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A study to evaluate if influenza virus vaccines (modRNA and saRNA) can prevent influenza infection in healthy adults.

Submission date
22/09/2022

Recruitment status
No longer recruiting

Registration date
19/12/2022

Overall study status
Completed

Last Edited
05/08/2025

Condition category
Infections and Infestations

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
The purpose of this study is to investigate the efficacy and safety of vaccination with Nucleoside-modified Messenger Ribonucleic Acid (ModRNA) and Self-amplifying Ribonucleic Acid (SaRNA) vaccines in preventing infection with A/Delaware/55/2019 (H1N1) influenza virus compared to an external placebo group and a licensed flu vaccine (quadrivalent influenza vaccines (QIV)).

Who can participate?
Healthy volunteers aged 18 to 55 years. Up to 240 participants will be enrolled on the study. Each participant will remain in the study for about 5 months from screening until their last follow-up visit.

What does the study involve?
The study is divided into 4 phases:
1. Screening phase: Screening will occur between Day -90 to Day -30. Historical generic screening data collected through the hVIVO generic screening process may be transferred to this study after the study-specific consent form has been signed by the participant.
2. Vaccination phase: Participants will be invited to clinic to be randomly allocated to receive a single intramuscular dose of either:
Part A: QIV or Monovalent modRNA vaccine preparation.
Part B: Two out of three of the following preparations will be used: bivalent saRNA vaccine, monovalent saRNA vaccine or a bivalent modRNA vaccine.
Participants are invited to attend clinic visits 1, 3 and 8 days after vaccination, with a telephone follow-up 14 days post-vaccination.
3. Quarantine phase: Participants will stay in the quarantine unit for approximately 11 days (from Day -2 to Day 8). Two days prior to the day of inoculation with influenza, participants will be admitted to quarantine where their eligibility will be reassessed and inoculated with influenza on day 0. Participants will undergo a range of clinical assessments and safety monitoring for the entirety of their stay in quarantine. Participants will be discharged from the quarantine unit on

Day 8.
4. Outpatient phase: Final follow-up visit 28 days (±3 days) after the day they receive the virus. Their symptoms will be reassessed, and a complete safety examination will be performed.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
Potential participants will be fully informed of the risks and requirements of the study and during the study, participants will be given any new information that may affect their decision to continue participation.

Risks from vaccination:
The full risk profile of the influenza modRNA vaccine is not yet known. The full risk profile of the influenza modRNA vaccine is not yet known. In a Pfizer modRNA Phase 1/2 study, 194 participants 65 to 85 years of age received influenza modRNA vaccine doses up to 30 mcg in substudy A of this clinical study, none of the safety assessments that were performed raised any concerns. In Substudy B of this clinical study, 449 participants received influenza modRNA vaccine doses between 30mcg and up to 60mcg. One participant who received the influenza modRNA vaccine at a dose level of 60 mcg developed a temporary increased level in a lab test that measures heart muscle damage as well as changes to their ECG after vaccination, but the participant did not have any symptoms. There was no confirmed diagnosis made after follow-up testing; however, this event may have been myocarditis/pericarditis, following a recent viral infection, or following vaccination. Myocarditis/pericarditis is a potential rare risk with this type of vaccine (please see further information below). This event was investigated by the study sponsor, and it was judged safe to continue further vaccinations. Further study is needed to fully characterise the safety profile of influenza modRNA vaccine; since the influenza modRNA vaccine is similar to other modRNA vaccines, like those developed recently to prevent COVID-19 (for example, BNT162b2, Comirnaty), similar risks could be expected. However, in larger enrolled populations, they could occur more or less frequently, and additional new risks may be identified.

Participants may experience an allergic reaction to the study drug even though this has not been seen in the previous study. Symptoms of an allergic reaction may include the following: headache, rash, flushing, swelling, shortness of breath, nausea, and vomiting. Participants will be closely monitored for any side effects.
The study virus may cause symptoms of rhinitis, nasal stuffiness, fever, malaise, myalgia (muscle aches), and sore throat. In healthy adults, influenza infection is usually mild and resolves without treatment within approximately 7 days.
Severe complications are not expected as these tend to occur almost exclusively in infants, the elderly, and persons of any age with chronic comorbidities and significant immune compromise and not in young, healthy cohorts with no
comorbidities of coinfections. Qualified medical and nursing staff in the quarantine unit will monitor daily for symptoms and manage any that develop.
Blood drawing may cause pain/tenderness, bruising, bleeding, light-headedness, dizziness, fainting and, rarely, infection or nerve damage. Procedures will be in place to avoid injury.
Blood tests may indicate that a participant has an infection or illness. The hVIVO doctor will provide a referral letter to the participants' GP with consent.
Collection of nasal samples may cause discomfort, sneezing, watery eyes, irritated nose or nose bleeding. Sample collection will be performed by appropriately qualified and trained study staff to minimise the discomfort.
If a participant ever had a herpes infection (e.g., cold sores, genital herpes, or shingles), there is a small possibility that this infection could return after challenge.

Participants will be instructed to inform the study staff if they currently have an active herpes infection or have had one during the 30 days before enrolment
The study virus is usually absent from the nose by the time participants are discharged from quarantine. This will be confirmed by testing a nasal swab sample by using a qualitative virus antigen test or polymerase chain reaction (PCR) to determine participants' suitability for departure.

Where is the study run from?
hVIVO Services Ltd (UK)

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

Who is funding the study?
Pfizer (UK)

Who is the main contact?
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Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
1006279

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
PIR-CSV-001, IRAS 1006279

Study information

Scientific Title
A Phase IIa, randomised, double-blind, external placebo-controlled and internal comparator-controlled study to evaluate the safety, immunogenicity, and efficacy of influenza virus vaccines (modRNA and saRNA) in a human viral challenge model in healthy adult participants

Study objectives
Primary objective:
1. To assess the effect of vaccination with modRNA, saRNA and QIV influenza vaccines in reducing the influenza viral loads due to H1N1 when compared to an external placebo group

Secondary objectives:
1. To further evaluate the effect of modRNA, saRNA, and QIV influenza vaccines in reducing viral loads after influenza viral challenge, compared to an external placebo group
2. To evaluate the effect of the study vaccines in shortening viral shedding after influenza viral challenge, compared to an external placebo group
3. To evaluate the effect of the study vaccines in reducing the incidence of lab-confirmed influenza infection, compared to an external placebo group
4. To further evaluate the effect of the study vaccines in reducing the incidence of lab-confirmed symptomatic influenza infection, compared to an external placebo group.
5. To evaluate the effect of study vaccines in reducing the severity of clinical symptoms after influenza viral challenge, compared to an external placebo group
6. To evaluate the effect of study vaccines in reducing the duration of clinical symptoms due to influenza viral challenge, compared to an external placebo group
7. To evaluate the safety and reactogenicity of the study vaccines, compared to an external placebo group

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 09/12/2022, London - Surrey Borders Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, UK; +44 (0)20 7104 8057; surreyborders.rec@hra.nhs.uk), ref: 22/LO/0742

Study design
Interventional double-blind randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Other

Study type(s)
Treatment

Participant information sheet

Health condition(s) or problem(s) studied
Influenza Virus

Interventions
A total of up to 240 participants will be randomised to receive one of four active treatments via a single intramuscular injection.

Part A (n = up to 120, randomised 1:1 for n = 50 evaluable participants per arm):
• Monovalent modRNA HA (0.3 – 1 ml)
• Licensed Quadrivalent IV (0.5 ml)

Part B (n = up to 120, randomised 1:1 for n = 50 evaluable participants per arm):
• Bivalent saRNA* (0.3 – 1 ml)
• Bivalent modRNA HA+NA* (0.3 – 1 ml)
• Monovalent saRNA* (0.3 – 1 ml)
* Two of these three treatments will be administered in this study; the exact treatments will be determined based on emerging data.

A designated unblinded statistician, separate from the conduct or analysis of the study, will be responsible for the computer-generated randomisation schedule. Sealed copies of the randomisation code will be stored in a secure location.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Nucleoside-modified Messenger Ribonucleic Acid (ModRNA) HA, Nucleoside-modified Messenger Ribonucleic Acid (ModRNA) NA, Self-amplifying Ribonucleic Acid (saRNA), Self-amplifying Ribonucleic Acid (saRNA), Quadrivalent Influenza Vaccine (split virion, inactivated), suspension for injection

Primary outcome measure

To evaluate the reduction in one or more of the following endpoints within the primary endpoint family:
1. Area under the viral load-time curve (VL-AUC) of influenza challenge virus as determined by qRT-PCR on nasal samples collected twice daily starting from Day 1 (pm) up to planned discharge from quarantine (Day 8, am)
2. Peak viral load of influenza as defined by the maximum viral load determined by quantifiable qRT-PCR measurements on nasal samples collected twice daily starting from Day 1 (pm) up to planned discharge from quarantine (Day 8, am)
3. RT-PCR-confirmed moderately severe influenza infection, defined as:
3.1. RT-PCR-confirmed influenza infection (two quantifiable [≥lower limit of quantification {LLOQ}] qRT-PCR measurements [reported on 2 or more consecutive days], starting from Day 1 [pm] up to planned discharge from quarantine [Day 8, am]), AND
3.2. Any symptoms of grade ≥2 at a single timepoint
4. RT-PCR-confirmed febrile influenza infection, defined as:
4.1. RT-PCR-confirmed influenza infection (two quantifiable [≥LLOQ] qRT-PCR measurements [reported on two or more consecutive days], starting from Day 1 [pm] up to planned discharge from quarantine [Day 8, am]), AND
4.2. A temperature of ≥37.9°C from Day 1 up to planned discharge from quarantine (Day 8, am)

Secondary outcome measures

1. VL-AUC of influenza challenge virus as determined by tissue culture on nasal samples collected twice daily starting from Day 1 (pm) up to planned discharge from quarantine (Day 8, am)
2. VLPEAK of influenza as defined by the maximum viral load determined by quantitative viral culture measurements in nasal samples collected twice daily starting from Day 1 (pm) up to planned discharge from quarantine (Day 8, am)
3. Duration of quantifiable influenza, assessed by qRT-PCR measurements in nasal samples, starting from Day 1 (pm) up to planned discharge from quarantine (Day 8, am). Duration is defined as the time (hours) from first quantifiable (≥LLOQ) until first confirmed <LLOQ assessment after their peak measure (after which no further virus is quantified)
4. Duration of quantifiable influenza viral culture measurements in nasal samples, starting from Day 1 (pm) up to planned discharge from quarantine (Day 8, am). Duration is defined as the time (hours) from first quantifiable (≥LLOQ) until first confirmed <LLOQ assessment after their peak measure (after which no further virus is quantified)
5. RT-PCR-confirmed influenza infection defined as two quantifiable (≥LLOQ) RT-PCR measurements (reported on two or more independent nasal samples over 2 days), starting from Day 1 (pm) up to planned discharge from quarantine (Day 8, am)
6. RT-PCR-confirmed symptomatic influenza infection, defined as:
6.1. RT-PCR-confirmed influenza infection (two quantifiable [≥LLOQ] qRT-PCR measurements [reported on two or more consecutive days], starting from Day 1 [pm] up to planned discharge from quarantine [Day 8, am]), AND
6.2. Symptom score totalling ≥2 at a single timepoint
7. Area under the curve over time of total symptoms score (TSS-AUC) as measured by graded symptom scoring system collected three times daily, starting from Day 1 (am) up to planned discharge from quarantine (Day 8, am).
8. Peak daily symptom score: individual maximum daily sum of symptom score, starting from Day 1 (am) up to planned discharge from quarantine (Day 8, am)
9. Peak symptoms diary card score: peak TSS as measured by graded symptom scoring system collected 3times daily, starting from Day 1 (am) up to planned discharge from quarantine (Day 8, am)

10. Duration of clinical symptoms: any symptoms, starting from Day 1 (am) up to planned discharge from quarantine (Day 8, am)
11. Duration of clinical symptoms: grade 2 or higher symptoms, starting from Day 1 (am) up to planned discharge from quarantine (Day 8, am)
12. Occurrence of adverse events (AEs) (solicited and unsolicited) up to the Day 28 (±3 days) follow-up visit, including any serious adverse events (SAEs)
13. Occurrence of unsolicited AEs of special interest (AESIs) up to the Day 28 (±3 days) follow-up visit. AESIs are: a confirmed diagnosis of myocarditis or pericarditis

Overall study start date
15/09/2022

Completion date
31/08/2023

Eligibility

Key inclusion criteria
1. An informed consent document signed and dated by the subject and the investigator.
2. Males and females 18 to 55 years inclusive on the day of signing the consent form.
3. A total body weight ≥50 kg and body mass index (BMI) ≥18 kg/m2 and ≤35kg/m2.
4. In good health with no history, or current evidence, of clinically significant medical conditions, and no clinically significant test abnormalities that will interfere with participant safety, as defined by medical history, physical examination, (including vital signs), ECG, and routine laboratory tests as determined by the investigator.
5. Participants will have a documented medical history either prior to entering the study or following medical history review with the study physician at screening.
6. The following criteria are applicable to female participants participating in the study.
6.1. Females of childbearing potential must have a negative pregnancy test prior to enrolment.
6.2. Females of non-childbearing potential:
6.2.1. Postmenopausal females defined as amenorrhea for ≥12 months with no alternative medical cause. A high follicle-stimulating hormone (FSH) level, within appropriate postmenopausal range, may be used to confirm postmenopausal state in the absence of combined hormonal contraception or hormone replacement therapy. If there is <12 months of amenorrhea, 2 FSH samples are required at least 4 to 6 weeks apart.
6.2.2. Documented status as being surgically sterile (e.g., tubal ligation, hysterectomy, bilateral salpingectomy, and bilateral oophorectomy).
7. The following criteria apply to female and male participants:
7.1. Female participants of childbearing potential must use 1 or more highly effective contraception. Hormonal methods must be in place from at least 2 weeks prior to the first study visit. The contraception use must continue until 28 days after the date of viral change. Highly effective contraception is as described below:
Established use of hormonal methods of contraception described below (for a minimum of 2 weeks prior to first study visit). When hormonal methods of contraception are used, male partners are required to use a condom with a spermicide.
7.2. Combined (oestrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation:
7.2.1. oral
7.2.2. intravaginal
7.2.3. transdermal
7.3. progestogen-only hormonal contraception associated with inhibition of ovulation:

7.3.1. oral
7.3.2. injectable
7.3.3. implantable
7.4 Intrauterine device
7.5. Intrauterine hormone-releasing system
7.6. Bilateral tubal ligation
7.7. Male sterilisation (with the appropriate post vasectomy documentation of the absence of sperm in the ejaculate) where the vasectomised male is the sole partner for that woman.
7.8. True abstinence -sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the participant.
8. Serosuitable for the challenge virus

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
Both

Target number of participants
240

Total final enrolment
285

Key exclusion criteria
1. History of, or currently active, symptoms or signs suggestive of upper or lower respiratory tract (LRT) infection within 4 weeks prior to the first study visit.
2. Any history or evidence of any clinically significant or currently active cardiovascular, respiratory, dermatological, gastrointestinal, endocrinological, haematological, hepatic, immunological (including immunosuppression), metabolic, urological, renal, neurological, or psychiatric disease and/or other major disease that, in the opinion of the PI/investigator may interfere with a participant completing the study and necessary investigations. Any other major disease that, in the opinion of the Investigator, may put the subject at undue risk, or interfere with a subject completing the study and necessary investigations. Other conditions may apply as per protocol.
3. Any participants who have smoked ≥10 pack years at any time (10 pack years is equivalent to one pack of 20 cigarettes a day for 10 years).
4. Female participants who:
4.1. Are breastfeeding, or
4.2. Have been pregnant within 6 months prior to the study, or

4.3. Have a positive pregnancy test at any point during screening or prior to inoculation.
5. Lifetime history of anaphylaxis and/or a lifetime history of severe allergic reaction. Significant intolerance to any food or drug in the last 12 months, as assessed by the PI.
6. Venous access deemed inadequate for the phlebotomy and cannulation demands of the study.
7.1. Any significant abnormality altering the anatomy of the nose in a substantial way or nasopharynx that may interfere with the aims of the study and, in particular, any of the nasal assessments or viral challenge (historical nasal polyps can be included, but large nasal polyps causing current and significant symptoms and/or requiring regular treatments in the last month will be excluded).
7.2. Any clinically significant history of epistaxis (large nosebleeds) within the last 3 months of the first study visit and/or history of being hospitalised due to epistaxis on any previous occasion.
7.3. Any nasal or sinus surgery within 3months of the first study visit.
8.1. Evidence of vaccinations within the 4weeks prior to the planned date with vaccine.
8.2. Intention to receive any vaccination(s) before the last day of follow-up.
8.3. No travel restrictions apply after the Day 28 [±3 days] follow-up visit.
9. Receipt of blood or blood products, or loss (including blood donations) of 550mL or more of blood during the 3 months prior to the planned dosing with vaccine or planned during the 3months after the final visit.
10.1. Receipt of any investigational drug within 3 months prior to the planned date of dosing with vaccine.
10.2. Receipt of 3 or more investigational drugs within the previous 12months prior to the planned date of dosing with vaccine.
10.3. Prior inoculation with a virus from the same virus-family as the challenge virus.
10.4. Prior participation in another HVC study with a respiratory virus in the preceding 3 months, taken from the date of viral challenge in the previous study to the date of expected viral challenge in this study.
11.1. Use or anticipated use during the conduct of the study of concomitant medications (prescription and/or non-prescription), including vitamins or herbal and dietary supplements within the specified windows, unless in the opinion of the study physician/PI, the medication will not interfere with the study procedures or compromise participant safety.
11.2. Over-the-counter medications (e.g., paracetamol or ibuprofen) where the dose taken over the preceding 7 days prior to the planned date of dosing with vaccine has exceeded the maximum permissible 24-hour dose (e.g., ≥4 grams paracetamol or ≥1.2g ibuprofen over the preceding week).
11.3. Systemic antiviral administration within 4 weeks of the planned date of dosing with vaccine.
12.1. Confirmed positive test for drugs of abuse and cotinine on first study visit. One repeat test is allowed at PI discretion.
12.2. Recent history or presence of alcohol addiction, or excessive use of alcohol (weekly intake in excess of 28 units alcohol; 1 unit being a half glass of beer, a small glass of wine, or a measure of spirits), or excessive consumption of xanthine-containing substances (e.g., daily intake in excess of 5 cups of caffeinated drinks, e.g., coffee, tea, cola).
13. A forced expiratory volume in 1 second (FEV1) <80%.
14. Positive HIV, hepatitis B virus, or hepatitis C virus test.
15. Presence of fever, defined as participant presenting with a temperature reading of ≥37.9C on the day of vaccine dosing or upon admission to quarantine.
16. Those employed or immediate relatives of those employed at hVIVO or the sponsor.
17. Any other reason that in the opinion of the investigator raises a concern that the participant will be unsuitable.

Date of first enrolment
13/12/2022

Date of final enrolment
15/05/2023

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
hVIVO Services Ltd.

Sponsor details
Queen Mary BioEnterprises Innovation Centre
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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Pfizer UK

Alternative Name(s)
Pfizer Ltd, Pfizer Limited

Funding Body Type
Private sector organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
Internal report
Publication on website
Other publication
Other
Information about this study and a summary of the results will be available on publicly accessible clinical trials databases e.g. http://www.ClinicalTrials.gov, https://www.isrctn.com/
This will not include information that could identify participants.

Intention to publish date
31/08/2024

Individual participant data (IPD) sharing plan
All data generated or analysed during this study will be included in the subsequent results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Basic results		29/07/2025	29/07/2025	No	No