Randomised, double-blind, placebo-controlled study to evaluate the safety, tolerability, immunogenicity and shedding of live-attenuated RSV vaccine in healthy adults

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- To assess the safety and tolerability of live-attenuated RSV vaccine in healthy adults.- To assess the immunogenicity of the live-attenuated RSV vaccine (systemic and mucosal immunity) - To assess the viral load/shedding of the live-attenuated RSV...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Respiratory tract infections
Study type	Interventional

Summary

ID

NL-OMON47495

Source
ToetsingOnline

Brief title
Live-attenuated RSV vaccine in healthy adults

Condition

- Respiratory tract infections

Synonym
Respiratory Syncytial Virus (RSV)

Research involving
Human

Sponsors and support

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

Intervention

Keyword: RSV Vaccine

Outcome measures

Primary outcome

Safety and tolerability endpoints

(Serious) adverse events will be collected throughout the study at every study visit, solicited (via a questionnaire in a e-diary app) as well as non-solicited. Laboratory safety and vital signs will be obtained multiple times during the course of the study. Tolerability will be assessed via a visual analogue scale (naso-oropharyngeal pain). Assessments will be performed according to the Visit and Assessment Schedule.

Immunogenicity endpoints

The capacity of the RSV*G vaccine to induce a humoral immune response both systemically and mucosally will be evaluated. Therefore, RSV neutralizing antibodies and RSV-specific immunoglobulin (Ig) A will be measured in nasal washes. In addition, blood samples will be taken to also determine neutralizing antibodies, Palivizumab competing antibodies, F-specific antibodies and (if relevant) specificity for different F protein epitopes.

Viral load / shedding endpoints

The viral load in nasal washes will be performed in order to evaluate the

ability of RSV*G to replicate and to evaluate the shedding.

Secondary outcome

Not applicable

Study description

Background summary

Respiratory Syncytial Virus (RSV) is still the leading cause of hospitalization of children under 5 years of age. Currently, there is no effective treatment licensed for an ongoing RSV infection. Therefore, Intravacc develops a live-attenuated recombinant RSV vaccine. With reverse genetics, a virus was constructed from which the coding sequence for the G attachment protein was deleted from the RSV genome. This construct (RSV*G) lacks the G protein resulting in severely impaired binding to host cells and therefore reducing infectivity. Due to this attenuation and limited spread, the vaccine is expected to induce an effective immune response, without inducing RSV symptoms. This phase I trial evaluates the safety, tolerability, immunogenicity and shedding of the RSV vaccine in healthy adults

Study objective

- To assess the safety and tolerability of live-attenuated RSV vaccine in healthy adults.
- To assess the immunogenicity of the live-attenuated RSV vaccine (systemic and mucosal immunity)
- To assess the viral load/shedding of the live-attenuated RSV vaccine
- To assess longevity of antibody response 6 months after immunization (if the vaccine was able to induce a significant increase in antibody titers on day 28)

Study design

This study is conducted in a double blind, randomised, placebo-controlled single-dose fashion in healthy adult volunteers.

Intervention

RSV*G or placebo

Study burden and risks

The risks associated with the administration of RSV*G to humans have not yet been identified, as this vaccine candidate has not yet been administered to humans before. However, due to the nature of this type of vaccines, the adverse events are expected to be mild and of short duration. Due to the attenuation (deletion of G protein) immunization with RSV*G is expected to be without harmful effects. Furthermore, most humans have pre-existing immunity against RSV and therefore it is unlikely that RSV*G will cause a measurable infection in healthy adults. If infection with the RSV*G occurs, it is most likely asymptomatic. If infection becomes symptomatic, symptoms may resemble infection with wt-RSV with symptoms, such as rhinorrhea, pharyngitis, sneezing, and cough.

Subjects receiving the vaccine might benefit from the immunization. Activation of the immune response against RSV might protect them against disease related to natural RSV infection.

The potential risks of venepuncture for blood sampling are mild pain and haematoma, and are considered low.

The major benefit is for the public at large since the final objective of this project is to protect infants against severe disease and mortality due to RSV infection.

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

1. Healthy male or female, 18-50 years of age, inclusive at screening;
2. Body mass index (BMI) * 18.0 and < 32.0 kg/m2;
3. Good health, based upon the results of medical history, physical examination, vital signs, ECG, and laboratory profiles of both blood and urine;
4. Pre-existing virus neutralization antibody titers (VNT) against RSV * 9.6 log2 (titer) at screening;
5. Willing to comply with effective contraception during the study if subject is male or woman of child bearing potential, up to 90 days after the vaccine administration;
6. Signed informed consent prior to any study-mandated procedure;
7. The ability to communicate well with the Investigator in the Dutch language
8. Willing to comply with the study restrictions.

Exclusion criteria

1. Immune-compromised (known or expected immune deficiency, disease, or use of medication that may affect the immune system);
2. Close contact with infants (<2 years of age) and immune-compromised individuals, during 14 days starting from day of vaccine administration;
3. Chronic airway diseases;
4. Airway infection in the period of 14 days before first vaccine administration;
5. Active hay fever or other allergies that involve the airways;
6. Any confirmed significant allergic reactions (urticaria or anaphylaxis) against any drug, or multiple drug allergies;
7. Any anatomic or neurologic abnormality impairing the gag reflex, or associated with an increased risk of aspiration, or any abnormality significantly altering the anatomy of the nose or nasopharynx;
8. History of frequent epistaxis (nose bleeds);
9. Evidence of any other active or chronic disease (haematologic, renal, hepatic, cardiovascular, neurologic, endocrinal, gastrointestinal, oncologic, pulmonary, immunologic, or psychiatric disorders) or condition that could interfere with, or for which the treatment of might interfere with, the conduct of the study, or that would pose an unacceptable risk to the

subject in the opinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, and body temperature) and ECG. Minor deviations from the normal range may be accepted, if judged by the Investigator to have no clinical relevance.
10. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including blood chemistry, haematology and urinalysis). In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects.
11. Positive Hepatitis B surface antigen, Hepatitis B antibodies, Hepatitis C antibody, or human immunodeficiency virus antibody at screening;
12. If a woman, pregnant, or breast-feeding, or planning to become pregnant during the study or 90 days after vaccine administration;
13. Use of any medications (prescription or over-the-counter (OTC)), within 14 days of vaccine administration, or less than 5 half-lives (whichever is longer). Exceptions is paracetamol (up to 4 g/day). Other exceptions will only be made if the rationale is clearly documented and accepted by the investigator.
14. History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 21 units alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquillisers, or any other addictive agent;
15. Smoking in the 90 days preceding screening;
16. Positive test for drugs of abuse at screening or pre-dose;
17. Participation in an investigational drug or device study within 3 months prior to first dosing or more than 4 times a year;
18. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening or intention to donate blood or blood products during the study;
19. Any known factor, condition, or disease that might interfere with treatment compliance, study conduct or interpretation of the results.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-05-2018
Enrollment:	48
Type:	Actual

Medical products/devices used

Product type:	Medicine
Generic name:	Genetic modified organism
Product type:	Medicine
Brand name:	RSV□G

Ethics review

Approved WMO Date:	15-01-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	16-04-2018
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-07-2018
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-08-2018
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	EUCTR2016-002437-30-NL
CCMO	NL58147.000.17