A phase 3, randomized, double-blind trial to evaluate the safety and immunogenicity of a 20-valent pneumococcal conjugate vaccine given as a series of 2 infant doses and 1 toddler dose in healthy infants

Published: 22-06-2020
Last updated: 17-01-2025

Primary Safety Objective: To describe the safety profile of 20vPnC

Ethical review	Approved WMO
Status	Completed
Health condition type	Therapeutic procedures and supportive care NEC
Study type	Interventional

Summary

ID

NL-OMON49743

Source
ToetsingOnline

Brief title
9002/0612 (B7471012)

Condition

- Therapeutic procedures and supportive care NEC

Synonym
infections caused by the pneumococ bacteria, Pneumococcal Infections

Research involving
Human

Sponsors and support

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

Intervention

Keyword: 20vPnC, Phase 3, Vaccine

Outcome measures

Primary outcome

Primary Safety Objective:

- To describe the safety profile of 20vPnC

Primary Concomitant Immunogenicity Objective

- To demonstrate that the immune responses induced by concomitant vaccine antigens given with 20vPnC are noninferior to immune responses induced by concomitant vaccine antigens given with 13vPnC at 1 month after Dose 3

Primary Pneumococcal Immunogenicity Objectives:

- To demonstrate that the percentages of participants with predefined serotype-specific IgG concentrations for the 13 serotypes in the 20vPnC group are noninferior to the percentages of the corresponding serotypes in the 13vPnC group at 1 month after Dose 3
- To demonstrate that the percentages of participants with predefined serotype-specific IgG concentrations for the 7 additional serotypes in the 20vPnC group are noninferior to the lowest percentage among the 13 serotypes in the 13vPnC group at 1 month after Dose 3

- To demonstrate that the serotype- specific IgG GMCs for the 13 serotypes in

the 20vPnC group are noninferior to the GMCs for

the corresponding serotypes in the 13vPnC group at 1 month after Dose 3

-To demonstrate that the serotype- specific IgG GMCs for the 7 additional

serotypes in the 20vPnC group are noninferior to the lowest IgG GMCs among the

13 serotypes in the 13vPnC group at 1 month after Dose 3

Secondary outcome

Secondary Pneumococcal Immunogenicity Objective:

- To further describe the immune responses induced by 20vPnC

Secondary Concomitant Immunogenicity Objective

- To further describe the immune responses induced by specific concomitant

vaccine antigens given with 20vPnC or 13vPnC

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Study description

Background summary

2.1 Study Rationale

This study is part of the Phase 3 clinical development program to support the use of 20vPnC in the pediatric population. The purpose of the study is to generate key safety and immunogenicity data to support licensure in this population. The targeted age of the population for this study, infants born at >36 weeks of gestation and *42 to *112 days of age, has been selected as the routinely recommended vaccination schedule for pneumococcal conjugate vaccines and other vaccines in infants, starting at approximately 2 months of age.

The participants will be administered either 20vPnC or 13vPnC in a series of 2 infant doses and 1 toddler dose (at 2, 4, and 11-12 months of age). Data will

also be generated on key routine pediatric vaccines given concomitantly with 20vPnC or 13vPnC.

Study objective

Primary Safety Objective: To describe the safety profile of 20vPnC

Study design

4.1 Overall Design
This Phase 3, multicenter, randomized, double-blind study will be conducted at investigator sites in Europe, and possibly other countries. This study is part of the Phase 3 pediatric clinical development program to support the use of 20vPnC in the pediatric population. The purpose of the study is to generate data on the safety and immunogenicity of 20vPnC in infants when administered in a series of 2 infant doses and 1 toddler dose (at 2, 4, and 11-12 months of age). Data will also be generated on key routine pediatric vaccines given concomitantly with 20vPnC or 13vPnC. 13vPnC will serve as an active comparator.

Approximately 1200 infants >36 weeks of gestation and *42 to *112 days of age at the time of consent by a parent(s)/legal guardian(s) will be enrolled into this study. Participants will be randomized in a 1:1 ratio to receive either 20vPnC or 13vPnC (control vaccine) by site- based randomization. At 2, 4, and 11 to 12 months of age (Doses 1 [Visit 1], 2 [Visit 2], and 3 [Visit 4], respectively), participants will receive the same vaccine (either 20vPnC or 13vPnC) for all 3 doses. Blood will be drawn from all participants for immunogenicity assessments 1 month after Dose 2 (5 months of age), prior to receipt of Dose 3 (11-12 months of age), and 1 month after Dose 3 (13 months of age). A subset of participants (participants at certain investigator sites) will also have blood drawn for immunogenicity assessments prior to Dose 1 and prior to Dose 2.

On Day 1 (Visit 1, Dose 1 vaccination) of the study, participants will be assessed for eligibility and information will be collected, including medical history and vaccine history. Vaccines administered during pregnancy and intrapartum antibiotic use (yes/no) will also be collected (if available). In a subset of participants (participants at selected investigator sites), blood will be drawn prior to Dose 1. All participants will receive Dose 1 of 20vPnC or 13vPnC. The 13vPnC and 20vPnC will be matched in appearance and will be prepared and administered by a site staff member or designee. Specific concomitant vaccination containing DTaP, HBV, IPV, and Hib antigens will also be administered at this visit.
Participants will be observed for 30 minutes after vaccination, and any reactions occurring during that time will be recorded as AEs.

The participant*s parent(s)/legal guardian(s) will be provided with an e-diary (or e-diary application), digital thermometer, and measuring device and instructed to collect prompted local reactions (redness, swelling, and pain at the injection site) and systemic events (fever, decreased appetite, drowsiness/increased sleep, and irritability) occurring 7 days after each vaccination. Use of antipyretic/pain medications will also be prompted for and collected daily in the e-diary for 7 days after vaccination. The participant*s parent(s)/legal guardian(s) will be instructed to contact the study staff if the participant experiences redness or swelling
>14 caliper units, severe pain at the 20vPnC or 13vPnC injection site, or fever >40.0°C (>104.0°F) in the 7 days after vaccination, or has an emergency room visit or hospitalization.

Participants will return for Visit 2 (42 to 63 days after Visit 1).
Participants will be assessed for continued eligibility and information will be collected from the participant*s parent(s)/legal guardian(s) on AEs, including nonserious AEs, SAEs, NDCMCs, and e-diary follow-up (as needed). Concomitant medications used to treat SAEs and NDCMCs will be recorded, as will information on nonstudy vaccinations given since the last visit. An NDCMC is defined as a significant disease or medical condition, not previously identified, that is expected to be persistent or is otherwise long-lasting in its effects. A subset of participants will have blood drawn for immunogenicity assessment at this visit prior to
Dose 2. Dose 2 of 20vPnC or 13vPnC will be administered. Specific concomitant vaccination containing DTaP, HBV, IPV, and Hib antigens will also be administered at this visit. Participants will be observed for 30 minutes after vaccination and any reactions occurring during that time will be recorded as AEs. The participant*s parent(s)/legal guardian(s) will be instructed to collect prompted local reactions and systemic events occurring 7 days after vaccination. Use of antipyretic/pain medications will also be prompted for and collected daily in the e-diary for 7 days after vaccination. The participant*s parent(s)/legal guardian(s) will be instructed to contact the study staff if the participant experiences redness or swelling >14 caliper units, severe pain at the 20vPnC or 13vPnC injection site, or fever >40.0°C (>104.0°F) in the 7 days after vaccination or has an emergency room visit or hospitalization.

Participants will return for Visit 3 (28 to 42 days after Visit 2).
Participants will be assessed for continued eligibility and information will be collected from the participant*s parent(s)/legal guardian(s) on AEs, SAEs, NDCMCs, and e-diary follow-up (as needed). The e-diary will be collected (if applicable). Concomitant medications used to treat SAEs and NDCMCs will be recorded, as will information on nonstudy vaccinations given since the last visit. Blood will be taken for immunogenicity assessment.

Participants will return for Visit 4 (335 to 386 days of age). Participants will be assessed for continued eligibility and information will be collected

from the participant*s parent(s)/legal guardian(s) on SAEs and NDCMCs. Concomitant medications used to treat SAEs and NDCMCs will be recorded, as will information on nonstudy vaccinations given since the last visit. Blood will be taken for immunogenicity assessment prior to vaccination. Dose 3 will be administered at this visit. Specific concomitant vaccine containing DTaP, HBV, IPV, and Hib antigens will also be administered.

Specific vaccines containing MMR and varicella antigens are also to be administered at this visit. The MMR and varicella vaccines are intended to be given to all participants.
However, in case of circumstances due to local practice/recommendations, some sites may not administer them to their participants at Dose 3, in which case MMR and varicella vaccines will be considered nonstudy vaccines. Participants will be observed for 30 minutes after vaccination and any reactions occurring during that time will be recorded as AEs. The participant*s parent(s)/legal guardian(s) will be reissued an e-diary (if applicable). The participant*s parent(s)/legal guardian(s) will be instructed to collect prompted local reactions and systemic events occurring 7 days after vaccination. Use of antipyretic/pain medications will also be prompted for and collected daily in the e-diary for 7 days after vaccination. The participant*s parent(s)/legal guardian(s) will be instructed to contact the study staff if the participant experiences redness or swelling >14 caliper units, severe pain at the 20vPnC or 13vPnC injection site, or fever >40.0°C (>104.0°F) in the 7 days after vaccination, or has an emergency room visit or hospitalization.

All participants will return for Visit 5 (28 to 42 days after Visit 4).
Information will be collected from the participant*s parent(s)/legal guardian(s) on AEs, SAEs, NDCMCs, and e-diary follow-up (as needed).
Concomitant medications used to treat SAEs or NDCMCs will be recorded, as will information on nonstudy vaccinations given since the last visit.
Blood will be taken for immunogenicity assessment. Other licensed nonstudy vaccines may be administered after the blood draw at this visit.

Intervention

6. STUDY INTERVENTION
Study intervention is defined as any investigational intervention(s), marketed product(s), placebo, or medical device(s) intended to be administered to a study participant according to the study protocol.

For the purposes of this protocol, the term investigational product may be used synonymously with study intervention.

Study Intervention(s) Administered
20vPnC is a sterile liquid suspension formulation containing saccharides from pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B,

18C, 19A, 19F, 22F, 23F,
and 33F individually conjugated to CRM197. The vaccine is formulated to contain 2.2 µg of each saccharide, except for 4.4 µg of 6B, per 0.5-mL dose. The vaccine contains 5 mM succinate buffer, 150 mM sodium chloride, 0.02% polysorbate 80, and 125 µg aluminum as aluminum phosphate, per 0.5-mL dose.

13vPnC is a sterile liquid suspension formulation containing saccharides from pneumococcal serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F individually conjugated to CRM197. The vaccine is formulated to contain 2.2 µg of each saccharide, except for 4.4 µg
of 6B, per 0.5-mL dose. The vaccine contains 295 *g succinate buffer, 0.85% sodium chloride, 100 *g polysorbate 80, and 125 µg aluminum as aluminum phosphate, per 0.5-mL dose.

The 13vPnC supply is considered representative of Prevnar 13, as it is manufactured according to the approved Prevnar 13 commercial drug product process using commercially released vaccine drug substances.

20vPnC and 13vPnC, supplied as syringes, are both white suspensions and have a matching appearance.

DTaP, HBV, IPV, and Hib vaccine (supplied as a vial and a prefilled syringe) is a vaccine indicated for active immunization against diphtheria, tetanus, pertussis, hepatitis B caused by all known subtypes of hepatitis B virus, poliomyelitis, and Hib infection, respectively. See the investigational product manual (IP manual) and applicable SRSD.

MMR vaccine (supplied as a vial and prefilled syringe with solvent) is a live virus vaccine for vaccination against measles (rubeola), mumps, and rubella (German measles). See the IP manual and applicable SRSD provided.

Varicella vaccine (supplied as a vial and prefilled syringe with solvent) is a live virus vaccine for vaccination against varicella. See the IP manual and applicable SRSD.

Investigational product will be supplied by Pfizer as prefilled syringes or vials. Each syringe/vial will be packaged in a carton with a label and a tamper-evident seal, and will be labeled as required per country requirement (refer to the IP manual).

Administration
Participants will receive 1 dose of 20vPnC or 13vPnC at each vaccination visit (Visits 1, 2, and 4) in accordance with the study*s SoA.

Participants will also receive 1 dose of DTaP, HBV, IPV, and Hib vaccine at Visits 1, 2, and

4. Participants are also to receive MMR and varicella vaccines at Visit 4 in accordance with the study*s SoA. The MMR and varicella vaccines are intended to be given to all participants. However, in case of circumstances due to local practice/recommendations, some sites may not administer them to their participants at Dose 3, in which case MMR and varicella vaccines will be considered nonstudy vaccines. If MMR and varicella vaccines are not given with Dose 3, and administered based on local practice/recommendations, they are not to be given during the interval <28 days before Dose 3 through the Visit 5 blood draw after Dose 3.

20vPnC and 13vPnC should be administered intramuscularly by injecting 0.5 mL into the anterolateral thigh muscle of the left leg at the vaccination visits.

The DTaP, HBV, IPV, and Hib vaccine will be administered concomitantly with 20vPnC or 13vPnC and must be given in a limb other than the site of administration of 20vPnC or 13vPnC, as appropriate for the age of the child and the route of administration (ie, intramuscular or subcutaneous).

The MMR and varicella vaccines will be administered concomitantly with 20vPnC or 13vPnC and must be given in a limb other than the site of administration of 20vPnC or 13vPnC, as appropriate for the age of the child and the route of administration (ie, intramuscular or subcutaneous).

Standard vaccination practices must be observed and vaccine must not be injected into blood vessels. Appropriate medication and other supportive measures for management of an acute hypersensitivity reaction should be available in accordance with local guidelines for standard immunization practices.

Administration of investigational products should be performed by an appropriately qualified, Good Clinical Practice (GCP)-trained, and vaccine-experienced member of the study staff (eg, physician, nurse, physician*s assistant, nurse practitioner, pharmacist, or medical assistant) as allowed by local, state, and institutional guidance.

Investigational product administration details will be recorded on the case report form (CRF).

Study burden and risks

Please refer to the subject information sheet and the Reference Safety Information (RSI) in the Investigator's Brochure for a complete overview of the risks of participation.

Contacts

Public
Pfizer

235 East 42nd Street 235 East 42nd Street
New York NY 10017
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Scientific
Pfizer

235 East 42nd Street 235 East 42nd Street
New York NY 10017
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

Section 5.1 in protocol
1. Male or female infants born at >36 weeks of gestation and 2 months of age (*42 to *112 days) at the time of consent (the day of birth is considered day of life 1).
2. Participants whose parent(s)/legal guardian(s) are willing and able to comply with all scheduled visits, treatment plan, and other study procedures.
3. Healthy infants determined by clinical assessment, including medical history and clinical judgment, to be eligible for the study.
4. Expected to be available for the duration of the study and whose parents(s)/legal guardian can be contacted by telephone during study participation.
5. Participants whose parent(s)/legal guardian(s) is capable of giving signed informed consent as described in Appendix 1, which includes compliance with the

requirements and restrictions listed in the ICD and in this protocol.

Exclusion criteria

Section 5.2 in protocol

1. History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of investigational product or any diphtheria toxoid*containing vaccine.
2. Significant neurological disorder or history of seizure including febrile seizure or significant stable or evolving disorders such as cerebral palsy, encephalopathy, hydrocephalus, or other significant disorders. Does not include resolving syndromes due to birth trauma, such as Erb*s palsy and/or hypotonic-hyporesponsive episodes.
3. Major known congenital malformation or serious chronic disorder
4. History of microbiologically proven invasive disease caused by S pneumonia
5. Known or suspected immunodeficiency or other conditions associated with immunosuppression, including, but not limited to, immunoglobulin class/subclass deficiencies, DiGeorge syndrome, generalized malignancy, human immunodeficiency virus (HIV) infection, leukemia, lymphoma, or organ or bone marrow transplant.
6. Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection.
7. Congenital, functional, or surgical asplenia
8. Other acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the participant inappropriate for entry into this study.
9. Previous vaccination with any licensed or investigational pneumococcal vaccine, or planned receipt through study participation.
10. Prior receipt of diphtheria, tetanus, pertussis, poliomyelitis, and/or Hib vaccine
11. Currently receives treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, or planned receipt through the last blood draw. If systemic corticosteroids have been administered short term (<14 days) for treatment of an acute illness, participants should not be enrolled into the study until corticosteroid therapy has been discontinued for at least 28 days before investigational product administration. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin, eyes, or ears) corticosteroids are permitted.
12. Receipt of blood/plasma products or immunoglobulins (including hepatitis B immunoglobulin) since birth or planned receipt through the last planned blood draw in the study (Visit 5, 13-month visit).
13. Participation in other studies involving investigational drug(s),

investigational vaccines, or investigational devices within 28 days prior to study entry and/or during study participation or intrauterine exposure to investigational vaccines. Participation in purely observational studies is acceptable.
14. Children or grandchildren who are direct descendants of investigator site staff members or Pfizer employees who are directly involved in the conduct of the study

Study design

Design

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	08-04-2021
Enrollment:	40
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	20-valent Pneumococcal Conjugate Vaccine (20vPnC)
Product type:	Medicine
Brand name:	Infanrix Hexa
Generic name:	J07CA09
Registration:	Yes - NL intended use
Product type:	Medicine

Brand name:	M-M-RVAXPRO
Generic name:	J07BD52
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Prevenar 13
Generic name:	J07AL02
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Varilrix 10 3.3 PFU/0.5ml, powder and solvent for solution for injection
Generic name:	J07B K01

Ethics review

Approved WMO Date:	22-06-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	12-10-2020
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-02-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	24-03-2021
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	15-09-2021

Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	30-09-2021
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
Other	17980
EudraCT	EUCTR2019-003306-27-NL
CCMO	NL74110.000.20

Study results

Date completed:	11-03-2022
Results posted:	18-11-2022
Actual enrolment:	14

First publication
08-10-2022