Safety, tolerability and immunogenicity of intradermal mRNA SARS-CoV2 vaccination in patients with Fibrodysplasia Ossificans Progressiva

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This study has been transitioned to CTIS with ID 2024-518686-10-00 check the CTIS register for the current data. To describe and investigate safety and tolerability of the intradermal delivery of two fractional doses of 3/3 µg Comirnaty Original/...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Interventional

Summary

ID

NL-OMON53330

Source
ToetsingOnline

Brief title
IVY

Condition

- Musculoskeletal and connective tissue disorders congenital
- Musculoskeletal and connective tissue disorders congenital

Synonym
Fibrodysplasia ossificans progressiva, FOP, Stone man syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Beurs verkregen van FOP patientenvereniging

Intervention

Keyword: Fibrodyplasia ossificans progressiva, heterotopic ossification, SARS-CoV-2, Vaccination

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: flare-up, fever, fatigue, headache, chills, vomiting, diarrhoea, new

or worsened muscle pain, and new or worsened joint pain.

Use of corticosteroids, antipyretics and painkillers

Secondary outcome

• SARS-CoV 2 WT neutralising antibody titres rate on Day 1 and Day 43

• SARS-CoV-2-spike protein-specific binding IgG level on Day 1 and Day 43

• B-cell and T-cell responses on day 1 and day 43

Study description

Background summary

Patients with Fibrydysplasia Ossificans Progressiva (FOP) have an increased risk of fatal SARS-CoV-2 infection due to their restricted pulmonary function though are unable receive the approved intramuscular vaccination. Intramuscular vaccination will likely cause a flare-up and subsequent heterotopic ossification (HO). Current treatment guidelines also recommend to avoid all intramuscular (IM) vaccinations and advise to immunize through subcutaneous vaccination when possible. Actual data on vaccine tolerability, safety and immunogenicity is however limited. Lanchoney et al reported that IM injection of diphtheria-pertussis-tetanus (DPT) vaccines caused flare-ups and subsequent HO in 27% of children with FOP. Kou et al. followed up on patients who had received mRNA COVID-19 vaccination and reported that 1 out of 12 patients experienced a flare-up and subsequent HO after IM vaccination.

Normally, vaccines are administered into the muscle. However, the skin (dermis) contains a much higher density of antigen presenting dendritic cells than does muscle. The skin lymphatic system is extensively organised into several plexus systems, which aids efficient transport of vaccine antigen and antigen presenting dendritic cells to the regional lymph nodes. 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. This principle has already been demonstrated for rabies, yellow fever, inactivated polio and seasonal influenza vaccine. At the moment, a research group at the LUMC is performing the IDSCOVA-trial, evaluating the tolerability, safety and immunogenicity of intradermal mRNA SARS-CoV-2 vaccination compared to standard intramuscular vaccination.

In preclinical studies the intradermal route has been shown to be a very effective way for mRNA vaccine administration. At the moment, a research group at the LUMC is performing the IDSCOVA-trial, evaluating the tolerability, safety and immunogenicity of intradermal mRNA SARS-CoV-2 vaccination compared to standard intramuscular vaccination in healthy adults. Results in a preprint show that 20µg ID elicited a sufficient antibody response in all subjects with significantly less systemic sides effects such as fever, myalgia, joint pains and headaches. If the intradermal route is also a safe and effective route of vaccination in patients with FOP, it would prove a preferred alternative to intramuscular vaccination in patients with FOP.

At the moment, the omicron variant is the dominant variant in the Netherlands. Due to policy decisions, the moderna vaccine is not currently available in the Netherlands. To best accomodate the current corona situation in the Netherlands, we will vaccinate the patients with the 3/3 µg Comirnaty Original/Omicron BA.4-5 vaccin intradermally.

Study objective

This study has been transitioned to CTIS with ID 2024-518686-10-00 check the CTIS register for the current data.

To describe and investigate safety and tolerability of the intradermal delivery of two fractional doses of 3/3 µg Comirnaty Original/Omicron BA.4-5 vaccin in patients with Fibrodysplasia Ossificans Progressiva. Additionally to measure the immunogenicity through SARS-CoV 2 neutralising antibody, SARS-CoV-2-spike protein-specific binding IgG and IgA antibody levels and RBD-specific IgG antibody levels with be measures in all participants at D0, D29 and D57.

Study design

Prospective interventional cohort study

Intervention

Participants will receive 3/3 µg Comirnaty Original/Omicron BA.4-5 vaccine followed by a second dose on day 28 through the intradermal route.

Study burden and risks

FOP patients have an increased risk of severe SARS-CoV-2 infection due to (severe) reduced lung function, but can usually not be vaccinated intramuscularly because of the risk of heterotopic ossification. Previous research has shown that intradermal COVID19 vaccination is safe and effective in healthy volunteers. If this also turns out to be the case in FOP patients, this vulnerable population can be protected against serious disease. This justifies the potential risk of more pronounced local side effects from intradermal injection and venipuncture.

Contacts

Public
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
Amsterdam 1081HV
NL
Scientific
Vrije Universiteit Medisch Centrum

De Boelelaan 1117
Amsterdam 1081HV
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• Fibrodysplasia ossificans progressiva as determined by confirmation of any causative genetic mutation in the ACVR1 gene
• 18 years or older
• Participants who are willing and able to comply with all scheduled visits, vaccination tests and other study procedure
• Capable of giving personal signed consent as described in appendix 1, which includes compliance with the requirements and restrictions listed in the ICD and this protocol

Exclusion criteria

• 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 SARS-CoV-2 infection.
• Current clinical complaints consistent with SARS-CoV-2 infection (three or more of the following complaints: headache, loss of smell, sore throat, hoarseness, cough, chest pain, shortness of breath, fatigue, diarrhea, fever).
• SARS-CoV-2 vaccination 6 months prior to participation.
• 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.
• SARS-CoV-2 PCR-positive EMA approved lateral flow test at the screening before receipt of fist vaccine dose
• 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 phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	28-07-2023
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Comirnaty Original/Omicron BA.4-5 vaccine

Ethics review

Approved WMO

Date:	10-03-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	19-06-2023
Application type:	First submission
Review commission:	METC Amsterdam UMC

Approved WMO

Date:	24-07-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EU-CTR	CTIS2024-518686-10-00
EudraCT	EUCTR2022-000692-39-NL
CCMO	NL83562.018.22