A Phase 1, randomized, double-blind, controlled trial to evaluate the safety and immunogenicity of increasing intranasal doses or of three intramuscular doses of the adjuvant Gram-positive Enhancer Matrix (GEM) administered with a standard dose of trivalent inactivated influenza vaccine (TIV) antigens, compared to a standard dose of TIV antigens administered either intranasally or intramuscularly in healthy adult volunteers; followed by a randomized, double-blind, controlled evaluation of safety

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To assess the safety, reactogenicity, and tolerability of increasing GEM intranasal doses (1.25 mg, 2.5 mg and 5.0 mg) and intramuscular doses (0.05, 0.1, 0.2 mg) of the GEM adjuvant, each administration containing as well a standard 2010/2011 Flu...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Viral infectious disorders
Study type	Interventional

Summary

ID

NL-OMON36678

Source
ToetsingOnline

Brief title
FluGem in healthy adult and elderly volunteers

Condition

- Viral infectious disorders

Synonym
griep vaccination

Research involving
Human

Sponsors and support

Primary sponsor: Mucosis
Source(s) of monetary or material Support: Mucosis

Intervention

Keyword: Adjuvant, Influenza, Vaccine

Outcome measures

Primary outcome

The primairy study parameters are safety and tolerability parameters

Secondary outcome

The secondairy study parameters is the immunogenicity of the combination GEM +

vaccin:

Haemaglutination Inhibition Titers

Mucosal IgA

Total and subtype IgG

Cell Medicated Immunity

Microneutralization with mucosal IgA

Study description

Background summary

Prophylaxis of influenza relies on annual flu vaccination with seasonal flu vaccines matching the expected circulating strains. Trivalent inactivated vaccines (TIV) are among the most used flu vaccines. They offer a good protection in adults; however, children less than 5 year-old and elderly of 65 years and older are still significantly exposed to the risk of infection, due to a still immature or to a senescent immune system, respectively. This limited and unpredictable immune response may result, particularly in elderly with associated pathologies, in hospitalization and potentially death. There is therefore still a large medical need in these age groups, where flu prophylaxis would be much needed.

Study objective

To assess the safety, reactogenicity, and tolerability of increasing GEM intranasal doses (1.25 mg, 2.5 mg and 5.0 mg) and intramuscular doses (0.05, 0.1, 0.2 mg) of the GEM adjuvant, each administration containing as well a standard 2010/2011 Flu antigens dose and compare results with those recorded following the intranasal and intramuscular administration of a standard plain TIV antigens dose (without the GEM adjuvant)

Study design

Double-blind, randomised trial

Intervention

The intranasal administration of the 2010/2011 flu vaccine alone or with increasing doses of the GEM adjuvant OR the intramuscular administration of the 2010/2011 flu vaccine alone of with increasing doses of the GEM adjuvant.

Study burden and risks

Local or systemic adverse reactions, such as Local (injection site) reactions, such as swelling, redness or bruising, can occur as a direct result of vaccination.Based on the previous studies with flu vaccines, the majority of local reactions due to the administration of the flu antigens would be expected to be absent or mild in severity, with moderate severity being reported in <10%

of subjects. GEM has never being tested in humans. Toxicological studies however did not reveal any specific local tolerability issue.

GEM has never been administered to humans. Toxicological studies did not reveal any specific intranasal tolerability issue.
Among the 17 intramuscularly dosed subjects, 5 subjects experienced severe pain in the injected arm. Therefore it was decided to change the i.m. dose of 0.1 mg GEM in adults and to increasing doses of 0.05, 0.1, 0.2 mg GEM in elderly.
After dosing of 9 adults with 0.1 mg i.m. GEM/plac the stopping rule of 2 subjects with severe pain in the arm was reached. The Safety and Monitoring Committee decided to continue with the 0.05 mg i.m. dose in adult subjects only.

There is a small change on rare side effect such as allergic reaction.
Head ache can happen due to fasting. the canula for blood drawing might sometime lead to a bruis.

This study will provide the first data on the tolerability, safety and immunogenicity of the adjuvant GEM administered either intramuscularly or intranasally together with trivalent inactivated flu antigens (sub-unit vaccine) . Adjuvants are a possible way to increase the immune response to antigens in poor responders, such as elderly people. The rate of flu related morbidity and mortality is still unacceptably high. Ways of improving immunogenicity in the elderly (as well as in infants and young children) are therefore needed.

Vaccinated subjects could have some unknown degree of protection against flu in the following season depending on the circulating strains. This should in no way be regarded as a replacement for standard flu prophylaxis as recommended by Health Authorities.

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

• Male or female aged 18 - 49 years inclusive ;OR ;• Male or female aged 65 years or older ;• Able to give written informed consent to participate;• Comprehension of the study requirements, expressed availability for the required study period, and ability to attend scheduled visits and to be contacted by telephone throughout the follow-up period.;• Healthy- Subjects must be free of any clinically significant disease, as determined by medical history, physical examination, vital signs, and safety laboratory examinations at baseline;• A Body Mass Index (BMI) between 18 and 32, inclusive. BMI = weight (kg)/height2 (m2). ;• Subjects* clinical laboratory tests (CBC, blood chemistry, and urinalysis) must be within normal limits or clinically acceptable to the investigator and within allowed expanded range supplied by sponsor. Subject*s liver function test results (ie, AST, ALT) must not be elevated above the normal limits at Screening;• The Screening 12 lead ECG conduction intervals must be within gender specific normal range (QTc males * 430 msec, PR interval * 200 msec).;• Vital sign measurements (taken after ~3 minutes in a supine position) must be within the following ranges: (Individuals with values outside (or indicate lower or higher) of these ranges may be enrolled if clinically acceptable to the investigator and sponsor.) ;o oral body temperature, between 35.0*C and 37.5*C;o systolic blood pressure, 90 to 140 mm Hg;o diastolic blood pressure, 45 to 90 mm Hg;o pulse rate, 40 to 100 bpm;• ;• ;• Women of childbearing potential must have a negative urine pregnancy test within 24 hours preceding receipt of each dose. and / or should fulfill one of the following criteria:;A At least one year post-menopausal;;B. Surgically sterile;C Willing to abstain from sexual intercourse or use another reliable form of contraception approved by the Investigator (e.g., intrauterine device, female condom, diaphragm with spermicide, cervical cap, use of condom by the sexual partner or a sterile sexual partner) for 30 days prior to first vaccination, throughout study duration and until 28 days after vaccination.

Exclusion criteria

• Presence of significant uncontrolled medical or psychiatric illness (acute or chronic). This includes institution of a new medical or surgical treatment, or a significant dose alteration for uncontrolled symptoms or drug toxicity within 3 months of screening ;• Receipt of a 2010/2011 influenza vaccine in the vaccination season 2010/2011.;• HI titers against the vaccine strains >= 1:10 for 2 or more strains;• Subjects who are positive for hepatitis B surface antigen, hepatitis C antibodies or HIV.;• Subjects positive for Hematuria on screening urinalysis.;• Positive serology for HIV-1 or HIV-2.;• Cancer, or treatment for cancer, within 3 years, excluding basal cell carcinoma or squamous cell carcinoma, which is allowed.;• Presence of any medical condition that may be associated with impaired immune responsiveness, including diabetes mellitus.;• Presently receiving or history of receiving, during the preceding 3-month period, any medications or other treatments that may adversely affect the immune system such as allergy injections, immune globulins, interferon, immunomodulators, cytotoxic drugs or other drugs known to be frequently associated with significant major organ toxicity, or systemic corticosteroids (oral or injectable). Topical corticosteroids will be allowed. ;• Receipt or planned administration of a non-study vaccine within 30 days prior to vaccination and during the study. If for a subject included in the study, immunization on an emergency basis with Tetanus Toxoids Adsorbed for adult use (Td or Tdap) becomes necessary, the subject will remain in the study provided the tetanus vaccine is administered up to 8 days before the second dose of the study vaccine or at least 8 days after a dose of study vaccine. Administration of study vaccine can be delayed if a non-study vaccine has been administered and will be given as soon as acceptable, as described above.;• Positive history of illicit drug or alcohol abuse within the previous 6 months or positive drug or alcohol screen.;• History of anaphylactic type reaction to injected vaccines.;• History of drug or chemical abuse in the year before the study.;• Treatment with another investigational medicinal product (IMP) within 3 months prior to screening or more than 4 times in the past year.;• Receipt of any investigational product or nonregistered drug within the 30 days prior to vaccination or currently enrolled in any investigational drug study or intends to enroll in such a study within the ensuing study period.;• Receipt of blood or blood products 8 weeks prior to vaccination or planned administration during the study period.;• Loss of blood outside the limits of Sanquin within 3 months prior to screening. ;• Donation of blood or blood products within 8 weeks prior to vaccination or at any time during the study.;• Acute disease within 72 hours prior to vaccination, defined as the presence of a moderate or severe illness (as determined by the Investigator through medical history and physical examination) with or without fever, or a fever >38ºC. Study vaccine can be administered to persons with a minor illness, such as diarrhea. However, in subjects suffering from mild upper respiratory tract infection with or without low-grade fever, vaccination must be delayed until the subject has recovered.;• Any condition that, in the Investigator*s opinion, might interfere with the primary study objectives.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Active
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	08-03-2011
Enrollment:	134
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	FluGem

Ethics review

Approved WMO Date:	13-01-2011
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-02-2011
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-04-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den

	Haag)
Approved WMO Date:	01-06-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-06-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-06-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	04-10-2011
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)

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	EUCTR2010-024346-30-NL

Register	ID
CCMO	NL35116.000.10