Switching of COVID-19 vaccines: A solution for the problems? A multicentre, randomised, single blind, controlled trial among HealthCare Workers (HCW) vaccinated with Janssen: the SWITCH trial.

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Primary objectivesMeasuring the SARS-CoV-2-specific immune response against SARS-CoV-2 after inoculation with a single-dose Janssen compared to a homologous vaccination regimen with Janssen /Janssen and the comparison of a homologous vaccination...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON52043

Source
ToetsingOnline

Brief title
SWITCH

Condition

- Viral infectious disorders

Synonym
COVID-19 vaccinations

Research involving

Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: COVID-19, Immune-response, Vaccination

Outcome measures

Primary outcome

Primary objectives

Measuring the SARS-CoV-2-specific immune response against SARS-CoV-2 after inoculation with a single-dose Janssen compared to a homologous vaccination regimen with Janssen /Janssen and the comparison of a homologous vaccination regimen (Janssen/Janssen) with a heterologous vaccination regimen (Janssen/Pfizer + Janssen/Moderna).

Main endpoint

The immune response to SARS CoV-2 28 days after the second vaccination is the primary endpoint.

December 2021

Measuring the SARS-CoV-2 specific immune response to SARS-CoV-2 after inoculation with Pfizer 30 micrograms 6 months after priming versus 3 months.

Main endpoint

The immune response to SARS CoV-2 28 days after the second vaccination is the primary endpoint.

February 2022

Extra boost

Measuring the SARS-CoV-2 specific immune response against SARS-CoV-2 after inoculation with Pfizer 30 micrograms (as second boost) and comparing this immune response between the different groups (J/J, J/P and J/M).

Waning

Pharmacokinetic comparison of the decline of the immune response between the different groups (J/J, J/P and J/M).

Non-responders

Finding an indicator to predict/identify non-responders.

Secondary outcome

Secondary objectives

1. To assess adverse events after SARS-CoV-2 vaccination.

2. To evaluate development of antibody and cellular response after homologues versus heterologues vaccination

3. To assess durability of the antibody response

4. To analyze the SARS-CoV-2-specific T and B cell response after vaccination

Study description

Background summary

The first vaccines against COVID-19 were available in the Netherlands from January 2021. The ability to combine vaccinations could make vaccination campaigns more flexible in the future. It could speed up the process and reduce the impact of supply disruptions. It can also elicit a broader immune response (in terms of neutralizing antibodies and T-cell responses). These results support the need to conduct clinical trials in humans to investigate the safety and immunogenicity of heterologous vaccination regimens. Several studies have already been set up to look at the safety and immunogenicity of a heterologous vaccination regimen. These studies are ongoing in the UK and Spain where they are combining Pfizer and AstraZeneca and vice versa (Com-COV & CombiVacS). For these reasons, we decided to focus our study on adeno priming with Janssen, which is not studied in other ongoing studies. As the vaccination rate in The Netherlands is increasing rapidly, we decided to include HCW vaccinated once with Janssen.

December 2021
All healthcare workers now have the option of a boost with Pfizer 30 micrograms. This boost has already been investigated in the SWITCH and the Health Council has made this decision based on this, among other things.
The main aim of this study is to determine whether there is a difference in the production of antibodies of a dose of Pfizer 30 micrograms adminstered 6 months after priming versus 3 months after priming. We also study the formation of immune cells after vaccination and the occurrence of side effects.

February 2022
In mid-December, the government decided to advise everyone who had their last COVID-19 vaccination 3 months or more ago to get a boost. This applies to all our groups; Janssen/Janssen, Janssen/Moderna and Janssen/Pfizer (boosted at the end of July/August). And later possibly also for Janssen/- who had their boost last December (2021).

We also want to take extra blood from a small sample (monthly) to map the kinetics (waning) of the decrease in the immune response. This concerns 15 people from each group (J/J, J/P, J/M).

Finally, we want to compare the 21 non-responders (defined as insufficient IgG antibodies (+/- 4 months) after their prime with Janssen) with the 21 highest responders from the J/- group. To this end, the immune response of these subjects to previous vaccinations (national vaccination program, hepatitis B, influenza) will be examined.

Study objective

Primary objectives
Measuring the SARS-CoV-2-specific immune response against SARS-CoV-2 after inoculation with a single-dose Janssen compared to a homologous vaccination regimen with Janssen /Janssen and the comparison of a homologous vaccination regimen (Janssen/Janssen) with a heterologous vaccination regimen (Janssen/Pfizer + Janssen/Moderna).

Main endpoint
The immune response to SARS CoV-2 28 days after the second vaccination is the primary endpoint.

Secondary objectives
1. To assess adverse events after SARS-CoV-2 vaccination.
2. To evaluate development of antibody and cellular response after homologues versus heterologuest vaccination
3. To assess durability of the antibody response
4. To analyze the SARS-CoV-2-specific T and B cell response after vaccination

December 2021

Primary Goals
Measuring the SARS-CoV-2 specific immune response to SARS-CoV-2 after inoculation with Pfizer 30 micrograms 6 months versus 3 months.

Secondary Objectives
1. To assess adverse reactions after SARS-CoV-2 vaccination.
2. Evaluation of the development of antibody and cellular response after the heterologous versus homologous vaccination
3. To Assess the Durability of the Antibody Response
4. Analysis of SARS-CoV-2 Specific T and B Cell Responses After Vaccination

February 2022
Extra boost
Measuring the SARS-CoV-2 specific immune response against SARS-CoV-2 after inoculation with Pfizer 30 micrograms (as second boost) and comparing this immune response between the different groups (J/J, J/P and J/M).

Waning
Pharmacokinetic comparison of the decline of the immune response between the different groups (J/J, J/P and J/M).

Non-responders
Finding an indicator to predict/identify non-responders.

Study design

A multicentre, randomized, single-blind, controlled study. Only registered, available vaccines will be administered (Pfizer, Moderna and Janssen). For administration of the first vaccine, participants are randomized to a single dose, homologous vaccination strategy (two of the same vaccines) or a heterologous vaccination strategy (two different vaccines). Blood will be drawn at 4 different times: day 0 (before 2nd vaccination), on day 28 (primary endpoint), day 180 ((+/- 14 days) and day 365 (+/- 14 days). The primary outcome parameter is similar to the other studies (humoral response at 28 days after 2nd vaccination). Questionnaires will be used to check for adverse events after each vaccination and to evaluate any breakthrough SARS-CoV-2 infections and outcome despite vaccination.

December 2021
We would like to boost the Janssen solo group with Pfizer 30 micrograms.

The research is being conducted among the participants of the Janssen solo group. That was about 108. In the meantime, 18 have lost weight because these people were insufficiently protected against COVID based on their antibodies. These people have already been vaccinated.

February 2022
Extra boost: A second boost with Pfizer 30 micrograms is offered to the groups J/J, J/M and J/P.

Waning: all participants from groups J/J, J/M and J/P are asked if they would like to participate in a study on the decline of the immune response over time.

Non-responders: the non-responders and high responders of the J/ group (at the time of Study Visit 2 - +/- 4 months after prime with Janssen) are asked whether they want to participate in a study to find out why someone makes a reduced immune response to a single vaccination with Janssen.

Intervention

All adults in the Netherlands are vaccinated on a voluntary basis, the intervention is aimed at comparing homologous versus heterologous vaccination strategy.
Key endpoints: The immune response to SARS CoV-2 after vaccination at various time points, with antibody response 28 days after the second vaccination being the primary endpoint.

December 2021
The participants will be boosted with Pfizer 30 microgram.

Study burden and risks

RISK - BENEFIT ANALYSIS

1. The group of persons that will be approached for this study are all Health Care Workers. This means that they belong to a group of HCW with a higher exposure to COVID-19 during their work. On the other hand, due to a shortage of vaccines this group is not yet assigned to vaccination. By offering them to participate to this trial, these HCW (and their family) can be accelerated protected to COVID infections.
2. Full vaccination with two boosters can at this moment only be assured if combinations of vaccines are applied. Vaccination with only one booster is not recommended by virologists.
3. If combination of two different vaccines will not lead to sufficient protection as seen in the titer of neutralizing antibodies, this will be identified within 2 months after the first injection. This can be the case for both an individual or a group. If this appears, adequate measures will be taken to reassure the safety of the HCW.
4. As two different vaccines will be administered, it may be the case that through vaccinations with slightly different vaccines the immune-response may even be improved.
5. With the upcoming Variants of Concern (e.g. the british variant), it has been suggested that the present vaccines could be changed a bit to improve the vaccination against these variants. In that case it might even be a necessity to combine vaccines to cover all different VoC.
6. It is difficult to predict whether the occurrence of adverse events will increase or decrease. In the comirnaty-trial can be seen that the systemic adverse events are increased after the 2nd dose. Most of these adverse reactions can be seen as an immune response. As the 2nd dose in this study differs from the 1st, the immune response may be less prominent in the first 2 days.
7. The occurrence of anaphylaxis might increase as the HCW are exposed to two different regimens. The incidence of anaphylaxis appears to be so low that this might not be of clinical significance. To mitigate the occurence of anaphylaxis the HCW will be monitored after the 1st and the 2nd dose for at least 15 minutes.
8. It is important to state that the vaccines for this study will NOT be retrieved from a stock reserved for patients or other persons.In the past days we have shown that we get more vaccinations from 1 flacon than stated by the manufacturer. The extra flacons that will be gained by this method will be used for this study. This statement is strengthened by the cooperation of hospital pharmacists from the region who support this trial.
9. As stated in the introduction of the study, due to shortages, logistic problems and reservations of vaccines for the 2nd booster, the velocity of vaccination is hampered all over the world. If this non-inferiority study concludes that boosting the immune system against COVID-19 can be done with

different vaccines, this has a huge societal impact for the world.

December 2021
10. All HCW will be vaccinated anyway with Pfizer 30 microgram.

Conclusion
Based on the considerations mentioned above and weighing both the risks and the benefits of this trial, we conclude that there is a positive risk-benefit analysis to proceed with this trial.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

All HCW who work in the health care facility without contra-indications, vaccinated already once with Janssen.

December 2021
Only participants from the SWITCH in the Janssen solo group will be included.

Exclusion criteria

1. HCW younger than 18
2. HCW that are pregnant or have a wish to become pregnant within 6 months
3. All regular contra-indications of the vaccines will be applied
4. HCW with a confirmed SARS-COVID-19 infection

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	26-06-2021
Enrollment:	461
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Comirnaty (Pfizer)
Product type:	Medicine
Brand name:	Janssen
Product type:	Medicine
Brand name:	Moderna

Ethics review

Approved WMO Date:	22-03-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	31-03-2021
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-04-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-06-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	22-11-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	24-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	07-03-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO	

Date:	08-03-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	28-04-2022
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	EUCTR2021-000701-24-NL
CCMO	NL76782.078.21