A phase 3 study to evaluate the efficacy, immunogenicity, and safety of Respiratory Syncytial Virus (RSV) prefusion F subunit vaccine in adults

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ObjectivesPrimary Efficacy:To demonstrate the efficacy of RSVpreF in preventing LRTI-RSV in the first RSV season following vaccination.Primary Safety:To describe the safety profile of RSVpreF as measured by the percentage of participants reporting...

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

Summary

ID

NL-OMON52252

Source
ToetsingOnline

Brief title
C3671013 (9002/0849)

Condition

- Viral infectious disorders

Synonym
Respiratory Syncytial Virus (RSV), Virus disease

Research involving
Human

Sponsors and support

Primary sponsor: Pfizer

Source(s) of monetary or material Support: Industry

Intervention

Keyword: Phase 3, Respiratory Syncytial Virus (RSV), Vaccine

Outcome measures

Primary outcome

Primary Efficacy:

In participants in compliance with the key protocol criteria (evaluable

efficacy population):

1. VE, defined as the relative risk reduction of first-episode LRTI-RSV cases

with >=2

LRTI signs/symptoms in the RSVpreF group compared to the placebo group in the

first RSV season (starting on Day 15 after study vaccination) and in compliance

with the key protocol criteria (evaluable efficacy population).

2. VE, defined as the relative risk reduction of first-episode LRTI-RSV cases

with >=3 LRTI signs/symptoms in the RSVpreF group compared to the placebo group

in the first RSV season (starting on Day 15 after study vaccination).

Primary Safety:

In participants receiving study intervention:

1. The proportion of participants reporting prompted local reactions within 7

days following study intervention administration in a subset of participants.

2. The proportion of participants. reporting prompted systemic events within 7

days following study intervention administration in a subset of participants.

3. The proportion of participants reporting AEs through 1 month following study

intervention administration.

4. The proportion of participants reporting NDCMCs throughout the study.

5. The proportion of participants reporting SAEs throughout the study.

Secondary outcome

Key Secondary Efficacy:

In participants in compliance with the key protocol criteria (evaluable

efficacy population):

VE, defined as the relative risk reduction of first- episode sLRTI-RSV cases in

the RSVpreF group compared to the placebo group in the first RSV season

(starting on Day 15 after study vaccination).

Secondary Efficacy:

In participants in compliance with the key protocol criteria (evaluable

efficacy population):

- VE, defined as the relative risk reduction of first-episode LRTI-RSV cases

with >=2 LRTI signs/symptoms in the RSVpreF group compared to the placebo group:

• starting on Day 15 after study vaccination through 2 RSV seasons.

• starting on Day 15 after study vaccination through 3 RSV seasons.

VE, defined as the relative risk reduction of first- episode LRTI-RSV cases

with >=3 LRTI signs/symptoms in the RSVpreF group compared to the placebo group

• starting on Day 15 after study vaccination through 2 RSV seasons.

• starting on Day 15 after study vaccination through 3 RSV seasons.

In participants in compliance with the key protocol criteria (evaluable

efficacy population):

• VE, defined as the relative risk reduction of first-episode LRTI-RSV cases with >=2 LRTI signs/symptoms in the RSVpreF group compared to the placebo group, in the second RSV season and in the third RSV season.

• VE, defined as the relative risk reduction of first-episode LRTI-RSV cases with >=3 LRTI signs/symptoms in the RSVpreF group compared to the placebo group, in the second RSV season and in the third RSV season.

In participants in compliance with the key protocol criteria (evaluable efficacy population):

- VE, defined as the relative risk reduction of first-episode ARI-RSV cases in the RSVpreF group compared to the placebo group:

• in the first RSV season (from Day 15), in the second RSV season, and in the third RSV season.

• starting on Day 15 after study vaccination through the first 2 RSV seasons, and through all 3 RSV seasons,.

In participants in compliance with the key protocol criteria (evaluable efficacy population):

- VE, defined as the relative risk reduction of first-episode sLRTI-RSV cases in the RSVpreF group compared to the placebo group:

• from Day 15 through the 2 RSV seasons.

• starting on Day 15 after study vaccination through 3 RSV seasons.

In participants in compliance with the key protocol criteria (evaluable efficacy population):

- VE, defined as the relative risk reduction of first- episode sLRTI-RSV cases in the RSVpreF group compared to the placebo group, in the second RSV season and in the third RSV season.

Secondary Immunogenicity:

In the immunogenicity subset participants in compliance with the key protocol criteria (evaluable immunogenicity population):

1. GMT of NT for RSV A and RSV B at each time point after vaccination.

2. GMT of NT for RSV A and RSV B before vaccination.

3. GMFR of NT for RSV A and RSV B from before vaccination to each time point after vaccination.

4. GMC of RSVpreF-binding IgG at each time point after vaccination.

5. GMC of RSVpreF-binding IgG before vaccination.

6. GMFR of RSVpreF-binding IgG from before vaccination to each time point after vaccination.

Study description

Background summary

RSV is an important cause of severe respiratory disease in older adults and is associated with a high morbidity and mortality. After RSV natural infection, immunity is considered to be short-lived. Currently, there is no licensed vaccine to prevent RSV disease. Current treatments consist primarily of supportive care. The only available prophylactic measure is an RSV fusion glycoprotein (F)-specific monoclonal, which is limited to use in high-risk

infants and requires costly, monthly injections. Therefore, there is an important unmet medical need to develop an effective vaccine to boost the immune response sufficiently to protect older adults against RSV disease.

The vaccine investigated in this study is a bivalent RSV prefusion F subunit vaccine (RSVpreF) developed by Pfizer. The RSV F glycoprotein facilitates fusion of the virion and host cell membrane through a dramatic transition from an unstable but highly immunogenic prefusion conformation to the more stable postfusion state. Preclinical studies show that prefusion F elicits much higher neutralizing antibody titers than postfusion F and that the most potent neutralizing antibodies from postinfection human sera target the prefusion form. RSVpreF is composed of engineered, stabilized, trimeric, prefusion F glycoproteins matching the 2 subgroups (A and B) to help ensure the broadest coverage against RSV illness.

Study objective

Objectives
Primary Efficacy:
To demonstrate the efficacy of RSVpreF in preventing LRTI-RSV in the first RSV season following vaccination.

Primary Safety:
To describe the safety profile of RSVpreF as measured by the percentage of participants reporting local reactions, systemic events, AEs, and SAEs.

Key Secondary Efficacy:
To demonstrate the efficacy of RSVpreF in preventing RSV-associated severe lower respiratory tract illness (sLRTI-RSV) in the first RSV season following vaccination.
Secondary Efficacy:
To describe the efficacy of RSVpreF in preventing
- LRTI-RSV across multiple RSV seasons following vaccination
- LRTI-RSV in the second and third RSV seasons
- ARI-RSV at each RSV season and across multiple RSV seasons following vaccination- sLRTI-RSV across multiple RSV seasons following vaccination
- sLRTI- RSV in the second and third RSV seasons.

Secondary Immunogenicity:
To describe the immune responses induced by RSVpreF following vaccination.

Study design

This is a Phase 3, multicenter, randomized, double-blind, placebo-controlled study to assess the safety, immunogenicity, and efficacy of bivalent RSVpreF in adults 60 years of age and older.

Intervention

Group 1. The people in this group will get the RSVpreF vaccine.
Group 2. The people in this group will get a placebo.

Study burden and risks

As of June 2021, RSVpreF has been studied in 3 completed and 3 ongoing clinical trials in healthy adults and pregnant women and was shown to be well tolerated, with an acceptable safety profile, and highly efficacious in the human challenge model.

Contacts

Public
Pfizer

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New York NY10017
US
Scientific
Pfizer

East 42nd Street 235
New York NY10017
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age

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

Inclusion criteria

1. Participants who are willing and able to comply with all scheduled visits, vaccination plan, laboratory tests, lifestyle considerations, frequent symptom assessment by mobile device application, and other study procedures, including collection of nasal swabs by themselves and by study staff when indicated.
2. Healthy participants who are determined by medical history, physical examination (if required), and clinical judgment of the investigator to be eligible for inclusion in the study.
Note: Healthy participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks before enrollment, can be included. Specific criteria for participants with known stable infection with HIV, HCV, or HBV can be found in Section 10.8.
3. Adults who are ambulatory and live in the community, or in assisted-living or long-term care residential facilities that provide minimal assistance, such that the participant is primarily responsible for self-care and activities of daily living.
4. Capable of giving signed informed consent as described in Section 10.1, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol.
5. Male or female participants >=60 years of age.
* Male participants able to father children must agree to use a highly effective method of contraception from the time of informed consent through at least 28 days after study intervention administration (see Section 10.3.1).
* Female participants must not be of childbearing potential (see Section 10.3.3).

Exclusion criteria

1. Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection.
2. History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s) or any related vaccine.
3. Serious chronic disorder including metastatic malignancy, end-stage renal disease with or without dialysis, clinically unstable cardiac disease, or any other disorder that, in the investigator*s opinion, excludes the participant from participating in the study.
4. Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.
5. Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may

increase the risk of study participation or, in the investigator*s judgment, make the participant inappropriate for the study.
6. Participation in other studies involving study intervention within 28 days prior to consent and/or through and including the 6-month follow-up visit (Visit 3). Note: This criterion does not apply to participants who are participating in a follow-up period for another study involving a study intervention that is an investigational drug or vaccine, if receipt of the last dose was at least 12 months prior to consenting for this study and there is no further dosing anticipated from the previous study during the participant's participation in this study.
7. Individuals who receive chronic systemic treatment with immunosuppressive therapy, including cytotoxic agents, monoclonal antibodies, systemic corticosteroids, or radiotherapy, eg, for cancer or an autoimmune disease, from 60 days before study intervention administration or planned receipt throughout the study. If systemic corticosteroids have been administered short term (<14 days) for treatment of an acute illness, participants should not be enrolled in the study until corticosteroid therapy has been discontinued for at least 28 days before study intervention administration. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin or eyes) corticosteroids are permitted. Note: Participants with COPD or asthma can be enrolled if chronic corticosteroids do not exceed a dose equivalent to 10 mg/day of prednisone.
8. Receipt of blood/plasma products or immunoglobulin within 60 days before study intervention administration.
9. Previous vaccination with any licensed or investigational RSV vaccine or planned receipt during study participation.
10. Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	28-10-2021
Enrollment:	5000
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	PF-06928316 (Respiratory Syncytial Virus (RSV) Vaccine)

Ethics review

Approved WMO Date:	03-08-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	01-10-2021
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	11-10-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	18-10-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-10-2021
Application type:	Amendment

Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-10-2021
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Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	28-10-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	25-11-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	29-04-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	06-07-2022
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-07-2022
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	EUCTR2021-003693-31-NL
CCMO	NL78577.000.21
Other	US IND number 17931; NCT05035212