# 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<br>Units: Subjects | | | |
| Adults (18-64 years) | 2755 | 2755 | |
| From 65-84 years | 2096 | 2096 | |
| 85 years and over | 17 | 17 | |
| Age continuous<br>Units: years | | | |
| arithmetic mean | 60.0 | | |
| standard deviation | ± 13.6 | - | |
| Gender categorical<br>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<br>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<br>Units: years | | | |
| arithmetic mean | 67.4 | 65.3 | 57.8 |
| standard deviation | ± 12.2 | ± 12.6 | ± 13.3 |

| Gender categorical<br>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<br>2. Addition of a questionnaire about general patient characteristics<br>3. Addition of a questionnaire about behavioural changes with regard to preventive measures during the pandemic<br>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