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SYNOPSIS

Study Title: Final Report: A Phase 3, Randomized, Double-Blind, Third-Party-Unblinded Trial to Evaluate the Safety and Immunogenicity of a 20-Valent Pneumococcal Conjugate Vaccine in Pneumococcal Vaccine-Naïve Adults 60 Years of Age and Older in Japan, Korea, and Taiwan

Study Number: B7471009

Regulatory Agency or Public Disclosure Identifier Number: NCT04875533

Study Phase: Phase 3

Name of Study Intervention: 20-valent Pneumococcal Conjugate Vaccine (20vPnC)

Name of Sponsor/Company: Pfizer Inc.

CSR Version and Report Date: Final CSR (LPLV) Version 1.0; 13 March 2023

Number of Study Center(s) and Investigator(s):

This study was conducted at 28 sites in Japan, Korea, and Taiwan.

A list of study centers and investigators involved in this study is provided in Appendix 16.1.4.1.

Publications:

None

Study Period:

Study Initiation Date (Frist Participant First Visit [FPFV]): 14 June 2021

Study Completion Date (Last Participant Last Visit [LPLV]): 13 May 2022

This study was neither discontinued nor interrupted.

Rationale:

Pfizer has developed a 20vPnC candidate to expand protection against pneumococcal disease beyond that covered by current pneumococcal vaccines in children and adults. 20vPnC has the same composition as 13vPnC (Prevenar 13®) but contains an additional 7 pneumococcal conjugates to protect against serotypes responsible for a substantial burden of remaining pneumococcal disease. 20vPnC uses the same platform and contains the same excipients as 13vPnC. 20vPnC was evaluated in a clinical development program in adults, and data from overseas Phase 3 studies in participants 18 years of age and older provided evidence that the

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safety profile was acceptable and similar to 13vPnC and induced immune responses that supported licensure for an adult (≥18 years of age) indication in the US, EU, Great Britain, and Canada.

The purpose of this study was to assess the safety and immunogenicity of 20vPnC in adults ≥60 years of age in Japan, Korea, and Taiwan and to help support use of 20vPnC in the adult population in these countries/regions.

Objectives, Estimands and Endpoints:

Table S1. Objectives, Estimands and Endpoints

Type	Objective	Estimands	Endpoints
Primary			
Safety	To describe the safety profile of 20vPnC.	In participants receiving at least 1 dose of study intervention and having safety follow-up after vaccination from each vaccine group: • The percentage of participants reporting prompted local reactions within 10 days after the first vaccination (20vPnC or 13vPnC). • The percentage of participants reporting prompted systemic events within 7 days after the first vaccination (20vPnC or 13vPnC). • The percentage of participants reporting AEs within 1 month after vaccination with 20vPnC or 13vPnC. • The percentage of participants reporting SAEs within 1 month after vaccination with 20vPnC or 13vPnC.	• Prompted local reactions (redness, swelling, and pain at the injection site) • Prompted systemic events (fever, headache, fatigue, muscle pain, and joint pain). • AEs • SAEs

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Table S1. Objectives, Estimands and Endpoints

Immunogenicity	To demonstrate that the immune responses to the 13 serotypes in 13vPnC (1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F) induced by 20vPnC are noninferior to the immune response induced by 13vPnC.	In participants in compliance with the key protocol criteria (evaluable participants): • For each of the 13 serotypes: GMR of serotype-specific OPA titers 1 month after 20vPnC to the serotype-specific OPA titers 1 month after 13vPnC.	• Serotype-specific OPA titers
	To demonstrate that the immune responses to the 7 additional serotypes in 20vPnC (8, 10A, 11A, 12F, 15B, 22F, and 33F) induced by 20vPnC are noninferior to the immune response induced by PPSV23.	In evaluable participants: • For each of the 7 additional serotypes: GMR of serotype-specific OPA titers 1 month after 20vPnC to the serotype-specific OPA titers 1 month after PPSV23.	• Serotype-specific OPA titers

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Table S1. Objectives, Estimands and Endpoints

Secondary			
Immunogenicity	To describe the immune responses to all 20 serotypes induced by 20vPnC.	In evaluable participants for each of the 20 serotypes: • Serotype-specific OPA GMTs 1 month after vaccination* in each vaccine group. • GMFRs in serotype-specific OPA titers from before to 1 month after vaccination* in each vaccine group. • Percentage of participants with ≥4-fold rise in serotype-specific OPA titers from before to 1 month after vaccination* in each vaccine group. • Percentage of participants with serotype-specific OPA titers greater than or equal to the LLOQ 1 month after vaccination* in each vaccine group.	• Serotype-specific OPA titers

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Table S1. Objectives, Estimands and Endpoints

Safety	To describe the reactogenicity profile of PPSV23 following 13vPnC in Japanese participants (only for participants enrolled at Japan sites).	In participants receiving at least 1 dose of study intervention and having safety follow-up after vaccination from each vaccine group: • The percentage of participants reporting prompted local reactions within 10 days after the second vaccination (PPSV23 or saline). • The percentage of participants reporting prompted systemic events within 7 days after the second vaccination (PPSV23 or saline).	• Prompted local reactions (redness, swelling, and pain at the injection site) • Prompted systemic events (fever, headache, fatigue, muscle pain, and joint pain)

* Note: "1 month after vaccination" refers to 1 month after vaccination with 20vPnC (20vPnC/saline group), or 1 month after vaccination with 13vPnC for the 13 matched serotypes or PPSV23 for the 7 additional serotypes (13vPnC/PPSV23 group).
Abbreviations: 13vPnC = 13-valent pneumococcal conjugate vaccine, 20vPnC = 20-valent pneumococcal conjugate vaccine, AE = adverse event, GMR = geometric mean ratio, LLOQ = lower limit of quantitation, OPA = opsonophagocytic activity, PPSV23 = 23-valent pneumococcal polysaccharide vaccine, SAE = serious adverse event,

Methodology:

This was a Phase 3, multicenter, randomized, double-blind, third-party-unblinded study. Approximately 1400 participants 60 years of age and older at enrollment were randomized into 2 groups in a 1:1 ratio by center-based randomization stratified by age (60 to 64 year of age and ≥65 years of age): 20vPnC/saline group and 13vPnC/PPSV23 group. Each participant was randomized to receive either 20vPnC or 13vPnC (control vaccine) at Vaccination 1. Participants who received 20vPnC at Vaccination 1 in the 20vPnC/saline group received saline at Vaccination 2 (1 month after Vaccination 1). Participants who received 13vPnC at Vaccination 1 in the 13vPnC/PPSV23 group received PPSV23 at Vaccination 2 (1 month after Vaccination 1).

Immunogenicity Evaluations

Blood samples were collected from all participants at Visit 1 (prior to administration of 20vPnC or 13vPnC), at Visit 2 (prior to administration of saline or PPSV23), and at Visit 3.

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OPA titers for serotypes present in 20vPnC (1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F) were determined on all sera collected prior to study vaccination and 1 month (28 to 42 days) after Vaccination 1. OPA titers for the 7 additional serotypes only were determined on sera collected 1 month (28 to 42 days) after Vaccination 2.

Safety Evaluations

Participants recorded local reactions for 10 days, and systemic events and antipyretic/pain medication usage for 7 days, each evening following Vaccination 1 (Day 1 was the day of vaccination) using an e-diary (in a provisioned device or an application on a personal device). For Japan sites only, the participants were asked to complete an e-diary after Vaccination 2.

AEs and SAEs were reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative). The AEs and SAEs were collected from the time the participant provided informed consent, through and including Visit 3.

Number of Participants (planned and analyzed):

This study planned to enroll approximately 1400 participants. A total of 1425 participants were randomized in the study with 1421 participants included in the safety population, 1377 participants included in the 13-matched immunogenicity population and 1382 participants in the evaluable 7-additional immunogenicity population.

Diagnosis and Main Criteria for Inclusion and Exclusion:

Key inclusion/exclusion criteria were as follows:

Inclusion Criteria:

- Male or female participants ≥60 years of age at the time of consent.
- Adults determined by clinical assessment, including medical history and clinical judgment, to be eligible for the study, including adults with preexisting stable disease, defined as disease not requiring significant change in therapy in the previous 6 weeks or hospitalization for worsening disease within 12 weeks before receipt of study intervention.

  For adults 60 through 64 years of age enrolled at Japan sites only:

  - Participants were required to have a preexisting chronic stable disease with an elevated risk for pneumococcal disease (eg, chronic cardiac disease, chronic pulmonary disease, chronic hepatic disease, diabetes mellitus, and/or chronic renal disorders).

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Exclusion Criteria:

- History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of 20vPnC, 13vPnC, or any other diphtheria toxiod-containing vaccine or PPSV23.

- Serious chronic disorder, including metastatic malignancy, severe COPD requiring supplemental oxygen, end-stage renal disease with or without dialysis, cirrhosis of the liver, clinically unstable cardiac disease, or any other disorder that, in the investigator's opinion, excludes the participant from participating in the study.

- Previous vaccination with any licensed or investigational pneumococcal vaccine, or planned receipt through study participation.

Study Interventions, Dose, Mode of Administration, and Batch Number(s):

Participants received either 20vPnC or 13vPnC (control vaccine) at Vaccination 1. Participants who received 20vPnC at Vaccination 1 received saline at Vaccination 2. Participants who received 13vPnC at Vaccination 1 received PPSV23 at Vaccination 2.

At Vaccination 1 (Visit 1), a 0.5-mL dose of 20vPnC or 13vPnC was administered intramuscularly in the deltoid muscle of the nondominant arm by a blinded site staff member. At Vaccination 2 (Visit 2), a 0.5-mL dose of saline or PPSV23 was prepared and administered by third-party unblinded site staff member(s) and was administered intramuscularly in the deltoid muscle of the nondominant arm to blinded participants.

The manufacturing lot numbers for the study interventions dispensed in this study are provided in Table S2.

Table S2. Study Intervention Administered

Investigational Product	Manufacturer	Vendor Lot Number	Pfizer Lot Number[a]
20vPnC	Pfizer	DW1636	20-002030
13vPnC	Pfizer	DN3806	20-001731
PPSV23	Merck & Co., Inc	T032855	20-AE-00068
		T038629	21-AE-00071
		T032852	21-AE-00164
Placebo (0.9% Sodium Chloride for Injection)	Pfizer	CW7633	19-004626

a. Lot number assigned to the investigational product by Pfizer Global Clinical Supply.
Protocol B7471009 Investigational Product Lot Numbers Table – Version 1.0, 10Nov2022.

Duration of Study Intervention:

Each participant was in the study for approximately 2 months.

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Summary of Results:

Demographic and Other Baseline Characteristics:

A total of 1425 participants were randomized in the study to receive either 20vPnC/saline or 13vPnC/PPSV23, 1421 (99.7%) received Vaccination 1, 1394 (97.8%) received Vaccination 2, and 1391 (97.6%) completed all visits in the study. Disposition was similar in the 2 vaccine groups and the most common reason for withdrawal was "withdrawal by participant".

The demographic characteristics and smoking history of the safety population were generally similar in the 20vPnC/saline and 13vPnC/PPSV23 groups. There were 832, 349, and 240 participants in Japan, Korea, and Taiwan, respectively. There were more male than female participants. The majority of the participants (59%) never smoked.

Immunogenicity Results:

- The immune responses to all 13-matched vaccine serotypes induced by 20vPnC were noninferior to those induced by 13vPnC.
- The immune responses to 6 of the 7 additional vaccine serotypes induced by 20vPnC were noninferior to those induced by PPSV23.
- Serotype 8 narrowly missed the statistical NI criterion 1 month after 20vPnC. However, the serotype 8 immune response is expected to be similarly protective as the 19 vaccine serotypes in 20vPnC that met NI, based on OPA GMT, GMFR, proportion of participants with a ≥4-fold rise in OPA titers, and proportion of participants with OPA titers ≥ LLOQ.
- Robust immune responses to all 20 vaccine serotypes 1 month after 20vPnC were observed in adults ≥60 years of age, based on OPA GMTs, GMFRs, proportions of participants with a ≥4-fold-rise in OPA titers, and proportions of participants with OPA titers ≥ LLOQ.
- Immune responses to all 20 vaccine serotypes were increased after 20vPnC for each of the 3 countries.

Safety Results:

- The proportions of participants who reported prompted local reactions and systemic events were similar in the 2 groups. Most local reactions and systemic events were mild or moderate in severity.
- Rates of AEs within 1 month after 20vPnC or 13vPnC were similar in the 2 groups. No safety concerns were identified.
- The proportions of participants reporting any SAEs were low and similar in the 2 groups. [redacted]

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[redacted] No SAEs were considered related to 20vPnC in this study.

Conclusions:

20vPnC was observed to have a tolerability and safety profile similar to 13vPnC. Based on the robust immune responses and comparability to licensed pneumococcal vaccines (13vPnC and PPSV23) for applicable serotypes, these data support that 20vPnC will be protective against pneumococcal disease due to the 20 serotypes in adults 60 years of age and older in Japan, Korea, and Taiwan.