Optimal Booster Strategy for SARS-CoV-2 Vaccination in Kidney Transplant patients

Published: 13-09-2021
Last updated: 05-04-2024

To assess the efficacy (expressed as percentage of responders) of various COVID-19 booster vaccination strategies in kidney transplant patients that failed to mount a sufficient antibody response after two primary doses of the mRNA-1273 vaccine.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON50602

Source
ToetsingOnline

Brief title
Recovac Booster Study

Condition

- Other condition
- Renal disorders (excl nephropathies)

Synonym
kidney transplant

Health condition

niertransplantatie

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Booster, Kidney transplant, SARS-CoV-2 vaccination

Outcome measures

Primary outcome

The primary endpoint is the percentage of subjects with a serum anti-S1 IgG concentration *10 BAU/mL at 28 days after the third vaccine administration.

Secondary outcome

o SARS-CoV-2 specific antibody concentrations in serum at 28 days after the 3rd vaccine administration

o SARS-CoV-2 specific antibody concentrations in serum at 6 and 12 months after the 3rd vaccine administration

o The titer of neutralizing anti-SARS-CoV-2 antibodies at 28 days after the 3rd vaccine administration

o SARS-CoV-2 specific antibody concentrations in nasal mucosal fluid at 28 days and 6 months after the 3rd vaccine administration

o SARS-CoV-2 specific T cell responses at 28 days after the third vaccine administration by:

* Measuring interferon-gamma concentration in whole blood after ex vivo stimulation with SARS-CoV-2 specific peptides

* Measuring ex vivo production of T cell related cytokines by peripheral blood mononuclear cells (PBMC) in ELISpot assays

o Incidence of acute rejection within 6 months after the third vaccine administration

o Safety in terms of incidence of solicited local and systemic adverse events (AEs) within one week after vaccine administration graded according to severity. The following items will be specifically addressed:

* Percentage of participants reporting local reactions (pain at the injection site, redness and swelling) within 7 days after vaccine administration

* Percentage of participants reporting systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new of worsened muscle pain, and new or worsened joint pain) within 7 days after vaccine administration

* Percentage of participants with serious adverse events within 6 months after the third vaccine administration

Study description

Background summary

COVID-19 is associated with severely increased morbidity and mortality in kidney transplant patients. Therefore, effective SARS-CoV-2 vaccination is of great clinical importance in these patients. Available data show that the humoral and cellular immune response after a standard regimen of two mRNA vaccinations is severely attenuated in kidney transplant patients compared to controls, especially when their immunosuppressive regimen contains mycophenolate mofetil (MMF) / mycophenolic acid (MPA). A booster strategy is therefore required to improve the efficacy of vaccination.

Study objective

To assess the efficacy (expressed as percentage of responders) of various COVID-19 booster vaccination strategies in kidney transplant patients that failed to mount a sufficient antibody response after two primary doses of the mRNA-1273 vaccine.

Study design

Prospective open label randomized multicentre study.

Intervention

In stratum A, patients will be randomized to one of two booster strategies:
* A1: 3rd dose of mRNA-1273 (100 *g, i.m)
* A2: 3rd dose of mRNA-1273 (100 *g, i.m), with temporary discontinuation of MMF/MPA during one week before and one week after the 3rd dose

In stratum B, patients will be randomized to one of three booster strategies:
* B1: 3rd dose of mRNA-1273 (100 *g, i.m)
* B2: 3rd dose of mRNA-1273 (100 *g, i.m) in both upper arms
* B3: Ad26.COV2.S vaccine (Janssen, 5x1010 viral particles i.m.)

Study burden and risks

In general:
Risks are associated with 4 or 6 venapunctions with a maximum of 62,5 ml withdrawal of blood per session.

Specific:
In group A2 subjects will interrupt the use of MMF/MPA during two weeks. This temporary interruption of the use of one of the immunosuppressive drugs may theoretically increase the risk of graft rejection. These subjects will have two more bloodsamples drawn (at one and two weeks after discontinuing immunosuppressives) to monitor this risk.

In group B2 standard dose of 100*g mRNA-1273 will be given in both arms, what makes a double dose.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9700RB
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1

Groningen 9700RB
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. Age 18 years or older
2. Received 2 doses of mRNA-1273 according to the recommended vaccination schedule, with the last administration within the last nine months
3. Insufficient response to vaccination, defined as anti-spike IgG in serum < 10 BAU/mL measured between 25 and 56 days after the second dose of the mRNA-1273 vaccine with a validated test
4. Capable of understanding the purpose and risks of the study, fully informed and given written informed consent (signed informed consent form has been obtained)

Additional inclusion criteria to be eligible for stratum A:
5. Maintenance immunosuppressive therapy consisting of a calcineurin inhibitor (tacrolimus or cyclosporine), MMF/MPA, and prednisone
6. In case of tacrolimus treatment: last tacrolimus pre-dose level while on current dosage above 4 *g/l
7. In case of cyclosporine treatment: last cyclosporine pre-dose level while on current dosage above 75 *g/l
8. Prednisone dose at least 5 mg/day
9. First or second transplantation
10. Calculated level of panel reactive antibodies prior to last transplantation below 85%
11. No signs of acute rejection during the preceding year

Exclusion criteria

1. Multi-organ transplant recipient
2. Previous or active COVID-19 disease
3. Active malignancy, except non-melanoma skin cancer
4. Inherited immune deficiency
5. Infection with Human Immunodeficiency Virus (HIV)
6. Administration of T cell, B cell, or plasma cell depleting antibodies during the last 6 months
7. Any vaccination within a month before enrolment

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-11-2021
Enrollment:	460
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	COVID-19 Vaccine Janssen
Product type:	Medicine
Brand name:	Spikevax

Ethics review

Approved WMO Date:	13-09-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-10-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-01-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	06-04-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	15-07-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2021-004558-44-NL
CCMO	NL78963.042.21