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A trial to evaluate the ability to provoke an immune response and the safety of mRNA-1273.529 (Omicron Variant) in comparison with mRNA-1273 (prototype) booster vaccine

Submission date
22/01/2022

Recruitment status
No longer recruiting

Registration date
18/03/2022

Overall study status
Completed

Last Edited
01/04/2022

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[_] Record updated in last year

Plain English summary of protocol

Background and study aims
An outbreak of COVID-19 caused by the novel coronavirus SARS-CoV-2 has spread throughout the world. There are now a number of vaccines that have been approved to prevent COVID-19.

Vaccines serve to prepare the immune system for fighting infection and preventing illness. The immune system produces antibodies which recognise viruses and make them harmless. COVID-19 vaccines boost the immune system to produce enough antibodies against SARS-CoV-2 so in case of an infection, the virus does not cause illness. The mRNA-1273 vaccine has been approved for emergency use for prevention of COVID-19. The mRNA-1273.529 vaccine targets the omicron strain of SARS-CoV-2 and is not yet approved.

The purpose of this study is to compare the body's immune response to a booster dose of mRNA-1273 vaccine compared to mRNA-1273.529 vaccine.

Who can participate?
Healthy people who are at least 16 years old and have already received 2 or 3 doses of an authorised or approved COVID-19 vaccine may be eligible to participate.

What does the study involve?
Participants will be randomised in a 1:1 ratio to receive either the mRNA-1273 or mRNA-1273.529 vaccine. They will remain in the study for 12 months. They will attend the clinic for visits at screening, Day 1, (Day 8), and Months 1, 3, 6 and 12. They will also have 3 or 4 safety phone calls during this time. Procedures during the visits will include physical examination, vital signs, nasopharyngeal swab, blood sampling and participants will need to complete an e-diary.

What are the possible benefits and risks of participating?
Benefits:
Taking part in this study may be of no direct benefit to participants. However, the data gathered

during this study may help doctors learn more about the study vaccine and this may help others in the future.
Risks:
All vaccines can cause side effects. No studies of the mRNA-1273.529 vaccine in people are ongoing at this time. There may be similar side effects to the mRNA-1273 vaccine.
Some people experienced reactions that kept them from their usual daily activities. Most of these reactions lasted about 1 to 3 days. They mostly occurred within the first few days after vaccination and went away within a few days. These side effects were usually mild or moderate but were occasionally severe.
The most common side effects seen when the mRNA-1273 vaccine was given to adults were:
- Pain at the injection site
- Fatigue (tiredness)
- Headache
- Muscle aches or pain
- Joint aches or pain
- Chills
The most common side effects seen when the mRNA-1273 vaccine was given to adolescents were:
- Pain at the injection site
- Swelling at the injection site
- Redness at the injection site
- Fatigue (tiredness)
- Headache
- Muscle aches or pain
- Joint aches or pain
- Chills
- Gland swelling under the arm on the side of study vaccination
- Nausea/vomiting
- Fever

Where is the study run from?
St George's, University of London (UK)

When is the study starting and how long is it expected to run for?
January 2022 to March 2023

Who is funding the study?
ModernaTX, Inc. (USA)

Who is the main contact?
Dr Catherine Cosgrove, ccosgrov@sgul.ac.uk

Study website
https://connect.trialscope.com/studies/0a9015ce-4de7-49a8-8683-a2f5fe6fa455

Contact information

Type(s)
Principal Investigator

Contact name

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Additional identifiers

EudraCT/CTIS number
2022-000063-51

IRAS number
1004941

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
mRNA-1273-P305, IRAS 1004941, CPMS 51566

Study information

Scientific Title
A phase 2/3, randomized, observer-blind, active-controlled, multicenter study to evaluate the immunogenicity and safety of mRNA-1273.529 (B.1.1.529, Omicron Variant) in comparison with mRNA-1273 (prototype) booster vaccine

Study objectives
- To demonstrate non-inferiority of the immune response of mRNA-1273.529 compared to mRNA-1273 booster administered as a 4th dose against the B.1.1.529 strain at Day 29
- To evaluate the safety and reactogenicity of mRNA-1273.529 and mRNA-1273 administered as a booster dose
- To demonstrate the superiority of the immune response of mRNA-1273.529 compared to mRNA-1273 administered as a 4th dose against the B.1.1.529 strain at Day 29 or Month 3
- To demonstrate non-inferiority of the immune response of mRNA-1273.529 compared to mRNA-1273 booster administered as a 4th dose against theprototype strain at Day 29
- To evaluate the sero response rate (SRR) of mRNA-1273.529 and mRNA-1273 boosters administered as a 4th dose
- To evaluate the immunogenicity of mRNA-1273.529 booster compared to mRNA-1273 booster administered as a 3rd dose
- To evaluate the immunogenicity of mRNA-1273.529 booster compared to mRNA-1273 booster

administered as a 3rd or the 4th dose study vaccine
- To evaluate the immunogenicity of mRNA-1273.529 and mRNA-1273 booster at all evaluable time points after the vaccination administration

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 03/02/2022, Fast Track Research Ethics Committee (Health Research Authority, 2 Redman Place, Stratford, London, E20 1JQ, UK; no telephone number provided; fasttrack.rec@hra.nhs.uk), ref: 22/HRA/0060

Study design
Observer-blind stratified interventional randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Prevention

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet.

Health condition(s) or problem(s) studied
COVID-19 (SARS-CoV-2 infection)

Interventions
Study Arms:
mRNA-1273 (Moderna COVID-19 Vaccine, Spikevax®) 50 µg (mRNA)
mRNA-1273.529 (Moderna Omicron Variant Vaccine) 50 µg (mRNA)

All participants will have previously received 2 or 3 doses of an authorized/approved COVID-19 vaccine. Participants who had previously received 2 doses of a COVID-19 vaccine as a primary series will receive mRNA-1273.529 or mRNA-1273 as the third dose, and participants who have previously received a primary series and 1 booster dose will receive mRNA-1273.529 or mRNA-1273 as the 4th dose. Participants who will receive the 4th dose as part of the study must have previously received a mRNA vaccine as the 3rd dose of a COVID-19 vaccine. Participants who will receive the 3rd dose as part of the study may have previously received 2 doses of a mRNA or a non-mRNA COVID-19 vaccine.

Study visits: will consist of a Screening Visit (up to 28 days before the Day 1 visit), Vaccination Visit at Day 1 and subsequent study visits on Day 8 (for a subset of participants), Day 29 (Month 1), Day 85 (Month 3), Day 179 (Month 6), and Day 359 (Month 12), with up to 13 months of study participation. Unscheduled visits for potential symptoms of COVID-19 will include PCR testing.

Randomisation: Randomization will be performed using an interactive response technology (IRT). Approximately 2,924 participants will be randomized in a 1:1 ratio to receive a single dose of either 50 µg of mRNA-1273.529 or 50 µg of mRNA-1273 (active control). Randomization will be stratified by age groups (16 to <65 years or ≥65 years) and number of booster doses received (to receive study vaccine as the 4th dose or to receive study vaccine as the 3rd dose). At least ≥90% of participants will receive study vaccine as the 4th dose.

Intervention Type
Biological/Vaccine

Phase
Phase II/III

Drug/device/biological/vaccine name(s)
mRNA-1273.529, mRNA-1273 booster

Primary outcome measure
To demonstrate non-inferiority of the immune response of mRNA-1273.529 compared to mRNA-1273 booster administered as a 4th dose against the B.1.1.529 strain at Day 29:
1. Geometric mean titer (GMT) of mRNA 1273.529 and mRNA-1273 against both the B.1.1.529 and prototype strain at Day 29 after study vaccine administration
2. Ratio of GMTmRNA-1273.529/GMTmRNA-1273 against the B.1.1.529 strain at Day 29 after study vaccine administration
3. Geometric mean fold rise (GMFR) of mRNA-1273.529 against the B.1.1.529 strain at Day 29 after study vaccine administration

To evaluate the safety and reactogenicity of mRNA-1273.529 and mRNA-1273 administered as a booster dose :
4. Solicited local and systemic reactogenicity ARs during a 7-day follow up period after vaccination
5. Unsolicited adverse events (AEs) during the 28-day follow-up period after vaccination
6. SAEs, medically attended AEs (MAAEs), AEs leading to withdrawal, and AEs of special interest (AESIs) from Day 1 to end of study

Secondary outcome measures
To demonstrate superiority of the immune response of mRNA-1273.529 compared to mRNA-1273 administered as a
4th dose against the B.1.1.529 strain at Day 29 or Month 3:
1. GMT of mRNA-1273.529 and mRNA-1273 against the B.1.1.529 strain at Day 29 and Month 3 after study vaccine administration
2. Ratio of GMTmRNA-1273.529/GMTmRNA-1273 against the B.1.1.529 strain at Day 29 and Month 3 after study vaccine administration

To demonstrate non-inferiority of the immune response of mRNA-1273.529 compared to mRNA-1273 booster administered as a 4th dose against the prototype strain at Day 29:
3. GMT of mRNA-1273.529 and mRNA-1273 against the prototype strain at Day 29 after study

vaccine administration
4. Ratio of GMTmRNA-1273.529/GMTmRNA-1273 against the prototype strain at Day 29 after study vaccine administration
5. GMFR of mRNA-1273.529 against the prototype strain at Day 29 after study vaccine administration

To evaluate the seroresponse rate (SRR) of mRNA-1273.529 and mRNA-1273 boosters administered as a 4th dose:
6. SRR against the B.1.1.529 strain
7. SRR against the prototype strain

To evaluate the immunogenicity of mRNA-1273.529 booster compared to mRNA-1273 booster administered as a 3rd dose:
8. GMT of mRNA-1273.529 against both the B.1.1.529 and the prototype strain at Day 29 after study vaccine administration
9. Ratio of GMTmRNA-1273.529/GMTmRNA-1273 against the B.1.1.529 strain at Day 29 after study vaccine administration
10. Ratio of GMTmRNA-1273.529/GMTmRNA-1273 against the prototype strain at Day 29 after study vaccine administration
11. GMFR of mRNA-1273.529 against both the B.1.1.529 and prototype strain at Day 29 after study vaccine administration
12. SRR against both the B.1.1.529 and prototype strain

To evaluate the immunogenicity of mRNA-1273.529 booster compared to mRNA-1273 booster administered as a 3rd or the 4th dose study vaccine:
13. GMT of mRNA-1273.529 against both the B.1.1.529 and the prototype strain at Day 29 after study vaccine administration
14. Ratio of GMTmRNA-1273.529/GMTmRNA-1273 against the B.1.1.529 strain at Day 29 after study vaccine administration
15. Ratio of GMTmRNA-1273.529/GMTmRNA-1273 against the prototype strain at Day 29 after study vaccine administration
16. GMFR of mRNA-1273.529 against both the B.1.1.529 and prototype strain at Day 29 after study vaccine administration
17. SRR against both the B.1.1.529 and prototype strain GMT of mRNA-1273.529 and mRNA-1273 againstvariant and the prototype strains at all evaluable time points after study vaccine administration

To evaluate the immunogenicity of mRNA-1273.529 and mRNA-1273 booster at all evaluable time points after the vaccination administration
18. GMT of mRNA-1273.529 and mRNA-1273 against variant and the prototype strains at all evaluable time points after study vaccine administration
19. Ratio of GMTmRNA-1273.529/GMTmRNA-1273 against variant and prototype strains at all evaluable time points after study vaccine administration
20. GMFR of mRNA-1273.529 and mRNA-1273 against variant and prototype strains at all evaluable time points after study vaccine administration
21. SRR against variant and prototype strains at all evaluable time points after study vaccine administration

To assess for symptomatic and asymptomatic SARS-CoV-2 infection after vaccination with mRNA-1273.529 booster or mRNA-1273 booster:
22. Reverse transcriptase polymerase-chain reaction (RT-PCR)- confirmed symptomatic or asymptomatic SARS-CoV-2 infection

To evaluate the immunogenicity of mRNA-1273.529 booster against other variant strains:
23. GMT of mRNA-1273.529 against other ariant strains (eg, Alpha, Beta, Delta) at Day 29 after study vaccine administration
24. Ratio of GMTmRNA-1273.529/GMTmRNA-1273 gainst other variant strains at Day 29 after study vaccine administration
25. GMFR of mRNA-1273.529 against other variant strains at Day 29 after study vaccine administration
26. SRR against other variant strains

To evaluate cellular immunogenicity in a subset of participants
27. Frequency, magnitude, and phenotype of virus-specific T-cell and B-cell responses measured by flow cytometry or other methods, and to perform targeted repertoire analysis of T-cells and B-cells after vaccination

To evaluate the genetic and/or phenotypic relationships of solated SARSCoV-2 strains to the vaccine sequence
28. Characterize the SARS-CoV-2 spike genetic sequence of viral isolates and compare with the vaccine sequence
29. Characterize the immune responses to vaccine breakthrough isolates

30. Safety follow-up measured using an eDiary that prompts every two weeks from Day 43 through Day 359 for surveillance for COVID-19 and significant changes in health

Overall study start date
20/01/2022

Completion date
17/03/2023

Eligibility

Key inclusion criteria
1. Male or female, at least 16 years of age at the time of consent (Screening Visit)
2. Investigator’s assessment that participant understands and is willing and physically able to comply with protocol-mandated follow-up, including all procedures
3. Participant has provided written informed consent for participation in this study, including all evaluations and procedures as specified in this protocol
4. Female participants of nonchildbearing potential may be enrolled in the study. Nonchildbearing potential is defined as bilateral tubal ligation > 1 year prior to the Screening Visit, bilateral oophorectomy, hysterectomy, or postmenopausal (defined as amenorrhea for ≥ 12 consecutive months prior to the Screening Visit without an alternative medical cause). A follicle stimulating hormone (FSH) level may be measured at the discretion of the investigator to confirm postmenopausal status
5. Female participants of childbearing potential may be enrolled in the study if the participant fulfills all the following criteria:
5.1 Has a negative pregnancy test at the Screening Visit and on the day of vaccination prior to vaccine dose being administered on Day 1.
5.2 Has practiced adequate contraception or has abstained from all activities that could result in pregnancy for at least 28 days prior to the first dose (Day 1). Adequate female contraception is defined as consistent and correct use of a local health authority approved contraceptive method

in accordance with the product label.
5.3 Has agreed to continue adequate contraception through 90 days following vaccine administration
6. Has received 2 prior doses of one of the following approved/authorized COVID-19 vaccines: Moderna, Pfizer/BioNTech, Oxford/AstraZeneca, Janssen. A heterologous vaccine regimen is acceptable
7. Participants who will receive the 4th dose as part of the study must have previously received a mRNA vaccine (Moderna or Pfizer/BioNTech) as the 3rd dose of a COVID-19 vaccine. Participants who will receive the 3rd dose as part of the study may have previously received 2 doses of an approved/authorized mRNA or a non-mRNA COVID-19 vaccine (a heterologous vaccine regimen is acceptable).

Participant type(s)
Healthy volunteer

Age group
Mixed

Sex
Both

Target number of participants
2924

Key exclusion criteria
1. Had significant exposure to someone with SARS-CoV-2 infection or COVID-19 in the past 14 days, as defined by the CDC as a close contact (without PPE) of someone who has had COVID 19.
2. Participant is acutely ill or febrile (temperature ≥ 38.0°C/100.4°F) 72 hours prior to or at the Screening Visit or Day 1. Participants meeting this criterion may be rescheduled within the 28-day screening window and will retain their initially assigned participant number.
3. Had tested positive for SARS-CoV-2 by approved/authorized lateral flow/rapid antigen or PCR test on 08 November 2021 or later.
4. Has received a COVID-19 vaccine within 3 months of the Screening Visit.
5. Has received a total of 4 doses or more of COVID-19 vaccine.
6. Has received a COVID-19 vaccine at a dose different from the authorized/approved dose.
7. History of a diagnosis or condition that, in the judgment of the Investigator, is clinically unstable or may affect participant safety, assessment of safety endpoints, assessment of immune response, or adherence to study procedures. Clinically unstable is defined as a diagnosis or condition requiring significant changes in management or medication within the 2 months prior to screening and includes ongoing workup of an undiagnosed illness that could lead to a new diagnosis or condition.
8. Reported history of congenital or acquired immunodeficiency, immunosuppressive condition, or immune-mediated disease requiring immunosuppressive treatment or other immunosuppressive condition.
9. Dermatologic conditions that could affect local solicited AR assessments (eg, tattoos, psoriasis patches affecting skin over the deltoid areas).
10. Reported history of anaphylaxis or severe hypersensitivity reaction after receipt of any components of mRNA vaccine.
11. Reported history of bleeding disorder that is considered a contraindication to intramuscular (IM) injection or phlebotomy.
12. Any medical, psychiatric, or occupational condition, including reported history of substance

abuse, that, in the opinion of the Investigator, might pose additional risk due to participation in the study or could interfere with the interpretation of study results. Asymptomatic conditions and conditions with no evidence of end organ involvement (eg, mild hypertension, dyslipidemia) are not exclusionary, provided that they are being appropriately managed and are clinically stable (ie, unlikely to result in symptomatic illness within the time course of this study). Illnesses or conditions may be exclusionary, even if otherwise stable, due to therapies used to treat them (eg, immune modifying treatments), at the discretion of the Investigator.
13. Has received systemic immunosuppressants or immune-modifying drugs for > 14 days in total within 181 days prior to screening (for corticosteroids ≥ 10 mg/day of prednisone equivalent) or is anticipating the need for immunosuppressive treatment at any time during participation in the study.
14. Has received or plans to receive any licensed vaccine ≤ 28 days prior to the study injection (Day 1) or plans to receive a licensed vaccine within 28 days after the study injection (with the exception that approved seasonal influenza vaccine may be received by at least 7 and preferably 14 days apart from the study injection).
15. Has received systemic immunoglobulins or blood products within 90 days prior to the Screening Visit or plans to receive during the study.
16. Diagnosis of malignancy within previous 10 years (excluding nonmelanoma skin cancer).
17. Has donated ≥ 450 mL of blood products within 28 days prior to the Screening Visit or plans to donate blood products during the study.
18. Has participated in an interventional clinical study within 28 days prior to the Screening Visit based on the medical history interview or plans to do so while participating in this study.
19. Is an immediate family member or household member of study personnel, study site staff, or Sponsor personnel.

Date of first enrolment
16/02/2022

Date of final enrolment
30/04/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Salford Royal Hospital
Stott Lane
Eccles
Salford
United Kingdom
M6 8HD

Study participating centre

University College London Hospitals NHS Foundation Trust
250 Euston Road
London
United Kingdom
NW1 2PG

Study participating centre
Castle Hill Hospital
Castle Road
Cottingham
United Kingdom
HU16 5JX

Study participating centre
Royal United Hospital
Combe Park
Bath
United Kingdom
BA1 3NG

Study participating centre
Gloucestershire Royal Hospital
Great Western Road
Gloucester
United Kingdom
GL1 3NN

Study participating centre
Royal Cornwall Hospital (treliske)
Treliske
Truro
United Kingdom
TR1 3LJ

Study participating centre
The Royal Victoria Infirmary
Queen Victoria Road
Newcastle upon Tyne
United Kingdom
TS1 4LP

Study participating centre
Chelsea & Westminster Hospital
Chelsea and Westminster Hospital NHS Foundation Trust
369 Fulham Road
London
United Kingdom
SW10 9NH

Study participating centre
Royal Free Hospital
Royal Free London NHS Foundation Trust
Pond Street
London
United Kingdom
NW3 2QG

Study participating centre
Bradford Royal Infirmary
Duckworth Lane
Bradford
United Kingdom
BD9 6RJ

Study participating centre
Aberdeen Royal Infirmary
Foresterhill Road
Aberdeen
United Kingdom
AB25 2ZN

Study participating centre
Kings College Hospital
Mapother House
De Crespigny Park
Denmark Hill
London
United Kingdom
SE5 8AB

Study participating centre
Portsmouth Research Hub
John Pounds Community Centre
23 Pounds Gate
Queen Street
Portsmouth
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PO1 3HN

Study participating centre
Northern General Hospital
Northern General Hospital NHS Trust
C Floor, Huntsmnan Building
Herries Road
Sheffield
United Kingdom
S5 7AU

Study participating centre
Wansford and Kingscliffe Practice
Old Hill Farm
Yarwell Road
Wansford
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PE8 6PL

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Royal Devon & Exeter Hospital
Royal Devon and Exeter NHS Foundation Trust
Barrack Road
Exeter
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EX2 5DW

Study participating centre
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Derriford Road
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Study participating centre
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SW17 0QT

Sponsor information

Organisation
ModernaTX, Inc. (USA)

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
ModernaTX, Inc

Results and Publications

Publication and dissemination plan
Peer reviewed scientific journals
Internal report
Conference presentation
Publication on website
Submission to regulatory authorities

Intention to publish date
17/03/2024

Individual participant data (IPD) sharing plan
The sponsor is committed to responsible sharing of clinical data with the goal of advancing medical science and improving patient care. Independent researchers will be permitted to use anonymised data collected from participants during this study to conduct additional scientific research, which may be unrelated to the study vaccine. The data provided to external researchers will not include identifiable information.

IPD sharing plan summary
Available on request