A Phase 3, observer-blind, randomized, placebo controlled study to evaluate the non inferiority of the immune response and safety of the RSVPreF3 OA investigational vaccine in adults 50-59 years of age, including adults at increased risk of respiratory syncytial virus lower respiratory tract disease, compared to older adults >=60 years of age.

Published: 19-08-2022
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Primary objective:To demonstrate the non-inferiority (NI) of the humoral immune response in healthy participants 50-59 YOA compared to OA (>=60 YOA) for the RSV-A strain after RSVPreF3 OA investigational vaccine administration.To demonstrate the...

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

Summary

ID

NL-OMON53679

Source
ToetsingOnline

Brief title
219238 - RSV OA=ADJ018

Condition

- Respiratory tract infections

Synonym
respiratory syncytial virus (RSV)-associated (subtypes A and B) disease, RSV infection

Research involving
Human

Sponsors and support

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

Intervention

Keyword: immune response, lower respiratory tract disease, Older Adults, RSV

Outcome measures

Primary outcome

RSV-A neutralization titers expressed as group:

- GMT ratio (OA-RSV/Adults-HA-RSV), 1 month after the RSVPreF3 OA

investigational vaccine administration.

- SRR difference (OA-RSV - Adults-HA-RSV), 1 month after the RSVPreF3 OA

investigational vaccine administration compared to baseline

RSV-B neutralization titers expressed as group:

- GMT ratio (OA-RSV/Adults-HA-RSV), 1 month after the RSVPreF3 OA

investigational vaccine administration.

- SRR difference (OA-RSV - Adults-HA-RSV), 1 month after the RSVPreF3 OA

investigational vaccine administration compared to baseline

Secondary outcome

Percentage of participants reporting:

- each solicited administration site event with onset within 4 days after study intervention administration

- each solicited systemic event with onset within 4 days after study intervention administration

- unsolicited AEs within 30 days after study intervention administration

- any SAEs and pIMDs after study intervention administration up to Month 6.

- SAEs and pIMDs related to study intervention administration after study intervention administration up to study end

- any fatal SAEs after study intervention administration up to study end

RSV-A and RSV-B neutralization titers expressed as GMT, at pre-study intervention administration, 1 month, 6 months and at 12 months after study intervention administration.

(sub study not conducted in the Netherlands)

CMI response expressed as group geometric mean of the frequency of RSVPreF3-specific CD4+ and/or CD8+ T cells expressing at least 2 activation markers, 1 month, 6 months and at 12 months after study intervention administration, in a subset of participants

Tertiary:

RSV-A and RSV-B neutralization titers expressed as GMT, at pre-study intervention administration, 1 month, 6 months and at 12 months after study intervention administration, by baseline co-morbidities.

Any further exploratory immunology such as but not limited to:

- Antibodies against specific protein F epitopes or other RSV strains

- Potential new immunological markers for protection

- Frequency of RSVPreF3-specific CD4+ and/or CD8+ T cells expressing one or any

combination of immune marker(s)

Study description

Background summary

RSV is an RNA virus of which 2 antigenically distinct subtypes exist, referred to as RSV A and RSV-B. RSV is a highly contagious human pathogen that causes respiratory tract infections in people of all ages. In temperate climates throughout the world, RSV predictably causes fall-winter epidemics. In (sub) tropical regions, viral activity is more endemic, and outbreaks are less temporally focused.

RSV is one of the important viral pathogens identified in adults with acute respiratory infections and is increasingly recognized as a cause of serious illness in high-risk adults, including those with chronic lung and heart disease. In a prospective cohort study over 4 RSV seasons in healthy elderly patients (>=65 YOA) and high-risk adults (>=21 YOA) with chronic heart or lung disease, RSV infection developed annually in 3% to 7% of healthy elderly patients and in 4% to 10% of high-risk adults. Healthy elderly patients with RSV infection required fewer visits to the doctor*s office compared to those with influenza. Utilization of health care services among high-risk adults with either RSV infection or influenza was similar. RSV infection in the elderly and high-risk adults has a disease burden similar to that of a non-pandemic influenza A in a population with a high rate of influenza vaccination.

In different populations of patients with chronic morbidities both the prevalence and incidence of RSV infections is increased, leading to an increase in need for medical care and hospitalization in high income countries. A major US study reported incidence of RSV-related hospitalizations among different types of high-risk patients of different age groups, in 2 different settings. Adults with COPD had 3.2-13.4 times higher hospitalization rates than those without COPD. Adults with asthma had 2.0 - 3.6 times higher estimated hospitalization rates than those without asthma. Adults with diabetes had 2.4-11.4 times higher hospitalization rates than those without diabetes. Adults with CAD had estimated RSV hospitalization rates 3.7-7.0 times higher than

those without CAD. Estimated IRRs for CHF were the largest; adults with CHF had 4.0 33.2 times higher hospitalization rates than those without CHF. Estimated IRRs for CHF were highest in the youngest age group and declined with increasing age. Different European, Asian and US studies have reported an exacerbation of either COPD, asthma, interstitial pulmonary fibrosis or cystic fibrosis ranging from 2.2% to 17%. Patients with chronic renal disease as well as those with chronic liver disease have impaired immune functions due to their disease pathogenesis, which is associated, in general, with increased susceptibility to infections.

Study objective

Primary objective:
To demonstrate the non-inferiority (NI) of the humoral immune response in healthy participants 50-59 YOA compared to OA (>=60 YOA) for the RSV-A strain after RSVPreF3 OA investigational vaccine administration.
To demonstrate the NI of the humoral immune response in healthy participants 50-59 YOA compared to OA (>=60 YOA) for the RSV-B strain after RSVPreF3 OA investigational vaccine administration.
To demonstrate the NI of the humoral immune response in participants 50-59 YOA at increased risk of RSV-LRTD compared to OA (>=60 YOA) for the RSV-A strain after RSVPreF3 OA investigational vaccine administration.
To demonstrate the NI of the humoral immune response in participants 50-59 YOA at increased risk of RSV-LRTD compared to OA (>=60 YOA) for the RSV-B strain after RSVPreF3 OA investigational vaccine administration.
To evaluate the safety and reactogenicity after the RSVPreF3 OA investigational vaccine administration.

Secondary Objectives:
To evaluate the humoral immune response to the RSVPreF3 OA investigational vaccine until 12 months post-study intervention administration.

(Sub study, not in the Netherlands)
To evaluate the CMI response after RSVPreF3 OA investigational vaccine administration until 12 months post-study intervention administration.

Tertiary
(Tertiary objectives, endpoints, and estimands are optional and might be assessed only if needed; therefore, not all testing might be performed and reported)
To evaluate the humoral immune response to the RSVPreF3 OA investigational vaccine in participants 50-59 YOA at increased risk of RSV LRTD, by baseline co-morbidities.
To further characterize immune responses to the RSVPreF3 OA investigational vaccine

Study design

Overall Design:
Experimental design: Phase 3, observer/participant-blind, randomized, placebo-controlled study with 2 cohorts:

Cohort 1 (adults 50-59 YOA) n=1140, with 2 sub-cohorts (Adults-HA (Healthy Adults) and Adults AIR (at increased risk)) and 4 parallel groups:
o Adults-HA-RSV Group n=380
o Adults-HA-Placebo Group n=190
o Adults-AIR-RSV Group n=380
o Adults-AIR-Placebo Group n=190

Cohort 2 (adults >=60 YOA) with a single group (OA-RSV Group) n=380

Duration of the study: approximately 12 months for all participants.
Primary completion date: Day 31 (1 month after the administration of study intervention).
Control: placebo saline solution.

Vaccination schedule: Participants will receive a single dose of study intervention (either RSVPreF3 OA investigational vaccine or placebo) at Visit 1 (Day 1).

Intervention

Participants will receive a single dose of study intervention (either RSVPreF3 OA investigational vaccine or placebo) at Visit 1.
Study participants must be observed closely for at least 30 minutes after the administration of the study intervention(s). Appropriate medical treatment must be readily available during the observation period in case of anaphylaxis, syncope.

Study burden and risks

Severe allergic reaction (including itchy skin rash, swelling of the face, difficulty in breathing and swallowing, or a sudden drop in blood pressure) have been rarely reported after vaccination.
Syncope (fainting) can occur after or even before any vaccination as a stress response to the needle injection

Observed 1 op 10:
Pain at injection site
Redness at injection site
Swelling at injection site

People who have received vaccines that contain an adjuvant have very rarely (up to 1 in 10 000 people) developed autoimmune diseases, which can sometimes be serious and lifelong.

Procedures:
When giving blood the subject may feel dizzy, faint or experience mild pain, bruising, irritation, or redness from the needle.

Contacts

Public
GlaxoSmithKline

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• Participants who, in the opinion of the investigator, can and will comply with the requirements of the protocol

Cohort1
• A male or female participant 50-59 YOA
• Female participants migth be of childbearing potential..
• Female participants of childbearing potential may be enrolled in the study, if the participant:
- has practiced adequate contraception from 1 month prior to study intervention administration until study end for this study, and
- has a negative pregnancy test on the day of study intervention administration.

For participants in the Adults-HA (Healthy Adults) Sub-cohort:
• Healthy participants as established by medical history and clinical examination before entering into the study.
• Participants with chronic stable medical conditions with or without specific treatment

For participants in the Adults-AIR (At increased Risk) Sub cohort:
• Chronic pulmonary disease resulting in activity restricting symptoms or use of long term medication:
- Chronic obstructive pulmonary disease (COPD); Grade 2-4
- Asthma
- Cystic fibrosis
- Other chronic respiratory diseases: lung fibrosis, restrictive lung disease, interstitial lung disease, emphysema or bronchiectasis
• Chronic cardiovascular disease
- Chronic heart failure (CHF)
- Pre-existing coronary artery disease (CAD not otherwise specified)
- Cardiac arrhythmia
• Diabetes mellitus: types 1 and 2
• Other diseases at increased risk for RSV-LRTD disease
- Chronic kidney disease
- Chronic liver disease

For participants in Cohort 2 (OA-RSV Group)
• A male or female participant >=60 YOA
• Participants with chronic stable medical conditions with or without specific treatment
• Participants living in the general community or in an assisted-living facility that provides minimal assistance.

Exclusion criteria

• Any confirmed or suspected immunosuppressive or immunodeficient condition
• History of any reaction or hypersensitivity likely to be exacerbated by any component of the study intervention.
• Hypersensitivity to latex.

• Unstable chronic illness.
• Any history of dementia or any medical condition that moderately or severely impairs cognition.
• Recurrent or uncontrolled neurological disorders or seizures.
• Significant underlying illness that in the opinion of the investigator would be expected to prevent completion of the study.
• Any medical condition that in the judgment of the investigator would make intramuscular injection unsafe.
• Use of any investigational or non-registered product, or planned use during the study period.
• Planned or actual administration of a vaccine not foreseen by the study protocol in the period starting 30 days before and ending 30 days after the dose of study intervention administration, with the exception of inactivated and subunit influenza vaccines or COVID-19 vaccines.
• Previous vaccination with an RSV vaccine, including investigational RSV vaccines.
• Chronic administration of immune-modifying drugs and/or administration of long-acting immune modifying treatments or planned administration at any time up to the end of the study.
• Concurrently participating in another clinical study
• History of chronic alcohol consumption and/or drug abuse
• Pregnant or lactating female.
• Female planning to become pregnant or planning to discontinue contraceptive precautions.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL
Recruitment status: Recruitment stopped

Start date (anticipated):	20-12-2022
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	RSV OA=ADJ

Ethics review

Approved WMO Date:	19-08-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-12-2022
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-07-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	09-08-2023
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-01-2024
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	14-02-2024

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	EUCTR2022-001981-36-NL
Other	https://www.trialsummaries.com
CCMO	NL81616.000.22