFNO, mechanical ventilation) or an

indication to do so but due to due to previously agreed treatment restrictions

HFNO or mechanical ventilation is not initiated..

* Admission to an intensive care unit for progression of respiratory

insufficiency..

* No clinical improvement on day 7 after randomization or any day thereafter

after first day of treatment (based on oxygen use in patients that require

oxygen and based on clinical disease burden (including fever) in patients that

require no oxygen).

* Readmission for COVID-19.

Secondary outcome

* Severity of COVID-19 disease in patients that have no anti SARS-CoV-2

antibodies upon inclusion (*per protocol* analysis).

* Duration of hospitalization.

* 28 days overall mortality.

* The four individual endpoints that compose the primary endpoint.

* Time to complete recovery from COVID-19 related symptoms.

* Rate of viral decay

* Development of long-term persistent neutralizing antibodies against SARS-COV-2

* T-cell immunity as measured by in vitro specific T cell response to COVID-19

tetrameric antigens.

Study description

Background summary

The COVID-19 pandemic has unfortunately caused many infections and deaths around the world. COVID-19, the disease caused by infection with the SARS-CoV2 virus, can cause symptoms of varying degrees of severity. Some patients do not show serious symptoms, and other patients sometimes show serious symptoms such as pneumonia and thrombosis. There are a number of factors that increase the risk of serious illness or death, of which advanced age is the most important (Loannidis et al. 2020; Banerjee et al. 2020). Patients with a reduced immune system, in which the blood cells in particular do not function properly, have an increased risk of a serious course of various viral diseases (Chemaly et al. 2006; Aksoy et al. 2007) and therefore also run a higher risk of any course of the disease. COVID-19 disease (Parra-Bracamonte et al. 2020; Jee et al. 2020). To date, a number of treatment options have been proposed for all COVID-19 patients, of which steroid treatment in combination with supportive care measures remains the cornerstone (WHO living guideline 2020). Treatment with plasma antibodies has also been studied, but to date none of these therapies have been successful in reducing the severity of the disease associated with COVID-19 in hospitalized patients (covid19treatmentguidelines.nih.gov). This is because 80% of the severe COVID-19 patients included in this study quickly develop antibodies themselves. It has become clear that this treatment can help in elderly patients in the first three days after complaints arise. All in all, these antibodies seem to help early in the course of the disease when complaints are still mild, but not after this. Whether this antibody treatment still helps in the prevention of treatment of COVID-19 infections in immune-compromised patients after admission has not been studied.

Study objective

There have been reports of a more serious course of COVID-19 infections in patients with a reduced immune system, such as patients with congenital immune disorders, (haematological) malignancies or patients taking medications that suppress the immune system. These patients all have to deal with a reduced immune system, which makes it more difficult for them to make antibodies against the virus and to clear the virus from the body. Until now, no treatments have been found with good results for these patients. Treatment with antibodies from recovered COVID patients may be able to help patients with reduced immunity to clear up the COVID infection more quickly. As a result, it is expected that these patients will have to be admitted less long and the course of the COVID-19 disease will be less severe.

Study design

A phase II, multicenter, cohort specific, randomized controlled, comparative study.

Intervention

After randomization, one group (43 patients) receives treatment with Nanogam containing high titre neutralizing anti-SARS-CoV-2 antibodies (further referred to as Nanogam plus). The other group (43 patients) receives control treatment with Nanogam without high titre anti SARS-CoV-2 antibodies as control for Nanogam plus. Treatment is in a double blinded fashion.

Study burden and risks

Infusion of Nanogam plus or control (Nanogam); Viral PCR on day 1, 3, 7, 10, 14 and weekly until discharge, then on months 2, 3, 6, 12. Blood withdrawal weekly until discharge (mostly covered during standard of care blood withdrawal) and monthly
Monthly follow-up measurement of anti-SARS-CoV-2 antibodies in serum until 3 months after discharge. Monthly follow-up measurement of SARS-CoV-2 virus by PCR until 3 months after discharge.
The risks of Nanogam infusion are small and widely known. These consist mainly of infusion reactions or volume overload.
Benefits of this study may include a shorter disease course and a decrease in mortality.

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

- Patient is >= 18 years of age, diagnosed with COVID-19 based on a positive PCR or antigen test in combination with COVID-19 related symptoms (e.g. Fever, hypoxia, gastrointestinal symptoms).
- Hospitalized.
AND one of immunocompromised conditions/treatments below

B-cell inhibition related ICP
- Use of anti-CD19 or -CD20 directed antibody therapy in 6 months prior to inclusion.
- Previous or current treatment with drugs that significantly impair B cell function (e.g. ibrutinib, venetoclax, acalabrutinib, idelalisib etc) within 6 months prior to inclusion

Other immunosuppression/treatment related ICP
- Patients treated with bendamustine, purine analogues or anti-thymocyte globulin within 6 months prior to inclusion.
- Solid organ transplant patients that are taking systemic immunosuppressive drugs from at least three pharmacological classes. Or from at least two classes

in combination with negative anti-SARS-CoV-2 antibodies <= 96 hours prior to inclusion.

Cellular therapy related ICP
- Allogeneic hematopoietic stem cell transplant (HSCT) in 12 months prior to inclusion.
- HSCT for which systemic therapy against graft-versus-host-disease is used.
- Recipient of CAR-T cells < 2 years prior to inclusion.

Disease related ICP
- Chronic B-cell leukemia*s: CLL, HCL, PLL, multiple myeloma, Waldenströms macroglobulinemia

Congenital ICP
- Congenital disorder resulting in severe B-cell dysfunction or depletion requiring immunoglobulin suppletion (e.g. agammaglobulinemia).

Exclusion criteria

- Patient or legal representative is unable to provide written informed consent
- Life expectancy of < 28 days in the opinion of the treating physician
- Has previously participated in this study.
- Has previously received convalescent plasma with high level neutralizing anti-SARS-CoV-2 antibodies (either in other study or in compassionate use program).
- Known IgA deficiency (defined as absence of IgA and possibility of anti-IgA antibodies), patients with disease related reduced levels of IgA (e.g. in myeloma or lymphoma) may be included in the study.
- Known previous grade 3 or 4 hypersensitivity reactions to treatment with immunoglobulins
- Patient who has reached endpoint already at admission (direct adjunctive oxygen therapy in the form of high-flow nasal oxygen (HFNO), mechanical ventilation or ICU admission for other reason).

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel

Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Suspended
Start date (anticipated):	19-04-2021
Enrollment:	86
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	19-03-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-03-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	14-04-2021
Application type:	Amendment

Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	30-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-05-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	EUCTR2020-006075-15-NL
CCMO	NL76365.018.21