Clinical trial results:
Long term efficacy and safety of SARS-CoV-2 vaccination in Dutch patients with chronic kidney disease stage G4-G5, on dialysis or after kidney transplantation

Summary

EudraCT number	2021-001520-18
Trial protocol	NL
Global end of trial date	18 December 2023

Results information

Result version number	v1 (current)
This version publication date	30 May 2024
First version publication date	30 May 2024

Trial information

Trial identification

Sponsor protocol code	NL76839.042.21

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04841785
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UMCG
Sponsor organisation address	Hanzeplein 1, Groningen, Netherlands, 9713 GZ
Public contact	study coordinator, RECOVAC consortium, 0031 0503616161, a.l.messchendorp@umcg.nl
Scientific contact	study coordinator, RECOVAC consortium, 0031 0503616161, a.l.messchendorp@umcg.nl

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	19 April 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	18 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy of SARS-CoV vaccination by the incidence of COVID-19 in patients with chronic kidney disease stage G4-G5, on dialysis and patients after kidney transplantation who received SARS-CoV-2 vaccination

Protection of trial subjects:

This study investigates the effect of registered vaccines that are administered in the context of routine clinical care. Therefore there are no potential issues of concern for the investigated medicinal products of this study and no extra protection of trial subjects is implemented
The vaccinations will be administered according to the instructions of the manufacturers and to the most recent COVID-19 vaccination guideline for standard care provided by the Dutch National Institute for Public Health and the Environment (RIVM).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 March 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 4868
Worldwide total number of subjects	4868
EEA total number of subjects	4868

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	2755
From 65 to 84 years	2096
85 years and over	17

Subject disposition

Recruitment

Recruitment details:

Possible eligible participants were all prioritized for primary COVID-19 vaccination and vaccinated via participating hospitals. They were invited to receive a study PIF by a flyer which was handed during the second vaccination. The were asked to preferably go to a survey, where an electronic version of the PIF could be found and ICF signed.

Pre-assignment

Screening details:

Via this way, 1200 kidney transplant recipients, 6000 dialysis patients and 6000 patients with CKD stage 4/5 were approached.

Pre-assignment period milestones

Number of subjects started	4868
Number of subjects completed	4868

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	COVID-19 vaccination

Arm description:

All patients entered in this study received a COVID-19 vaccination via the national vaccination programme of the Netherlands. Available vaccines were:
1. COVID-19 Vaccine Moderna
2. Comirnaty/ COVID-19 mRNA vaccine BioNTech/Pfizer
3. COVID-19 Vaccine AstraZeneca
4. COVID-19 Vaccine Janssen

Arm type	Experimental
Investigational medicinal product name	COVID-19 Vaccine Moderna
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose (0.5 mL) contains 100 micrograms of messenger RNA (mRNA) (embedded in SM-102 lipid nanoparticles). COVID-19 Vaccine Moderna is administered as a course of 2 doses (0.5 mL each). It is recommended to administer the second dose 28 days after the first dose

Investigational medicinal product name	Comirnaty/ COVID-19 mRNA vaccine BioNTech/Pfizer
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

1 dose (0.3 mL) contains 30 micrograms of COVID-19 mRNA Vaccine (embedded in lipid nanoparticles). Comirnaty is administered intramuscularly after dilution as a course of 2 doses (0.3 mL each) at least 21 days apart (

Investigational medicinal product name	COVID-19 Vaccine AstraZeneca
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose (0.5 ml) contains:
Chimpanzee Adenovirus encoding the SARS-CoV-2 Spike glycoprotein (ChAdOx1-S)*, not less than 2.5 × 108 infectious units (Inf.U). The COVID-19 Vaccine AstraZeneca vaccination course consists of two separate doses of 0.5 ml each. The second dose should be administered between 4 and 12 weeks (28 to 84 days) after the first dose

Investigational medicinal product name	COVID-19 Vaccine Janssen
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

One dose (0.5 mL) contains:
Adenovirus type 26 encoding the SARS-CoV-2 spike glycoprotein* (Ad26.COV2-S), not less than 8.92 log10 infectious units (Inf.U). Individuals 18 years of age and older
COVID-19 Vaccine Janssen is administered as a single-dose of 0.5 mL by intramuscular injection only.

Number of subjects in period 1	COVID-19 vaccination
Started	4868
Completed	2862
Not completed	2006
Adverse event, serious fatal	278
Consent withdrawn by subject	56
Deteriorating health	5
Lost to follow-up	1656
Protocol deviation	11

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (overall period)

Reporting group description: -

Reporting group values	Overall trial (overall period)	Total	
Number of subjects	4868	4868	
Age categorical Units: Subjects			
Adults (18-64 years)	2755	2755	
From 65-84 years	2096	2096	
85 years and over	17	17	
Age continuous Units: years			
arithmetic mean	60.0		
standard deviation	± 13.6	-	
Gender categorical Units: Subjects			
Female	1963	1963	
Male	2905	2905	

Subject analysis sets	
Subject analysis set title	CKD G4/5
Subject analysis set type	Full analysis

Subject analysis set description:
Patients with chronic kidney disease stage G4/5

Subject analysis set title	Dialysis
Subject analysis set type	Full analysis

Subject analysis set description:
Subjects on dialysis (either hemodialysis or peritoneal dialysis)

Subject analysis set title	Kidney Transplant Recipients
Subject analysis set type	Full analysis

Subject analysis set description:
Patients that have a functioning kidney transplant

Reporting group values	CKD G4/5	Dialysis	Kidney Transplant Recipients
Number of subjects	393	945	3530
Age categorical Units: Subjects			
Adults (18-64 years)	104	373	2278
From 65-84 years	289	557	1250
85 years and over	0	15	2
Age continuous Units: years			
arithmetic mean	67.4	65.3	57.8
standard deviation	± 12.2	± 12.6	± 13.3

Gender categorical Units: Subjects			
Female	159	363	2089
Male	234	582	1441

End points

End points reporting groups

Reporting group title	COVID-19 vaccination

Reporting group description:

All patients entered in this study received a COVID-19 vaccination via the national vaccination programme of the Netherlands. Available vaccines were:
1. COVID-19 Vaccine Moderna
2. Comirnaty/ COVID-19 mRNA vaccine BioNTech/Pfizer
3. COVID-19 Vaccine AstraZeneca
4. COVID-19 Vaccine Janssen

Subject analysis set title	CKD G4/5
Subject analysis set type	Full analysis

Subject analysis set description:

Patients with chronic kidney disease stage G4/5

Subject analysis set title	Dialysis
Subject analysis set type	Full analysis

Subject analysis set description:

Subjects on dialysis (either hemodialysis or peritoneal dialysis)

Subject analysis set title	Kidney Transplant Recipients
Subject analysis set type	Full analysis

Subject analysis set description:

Patients that have a functioning kidney transplant

Primary: Incidence of COVID-19 in a two years period after SARS-CoV-2 vaccination

End point title	Incidence of COVID-19 in a two years period after SARS-CoV-2 vaccination[1]

End point description:

During the trial, the COVID-19 pandemic emerged, for which we were forced to adapt our endpoints somewhat. We have chosen to only report on COVID-19 after two vaccinations and before the third COVID-19 vaccination. There were too few patients in the CKD G4/5 group and Dialysis group to report on this endpoint.

End point type	Primary

End point timeframe:

Within two years after vaccination

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: As this is not a traditional study including comparisons between certain treatment groups, the statistical analysis that was applied for this specific endpoint could not be entered in EudraCT. For details on this analysis we would like to refer to a publication which can be found under 'More Information' PMID 38257814

End point values	Kidney Transplant Recipients			
Subject group type	Subject analysis set			
Number of subjects analysed	2885			
Units: subjects	62			

Statistical analyses

No statistical analyses for this end point

Secondary: The antibody response against the SARS-CoV-2 Receptor Binding Domain at 28 days after the 2nd COVID-19 vaccination.

End point title	The antibody response against the SARS-CoV-2 Receptor Binding Domain at 28 days after the 2nd COVID-19 vaccination.

End point description:

End point type	Secondary

End point timeframe:

28 days after second COVID-19 vaccination

End point values	CKD G4/5	Dialysis	Kidney Transplant Recipients	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	393	480	2468	
Units: BAU/mL				
median (inter-quartile range (Q1-Q3))	2097 (828 to 4077)	1375 (431 to 2896)	65.7 (8.25 to 573.1)	

Statistical analyses

No statistical analyses for this end point

Secondary: The antibody response against the SARS-CoV-2 Receptor Binding Domain at 28 days after the 3rd COVID-19 vaccination

End point title	The antibody response against the SARS-CoV-2 Receptor Binding Domain at 28 days after the 3rd COVID-19 vaccination

End point description:

End point type	Secondary

End point timeframe:

28 days after third COVID-19 vaccination

End point values	CKD G4/5	Dialysis	Kidney Transplant Recipients	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	40	242	1547	
Units: BAU/mL				
median (inter-quartile range (Q1-Q3))	1551 (459 to 3225)	1727 (570 to 4254)	318.4 (35.0 to 1146)	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
7 days after each COVID-19 vaccination	
Adverse event reporting additional description:	
AEs were categorized in local AEs (pain or erythema at injection site and myalgia) or systemic AEs (fever, arthralgia, fatigue, headache and other).	
Assessment type	Systematic

Dictionary used	
Dictionary name	Pre-defined
Dictionary version	1

Frequency threshold for reporting non-serious adverse events: 0 %

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: AEs are reported according to patient group (CKD G4/5, Dialysis, Kidney Transplant Recipients) and whitin these groups according to vaccine type and vaccine number in the publication that can be found under 'More Information' with PMID number: 36865021.
The EudraCT results template is not suitable to provide the specific numbers this way.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2021	1. The time range that blood can be collected after second COVID-19 vaccination is extended to 28 -14/+28 days after vaccination 2. Addition of a questionnaire about general patient characteristics 3. Addition of a questionnaire about behavioural changes with regard to preventive measures during the pandemic 4. With the addition of a third vaccination we have changed the protocol for collection of a blood sample after 6 months for those who received a third vaccination to collection of a blood sample 28 days after receiving a third vaccination

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/36245996

http://www.ncbi.nlm.nih.gov/pubmed/35123437

http://www.ncbi.nlm.nih.gov/pubmed/36789469

http://www.ncbi.nlm.nih.gov/pubmed/36865021

http://www.ncbi.nlm.nih.gov/pubmed/37533418

http://www.ncbi.nlm.nih.gov/pubmed/38428480

http://www.ncbi.nlm.nih.gov/pubmed/38257814