Establishing immunogenicity and safety of needle-free intradermal delivery by nanoporous ceramic skin patch of mRNA SARS-CoV-2 vaccine as a revaccination strategy in healthy volunteers

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Primary objective - to describe immunogenicity and safety in healthy volunteers of the intradermal dermal delivery of a single fractional dose of 20µg mRNA-1273 LNP vaccine (Spikevax, Moderna) more than 3 months after primary vaccination with...

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

Summary

ID

NL-OMON51606

Source
ToetsingOnline

Brief title
MILESTONE: iMmunogenicity IntradermaL cEramic Skin paTch sars-cOv-2 vacciNE

Condition

- Viral infectious disorders

Synonym
COVID-19 vaccination

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,MyLifeTechnologies

Intervention

Keyword: COVID-19, intradermal, skin patch, vaccine

Outcome measures

Primary outcome

Immunogenicity:

- SARS-CoV-2-spike protein-specific binding IgG antibody levels

Safety:

- Local reactions (pain at the injection site, redness, and swelling)

- Reaction regional lymph nodes (pain, swelling)

- Use of antipyretics and painkillers

- Systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or

worsened muscle pain, and new or worsened joint pain)

- AEs

- SAEs

Secondary outcome

- SARS-CoV-2-spike protein-specific binding IgG and IgA antibody levels and

RBD- specific binding IgG antibody levels in serum

- SARS-CoV 2 WT neutralizing antibody levels

Exploratory

- Number of Spike-protein specific proliferating B-cells, plasma cells and

B-memory cells

- INF-gamma concentration and other cytokine responses after over-night

incubation

Study description

Background summary

Currently, five vaccines are listed by the World Health Organization (WHO) for emergency use. These vaccines are limited in supply, especially in low- and middle-income countries, leading to substantial morbidity and mortality. A large unvaccinated population continues to pose a threat of a continuous emergence of new SARS-CoV-2 variants that may be more infectious, more malignant and more resistant to vaccines than current strains. Despite the COVID-19 Vaccines Global Access (COVAX) Facility initiated by the WHO to provide vaccine access for low-income countries, probably 80% of the vaccine needs of participating countries will not be met soon.
In addition, there is an increasing demand for revaccination of the (vulnerable) population globally, because of waning immunity which will further limit vaccine supplies. Exploring dose-sparing techniques, and future self-application of vaccine, could therefore provide the solution to immunise more people with the same vaccine stockpile.

The intramuscular injection (IM) is the standard inoculation route of vaccines. However, the skin (dermis) is much richer in antigen presenting dendritic cells than muscle [1]. In addition, the dermis contains an extensive lymphatic network, which aids efficient transport of vaccine antigen and antigen presenting Langerhans and dendritic cells to the regional lymph nodes [2]. As a consequence, a fractional vaccine dose introduced directly into the dermis (intradermal administration, ID) might be as effective as the intramuscular administration of the full standard dose to achieve a protective immune response. This principle has recently been demonstrated for the ID dermal delivery of one-fifth fractional dose mRNA-1273 (Spikevax, Moderna) vaccine [3].

However, needle-based immunisation has several limitations. Fear of needles makes immunisation a stressful event. In addition, needle stick injuries, as well as unsafe injection practices carry serious health risks. Therefore, the development of needle-free delivery has been identified as an important goal in global health care [4]. The WHO reported that microneedle vaccine delivery is

top priority and requires additional research to explore the benefits in more detail. A big advantage of intradermal delivery via a microneedle array/patch is not only the absence of needles and pain since no nerves are at the proximity where the needles are presented, but also the local delivery close to immune cells as with the above mentioned intradermal injection enables a much lower dose as compared to IM dosing. And since with the patch a larger skin surface is involved as compared to intradermal injection, even lower doses are possibly still immunogenic.

Study objective

Primary objective
- to describe immunogenicity and safety in healthy volunteers of the intradermal dermal delivery of a single fractional dose of 20µg mRNA-1273 LNP vaccine (Spikevax, Moderna) more than 3 months after primary vaccination with Comirnaty (Pfizer) vaccine.

Secondary objectives
- to describe the kinetics of the SARS-CoV-2 anti-Spike1 (S1) and Region Binding Domain (RBD) IgG and IgA binding antibodies elicited by intradermal or intramuscular delivery of mRNA-1273 vaccine in healthy volunteers after a single fractional dose of 20µg mRNA-1273 LNP vaccine
- to describe the kinetics of the SARS-CoV-2 neutralising antibodies elicited by intradermal or intramuscular delivery of mRNA-1273 vaccine in healthy volunteers after a single fractional dose of 20µg mRNA-1273 LNP vaccine

Exploratory objectives:
- to describe the kinetics of memory B-cell and plasma cell responses elicited by intradermal or intramuscular delivery of mRNA-1273 vaccine of a single fractional dose of 20µg mRNA-1273 LNP vaccine (Spikevax, Moderna)
- to describe the interferon-gamma release in whole blood in response to SARS-CoV 2 peptides after intradermal or intramuscular delivery of mRNA-1273 vaccine of a single fractional doses of 20µg mRNA-1273 LNP vaccine (Spikevax, Moderna)

Study design

This is a Phase 2a, open-label, randomised-controlled, proof-of-concept vaccine study

Intervention

Intervention group (n=10): Participants will receive 20 µg of mRNA-1273 vaccine through the intradermal route using a micro-needle delivery system.

Control group (n=10): Participants will receive 20 µg of mRNA-1273 vaccine

through the intramuscular route

Study burden and risks

Burden of receipt of the vaccine by intradermal (ID) administration (adverse events):
The mRNA-1273 vaccine (Spikevax, Moderna) has been approved for mass vaccination by the EMA in Europe and by the Medicine Evaluation Board in the Netherlands. The most frequent side effects of intramuscular administration of 100 µg mRNA-1273 vaccine were injection site pain (92%); fatigue (70%); headache (64%); myalgia (61%); arthralgia (46%); chills (45%); nausea and vomiting (23%); swelling axillar lymph nodes 20%); pyrexia (15%) and injection site swelling and redness (15%) usually mild or moderate in intensity and resolving within a few days after vaccination. Side effects were reported more frequently after the second dose. The frequency of anaphylactic reactions after the mRNA vaccine by Moderna is estimated to be around 2.5:1000,000 [5]. Three cases of Bell*s palsy have been reported in the vaccine group and one in the placebo group. In 19 young adults, pericarditis/myocarditis has been reported in a population of over 20 million doses.
In a recent study we showed that the ID administration of 10 µg and 20 µg mRNA-1273 vaccine with needle and syringe resulted in a robust, homogeneous, immune response with an acceptable safety profile in healthy adults aged 18-30 years [IDSCOVA]. The most commonly reported adverse reactions were short-lasting and consisted of mild pain, itching, erythema and swelling at the injection site. These local reactions are similar to those reported after intradermal vaccination with other vaccines.

Burden of postponing their regular booster (i.e. revaccination) in the national vaccination programme:
Participants are willing to postpone their regular COVID revaccination upon invitation by the municipal health center or general practitioner until the day after the final study sampling (D29), which is approximately four weeks after receiving the intervention. Participants who have postponed their regular COVID-19 revaccination through the national immunisation program to participate in this study will be offered their regular vaccination after D29 of the study.

Burden of participation in the study (time and blood volume):
Participation in the study requires four site visits. Screening (D0) will take 60 minutes, vaccination (D1) will take 90 minutes since the vaccine-patch formulation will have to be prepared on the day of the vaccination. Blood sampling on D29 will take 15 minutes. In total this is 165 minutes without travelling to and from the LUMC. During the visits blood will be collected for antibody testing (maximal total blood volume 100 mL in the study).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- Male or female participants between the ages of 18 and 50 years, inclusive at randomisation.
- Previously vaccinated with Comirnaty (Pfizer) or Spikevax (Moderna) at least 3 months before inclusion.
- Healthy participants who are determined by medical history and clinical judgment of the investigator to be eligible for inclusion in the study. Healthy participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalisation for worsening disease during the 6 weeks before enrolment, can be included.
- Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, and other study procedures.
- Participants are willing to postpone their regular COVID-19 revaccination

upon invitation by the municipal health center or general practitioner until four weeks after receiving the intervention (after the last sampling of D29+/-1).
- Capable of giving personal signed informed consent, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol.

Exclusion criteria

- Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behaviour or laboratory abnormality that may increase the risk of study participation or, in the investigator*s judgment, make the participant inappropriate for the study.
- History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (e.g., anaphylaxis) to any component of the study intervention(s).
- Receipt of medications intended to prevent COVID-19.
- Previous microbiological diagnosis of COVID-19 less than 3 months ago.
- Previous COVID-19 (re)vaccination other than Comirnaty (Pfizer) or Spikevax (Moderna) less than 3 months ago
- Individuals at high risk for severe COVID-19 (e.g. BMI > 40, diabetes, heart-end/or lung disease), who are planned to receive COVID vaccine within the next two months.
- Immunosuppressed individuals with known or suspected immunodeficiency, as determined by history.
- Individuals with an active autoimmune disease requiring therapeutic intervention.
- Receipt of systemic or topical corticosteroids.
- Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection.
- Women who are pregnant or breastfeeding.
- Planned pregnancy within four weeks after injection.
- Positive serological test for SARS-CoV-2 anti-N IgM and/or IgG antibodies at screening visit.
- SARS-CoV-2 PCR-positive mid-turbinate/throat swab at the screening before receipt of the vaccine dose.
- Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation.
- Receipt of any other non-study vaccine within 28 days, before receipt of the study dose.
- Anticipated receipt of any other non-study vaccine within 28 days, after the study dose administration.

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-05-2022
Enrollment:	20
Type:	Actual

Medical products/devices used

Generic name:	nanoporous ceramic skin patch
Registration:	No
Product type:	Medicine
Brand name:	Spikevax

Ethics review

Approved WMO Date:	22-03-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl
Approved WMO Date:	31-03-2022

Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	EUCTR2021-006754-31-NL
CCMO	NL80101.058.22

Study results