A two-stage, controlled, open-label, dose-ascending first-in-man study to assess the safety, tolerability and immunogenicity of a Twincer®-administered dry powder influenza vaccine

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To evaluate the safety, tolerability and immunogenicity of a Twincer®-administered dry powder influenza vaccine in healthy adults.

Ethical review	Approved WMO
Status	Will not start
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON44937

Source
ToetsingOnline

Brief title
Safety, tolerability and immunogenicity of Twincer®-Flu

Condition

- Viral infectious disorders

Synonym
influenza flu

Research involving
Human

Sponsors and support

Primary sponsor: Rijksuniversiteit Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Influenza, Powder, Twincer, Vaccine

Outcome measures

Primary outcome

For safety and tolerability: (1) Occurrence and intensity of subjects experiencing acute AEs 6hr after the study treatments (for stage I and II); (2) Occurrence of subjects experiencing >20% reduction in FEV after the study treatments (for stage I and II); (3) Occurrence and intensity of solicited and unsolicited local and systemic AEs after the study treatments (for stage II only); (4) Occurrence of SAEs and AESIs during the 180 day study period (for stage II only).

For immunogenicity (for stage II only): (1) Geometric mean titer (GMT) of serum hemagglutination inhibition (HAI) with 95% confidence interval (CI) on day 0, 21 and 180; (2) seroconversion rate (SCR) of HAI on day 21 and 180; (3) seroprotection rate (SPR) of HAI on 21 and 180; (4) Mean-fold increase in HAI titer from baseline. (5) Geometric mean concentration (GMC) of influenza-specific IgG in serum, nasal wash and sputum samples with 95% CI on day 0, 21 and 180; (5) GMC of influenza-specific IgA in serum, nasal wash and sputum samples with 95% CI on day 0, 21 and 180.

Secondary outcome

NA

Study description

Background summary

Vaccination has been adopted as the primary measurement for the prevention and control of influenza diseases. Current inactivated influenza vaccines given by parenteral routes pose limitations related to needle usage and are ineffective in stimulating mucosal immune responses. To overcome these, a safe and effective needle-free mucosal vaccination strategy is needed.

Study objective

To evaluate the safety, tolerability and immunogenicity of a Twincer®-administered dry powder influenza vaccine in healthy adults.

Study design

A two-stage, controlled, open-label, dose-ascending first-in-man study to assess the safety, tolerability and immunogenicity of a Twincer®-administered dry powder influenza vaccine. Volunteer study participants in the area of University Medical Center Groningen will be recruited. Subjects recruited for the first stage (arm 1) will be instructed to receive a single dose of Twincer®-administered dry powder excipient (inulin in HBS buffer). Physical examination and pulmonary function test (FEV/FVC) will be performed before and after the inhalation. Subjects will be monitored closely at the trial site for 6 hours after the inhalation. The second stage of the trial will only start after the safety confirmation from the first stage and will be conducted after the influenza epidemic season 2016-2017. A controlled and dose-ascending approach is used for the second stage. Subjects will be block randomized to receive Twincer®-administered dry powder excipient (arm 1) or Twincer®-administered dry powder influenza vaccine (starting from low dose (arm 2)). The safety follow-up for these subjects is as described earlier. In addition, solicited and unsolicited adverse events (AEs) will be collected by AE questionnaire/diary card during the first 21 days. Unsolicited, serious adverse events (SAEs) and adverse events of special interest (AESIs) will be followed for 180 days. Nasal wash, (induced) sputum and blood samples will be taken from all subjects before, 21 and 180 days after the IMP inhalation for the evaluation of influenza-specific humoral immune responses.

Intervention

Twincer®-administered dry powder excipient (inulin and HBS, arm 1) and Twincer®-administered dry powder influenza vaccine (at 15, 30 and 45 micrograms, arm 2-4).

Study burden and risks

Participants will be asked to come to the clinical site where they will be asked to inhale either inulin (an inert sugar) or influenza vaccine incorporated in an inulin matrix. Inhalation is done via the Twincer® inhaler and the inhalation hardly poses any discomfort to the participant. Lung function testing will be limited to general tests that are frequently performed in medical practice, except for some inhalation and exhalation exercises no specific burden will be posed on the participants. Clinical samples including nasal wash, sputum and blood (10 ml) will be collected 3 times during a 180 day study period. Sampling will be done according to stand medical procedures to minimize the burden to the participants. Sampling procedures will not cause unacceptable risks to the participants.
Inulin which is an inert sugar will be inhaled by the participants, However, this material poses minimal risk to the participants. Other inert sugars or sugar alcohols such as lactose, glucose and mannitol are used or have been used in commercial formulations for inhalation without any safety problems. Moreover extensive inhalation studies with powdered inulin were performed in animals showing no effect of the inhaled inulin. It is therefore not to be expected that the sugar used in this study will cause any safety risk.
The major risk related to this study is the occurrence of an uncontrolled inflammatory reaction to the inhaled influenza vaccine. The risk is minimized by using a single dose regimen with carefully-chosen study doses. The study doses are close to the dose used in an earlier trial where pulmonary influenza vaccination was given by liquid aerosols. Influenza vaccine liquid aerosols had been tested in over 4000 human subjects without causing a specific safety concern.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Healthy male or non-pregnant female (as indicated by a negative urine pregnancy test immediately prior to study treatment) between the ages of 18 and 59 years, inclusive; ;- Women of childbearing potential (not surgically sterile or postmenopausal for greater than or equal to one year) must agree to practice adequate contraception (i.e., barrier method, abstinence, and licensed hormonal methods) for the entire study period;;- Is in good health, as determined by vital signs (heart rate, blood pressure, body temperature), medical history, self-reported illness, general physical examination, electrocardiogram (EKG), blood chemistry test (electrolytes, renal/kidney function, liver function, C-reactive protein, complete blood count), chest x-ray and clinical judgment of the Investigator; ;- Able to understand and comply with planned study procedures;;- Able to provide written informed consent

Exclusion criteria

- Has a history of severe reactions following immunization with contemporary influenza virus vaccines.;- Is allergic to egg or egg products.;- Persons with immune deficiency/disorder, whether due to genetic defect, immunodeficiency disease, or immunosuppressive therapy.;- Has a positive urine pregnancy test prior to vaccination (if female of childbearing potential) or women who are breastfeeding.;- Has a history of any serious disease:;Acute disseminated encephalomyelitis (ADEM);;Active neoplastic disease;;Any hematologic malignancy;;Asthma/COPD or severe allergic disease;;Bleeding disorders;;Chronic Hepatitis B and/or C infection;;Chronic liver disease;;Diabetes mellitus;;Guillain-Barre;;HIV;;Rheumatism or other autoimmune diseases;;Severe renal disease;;Transplant recipients;;Unstable or progressive neurological disorders.;- Receipt of medicines/treatments that would affect evaluation of immunogenicity:;(1) Oral or parenteral steroids, high-dose inhaled steroids (greater than 800 micrograms/day of beclomethasone dipropionate or equivalent) or other immunosuppressive or cytotoxic drugs;;(2) Immunoglobulin or other blood products (within the 3 months prior to treatment in this study);;(3) Experimental agent (vaccine, drug,

biologic, device, blood product, or medication) within 1 month prior to treatment in this study, or expects to receive an experimental agent (during the 180 day study period).;(4) Influenza antiviral medication (within 1 month prior to treatment in this study).;- Has received any influenza vaccine within 6 months prior to treatment in this study.;- Has influenza-like illness within 6 months prior to treatment in this study.;- Has an acute illness, including an oral temperature greater than 38 degrees Celsius, within 1 week of treatment.;- Has a history of alcohol or drug abuse deemed unsuitable for inclusion by the investigator (based on the units used according to the trial subject);- Has a smoking habit deemed unsuitable for inclusion by the investigator (based on the units used according to the trial subject).;- Ineligible subject based on the judgement of the Investigator.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	48
Type:	Anticipated

Medical products/devices used

Generic name:	Twincer®
Registration:	Yes - CE intended use

Ethics review

Approved WMO

Date:	02-02-2016

Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-02-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-04-2017
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2014-003435-19-NL
CCMO	NL50399.042.16