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To test the efficacy, safety, and immunogenicity of the influenza virus vaccines (modRNA) in a human influenza B challenge model in healthy adult participants

Submission date
23/09/2023

Recruitment status
No longer recruiting

Registration date
24/11/2023

Overall study status
Completed

Last Edited
22/04/2025

Condition category
Infections and Infestations

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

Plain English summary of protocol

Background and study aims
This is a Phase 2a study to assess the efficacy, safety, and immunogenicity of a single vaccination with nucleoside-modified messenger ribonucleic acid (modRNA) vaccines administered to healthy adults, before being challenged with influenza B/Connecticut/1/21 virus. The vaccine arms from this study will be compared against placebo. In addition, a licensed QIV will be used as a comparator in this study. Each participant will remain in the study for about 5 months from screening until their last follow-up visit.

Who can participate?
Healthy volunteers aged between 18 and 55 years old

What does the study involve?
The study is divided into four phases:
1. Screening phase: Screening will occur between Day -120 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 one of four treatment groups to receive a single intramuscular dose of Licensed QIV or Placebo or quadrivalent influenza modRNA vaccine (qIRV) HA or trivalent influenza modRNA vaccine (tIRV) HA. Participants are invited to attend clinic visits 3 and 8 days after vaccination, with telephone follow-up 1 day and 14 days post-vaccination.
3. Quarantine phase: Participants will stay in the quarantine unit for approximately 11 days (from Day -2/-1 to Day 8). One to two days before 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 (or may remain longer at the PI's discretion).
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 performed.

What are the possible benefits and risks of participating?
The full risks of influenza modRNA vaccines are not yet known. Currently, approximately 25000 participants 18 years of age or older have received influenza modRNA vaccines in clinical studies. In all studies, individuals who receive study vaccine are checked for side effects. Currently the following risks have been determined to be related to influenza modRNA vaccine: Injection site pain, injection site swelling, injection site redness, enlarged lymph glands, muscle pain, joint pain, pain (most frequently described as body aches), headache, fatigue (tiredness), chills, fever, diarrhoea and nausea.
Myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the lining outside the heart) have occurred in some people who have received another modRNA vaccine, COVID-19 vaccine (also called Comirnaty or BNT162b2). With this vaccine, most cases have been mild and tend to recover within a short time. Some other cases require intensive care support and fatal cases have been observed. Cases have mainly been reported in younger men and following the second vaccination, however, there have been some cases reported in older males and females as well as following the first vaccination and booster vaccinations. The chance of having this occur is very low and, in most of these people, symptoms began within 14 days of vaccination.
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 about 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 the 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. A participant's discharge from quarantine is foreseen at Day 9 (9 days post inoculation), provided that, where appropriate, no virus is detected by qualitative virus antigen test (negative virus antigen test) or PCR test and the participant has no clinically significant symptoms.

Where is the study run from?
hVIVO (UK)

When is the study starting and how long is it expected to run for?
September 2023 to October 2024

Who is funding the study?
Pfizer (USA)

Who is the main contact?
Kingsley Eze, k.eze@hvivo.com
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Contact information

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Additional identifiers

Integrated Research Application System (IRAS)
1008256

Protocol serial number
PIR-CSV-002

Study information

Scientific Title

A Phase IIa, randomized, double-blind, placebo-controlled, comparator-controlled study to evaluate the efficacy, safety, and immunogenicity, of influenza virus vaccines (modRNA) in a human influenza b challenge model in healthy adult participants

Study objectives
The primary statistical hypothesis is that vaccination with at least one of the modRNA vaccines will significantly reduce the viral shedding and/or the incidence and/or the severity of disease after influenza viral challenge when compared to placebo.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 15/11/2023, East Midlands - Leicester Central Research Ethics Committee (2 Redman Place, London , E20 1JQ, United Kingdom; +44 (0)20 7972 2545; leicestercentral.rec@hra.nhs.uk), ref: 23/EM/0236

Primary study design
Interventional

Study design
Double-blind randomized placebo-controlled trial

Study type(s)
Safety, Efficacy

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

Interventions
Current interventions as of 21/03/2025:
Approximately 280 participants will be randomised to receive one of three active treatments or a placebo via a single intramuscular injection:
1. qIRV HA
2. tIRV HA
3. Licensed QIV
4. Placebo Product: Sodium Chloride 0.9% w/v) (0.5 ml)

*One of these two treatments will be administered in this study. The exact treatment 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 randomization schedule using SAS.

Previous interventions as of 16/01/2025:
Approximately 280 participants will be randomised to receive one of three active treatments or a placebo via a single intramuscular injection:
1. qIRV HA

2. tIRV HA
3. Licensed QIV (Flucelvax Tetra)
4. Placebo Product: Sodium Chloride 0.9% w/v) (0.5 ml)

*One of these two treatments will be administered in this study. The exact treatment 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 randomization schedule using SAS.

Original interventions:
Approximately 280 participants will be randomised to receive one of three active treatments or a placebo via a single intramuscular injection:
1. qIRV HA (0.3 - 1 ml)
2. qIRV HA + NA (0.3 - 1 ml) or* modRNA monovalent HA (0.3 - 1 ml)
3. Licensed QIV (Flucelvax Tetra) (0.5 ml)
4. Placebo Product: Sodium Chloride 0.9% w/v) (0.5 ml)

*One of these two treatments will be administered in this study. The exact treatment 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 randomization schedule using SAS.

Intervention Type
Biological/Vaccine

Phase
Phase II

Drug/device/biological/vaccine name(s)
qIRV HA, tIRV HA, licensed QIV

Primary outcome(s)
Current primary outcome measures as of 21/03/2025:
1. Area under the viral load-time curve (VLAUC) of influenza challenge virus as determined by quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) on nasal samples collected twice daily starting from Day 1 up to planned discharge from quarantine (Day 9).
2. Peak viral load (VLPEAK) 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 up to planned discharge from quarantine (Day 9)
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 two or more independent samples over 2 days]), starting from Day 1 up to planned discharge from quarantine (Day 9), AND
3.2. Any symptoms from the symptom diary card of grade ≥2 at a single time point, from Day 1 up to planned discharge from quarantine (Day 9).
4. RT-PCR-confirmed febrile influenza infection, defined as:
4.1. RT-PCR-confirmed influenza infection (2 quantifiable [≥LLOQ] qRT-PCR measurements [reported on 2 or more independent samples over 2 days]) starting from Day 1 up to planned discharge from quarantine (Day 9), AND

4.2. A febrile episode, as defined by a temperature of ≥37.9°C starting from Day 1 up to planned discharge from quarantine (Day 9).

Previous primary outcome measures:
1. Area under the viral load-time curve (VLAUC) of influenza challenge virus as determined by quantitative reverse transcriptase-polymerase chain reaction (qRT-PCR) on nasal samples collected twice daily starting from Day 1 up to planned discharge from quarantine (Day 8).
2. Peak viral load (VLPEAK) 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 up to planned discharge from quarantine (Day 8)
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 two or more independent samples over 2 days]), starting from Day 1 up to planned discharge from quarantine (Day 8), AND
3.2. Any symptoms from the symptom diary card of grade ≥2 at a single time point, from Day 1 up to planned discharge from quarantine (Day 8).
4. RT-PCR-confirmed febrile influenza infection, defined as:
4.1. RT-PCR-confirmed influenza infection (2 quantifiable [≥LLOQ] qRT-PCR measurements [reported on 2 or more independent samples over 2 days]) starting from Day 1 up to planned discharge from quarantine (Day 8), AND
4.2. A febrile episode, as defined by a temperature of ≥37.9°C starting from Day 1 up to planned discharge from quarantine (Day 8).

Key secondary outcome(s)

Current secondary outcome measures as of 21/03/2025:
1. VLAUC of influenza challenge virus as determined by viral culture on nasal samples collected twice daily starting from Day 1 up to planned discharge from quarantine (Day 9).
2. VLPEAK of influenza as defined by the maximum viral load determined by quantitative viral culture measurements on nasal samples collected twice daily starting from Day 1 up to planned discharge from quarantine (Day 9).
3. Duration of quantifiable influenza, as assessed by qRT-PCR measurements in nasal samples, starting from Day 1 up to planned discharge from quarantine (Day 8). 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 up to planned discharge from quarantine (Day 9). 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 samples over 2 days), starting from Day 1 up to planned discharge from quarantine (Day 9).
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 independent samples over 2 days]) starting from Day 1 up to planned discharge from quarantine (Day 9), AND
6.2. Symptom score totaling ≥2 at a single time point, from Day 1 up to planned discharge from quarantine (Day 9).
7. Area under the curve over time of total symptoms score (TSSAUC) as measured by graded symptom scoring system collected 3 times daily starting from Day 1 up to planned discharge from quarantine (Day 9).
8. Peak daily symptom score: individual maximum daily sum of symptom score starting from Day

1 up to planned discharge from quarantine (Day 9). Peak symptoms diary card score: peak total symptoms score (TSS), as measured by graded symptom scoring system collected 3 times daily, starting from Day 1 up to planned discharge from quarantine (Day 9).
9. Duration of clinical symptoms: any symptoms starting from Day 1 up to planned discharge from quarantine (Day 9).
10. Duration of clinical symptoms: grade 2 or higher symptoms starting from Day 1 up to planned discharge from quarantine (Day 9).

Safety:
1. Occurrence of solicited adverse events (AEs) for 14 days (±1 day) after vaccination and occurrence of unsolicited AEs up to the Day 28 (±3 days) follow-up visit, including any serious adverse events (SAEs).
2. 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.

Previous secondary outcome measures:
1. VLAUC of influenza challenge virus as determined by viral culture on nasal samples collected twice daily starting from Day 1 up to planned discharge from quarantine (Day 8).
2. VLPEAK of influenza as defined by the maximum viral load determined by quantitative viral culture measurements on nasal samples collected twice daily starting from Day 1 up to planned discharge from quarantine (Day 8).
3. Duration of quantifiable influenza, as assessed by qRT-PCR measurements in nasal samples, starting from Day 1 up to planned discharge from quarantine (Day 8). 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 up to planned discharge from quarantine (Day 8). 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 samples over 2 days), starting from Day 1 up to planned discharge from quarantine (Day 8).
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 independent samples over 2 days]) starting from Day 1 up to planned discharge from quarantine (Day 8), AND
6.2. Symptom score totaling ≥2 at a single time point, from Day 1 up to planned discharge from quarantine (Day 8).
7. Area under the curve over time of total symptoms score (TSSAUC) as measured by graded symptom scoring system collected 3 times daily starting from Day 1 up to planned discharge from quarantine (Day 8).
8. Peak daily symptom score: individual maximum daily sum of symptom score starting from Day 1 up to planned discharge from quarantine (Day 8). Peak symptoms diary card score: peak total symptoms score (TSS), as measured by graded symptom scoring system collected 3 times daily, starting from Day 1 up to planned discharge from quarantine (Day 8).
9. Duration of clinical symptoms: any symptoms starting from Day 1 up to planned discharge from quarantine (Day 8).
10. Duration of clinical symptoms: grade 2 or higher symptoms starting from Day 1 up to planned discharge from quarantine (Day 8).

Safety:
1. Occurrence of solicited adverse events (AEs) for 14 days (±1 day) after vaccination and

occurrence of unsolicited AEs up to the Day 28 (±3 days) follow-up visit, including any serious adverse events (SAEs).
2. 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.

Exploratory:
1. Total weight of mucus produced starting from Day 1 up to planned discharge from quarantine (Day 8).
2. Total number of tissues used by participants starting from Day 1 up to planned discharge from quarantine (Day 8).
3. Time to resolution from VLPEAK as defined by the maximum viral load determined by qRTPCR measurements in nasal samples.
4. Time to resolution is defined as the time (hours) from VLPEAK until first confirmed unquantifiable assessment (after which no further virus is detected).
5. Time to resolution from VLPEAK as defined by the maximum viral load determined by viral culture measurements in nasal samples.
Time to resolution is defined as the time (hours) from VLPEAK until first confirmed unquantifiable assessment (after which no further virus is detected).
6. Further sensitivity analysis may be performed on the above qRT-PCR-related incidence endpoints where detection by qRT-PCR is reported above the lower limit of detection (LLOD) instead of the LLOQ. Details will be provided in the statistical analysis plan (SAP).
7. Number (%) of participants with grade 2 or higher symptoms starting from Day 1 up to planned discharge from quarantine (Day 8).
8. Time to resolution from peak clinical symptoms as measured by graded symptom scoring system collected 3 times daily.
9. Time to resolution is defined as the time (hours) from peak clinical symptoms until first time with TSS = 0 after which no further increase above 0 is observed.
10. Clinical symptom-related endpoints may be further explored, as measured with either the full 13 or a subset of the 13 symptoms within the graded symptom scoring system.
11. Patient perception questionnaire results (presence or absence of cold, change in severity of cold) may be compared to other virological and symptomatic endpoints in relation to respiratory viral disease, including but not limited to construct validations.
12. Additional symptoms may be included in the symptom scoring system (or captured separately), depending on emerging data from the characterization of the challenge virus.

Completion date
14/10/2024

Eligibility

Key inclusion criteria
Current inclusion criteria as of 21/03/2025:
1. Written informed consent signed and dated by the participant and the investigator obtained before any assessment is performed.
2. Aged between 18 and 55 years old, inclusive, on the day prior to signing the consent form.
3. Serosuitable for the challenge virus. The serology result obtained from the influenza B virus antibody assay suggests that the participant is sensitive to influenza B virus infection (i.e., they are likely to be infected following inoculation with the challenge virus).
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), electrocardiogram (ECG), and routine laboratory tests as determined by the investigator.

Previous inclusion criteria:
1. Written informed consent signed and dated by the participant and the investigator obtained before any assessment is performed.
2. Aged between 18 and 55 years old, inclusive, on the day prior to signing the consent form.
3. A total body weight ≥50 kg and body mass index (BMI) ≥18 kg/m2 and ≤35 kg/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), electrocardiogram (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. Post-menopausal females defined as amenorrhea for 12 months or greater with no alternative medical cause. A high follicle-stimulating hormone (FSH) level, within appropriate post-menopausal range, may be used to confirm post-menopausal state in the absence of combined hormonal contraception or hormone replacement therapy. If there is less than 12 months of amenorrhea 2 FSH samples are required at least 4-6 weeks apart.
6.2.2. Documented status as being permanently 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 form of 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 for 1 complete menstrual cycle after the date of viral challenge. Highly effective contraception is as described below:
7.1.1. 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:
7.1.1.1. Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation:
7.1.1.1.1. Oral
7.1.1.1.2. Intravaginal
7.1.1.1.3. Transdermal
7.1.1.2. Progestogen-only hormonal contraception associated with inhibition of ovulation:
7.1.1.2.1. Oral
7.1.1.2.2. Injectable
7.1.1.2.3. Implantable
7.1.2. Intrauterine device
7.1.3. Intrauterine hormone-releasing system
7.1.4. Bilateral tubal ligation
7.1.5. Male sterilization (with the appropriate post-vasectomy documentation of the absence of sperm in the ejaculate) where the vasectomized male is the sole partner for that woman.
7.1.6. 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.
7.2. Male participants must agree to the contraceptive requirements below from the first study

visit and continuing until 28 days after the date of viral challenge:
7.2.1. Use a condom with a spermicide to prevent pregnancy in a female partner.
7.2.2. Male sterilization with the appropriate post-vasectomy documentation of theabsence of sperm in the ejaculate (please note that the use of condom withspermicide will still be required to prevent partner exposure). This applies onlyto males participating in the study.
7.2.3. True abstinence – sexual abstinence is considered a highly effective methodonly if defined as refraining from heterosexual intercourse during the entireperiod of risk associated with the study treatments. The reliability of sexualabstinence needs to be evaluated in relation to the duration of the clinical trialand the preferred and usual lifestyle of the participant.
7.3. In addition to the contraceptive requirements above, male participants must agree not to donate sperm following discharge from quarantine until 28 days after the date of viral challenge.
8. Serosuitable for the challenge virus. The serology result obtained from the influenza B virus antibody assay suggests that the participant is sensitive to influenza B virus infection (i.e., they are likely to be infected following inoculation with the challenge virus).

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
279

Key exclusion criteria
Current exclusion criteria as of 21/03/2025:
1. History of, or currently active, symptoms or signs suggestive of upper or lower respiratory tract 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, hematological, hepatic, immunological (including immunosuppression), metabolic, urological, renal, neurological, or psychiatric disease and/or other major disease that, in the opinion of the investigator, may interfere with a participant completing the study and necessary investigations.
3. Females who:
3.1. Are breastfeeding, or
3.2. Have been pregnant within 6 months prior to the study, or
3.3. Have a positive pregnancy test at any point during screening or prior to vaccination.
4. 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.

5. Venous access deemed inadequate for the phlebotomy and cannulation demands of the study.
6. Evidence of vaccinations within the 4 weeks prior to the planned date of vaccination.
6.1. Intention to receive any vaccination(s) before the last day of follow-up. (NB. No travel restrictions will apply after the Day 28 follow-up visit).
6.2. Receipt of influenza vaccine (or another IMP relating to the treatment of influenza) OR a diagnosis of influenza or influenza-like illness confirmed by a physician in the last 6 months prior to the planned date of vaccination.
7. Receipt of any immunoglobulin or monoclonal antibodies within 3 months (or 5 half-lives, whichever is greater) prior to the planned date of vaccination.
8. 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.
9. Any other medical, psychiatric, social, or occupational condition and/or responsibility that, in the opinion of the investigator, would interfere with, or serve as a contraindication to, protocol adherence or the assessment of safety (including reactogenicity) will deem the participant unsuitable for the study.
Any other reason that in the opinion of the investigator raises a concern that the participant will not be able to cope with quarantine requirements.

Previous exclusion criteria as of 16/01/2025:
1. History of, or currently active, symptoms or signs suggestive of upper or lower respiratory tract 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, hematological, hepatic, immunological (including immunosuppression), metabolic, urological, renal, neurological, or psychiatric disease and/or other major disease that, in the opinion of the investigator, may interfere with a participant completing the study and necessary investigations.
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3.2. Have been pregnant within 6 months prior to the study, or
3.3. Have a positive pregnancy test at any point during screening or prior to vaccination.
4. 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.
5. Venous access deemed inadequate for the phlebotomy and cannulation demands of the study.
6. Evidence of vaccinations within the 4 weeks prior to the planned date of vaccination.
6.1. Intention to receive any vaccination(s) before the last day of follow-up. (NB. No travel restrictions will apply after the Day 28 follow-up visit).
6.2. Receipt of influenza vaccine (or another IMP relating to the treatment of influenza) OR a diagnosis of influenza or influenza-like illness confirmed by a physician in the last 6 months prior to the planned date of vaccination.
7. Receipt of any immunoglobulin or monoclonal antibodies within 3 months (or 5 half-lives, whichever is greater) prior to the planned date of vaccination.
8. 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.
9. Any other medical, psychiatric, social, or occupational condition and/or responsibility that, in the opinion of the investigator, would interfere with, or serve as a contraindication to, protocol adherence or the assessment of safety (including reactogenicity) will deem the participant

unsuitable for the study.
Any other reason that in the opinion of the investigator raises a concern that the participant will not be able to cope with quarantine requirements.

Previous exclusion criteria:
1. History of, or currently active, symptoms or signs suggestive of upper or lower respiratory tract 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, hematological, hepatic, immunological (including immunosuppression), metabolic, urological, renal, neurological, or psychiatric disease and/or other major disease that, in the opinion of the investigator, may interfere with a participant completing the study and necessary investigations. The following conditions apply:
2.1. Participants with a history of resolved depression and/or anxiety may be included at the discretion of the PI. Participants with a history of stress-related illness, which is not ongoing or requiring current therapy, with good evidence of preceding stressors may also be included at the PI's discretion. As required, participants will be assessed prior to enrollment with a Patient Health Questionnaire (PHQ-9) and/or Generalized Anxiety Disorder Questionnaire (GAD-7) which must score less than or equal to 4 on admission.
2.2. Rhinitis (including hay fever) which is clinically active or a history of moderate to severe rhinitis, or history of seasonal allergic rhinitis likely to be active at the time of inclusion into the study and/or requiring regular nasal corticosteroids on an at least weekly basis, within 30 days of admission to quarantine will be excluded. Participants with a history of currently inactive rhinitis (within the last 30 days) or mild rhinitis may be included at the PI's discretion.
2.3. Atopic dermatitis/eczema which is clinically severe and/or requiring moderate to large amounts of daily dermal corticosteroids will be excluded. Participants with mild to moderate atopic dermatitis/eczema, taking small amounts of regular dermal corticosteroids, may be included at the PI's discretion.
2.4. Any concurrent serious illness including history of malignancy that may interfere with a participant completing the study. Basal cell carcinoma within 5 years of initial diagnosis or with evidence of recurrence is also an exclusion.
2.5. Participants reporting physician-diagnosed migraine can be included provided there are no associated neurological symptoms such as hemiplegia or visual loss. Cluster headache/migraine or prophylactic treatment for migraine is an exclusion.
2.6. Participants with physician-diagnosed mild irritable bowel syndrome not requiring regular treatment can be included at the discretion of the PI.
2.7. Participants with a history of asthma where their last symptoms/treatment were in adolescence and over 6 years ago may be included at the discretion of the PI. Any participants with symptoms or treatment in adulthood would be excluded.
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. Females 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 vaccination.
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 hospitalized due to epistaxis on any previous occasion.
7.3. Any nasal or sinus surgery within 3 months of the first study visit.

Prior or concomitant medications and assessments:
8.1. Evidence of vaccinations within the 4 weeks prior to the planned date of vaccination.
8.2. Intention to receive any vaccination(s) before the last day of follow-up. (NB. No travel restrictions will apply after the Day 28 follow-up visit).
8.3. Receipt of influenza vaccine (or another IMP relating to the treatment of influenza) OR a diagnosis of influenza or influenza-like illness confirmed by a physician in the last 6 months prior to the planned date of vaccination.
8.4. Receipt or plans to receive a modRNA-platform SARS-Cov-2 vaccine 28 days before or after the vaccination visit.
9. Receipt of blood or blood products, or loss (including blood donations) of 550 mL or more of blood during the 3 months prior to the planned date of vaccination or planned during the 3 months after the final visit.
10.1. Receipt of any investigational drug within 3 months (or 5 half-lives of the IMP used in the other study, whichever is greater) prior to the planned date of vaccination.
10.2. Receipt of 3 or more investigational drugs within the previous 12 months prior to the planned date of vaccination.
10.3. Prior inoculation with a virus from the same virus subtype as the challenge virus.
10.4. Prior inoculation with a virus from the same virus family as the challenge virus in the last 12 months
10.5. Prior participation in another HVC study with a respiratory virus in the preceding 3 months, taken from the date of the viral challenge in the previous study to the date of the expected viral challenge in this study.
10.6. Receipt of any immunoglobulin or monoclonal antibodies within 3 months (or 5 half-lives, whichever is greater) prior to the planned date of vaccination.
11. 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. Specifically, the following are excluded:
11.1. Herbal supplements, any medication or product for the symptoms of nasal congestion, or short- or long-acting antihistamines within 7 days prior to the planned date of vaccination.
11.2 Chronically used medications, vitamins, or dietary supplements, including any medications known to be potent inducers or inhibitors of cytochrome 450 (CYP) enzymes, within 21 days prior to the planned date of vaccination.
11.3. Over-the-counter medications (e.g., paracetamol or ibuprofen) where the dose taken over the preceding 7 days prior to the planned date of vaccination has exceeded the maximum permissible 24-hour dose (e.g., ≥4 g paracetamol over the preceding week).
11.4. Systemic anti-viral administration within 4 weeks of vaccination.
11.5. Use of any intranasal medication, including saline douches, within 30 days prior to admission.
12.1. Confirmed positive test for drugs of misuse and cotinine on first study visit. One repeat test is allowed at the PI's 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 ≥37.9°C pre-dose on the day of vaccination (Day -30 [±3 days]), and/or pre-challenge on Day 0.

Other:
16. Those employed or immediate relatives of those employed at hVIVO or Pfizer.
17. Any other medical, psychiatric, social, or occupational condition and/or responsibility that, in the opinion of the investigator, would interfere with, or serve as a contraindication to, protocol adherence or the assessment of safety (including reactogenicity) will deem the participant unsuitable for the study.
Any other reason that in the opinion of the investigator raises a concern that the participant will not be able to cope with quarantine requirements.

Date of first enrolment
08/04/2024

Date of final enrolment
14/10/2024

Locations

Countries of recruitment
United Kingdom

Study participating centre
-
United Kingdom
-

Sponsor information

Organisation
hVIVO (United Kingdom)

ROR
https://ror.org/00a4k5f23

Funder(s)

Funder type
Industry

Funder Name
Pfizer

Alternative Name(s)
Pfizer Inc., Pfizer Consumer Healthcare, Davis, Charles Pfizer & Company, Warner-Lambert, King Pharmaceuticals, Wyeth Pharmaceuticals, Seagen, Pfizer Inc

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United States of America

Results and Publications

Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary
Data sharing statement to be made available at a later date