Establishing the tolerability, safety and immunogenicity of intradermal delivery of mRNA SARS-CoV-2 vaccine in healthy adults

No registrations found.

Ethical review	Not applicable
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON20603

Source
Nationaal Trial Register

Brief title
IDSCOVA

Health condition

COVID-19

Sponsors and support

Primary sponsor: Leiden University Medical Center
Source(s) of monetary or material Support: Leiden University Medical Center, Dept. of Infectious Diseases

Intervention

Outcome measures

Primary outcome

- Nature, frequency and severity of local reactions. Solicited adverse events include: pain, redness and swelling at the injection site and pain and swelling at the regional lymph nodes
- Nature, frequency and severity of systemic events. Solicited adverse events include: fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain.
- Use of antipyretics and painkillers
- SARS-CoV-2 WT neutralizing antibody titers rate on Day 43
- SARS-CoV-2-spike protein–specific binding IgG level on D 43

Secondary outcome

- Kinetics of SARS-CoV 2 WT neutralizing antibody (seroconversion, GMT and GM fold rise) and of SARS-CoV-2-spike protein-specific binding IgG antibody levels and RBD- specific binding IgG antibody levels (seroconversion, GMC and GM fold rise) over time
- Positive SARS-CoV-2 PCR (with or without clinical symptoms) of nasopharyngeal/throat swab
- Seroconversion SARS-CoV-2 (Nucleocapsid Serology)
- Proportion of afucosylated IgG variants
- SARS-CoV-2 WT neutralizing antibodies in nasal fluid
- SARS-CoV-2-spike protein–specific binding IgG and IGA antibody levels and RBD- specific binding IgG and IGA antibody levels in nasal fluid
- Parameters quantifying germinal center activity
- Whole blood interferon-gamma release assay to SARS-CoV-2 antigen

Study description

Background summary

SUMMARY
Rationale: The intradermal route is a highly effective way to administer vaccines. As a consequence, a fractional vaccine dose introduced directly into the papillary dermis (intradermal administration, ID) might be as effective as the intramuscular administration of the full standard dose to achieve a protective immune response. Especially in circumstances of limited vaccine stockpiles, vaccination with a fractional dose through the intradermal route can be applied as a dose-sparing strategy. Because the vaccine is administered much more superficially, the local side effects, such as redness and induration, are more visible at the site of injection than after intramuscular injection.
Globally the race to national mass vaccination campaigns to protect against infection with SARS-CoV-2 has started. Production limitations threaten to delay the roll-out of the national vaccination campaigns. In preclinical studies the intradermal route has been shown to be a very effective way for mRNA vaccine administration. If the intradermal route would be a safe and effective route for a fractional dose of the mRNA COVID vaccine, many more people could be vaccinated with the same limited amount of vaccine.
vaccine.

Objectives:
Primary objectives:
- to describe tolerability, safety and immunogenicity in healthy adults of the intradermal delivery of one or two fractional doses of 10 µg and 20 µg mRNA-1273 LPN vaccine (Moderna).
- to compare the immunogenicity in healthy adults of the intradermal delivery of two fractional dose of 20 µg mRNA-1273 LPN with that of two doses of 20 µg mRNA-1273 vaccine through intramuscular delivery on Day 43.
- to determine non-inferiority of the virus neutralizing antibody response elicited by intradermal delivery of mRNA-1273 vaccine in healthy adults after two fractional doses of 20 µg with the responses to two doses of 100 µg mRNA-1273 vaccine through intramuscular delivery on Day 43. On group receives the fractional dose (20ug) intradermally via 'Mantoux technique' and one group with Bella-mu needle for intradermal administration.
Secondary objectives:
- to describe the kinetics of the humoral immune responses elicited by intradermal or intramuscular delivery of mRNA-1273 vaccine in healthy adults after 1 and 2 fractional doses of 20 µg, and standard intramuscular delivery of 100 µg.
- to document symptomatic and asymptomatic infection with SARS-CoV-2
Exploratory objectives:
- to describe the nasal mucosal immune response elicited by intradermal or intramuscular delivery of mRNA-1273 vaccine in healthy adults after 1 or 2 fractional doses of 20 µg, and standard intramuscular delivery of 100 µg
- to describe the glycosylation of SARS-CoV-2 antibodies elicited by intradermal or intramuscular delivery of mRNA-1273 vaccine in healthy adults after 1 or 2 fractional doses of 20 µg, and standard intramuscular delivery of 100 µg.
- to describe the T follicular helper cell kinetics elicited by intradermal or intramuscular delivery of mRNA-1273 vaccine in healthy adults after 1 or 2 fractional doses of 20 µg, and standard intramuscular delivery of 100 µg.
- to describe the memory B-cell and plasma cell response elicited by intradermal delivery of mRNA-1273 vaccine in healthy adults after 1 or 2 fractional doses of 20 µg, and standard intramuscular delivery of 100 µg.

Study design: This is a Phase 1/Phase 2a, open-label, randomized-controlled, dose-escalation, proof-of-concept vaccine study.

Study population: Health adults aged 18 - 30 years
Intervention group: Participants will receive 10 µg or 20 µg mRNA-1273 vaccine followed by a second dose on day 28 through the intradermal route.
Comparison group: Participants will receive 20 µg or 100 µg mRNA-1273 vaccine followed by a second dose on day 28 through the intramuscular route.

Main study parameters/endpoints:
- Local reactions and systemic events self-reported by e-diary on a daily basis over a 2-week period, as well as by structured interviews by telephone/video call on D2, D3, D4, D8, D15, D29, D30, D31, D32, D36, and D43
- Adverse events (AEs) from Dose 1 to one month after the last dose
- Serious AEs (SAEs) from Dose to six months after the last dose

- Seroconversion for anti-spike IgG antibodies (D0, D29, D36, D43, M7, M13)
- Geometric mean titers (GMT) for anti-spike IgG antibodies (D0, D29, D36, D43, M7, M13)
- Seroconversion for neutralizing antibodies to SARS-CoV2 (D0, D29, D36, D43, M7, M13)
- GMT for neutralizing antibodies to SARS-CoV2 (D0, D29, D36, D43, M7, M13)

Study objective

The intradermal vaccination of a fractional dose of mRNA-1273 LPN vaccine (Moderna) is safe and non-inferior in eliciting neutralizing antibodies against SARS-CoV-2 to the standard dose injected intramuscularly

Study design

D0, D2, D3, D4, D8, D15, D29, D30, D31, D32, D36, D43, M7, M13 (safety and immunogenicity, D = day, M = month)

Intervention

intradermal injection of a fractional dose (10 µg and 20 µg) mRNA-1273 LPN vaccine compared to intramuscular injection of the standard dose (100 µg) mRNA-1273 LPN vaccine

Contacts

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Eligibility criteria

Inclusion criteria

- Male or female participants between the ages of 18 and 30 years, inclusive at randomization.
- 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 hospitalization 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.
- Capable of giving personal signed informed consent as described in Appendix 1, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol.
- Females only: female volunteers of childbearing potential (i.e. have a uterus and are neither surgically sterilized nor postmenopausal) must not be pregnant or breastfeeding. They should agree to use adequate contraception at least up to four weeks following the final dose of mRNA-1273 vaccine

Exclusion criteria

- Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior 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 (eg, anaphylaxis) to any component of the study intervention(s).
- Receipt of medications intended to prevent COVID-19.
- Previous clinical or microbiological diagnosis of COVID-19.
- Individuals at high risk for severe COVID-19, 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 a history of autoimmune disease or 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 the final injection.
- Positive serological test for SARS-CoV-2 IgM and/or IgG antibodies at the screening visit.
- SARS-CoV-2 PCR-positive nasopharyngeal/throat swab at the screening before receipt of first 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 first study dose.
- Anticipated receipt of any other non-study vaccine within 28 days, after last study dose administration

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-03-2021
Enrollment:	150
Type:	Actual

IPD sharing statement

Plan to share IPD: Undecided

Ethics review

Not applicable

Application type:	Not applicable

Study registrations

Followed up by the following (possibly more current) registration

ID: 51021
Bron: ToetsingOnline
Titel:

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL9275
CCMO	NL76702.058.21
OMON	NL-OMON51021

Study results