Protocol B7471026

A PHASE 3, RANDOMIZED, DOUBLE-BLIND TRIAL TO DESCRIBE THE SAFETY AND IMMUNOGENICITY OF 20-VALENT PNEUMOCOCCAL CONJUGATE VACCINE WHEN COADMINISTERED WITH A BOOSTER DOSE OF BNT162b2 IN ADULTS 65 YEARS OF AGE AND OLDER

Statistical Analysis Plan

Version: 1

Date: 30 Jun 2021

[redacted]

[redacted]

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APPENDICES

1. VERSION HISTORY

Table 1. Summary of Changes

Version/ Date	Associated Protocol Amendment	Rationale	Specific Changes
1 30 Jun 2021	Original protocol 08 Apr 2021	N/A	N/A

2. INTRODUCTION

This SAP provides the detailed methodology for summary and statistical analyses of the data collected in Study B7471026. This document may modify the plans outlined in the protocol; however, any major modifications of the primary endpoint definition or its analysis will also be reflected in a protocol amendment.

2.1. Study Objectives, Endpoints, and Estimands

The estimands corresponding to each primary, secondary, CCI [redacted] objective are described in Table 2. In the primary safety objective evaluations, missing AE start dates will be imputed according to Pfizer safety rules (Section 5.3). No other missing information will be imputed in the safety analysis.

The estimands to evaluate the immunogenicity objectives are based on the evaluable population (see Section 4 or definition). Missing serology results will not be imputed. Immunogenicity results that are below the LLOQ will be set to 0.5 × LLOQ in the analysis.

Table 2. List of Primary, Secondary, CCI [redacted] Objectives, Endpoints, and Estimands

Objectives	Endpoints	Estimands
Primary		
Safety		
To describe the safety profile of 20vPnC and a booster dose of BNT162b2 when coadministered or administered alone	• Prompted local reactions at each injection site (redness, swelling, and pain at the injection site) • Prompted systemic events (fever, headache, chills, fatigue, muscle pain, and joint pain) • AEs • SAEs •	In participants receiving at least 1 dose of study intervention and having safety follow-up after vaccination, the percentage of participants reporting: • Prompted local reactions at each injection site for up to 10 days following vaccination • Prompted systemic events for up to 7 days following vaccination • AEs from vaccination at Visit 1 through approximately 1 month after vaccination • SAEs from vaccination at Visit 1 through 6 months after vaccination

Table 2. List of Primary, Secondary, CCI [redacted] Objectives, Endpoints, and Estimands

Objectives	Endpoints	Estimands
Secondary		
Pneumococcal Immunogenicity		
To describe the immune response elicited by 20vPnC when coadministered with a booster dose of BNT162b2 or when administered alone	• Pneumococcal OPA titers	In participants in compliance with the key protocol criteria (evaluable participants): • OPA GMTs approximately 1 month after vaccination
BNT162b2 Immunogenicity		
To describe the immune response elicited by a booster dose of BNT162b2 when coadministered with 20vPnC or when administered alone	• Full-length S-binding IgG levels	In evaluable participants: • GMCs of full-length S-binding IgG levels approximately 1 month after vaccination • GMFR in full-length S-binding IgG levels from before to approximately 1 month after vaccination

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2.2. Study Design

This Phase 3, multicenter, randomized, double-blind study will be conducted at investigator sites in the US. The purpose of this study is to describe the safety and immunogenicity of 20vPnC and a booster dose of BNT162b2 when administered together at the same visit compared to each of the vaccines given alone in adults ≥65 years of age.

Approximately 600 participants ≥65 years of age who received 2 doses of 30 µg BNT162b2 at least 6 months previously in Study C4591001 will be randomized at a 1:1:1 ratio to 1 of 3 groups with center-based randomization: the Coadministration group (20vPnC + BNT162b2), the 20vPnC-only group (20vPnC + saline), and the BNT162b2-only group (BNT162b2 + saline), stratified by prior pneumococcal vaccine status (no previous pneumococcal vaccine [naïve] or receipt of at least 1 dose of a pneumococcal vaccine [experienced]).

Blood will be collected at Visit 1 (prior to vaccination) and at Visit 2 (1 month after Visit 1), to assess immunogenicity. Participants will be observed for 30 minutes after vaccination and any reactions occurring during that time will be recorded as AEs.

Prompted local reactions (redness, swelling, and pain at the injection site) occurring at each injection site within 10 days after vaccination (where Day 1 is the day of vaccination) and prompted systemic events (fever, headache, chills, fatigue, muscle pain, and joint pain) and use of antipyretic/pain medications occurring within 7 days after vaccination (where Day 1 is the day of vaccination) will be collected via an e-diary after vaccination.

AEs will be collected from the signing of informed consent through Visit 2 (approximately 1 month after Visit 1). SAEs will be collected from the signing of informed consent through 6 months after Visit 1.

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

3.1. Primary Endpoints

3.1.1. Primary Safety Endpoints

- Prompted local reactions (redness, swelling, and pain at the injection site) within 10 days at each injection site.
- Prompted systemic events (fever, headache, chills, fatigue, muscle pain, and joint pain) within 7 days after vaccination.
- AEs within 1 month after vaccination.
- SAEs up to 6 months after vaccination.

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Severity and Maximum Severity

Redness and swelling will be measured and recorded in measuring device units (range: 1 to 21 and >21), and then categorized during analysis as mild, moderate, or severe based on the grading scale in Table 3. Measuring device units will be converted to centimeters according to the following scale: 1 measuring device unit = 0.5 cm. Pain at the vaccine injection site will be assessed by the participant as mild, moderate, or severe according to the grading scale in Table 3.

Table 3. Grading Scales for Local Reactions

Local Reaction	GRADE 1 Mild	GRADE 2 Moderate	GRADE 3 Severe	GRADE 4[a]
Redness	5 to 10 measuring device units = >2.0 to 5.0 cm	11 to 20 measuring device units = >5.0 to 10.0 cm	>20 measuring device units = >10.0 cm	Necrosis or exfoliative dermatitis
Swelling	5 to 10 measuring device units = >2.0 to 5.0 cm	11 to 20 measuring device units = >5.0 to 10.0 cm	>20 measuring device units = >10.0 cm	Necrosis
Pain at injection site	Does not interfere with activity	Interferes with activity	Prevents daily activity[b]	Emergency room visit or hospitalization for severe pain at the injection site

Abbreviations: CRF = case report form; e-diary = electronic diary.

Note: If the size of the redness and/or swelling falls between 2 measuring device units, the higher measuring device unit number will be recorded in the e-diary.

a. Grade 4 assessment should be made by the investigator; Grade 4 will not be collected in the e-diary but will be collected as an AE on the CRF. The severity of the local reaction should be graded using the AE severity grading scale.

b. Prevents daily activity, eg, results in missed days of work or is otherwise incapacitating.

For each local reaction after vaccination at each injection site, the maximum severity grade will be derived for the e-diary collection period (Day 1 through Day 10, where Day 1 is the day of vaccination) as follows:

> maximum severity grade = highest grade (maximum severity) within 10 days after vaccination (Day 1 through Day 10) among severity grades reported for that local reaction in the e-diary.

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The systemic events of headache, fatigue, chills, muscle pain, and joint pain will be assessed by participants as mild, moderate, or severe according to the grading scale in Table 4. Grade 4 will not be collected in the e-diary but will be collected as an AE on the CRF.

Table 4. Grading Scales for Systemic Events

	Mild Grade 1	Moderate Grade 2	Severe Grade 3[a]	Grade 4[b]
Fatigue (tiredness)	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	Emergency room visit or hospitalization for severe fatigue
Headache	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	Emergency room visit or hospitalization for severe headache
Chills	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	Emergency room visit or hospitalization for severe chills
Muscle pain	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	Emergency room visit or hospitalization for severe muscle pain

Table 4. Grading Scales for Systemic Events

	Mild Grade 1	Moderate Grade 2	Severe Grade 3[a]	Grade 4[b]
Joint pain	Does not interfere with activity	Some interference with activity	Prevents daily routine activity	Emergency room visit or hospitalization for severe joint pain

Abbreviations: CRF = case report form; e-diary = electronic diary.

a. Prevents daily routine activity, eg, results in missed days of work or is otherwise incapacitating; includes use of narcotics for analgesia.

b. Grade 4 assessment should be made by the investigator; Grade 4 systemic events will not be collected in the e-diary but will be collected as AEs on the CRF. The severity of the systemic event should be graded using the AE severity grading scale.

Oral temperature will be collected in the evening daily for 7 days following vaccination (Days 1 through 7, where Day 1 is the day of vaccination) and at any time during the 7 days that fever is suspected. Fever is defined as an oral temperature of ≥100.4°F (≥38.0°C). The highest temperature for each day will be recorded in the e-diary. In the event of a fever on Day 7, temperature will be collected daily until fever has resolved (1 day of temperature <100.4°F [<38.0°C]) in order to collect a stop date in the CRF. Temperature will be measured and recorded to 1 decimal place.

Temperatures recorded in degrees Fahrenheit will be programmatically converted to degrees Celsius for reporting. Fever will be grouped into ranges for the analysis according to Table 5.

Table 5. Ranges for Fever

≥38.0°C to 38.4°C
>38.4°C to 38.9°C
>38.9°C to 40.0°C
>40.0°C

Note: Fever is defined as temperature ≥38.0°C.

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[redacted]

3.1.1.4. Adverse Events

AEs will be categorized according to MedDRA terms. AEs will be collected from the signing of the ICD through Visit 2 (approximately 1 month after Visit 1). The primary-endpoint AEs within 1 month after vaccination will be summarized by SOC and PT on a participant level.

This primary endpoint will be supported by summaries and listings of related AEs, severe AEs, and immediate AEs (start time is within the first 30 minutes after vaccination).

Missing AE start dates will be imputed following the Pfizer data standard rules as described in Section 5.3.

3.1.1.5. Serious Adverse Events

SAEs will be categorized according to MedDRA terms. SAEs will be collected from the signing of the ICD through the end of the study and will be reported from vaccination through 1 month and also through 6 months after vaccination.

3.2. Secondary Endpoints

3.2.1. Secondary Pneumococcal Immunogenicity Endpoint

- Pneumococcal serotype-specific OPA titers approximately 1 month after vaccination.

OPA titers for the 20 pneumococcal serotypes (1, 3, 4, 5, 6A, 6B, 7F, 8, 9V, 10A, 11A, 12F, 14, 15B, 18C, 19A, 19F, 22F, 23F, and 33F) will be measured in sera collected at Visit 1 (before vaccination) and Visit 2 (1 month after vaccination) from the Coadministration and 20vPnC-only groups. Participants from these 2 groups will be identified for OPA testing by an independent unblinded statistician. Further details will be described in a memo to the unblinded statistician before any testing proceeds.

OPA titers above the LLOQ are considered accurate and their quantitated values will be reported. OPA titers below the corresponding LLOQ or denoted as BLQ will be set to 0.5 × LLOQ for analysis. Missing assay results will not be imputed.

3.2.2. Secondary BNT162b2 Immunogenicity Endpoints

- Full-length S-binding IgG levels approximately 1 month after vaccination.

- Full-length S-binding IgG level fold rises from before vaccination to approximately 1 month after vaccination. The fold rises will be the ratio of full-length S-binding IgG levels at Visit 2 to those at Visit 1.

IgG levels will be measured in the SARS-CoV-2 full-length S-binding assay in sera collected at Visits 1 and 2 from the Coadministration and BNT162b2-only groups. Participants from these 2 groups will be identified for testing by an independent unblinded statistician. Further details will be described in a memo to the unblinded statistician before any testing proceeds.

Results will be reported as IgG concentrations. IgG concentrations above the LLOQ are considered accurate and their quantitated values will be reported. Values below the LLOQ, denoted as BLQ, will be set to 0.5 × LLOQ for analysis.

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[redacted]

3.4. Baseline and Other Variables

Day 1 is defined as the day of vaccination at Visit 1. Measurements or samples collected prior to vaccination on Day 1 are considered the baseline data for the assessments.

The following variables will be summarized as part of the baseline characteristics:

- Demographics
- Medical history
- C [redacted]

[redacted]

[redacted]

- BMI
- [redacted]
- BNT162b2 vaccine history

[redacted]

- [redacted]

3.4.1. Demographics and Baseline Characteristics

The demographic variables are age at vaccination at Visit 1 (in years), sex (male or female), race (Black or African American, American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, White, multiracial, and not reported), and ethnicity (Hispanic or Latino[a] or of Spanish origin, not Hispanic or Latino[a] or of Spanish origin, and not reported). In cases where more than 1 category is selected for race, the participant would be counted under the category "multiracial" for analysis.

Age at the first vaccination in years will be derived based on the participant's birthday. For example, if the vaccination date is 1 day before the participant's 70th birthday, the participant is considered to be 69 years old. For participants who were randomized but not vaccinated, the randomization date will be used in place of the date of the first vaccination for age calculation. If the randomization date is also missing, then the informed consent date will be used for age calculation.

BMI will be calculated as: BMI = weight (kg) / [height (m)]^2, and classified as 2 BMI groups: <30 kg/m^2 and ≥30 kg/m^2.

[redacted]

[redacted]

3.4.3. Nonstudy Vaccines and Concomitant Medications

The name and date of administration of [redacted] prior 2 BNT162b2 vaccinations received in Study C4591001, and all nonstudy vaccinations received from the time of signing of the ICD through Visit 2 will be listed. Concomitant medications will be recorded only if they were used to treat SAEs from the time of signing of the ICD through Visit 3. Concomitant and prior vaccines and concomitant medications will be coded using the WHO Drug Dictionary.

3.5. Safety Endpoints

Local reactions, systemic events, AEs, and SAEs have been described above (Section 3.1.1) in the Primary Safety Endpoint section (Section 6.1.1).

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

Analysis populations are defined for the statistical analysis of safety and immunogenicity results in the table below. For the specified criteria in each population definition that are not associated with unblinded information (vaccination as randomized or as actually received), data for all participants will be assessed to determine if participants meet the criteria for inclusion in each analysis population prior to unblinding and releasing the database for the specified analysis, and the classifications will be documented per SOPs.

Population	Description
Enrolled	All participants who have a signed ICD.
Randomized	All participants who are assigned a randomization number in the IWR system.
Evaluable immunogenicity	All eligible randomized participants who receive the study intervention(s) as assigned at Visit 1, have at least 1 valid immunogenicity result from the blood sample collected within 20 to 49 days after vaccination(s) at Visit 1, and have no other major protocol deviations as determined by the clinician. In the analysis for BNT162b2 immunogenicity endpoints based on the evaluable immunogenicity population, data from participants with documented SARS-CoV-2 infection up to 1 month after vaccination with BNT162b2 will be excluded.

Population	Description
	Participants will be grouped according to the vaccine as randomized in the analysis based on the evaluable immunogenicity population.
CCI	[redacted]
Safety	All participants who receive at least 1 dose of the study intervention and have safety follow-up after vaccination. Participants will be analyzed according to the vaccine as administered in the analysis based on the safety population.

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E-diary data will be summarized among those in the safety population who report any e-diary data.

5. GENERAL METHODOLOGY AND CONVENTIONS

5.1. Hypotheses and Decision Rules

There are no formal comparisons and the study is not designed or powered for hypothesis testing.

5.2. General Methods

Time points for local reactions and systemic events refer to data within 10 days and 7 days, respectively, after vaccination.

Prompted local reactions, prompted systemic events, and AEs will be summarized after vaccination at Visit 1, by vaccine group.

CIs for all endpoints in the statistical analysis will be presented as 2-sided at the 95% level.

5.2.1. Analyses for Binary Data

Descriptive statistics for categorical variables (eg, proportions) are the percentage (%), the numerator (n) and the denominator (N) used in the percentage calculation, and the 95% CI where applicable.

The exact 95% CI for binary endpoints for each group will be computed using the F distribution (Clopper-Pearson).[1] The 95% CI for the between-group difference for binary endpoints will be calculated using the Miettinen and Nurminen[2] method.

5.2.2. Analyses for Continuous Data

Unless otherwise stated, descriptive statistics for continuous variables are n, mean, median, standard deviation, minimum, and maximum.

5.2.2.1. Geometric Mean

For immunogenicity results of serotype-specific OPA titers, full-length S-binding IgG levels CCI the geometric means will be computed along with associated 95% CIs. The GMTs/GMCs and associated 2-sided 95% CIs will be calculated as the means and CIs of the assay results on the natural logarithmic scale based on the t-distribution, and then exponentiating the results.

5.2.2.2. Geometric Mean Fold Rises

GMFRs will be calculated as the mean of the difference of logarithmically transformed assay results (later minus earlier) and exponentiating back to the original units. The associated 2-sided 95% CIs will be computed by exponentiating the CIs using Student's t-distribution for the mean difference on the natural log scale.

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5.3. Methods to Manage Missing Data

A partial AE start date (missing day, missing both month and day) will be imputed by assigning the earliest possible start date using all available information, such as the stop date of the AE and the vaccination date(s) from the same participant, following the Pfizer standard of handling incomplete AE start date. A complete missing start date for an AE is not allowed in the data collection.

The LLOQ for each assay will be provided by Vaccine Research and Development as part of the electronic data transfer or within the Clinical Testing Completion Memo prior to any statistical analysis of immunogenicity data. Assay results above the LLOQ will be reported, and values below the LLOQ, denoted as BLQ, will be set to 0.5 × LLOQ for analysis.

No additional imputation will be applied unless stated otherwise (see Section 3).

6. ANALYSES AND SUMMARIES

6.1. Primary Endpoint

6.1.1. Primary Safety Endpoint

6.1.1.1. Prompted Local Reactions

Prompted local reactions at each injection site after vaccination at Visit 1 will be summarized by vaccination group.

6.1.1.1.1. Main Analysis

- Estimand: The percentage of participants reporting prompted local reactions (redness, swelling, and pain at the injection site) at each injection site within 10 days after vaccination (Section 2.1).
- Analysis set: Safety population (Section 4).
- Analysis time point: Within 10 days after vaccination.
- Analysis methodology: Descriptive statistics.
- Intercurrent events and missing data: Missing values will not be imputed. CCI [redacted]
- Reporting results: The count and percentage of participants with the indicated endpoint and the associated 2-sided 95% Clopper-Pearson CI for each local reaction and "any local reaction" after vaccination at each injection site in each vaccine group will be presented by maxium severity level. The denominator used in the percentage calculation will be the number of participants with any e-diary data reported after vaccination.

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[redacted]

6.1.1.2. Prompted Systemic Events

Prompted systemic events after vaccination at Visit 1 will be summarized by vaccine group.

6.1.1.2.1. Main Analysis

- Estimand: The percentage of participants reporting prompted systemic events (fever, headache, chills, fatigue, muscle pain, and joint pain) within 7 days after vaccination (Section 2.1).
- Analysis set: Safety population (Section 4).
- Analysis time point: Within 7 days after vaccination.
- Analysis methodology: Descriptive statistics.
- Intercurrent events and missing data: Missing values will not be imputed. CCI [redacted]
- Reporting results: The count and percentage of participants with the indicated endpoint and the associated 2-sided Clopper-Pearson 95% CI for each systemic event and "any systemic event" after vaccination in each vaccine group will be presented by maxium severity levels. The denominator used in the percentage calculation will be the number of participants with any e-diary data reported after vaccination.

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[redacted]

6.1.1.3. Adverse Events

AEs from vaccination at Visit 1 through approximately 1 month after vaccination will be summarized.

6.1.1.3.1. Main Analysis

- Estimand: The percentages of participants reporting AEs within 1 month after vaccination at Visit 1 (Section 2.1).
- Analysis set: Safety population (Section 4).
- Analysis time point: Within 1 month after vaccination.
- Analysis methodology: Descriptive statistics.
- Intercurrent events and missing data: No missing values will be imputed except for partial AE start dates (Section 5.3).
- Reporting results: The numerator (n) and the denominator (N) used in the percentage calculation, the percentage (%), and the corresponding 2-sided 95% Clopper-Pearson CI for participants reporting any AE, each SOC, and each PT within each SOC will be presented by vaccine group.

If any nonserious AEs are reported to occur before vaccination at Visit 1 or between 1 month after the last vaccination received and the 6-month follow-up (between Visit 2 and Visit 3) (outside of the protocol-specified reporting window), they will not be summarized but will be included in the AE listings.

CCI [redacted]

6.1.1.4. Serious Adverse Events

6.1.1.4.1. Main Analyses

- Estimand: The percentage of participants reporting SAEs up to 6 months after vaccination (Section 2.1).
- Analysis set: Safety population (Section 4).
- Analysis time point: Up to 6 months after vaccination.
- Analysis methodology: Descriptive statistics.
- Intercurrent events and missing data: No missing values will be imputed except for partial SAE start dates (see Section 5.3).
- Reporting results: The numerator (n) and the denominator (N) used in the percentage calculation, the percentage (%), and the corresponding 2-sided 95% Clopper-Pearson CI for participants reporting any SAEs, each SOC, and each PT within each SOC will be presented by vaccine group.

6.2. Secondary Endpoints

6.2.1. Secondary Pneumococcal Immunogenicity Endpoint

6.2.1.1. Pneumococcal Serotype-Specific OPA Titers

6.2.1.1.1. Main Analysis

- Estimand: GMT of the serotype-specific OPA titers 1 month after vaccination.
- Analysis set: Evaluable immunogenicity population, CCI [redacted] (Section 4).
- Analysis time point: 1 Month after vaccination at Visit 1.
- Analysis methodology: GMTs and the 2-sided 95% CIs based on the t-distribution (Section 5.2.2.1).

- Reporting results: For each of the 20 vaccine serotypes, the GMTs and 95% CIs for serotype-specific OPA titer will be presented for the Coadministration group (20vPnC + BNT162b2) and the 20vPnC-only group (20vPnC + saline) 1 month after vaccination.

Figures:

Bar charts for observed GMTs and corresponding 95% CIs for the 20 serotypes will be plotted before vaccination at Visit 1 and 1 month after vaccination for the Coadministration group (20vPnC + BNT162b2) and the 20vPnC-only group (20vPnC + saline).

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6.2.2. Secondary BNT162b2 Immunogenicity Endpoint

6.2.2.1. Full-Length S-Binding IgG Levels

6.2.2.1.1. Main Analysis

- Estimand: GMCs of full-length S-binding IgG levels at approximately 1 month after vaccination.
- Analysis set: Evaluable immunogenicity population, CCI [redacted] (Section 4).
- Analysis time point: 1 Month after vaccination at Visit 1.
- Analysis methodology: GMCs and the 2-sided 95% CIs based on the t-distribution (Section 5.2.2.1).
- Reporting results: GMCs and 95% CIs for full-length S-binding IgG levels will be presented 1 month after vaccination for the Coadministration group (20vPnC + BNT162b2) and the BNT162b2-only group (BNT162b2 + saline).

Figures:

Bar charts for observed GMCs and corresponding 95% CIs for full-length S-binding IgG levels will be plotted before vaccination at Visit 1 and 1 month after vaccination for the Coadministration group (20vPnC + BNT162b2) and the BNT162b2-only group (BNT162b2 + saline).

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6.2.2.2. Fold Rises in Full-Length S-Binding IgG Levels

- Estimand: GMFR of full-length S-binding IgG levels from before to approximately 1 month after vaccination.
- Analysis set: Evaluable immunogenicity population, CCI [redacted] Section 4).
- Analysis time point: 1 Month after vaccination.
- Analysis methodology: Descriptive statistics (Section 5.2.2.2).
- Reporting results: The number of participants (n), GMCs before and 1 month after vaccination, GMFRs from before vaccination to 1 month after vaccination, and the corresponding 2-sided 95% CIs for full-length S-binding IgG levels will be presented for the Coadministration group (20vPnC + BNT162b2) and the BNT162b2-only group (BNT162b2 + saline).

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6.5. Baseline and Other Summaries and Analyses

6.5.1. Baseline Summaries

6.5.1.1. Demographic Characteristics

Demographic and baseline characteristics including age, sex, race, ethnicity, BMI, BMI groups, and prior pneumococcal vaccine status will be summarized by vaccine group for all participants in the safety population and evaluable immunogenicity population. Descriptive statistics (n and %) will be provided overall and in subgroup tables.

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[redacted]

6.5.1.2. Medical History

Each reported interim medical history term will be mapped to a SOC and PT according to MedDRA. Only the medical history that was new from enrollment into the C4591001 study was to be collected in the B7471026 study. The number and percentage of participants with an assigned vaccine having at least 1 diagnosis, overall and at each SOC and PT level, will be summarized by vaccine group for the safety population.

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[redacted]

[redacted]

6.5.2. Study Conduct and Participant Disposition

6.5.2.1. Participant Disposition

The number and percentage of randomized participants will be included in the participant disposition summary. In addition, the number and percentage of participants who received vaccination(s) at Visit 1, who completed through Visit 2, who completed the study, and who withdrew from the study, along with the reasons for withdrawal, will be tabulated by vaccine group (according to randomized group assignment). The reasons for withdrawal will be those as specified in the database.

Participants excluded from each analysis population will also be summarized separately, along with the reasons for exclusion, by vaccine group.

6.5.2.2. Blood Samples for Assay

The number and percentage of randomized participants providing blood samples within and outside of protocol-prespecified time frames at each time point will be tabulated by vaccine group.

CCI [redacted]

6.5.3. Study Vaccination Exposure

6.5.3.1. Vaccination Timing and Administration

A listing of participants showing the randomized vaccine group and the vaccines actually received will be presented for each vaccine group.

6.5.4. Nonstudy Vaccinations and Concomitant Medications Used to Treat SAEs

Each nonstudy vaccine will be listed according to the ATC fourth-level classification.

Concomitant medications used to treat SAEs will be listed by vaccine group for the safety population.

6.6. Safety Summaries and Analyses

The summaries and analyses of the safety measures local reactions, systemic events, AEs, and SAEs are described in the Primary Safety Endpoint section (Section 6.1.1).

7. INTERIM ANALYSES

7.1. Introduction

Not applicable.

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[redacted]

8. REFERENCES

1. Collett D. Statistical inference for binary data. Chapter 2. In: Modelling binary data. London, England: Chapman & Hall; 1991:17-42.

2. Miettinen O, Nurminen M. Comparative analysis of two rates. Stat Med. 1985;4(2):213-26.

9. APPENDICES

Appendix 1. List of Abbreviations

Abbreviation	Term
13vPnC	13-valent pneumococcal conjugate vaccine
20vPnC	20-valent pneumococcal conjugate vaccine
AE	adverse event
ATC	Anatomic Therapeutic Chemical
BLQ	below the limit of quantitation
BMI	body mass index
CI	confidence interval
CRF	case report form
e-diary	electronic diary
GMC	geometric mean concentration
GMFR	geometric mean fold rise
GMT	geometric mean titer
ICD	informed consent document
ID	identification
IgG	immunoglobulin G
IWR	interactive Web-based response
LLOQ	lower limit of quantitation
MedDRA	Medical Dictionary for Regulatory Activities
N/A	not applicable
OPA	opsonophagocytic activity
PPSV23	23-valent pneumococcal polysaccharide vaccine
PT	preferred term
RCDC	reverse cumulative distribution curve
S	spike protein
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SOC	system organ class
SOP	standard operating procedure
US	United States
WHO	World Health Organization