

2.7.3 SUMMARY OF CLINICAL EFFICACY

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LIST OF ABBREVIATIONS

| Abbreviation | Definition |
|---------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------|
| BMI | body mass index |
| CDC | (US) Centers for Disease Control and Prevention |
| CEF | MHC-class I restricted peptides originating from CMV, EBV, and flu (influenza) virus |
| CEFT | MHC-class II restricted peptides originating from CMV, EBV, Flu (influenza) virus and tetanus toxin |
| CI | confidence interval |
| CMV | cytomegalovirus |
| CoV | coronavirus |
| COVID-19 | coronavirus disease 2019 |
| CSR | clinical study report |
| DBP | diastolic blood pressure |
| EBV | Epstein-Barr-virus |
| ECMO | extracorporeal membrane oxygenation |
| ELISpot | enzyme-linked immuno-spot |
| FACS | fluorescence-activated cell sorting |
| FDA | (US) Food and Drug Administration |
| FIH | first-in-human |
| FiO ₂ | fraction of inspired oxygen |
| GMC | geometric mean concentration |
| GMFR | geometric mean-fold rise |
| GMT | geometric mean titer |
| HBV | hepatitis B virus |
| HCV | hepatitis C virus |
| HCS | human convalescent serum |
| HIV | human immunodeficiency virus |
| HLA | human leukocyte antigen |
| ICS | intracellular cytokine staining |
| ICU | intensive care unit |
| IFN | interferon |
| IgG | immunoglobulin G |
| IgM | immunoglobulin M |
| IL | interleukin |
| IMM | Immunogenicity set, defined as all participants who received at least one dose of study vaccine and had at least one post-baseline immunogenicity assessment |
| IRC | (US Study C4591001) internal review committee |
| IRR | illness rate ratio |
| LLOQ | lower limit of quantitation |
| LNP | lipid nanoparticle |
| MHC | major histocompatibility complex |
| modRNA | nucleoside-modified messenger RNA |
| mRNA | messenger RNA |
| NAAT | nucleic acid amplification test |
| N-binding | SARS-CoV-2 nucleoprotein binding |

| Abbreviation | Definition |
|---------------------|-----------------------------------------------------------------|
| P2 S | SARS-CoV-2 full-length, P2 mutant, prefusion spike glycoprotein |
| PaO ₂ | partial pressure of oxygen, arterial |
| PBMC | peripheral blood mononuclear cell |
| Pr | posterior probability |
| RBD | receptor binding domain |
| RNA | ribonucleic acid |
| RNA-LNP | RNA lipid nanoparticle |
| RR | respiratory rate |
| RT-PCR | reverse transcription–polymerase chain reaction |
| S protein, S | SARS-CoV-2 spike protein |
| SAP | statistical analysis plan |
| SARS | severe acute respiratory syndrome |
| SARS-CoV-2 | SARS coronavirus-2; virus causing the disease COVID-19 |
| SBP | systolic blood pressure |
| SCE | summary of clinical efficacy |
| SPO ₂ | oxygen saturation as measured by pulse oximetry |
| USA | United States |
| Th1/Th2 | helper T cell type 1/type 2 |
| VE | vaccine efficacy |

2.7.3. SUMMARY OF CLINICAL EFFICACY

Pfizer and BioNTech have developed an investigational vaccine intended to prevent Coronavirus Disease 2019 (COVID-19) caused by the virus, SARS-CoV-2. The vaccine, BNT162b2, is a nucleoside-modified mRNA-based vaccine formulated in lipid nanoparticles (LNPs) that encodes the SARS-CoV-2 full-length, P2 mutant, prefusion spike glycoprotein (P2 S).

This Summary of Clinical Efficacy (SCE) summarizes data from evaluations of efficacy and immunogenicity performed in 2 clinical studies of BNT162b2 that support the present marketing application. The proposed indication and dosing administration for BNT162b2 (30 µg) are:

Proposed indication: Active immunization to prevent COVID-19 in individuals 16 years of age and older

Dosing administration: administered intramuscularly as a series of two doses (0.3 mL each) 3 weeks apart.

The present submission comprises 2 studies conducted in individuals ≥ 12 years of age. The submission includes data from:

- Phase 1 of the first-in-human (FIH) dose-ranging study, BNT162-01; and
- Phase 1, 2, and 3 of the pivotal efficacy study, C4591001.

The studies are currently ongoing, and therefore data included in the submission and presented in this SCE are interim. Additional data will be provided in subsequent submissions.

2.7.3.1. Background and Overview of Clinical Efficacy/Immunogenicity

The core innovation of mRNA-based vaccines is based on in vivo delivery of a pharmacologically optimized, antigen-encoding RNA to induce robust neutralizing antibodies and a concomitant T cell response to achieve protective immunization with minimal vaccine doses.^{1,2,3} BioNTech has developed multiple RNA-LNP platforms, including nucleoside-modified RNA (modRNA), which has blunted innate immune sensor activating capacity and thus augmented antigen expression. Two modRNA vaccine candidates were evaluated in both the FIH dose-ranging study, conducted in Germany (BNT162-01), and in the Phase 1, dose-ranging portion of Study C4591001, conducted in the United States. The vaccines were:

- BNT162b1, which encodes a fragment of the SARS-CoV-2 S glycoprotein that contains the receptor binding domain (RBD); and
- BNT162b2, which encodes the full-length SARS-CoV-2 S glycoprotein with mutations that stabilize S in an antigenically optimal prefusion conformation that exposes neutralization-sensitive sites (P2 S).

Based on safety and immunogenicity results from both of these studies, as well as nonclinical data, a single candidate and dose level (BNT162b2, at 30 µg) was selected for further development.

In Phase 2/3 of Study C4591001, the efficacy of BNT162b2 was evaluated using a case accrual design. Based on initial assumptions regarding the COVID-19 attack rate in the placebo group and the anticipated non-evaluable rate among all participants, it was estimated that efficacy could be demonstrated in a population of approximately 43,998 participants (21,999 per group). Recruitment was expanded beyond the United States to include study centers in Argentina, Brazil, Germany, Turkey, and South Africa. Initially, 4 interim analyses were planned after accrual of 32, 62, 92, and 120 confirmed COVID-19 cases for the first primary efficacy endpoint. At each interim analysis, Vaccine efficacy (VE) was to be evaluated for the first primary objective only (ie, VE for the subgroup of participants with no serological or virological evidence of SARS-CoV-2 infection prior to vaccination and up to 7 days after receipt of the second dose). Overwhelming efficacy could be declared if the success criterion for the first primary endpoint was met at any of the 4 interim analyses, or the study could be stopped for lack of benefit if the futility criterion was met at any of the first 3 interim analyses. The final analysis was to be performed with accrual of 164 confirmed cases for the first primary efficacy endpoint.

For operational reasons, the first planned IA was not performed. Amendment 9 to the C4591001 protocol eliminated the planned interim analysis at 32 cases and provided for 3 interim analyses to be performed after accrual of *at least* 62, 92, and 120 cases. Thereafter, case accumulation was so rapid that the planned analysis at 62 cases was performed after 94 cases had been confirmed, and accrual of the 164 cases for the final analysis followed soon thereafter.

At the interim analysis (data cutoff date: 04 November 2020), the success criterion for the first primary endpoint was met, confirming the efficacy of BNT162b2 in preventing disease caused by SARS-CoV-2 virus in individuals ≥ 16 years of age. The results from this interim analysis of the first primary endpoint are included in this SCE, along with the results from analyses of all the other primary and secondary efficacy endpoints, which were conducted after accrual of at least 164 cases (final analysis data cutoff date: 14 November 2020). In addition, updated descriptive efficacy analyses based on an accrued 1165 confirmed cases of COVID-19 during blinded placebo-controlled follow-up (data cutoff date: 13 March 2021) were conducted.

Analyses of immunogenicity in Study C4591001 include data from adults ≥ 18 years of age up to 6 months after Dose 2 in Phase 1 and up to 1 month after Dose 2 in Phase 2.

Content of the Summary of Clinical Efficacy

This SCE provides an overview of the 2 studies included in the submission, describing study design and conduct, methods for evaluating vaccine efficacy and immunogenicity, and results from the efficacy and immunogenicity analyses, as outlined below.

| Content | Section |
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| Overview of study design and conduct for both studies | Section 2.7.3.1.1 |
| Methods for the evaluation of efficacy (Study C4591001) | Section 2.7.3.1.2 |
| Methods for the evaluation of immunogenicity for both studies | Section 2.7.3.1.3 |
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| Results of immunogenicity evaluations | |
| Phase 1 Candidate and dose selection (BNT162-01, C4591001) | Section 2.7.3.2.2.1 |
| Phase 2 Immunogenicity results (C4591001) | Section 2.7.3.2.2.2 |

2.7.3.1.1. Overview of the Clinical Development Program

This section provides an overview of study design and conduct for Phase 1/2 study BNT162-01 (Section 2.7.3.1.1.1) and Phase 1/2/3 study C4591001 ([Section 2.7.3.1.1.2](#)). Methods for the evaluation of efficacy, including the statistical analyses performed, are described for Study C4591001 in [Section 2.7.3.1.2](#); and methods for the evaluation of immunogenicity, including the statistical analyses performed, are described for both studies in [Section 2.7.3.1.3](#).

2.7.3.1.1.1. Phase 1/2 Study BNT162-01 – Study Design and Conduct

Study BNT162-01, conducted in Germany, is an ongoing, FIH, open-label, dose-level finding study designed to evaluate the safety and immunogenicity of several different candidate vaccines at various dose levels in order to identify vaccine candidates and dose levels for further evaluation.

The study initially enrolled healthy adults 18 to 55 years of age, but the protocol was later amended to include adults 56 to 85 years of age, with data evaluated separately for the 2 age groups. Healthy participants with preexisting stable disease, defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks prior to enrollment, were eligible for the study. Individuals with certain medical conditions that could affect participant safety or evaluation of vaccine safety or immunogenicity were excluded. A complete list of inclusion and exclusion criteria is available in the protocol ([Module 5.3.5.1 BNT162-01 Protocol Section 5](#)).

Study BNT162-01 evaluated 4 different vaccine candidates using various mRNA platforms. However, because only the 2 modRNA candidates were ultimately selected for progression in the development program, the 2 candidates based on other RNA platforms are not discussed further herein.

For each vaccine candidate, participants were to receive escalating/de-escalating dose levels (12 participants per dose level), with progression to subsequent dose levels based on review of safety data by a Safety Review Committee. Each modRNA vaccine was administered as a 2-dose regimen, given 21 days apart, with dose levels as follows:

For adults 18 to 55 years of age:

- BNT162b1: 1, 3, 10, 20, 30, 50, and 60 µg
- BNT162b2: 1, 3, 10, 20, and 30 µg

Note that based on the tolerability profile after the first dose of BNT162b1 at 60 µg, the Safety Review Committee recommended that a second dose at 60 µg not be administered.

For adults 56 to 85 years of age:

- BNT162b1: 10, 20, 30 µg
- BNT162b2: 10, 20, 30 µg

Blood samples for evaluation of immunogenicity were to be collected at baseline (immediately before Dose 1); 7 and 21 days after Dose 1; and 7, 14, 21, 28, 63, and 162 days after Dose 2.

Immune responses were principally evaluated based on functional antibody titers determined using the SARS-CoV-2 neutralization assay. In addition, cell-mediated immune response assays were used to characterize T cell responses at baseline and approximately 7 days after Dose 2. For information on immunogenicity evaluation methods, refer to [Section 2.7.3.1.3](#).

2.7.3.1.1.2. Phase 1/2/3 Pivotal Efficacy Study C4591001 – Study Design and Conduct

Study C4591001 is the ongoing Phase 1/2/3, randomized, placebo-controlled, observer-blind study in healthy individuals ≥ 12 years of age. Phase 1, conducted in the United States, comprised the dose-finding, vaccine candidate–selection portion of the study, while efficacy was evaluated in the Phase 2/3 portion of the study, in which enrollment was expanded to include sites in Argentina, Brazil, Germany, Turkey, and South Africa.

The study is observer-blinded, as the physical appearance of the investigational vaccine candidates and the placebo may differ. The participant, investigator, study coordinator, and other site staff are blinded; at the study site, only the dispenser(s)/administrator(s) of the study vaccines are unblinded. To facilitate rapid review of data in real time, sponsor staff were unblinded to vaccine allocation for the participants in Phase 1.

2.7.3.1.1.2.1. Phase 1 of Study C4591001

Initiated shortly after the FIH study BNT162-01, Phase 1 of Study C4591001 evaluated escalating dose levels of BNT162b1 and BNT162b2 in healthy adults 18 to 55 years of age or 65 to 85 years of age. As in Study BNT162-01, healthy participants with preexisting stable disease were eligible, although individuals with certain medical conditions or situations that could affect participant safety or evaluation of vaccine safety or immunogenicity were excluded. These included individuals at high risk for severe COVID-19 (eg, those with hypertension, diabetes mellitus, chronic pulmonary, liver, or kidney disease); and individuals who were immunocompromised (including infection with HIV or receipt of systemic corticosteroids); and those with autoimmune disease, HCV, or HBV). Individuals with a SARS-CoV-2 NAAT-positive nasal swab within 24 hours before receipt of study intervention or a positive serological test for SARS-CoV-2 IgM and/or IgG antibodies at the

screening visit were excluded. A complete list of inclusion and exclusion criteria is available in the protocol ([Module 5.3.5.1 C4591001 Protocol Section 5](#)).

Study vaccine was administered using the same 2-dose regimen as in Study BNT162-01 (21 days apart). An internal review committee (IRC) reviewed safety data to allow dose escalation or changes to continuation of dosing in specified groups. Escalation between dose levels was based on IRC review of at least 7-day post-Dose 1 safety data in this study and/or the Phase 1 study conducted in Germany (BNT162-01).

Each vaccine and dose level was first evaluated in a group of participants 18-55 years of age (randomized 4:1, with 12 receiving active vaccine and 3 receiving placebo). A given vaccine and dose level was administered to groups of participants 65-85 years of age (12 receiving active vaccine and 3 receiving placebo) only after the IRC had reviewed safety data for the RNA platform at the same, or a higher, dose level in the 18- to 55-year age group and deemed them acceptable. Further details regarding controlled enrollment to ensure safety at each dose level, progression between dose levels, and stopping rules are provided in the protocol ([Module 5.3.5.1 C4591001 Protocol Section 4.1](#)).

The following vaccine candidates and dose levels were evaluated in Phase 1:

- BNT162b1: 10, 20, 30, and 100 µg
- BNT162b2: 10, 20, and 30 µg

The IRC recommended that a second dose of BNT162b1 at 100 µg not be administered due to reactogenicity after the first dose (see [Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 9.8](#) and [Section 12.1](#)). Participants in this group instead received a second dose of BNT162b1 at the 10-µg dose level, and the 100-µg dose level was not administered to older adults receiving BNT162b1.

Blood for immunogenicity evaluations was collected immediately before Dose 1 and at visits taking place approximately 7 and 21 days after Dose 1; at 7, 14, and 28 days after Dose 2, and at 6, 12, and 24 months after Dose 2. Immune responses were evaluated using the SARS-CoV-2 neutralization assay and antigen specific (S1-binding or RBD-binding) IgG level assays. Refer to [Section 2.7.3.1.3](#) for information on immunogenicity evaluation methods.

2.7.3.1.1.2.2. Phase 2/3 of Study C4591001

Study Population

Initially, participants enrolled in Phase 2/3 were to be 18 to 85 years of age, in 2 age strata: 18 to 55 years (“younger participants”) and 56 to 85 years (“older participants”). It was intended that a minimum of 40% of participants would be in the >55-years stratum. The protocol was later amended to lower the minimum age of participants to 16 years and to remove the upper age limit (Protocol Amendment 6, 08 September 2020). Protocol Amendment 7 (06 October 2020) allowed for enrollment of adolescents 12 to 15 years of age as an additional age stratum. The 12- to 15-year stratum was expected to comprise up to approximately 2000 participants enrolled at selected investigational sites. Note that both of

these amendments were implemented after Phase 2 of the study had been fully enrolled (N=360 participants), and therefore the Phase 2 study population included only adults 18 to 85 years of age.

Enrollment criteria for Phase 2/3 were defined to ensure a broad study population representative of the “real-world” populations expected to receive the registered vaccine. 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, were eligible for the study. Individuals were to be, in the judgment of the investigator, at higher risk for acquiring COVID-19 (including, but not limited to, use of mass transportation, relevant demographics, and frontline essential workers). Individuals with medical conditions placing them at high risk of severe COVID-19 or in occupations with high risk of exposure to SARS-CoV-2 were eligible for the study. Also included were individuals with previous clinical or microbiological diagnosis of COVID-19 or with evidence of current or prior infection based on serology or nasal swab. Immunocompromised individuals were excluded, including those receiving immunosuppressive therapy or systemic corticosteroids (inhaled/nebulized corticosteroids were permitted). Initially, known infection with human immunodeficiency virus (HIV), hepatitis C virus (HCV), or hepatitis B virus (HBV) were exclusionary; however, Amendment 6 (08 September 2020) allowed enrollment of individuals with stable HIV, hepatitis B, or hepatitis C. Additional selection criteria are described in the protocol ([Module 5.3.5.1 C4591001 Protocol Section 5](#)).

Vaccine Administration

Based on review of safety and immunogenicity results through 1 week post-Dose 2 in both Study BNT162-01 and Study C4591001 Phase 1, as well as key results from non-human primate studies, the vaccine selected for efficacy evaluation in Phase 2/3 of Study C4591001 was BNT162b2 at the 30 µg dose level.

Participants were randomized in a 1:1 ratio to receive either:

- BNT162b2 (30 µg); or
- Placebo (normal saline).

Vaccines were administered by an unblinded administrator. Participants received a 2-dose regimen, administered approximately 21 days apart, at Visit 1 and at Visit 2, with Visit 2 intended to take place 19 to 23 days after Visit 1.

Scheduled Assessments

Blood samples were collected from all participants for immunogenicity assessments immediately before Dose 1 and 1 month after Dose 2 (Visit 3). Samples will also be collected at follow-up visits scheduled at 6 months, 12 months, and 24 months after Dose 2.

Nasal (midturbinate) swabs for detection of SARS-CoV-2 were performed at Visit 1 and at Visit 2.

The complete schedule of study activities, including all efficacy, immunogenicity, and safety evaluations is available in the protocol ([Module 5.3.5.1 C4591001 Protocol Section 1.3](#)).

Definition of Phase 2

Phase 2 of the study comprised the collection and evaluation of safety and immunogenicity data for 360 of the earliest enrollees into the Phase 2/3 portion of the study, selected for balance between the younger (18 to 55 years of age) and older (56 to 85 years of age) protocol-defined strata within each vaccine group (BNT162b2 or placebo). Immunogenicity data for the 360 Phase 2 participants through 1 month after Dose 2 are presented below in [Section 2.7.3.2.2.2](#). These participants were also included in the efficacy evaluation of the Phase 3 portion of the study.

2.7.3.1.2. Methods for the Evaluation of Efficacy – Study C4591001, Phase 2/3

Efficacy against confirmed COVID-19 was evaluated in Phase 2/3 of Study C4591001 using a case-accrual design. Under the assumption of a true vaccine efficacy (VE) rate of $\geq 60\%$ after the second dose of study intervention, a target of 164 first primary-endpoint cases of confirmed COVID-19 due to SARS-CoV-2 occurring at least 7 days after Dose 2 were sufficient to provide 90% power to conclude true VE $> 30\%$ with high probability.

Assuming a COVID-19 attack rate of 1.3% per year in the placebo group, accrual of 164 first primary-endpoint cases within 6 months, an estimated 20% nonevaluable rate, and 1:1 randomization, the required sample size was expected to be approximately 17,600 *evaluable* participants per group or 21,999 BNT162b2 recipients randomized in a 1:1 ratio with placebo, for a total sample size of 43,998. This was the number of participants initially targeted for Phase 2/3 and could be adjusted based on advice from the data monitoring committee's analyses of case accumulation and the percentage of participants who are seropositive at baseline.

Ongoing surveillance for potential cases of COVID-19 required participants who experienced symptoms of COVID-19 (as specified in the protocol) to contact the site immediately for assessment and case confirmation based on protocol-specified criteria (see [Section 2.7.3.1.2.2](#)).

2.7.3.1.2.1. Objectives and Endpoints for Efficacy Against Confirmed COVID-19

The primary efficacy objectives of the Phase 2/3 portion of the study were:

- To evaluate the efficacy of BNT162b2 against confirmed COVID-19 occurring from **7 days** after the second dose
 - in participants without evidence of infection before and during vaccination regimen (first primary objective), and
 - in participants with or without evidence of infection before and during vaccination regimen (second primary objective).

Secondary efficacy objectives were:

- To evaluate the efficacy of BNT162b2 against confirmed COVID-19 occurring from **14 days** after the second dose
 - in participants without evidence of infection before and during vaccination regimen;
 - in participants with or without evidence of infection before and during vaccination regimen.
- To evaluate the efficacy of BNT162b2 against confirmed **severe** COVID-19 occurring from **7 days** and from **14 days** after the second dose
 - in participants without evidence of infection before and during vaccination regimen;
 - in participants with or without evidence of infection before and during vaccination regimen.
- To describe the efficacy of BNT162b2 against confirmed COVID-19 (according to the CDC-defined symptoms) occurring from **7 days** and from **14 days** after the second dose
 - in participants without evidence of infection before and during vaccination regimen;
 - in participants with or without evidence of infection before and during vaccination regimen.

In addition, post hoc analyses (not specified in the protocol) were performed to describe the efficacy of BNT162b2 against confirmed severe COVID-19 (according to the CDC-defined severe symptoms).

The endpoint for each analysis was the incidence of disease (confirmed COVID-19, confirmed severe COVID 19, or confirmed COVID-19 according to the CDC-defined symptoms) per 1000 person-years of follow-up based on a nasal (midturbinate) swab positive for SARS-CoV-2 as determined by nucleic acid amplification test (NAAT) (central laboratory or locally confirmed). Only first occurrences of COVID-19 with onset of symptoms at least 7 days or 14 days after Dose 2 were included in the analyses.

The analyses were performed for endpoints as shown in [Table 1](#).

Table 1. Primary and Secondary Efficacy Analyses for Efficacy Against Confirmed COVID-19

| Efficacy Against Confirmed: | Occurring From (Days after Dose 2) | Incidence in Participants With/Without Infection Before and During Vaccination Regimen |
|-------------------------------------|-----------------------------------------------|-------------------------------------------------------------------------------------------------------|
| Primary Efficacy Endpoints | | |
| COVID-19 | | |
| First primary endpoint | 7 days | Without |
| Second primary endpoint | | With or Without |
| Secondary Efficacy Endpoints | | |
| COVID-19 | | |
| | 14 days | Without |
| | | With or Without |
| Severe COVID-19 | | |
| | 7 days | Without |
| | | With or Without |
| | 14 days | Without |
| | | With or Without |
| CDC-Defined COVID-19 | | |
| | 7 days | Without |
| | | With or Without |
| | 14 days | Without |
| | | With or Without |

2.7.3.1.2.2. Surveillance/Definitions /Case Determination for Confirmed COVID-19

Participants who developed any of the potential COVID-19 symptoms listed in the protocol ([Module 5.3.5.1 C4591001 Protocol Section 8.13](#)) were to contact the site immediately and, if confirmed, participate in an in-person or telehealth visit as soon as possible, optimally within 3 days of symptom onset. At the visit, investigators were to collect clinical information and results from local standard-of-care tests sufficient to confirm a diagnosis of COVID-19.

Confirmation of Infection with SARS-CoV-2: Investigators were to obtain a nasal swab (mid-turbinate) to be tested at a central laboratory using a reverse transcription–polymerase chain reaction (RT-PCR) test (Cepheid; FDA approved under emergency use authorization) to detect SARS-CoV-2. If the evaluation was conducted by telehealth, the participant was to self-collect a nasal swab and ship for assessment at the central laboratory. The central laboratory nucleic acid amplification–based test (NAAT) result was to be used for the case definition, unless no result was available from the central laboratory, in which case a local NAAT result could be used if it was obtained using one of the following assays:

- Cepheid Xpert Xpress SARS-CoV-2
- Roche cobas SARS-CoV-2 real-time RT-PCR test (EUA200009/A001)

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- Abbott Molecular/RealTime SARS-CoV-2 assay (EUA200023/A001).

Confirmed COVID-19 was defined (per FDA guidance)⁴ as the presence of at least 1 of the following symptoms and a positive SARS-CoV-2 NAAT (determined by the central laboratory or at a local testing facility using an acceptable test) during, or within 4 days before or after, the symptomatic period:

fever; new or increased cough; new or increased shortness of breath; chills;
new or increased muscle pain; new loss of taste or smell; sore throat; diarrhea;
vomiting.

Confirmed COVID-19 (according to the CDC-defined symptoms) was defined as above, adding the following to the list of symptoms:

fatigue; headache; nasal congestion or runny nose; nausea.⁵

Confirmed severe COVID-19 was defined (per FDA guidance)⁴ as confirmed COVID-19 and the presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness (RR \geq 30 breaths per minute, HR \geq 125 beats per minute, SpO₂ \leq 93% on room air at sea level, or PaO₂/FiO₂ $<$ 300 mm Hg);
- Respiratory failure (defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation, or ECMO);
- Evidence of shock (SBP $<$ 90 mm Hg, DBP $<$ 60 mm Hg, or requiring vasopressors);
- Significant acute renal, hepatic, or neurologic dysfunction*;
- Admission to an ICU;
- Death.

For post hoc analyses (not specified in the protocol), **confirmed severe COVID-19 (according to the CDC-defined severe symptoms)** was defined as COVID-19 illness events that resulted in hospitalization, admission to the ICU, intubation or mechanical ventilation, or death.⁶

2.7.3.1.2.3. Statistical Methods (Efficacy)

2.7.3.1.2.3.1. Efficacy Analysis Datasets

The efficacy evaluations were performed using data for the *evaluable efficacy population*, which included all eligible randomized participants who received all vaccinations as randomized, with Dose 2 received within the predefined window (19-42 days after Dose 1), and had no other important protocol deviations as determined by the clinician on or before 7 days after Dose 2 (for 7-day post vaccination efficacy endpoints) or on or before 14 days after Dose 2 (for 14-day post vaccination efficacy endpoints).

Efficacy evaluations were also performed for the ***Dose 1 all-available efficacy population*** (all randomized participants who received at least 1 vaccination) and the ***Dose 2 all-available efficacy population*** (all randomized participants who received 2 vaccination doses).

Vaccine efficacy evaluations for the primary endpoints were also performed for subgroups of participants by age, race, ethnicity, sex, and country, as well as by risk status and by comorbidity status. In addition, in analyses of cases among participants with or without evidence of prior infection, efficacy evaluations for the primary endpoints were also performed for subgroups of participants by baseline SARS-CoV-2 infection status.

2.7.3.1.2.3.2. Statistical Analyses for Efficacy

Interim and Final Analyses

The assessment of efficacy against confirmed COVID-19 was event-driven. Initially, 4 interim analyses were planned to be performed by an unblinded statistical team supporting the data monitoring committee after accrual of 32, 62, 92, and 120 confirmed COVID-19 cases for the first primary endpoint, with the final analysis performed after accrual of at least 164 cases. For operational reasons, the first planned IA (after 32 cases) was not performed. Amendment 9 to the C4591001 protocol eliminated the planned interim analysis at 32 cases and provided for 3 interim analyses to be performed after accrual of *at least* 62, 92, and 120 cases for the first primary endpoint. At each of the IAs, vaccine efficacy with respect to the first primary efficacy endpoint was to be assessed. At the final analysis (at least 164 cases) vaccine efficacy with respect to all efficacy endpoints was to be assessed.

VE against confirmed COVID-19 was estimated by $100 \times (1 - \text{IRR})$, where IRR was the ratio of COVID-19 illness rate in the BNT162b2 group to the corresponding illness rate in the placebo group. The Bayesian 95% credible interval and the posterior probability for the true vaccine efficacy greater than 30% conditioning on the available data, ie, $P[\text{VE} > 30\% | \text{data}]$, were calculated using a beta-binomial model and a pre-specified minimally informative beta distribution as prior. The calculation of posterior probability and 95% credible interval were adjusted for surveillance time. All efficacy endpoints were to be analyzed using the same Bayesian approach unless stated otherwise.

If the posterior probability of $\text{VE} > 30\%$ were greater than 99.5% at any pre-planned interim analysis, or greater than 98.6% at the final analysis, the vaccine efficacy of BNT162b2 would be declared.

If the predicted posterior probability of demonstrating vaccine efficacy at the final analysis were less than 5.0% at the analyses after accrual of at least 62 and at least 92 cases, the study would stop for lack of benefit (futility).

For the subgroup analyses of the efficacy endpoints, and for the analyses of efficacy for COVID-19 cases determined according to the CDC-defined symptoms, VE and the 2-sided 95% CI for VE was derived based on the Clopper and Pearson method adjusted for surveillance time.

Updated Efficacy Analyses

Updated efficacy analyses were performed for COVID-19 cases accrued during blinded placebo-controlled follow-up, up to the data cutoff date (13 March 2021). Updated descriptive efficacy analyses were conducted for the primary efficacy endpoints, including subgroup analyses, and for secondary efficacy endpoints of severe disease and CDC-defined severe disease cases occurring ≥ 7 days after Dose 2. The analyses for cases of COVID-19 occurring ≥ 14 days after Dose 2 were not updated.

The point estimate of VE in the blinded follow-up period and associated 2-sided 95% CI was derived using the Clopper Pearson method adjusted for surveillance time, and the posterior probability (ie, $P[VE > 30\% | \text{data}]$) was provided for the primary endpoints and secondary endpoints of severe disease.

Additional details of the analysis methods are provided in [Module 5.3.5.1 C4591001 6-Month Update Interim CSR Appendix 16.1.9 SAP Section 5.1.1](#) and [Section 6](#).

2.7.3.1.3. Methods for Evaluation of Immunogenicity

2.7.3.1.3.1. Measurement of the Immune Response

Serological Assays

Blood samples were collected for immunogenicity assessments at the visits specified in the protocols ([Module 5.3.5.1 C4591001 Protocol Section 1.3](#); [Module 5.3.5.1 BNT162-01 Protocol Section 1.3](#)). In both studies BNT162-01 and C4591001, immune responses were evaluated using 3 serological assays: the SARS-CoV-2 neutralization assay, the S1-binding IgG level assay, and the RBD-binding IgG level assay.^{7,8}

Details regarding the neutralization and binding assays are available in [Module 2.7.1 Summary of Biopharmaceutical Studies and Associated Analytical Methods](#) and [Module 5.3.1.4 Reports of Bioanalytical and Analytical Methods for Human Studies](#).

Human Convalescent Sera Panel for Serology Comparisons

To facilitate interpretation of immunogenicity data generated in both studies, a human convalescent serum (HCS) panel was obtained from Sanguine Biosciences (Sherman Oaks, CA), MT Group (Van Nuys, CA), and Pfizer Occupational Health and Wellness (Pearl River, NY).^{7,8} The 38 sera in the panel were collected from SARS-CoV-2 infected or COVID-19 diagnosed individuals 18 to 83 years of age ≥ 14 days after PCR-confirmed diagnosis at a time when they were asymptomatic. The serum donors had predominantly had symptomatic infections (35 of 38), including 1 who had been hospitalized. Data for SARS-CoV-2 serum neutralizing titers (geometric mean titers, GMTs) from the two clinical studies were compared with data for GMTs determined for the HCS panel.

CD4+ and CD8+ T Cell Responses

In addition, in Study BNT162-01, T cell mediated immune responses were evaluated using Enzyme-Linked Immuno-Spot (ELISpot) and intracellular cytokine staining (ICS) visualized

with fluorescence-activated cell sorting (FACS). Blood samples for evaluation of T cell responses were collected at baseline (before Dose 1) and at the visit that was to take place approximately 7 days after Dose 2 (~Day 29).

Cell mediated immune response data were also evaluated in post hoc analyses (not specified in the protocol) using blood collected for general research purposes on approximately Day 43 (21 days after Dose 2) Day 85 (63 days after Dose 2) and Day 184 (162 days after Dose 2). T cell responses were evaluated at these later time points for only a small number of participants who received BNT162b2 at doses of 10, 20, or 30 µg.

ELISpot

The ELISpot assay was used to measure the frequency of cytokine-secreting cells in samples of peripheral blood mononuclear cells (PBMCs) obtained from whole blood samples of vaccinated participants. Briefly, PBMCs enriched for CD4+ or CD8+ effector cells are placed in ELISpot plates pre-coated with antibodies specific for IFN-γ and are incubated overnight (≥18 hours) with peptides originating from the vaccine antigens (ie, from RBD or full-length S protein). IFN-γ secreted by CD4+ or CD8+ cells in response to stimulation by the peptides is bound to the plate by the coating antibody. After incubation, the plates are developed by addition of alkaline phosphatase conjugated secondary anti-IFN-γ antibody followed by enzyme substrate; each spot corresponds to the IFN-γ secreted by a single cell. Developed plates are read by an AID ELISpot Reader. Details of the ELISpot assay are available in the analytical interim report ([Module 5.3.5.1 BNT162-01 Interim CSR Appendix 16.1.14 GA-RB-022-01A v3](#)).

For benchmarking, the T cell responses (IFN-γ secretion) after stimulation by peptides derived from the vaccine antigens were compared to those after stimulation by recall antigens in the following assay peptide mixtures:

- **CEF:** MHC-class I restricted peptides originating from CMV, EBV, and Flu virus (cytomegalovirus, Epstein-Barr virus, and influenza virus), which are expected to stimulate IFN-γ production from CD8+ T cells in the majority of donors; the peptides included in this pool are short peptides which mainly stimulate CD8+ T cells.
- **CEFT:** MHC-class II restricted peptides originating from CMV, EBV, Flu (influenza) virus and Tetanus toxin, which are expected to stimulate IFN-γ production from CD4+ T cells in the majority of donors.

Intracellular Cytokine Staining with FACS

Intracellular cytokine staining (ICS) is a flow cytometry-based assay to detect the production and accumulation of cytokines intracellularly upon cell stimulation. PBMCs obtained from vaccinated participants were restimulated in a round-bottom 96-well plate with synthetic peptides covering the encoded antigens (RBD or full-length S protein). After stimulation of PBMCs, inhibitors of protein transport were added to retain the produced cytokines within the cells. In order to discriminate between antigen-specific CD4 and CD8 T cell responses, fluorescently labelled antibodies for CD4 and CD8 were used for staining of extracellular

surface markers. Next, PBMCs were fixed (with paraformaldehyde) and subsequently permeabilized for intracellular staining of CD4 and CD8, and of produced cytokines using fluorescently labelled, cytokine-specific antibodies (IFN γ , IL-2 and IL-4). After the staining procedure, cells were analyzed using FACS on a flow cytometer to visualize the proportions of vaccine antigen-specific Th1 and Th2 CD4⁺ T cells and cytotoxic CD8⁺ T cells producing each cytokine. For benchmarking, PBMCs from recovered COVID-19 patients were used. Details of the ICS/flow cytometry assay are available in the interim technical report, [Module 5.3.5.1 BNT162-01 Interim CSR Appendix 16.1.14 – R-20-0235 v2.0](#) (for BNT162b1) and [R-20-0241 v3.0](#) (for BNT162b2).

2.7.3.1.3.2. Immunogenicity Objectives and Endpoints

The methods described below apply to both Study BNT162-01 and Study C4591001, except as noted. The immunogenicity objectives and endpoints are listed for each study in [Module 5.3.5.1 BNT162-01 Protocol Section 3](#) and in [Module 5.3.5.1 C4591001 Protocol Section 3](#).

For the immunogenicity serological assay results (neutralizing titers, S1-binding IgG levels, and RBD-binding IgG levels), the estimands included:

- Geometric mean concentrations (GMCs) or geometric mean titers (GMTs) at protocol specified time points; (Note that GMT data were summarized for 50% neutralizing titers and for 90% neutralizing titers. The estimand of principal interest is the 50% neutralizing titer. The 90% neutralizing titer was primarily intended to assist in differentiation of the candidate vaccines in Phase 1, if needed, for the purpose of candidate selection. Results for 90% neutralizing titers are available in the CSR, but will not be discussed in this SCE.)
- Geometric mean fold-rise (GMFR) from before vaccination to subsequent protocol specified time points;
- Proportion of participants achieving ≥ 4 -fold rise from before vaccination to subsequent protocol-specified time point after vaccination (Study BNT162-01 and Study C4591001 Phase 1 only).

2.7.3.1.3.3. Immunogenicity Analysis Sets

In Study BNT162-01, immunogenicity evaluations were performed for the immunogenicity set (IMM), defined as all participants who received at least one dose of study vaccine and had at least one post-baseline immunogenicity assessment.

In Study C4591001, immunogenicity analyses are primarily based on the Dose 1 and Dose 2 evaluable immunogenicity populations. Additional analyses were to be performed based on the all-available populations if there was a large enough difference in sample size between the all-available immunogenicity population and the evaluable immunogenicity population. The criteria for each population are shown below. Participants were analyzed according to the vaccine group to which they were randomized.

| | |
|-------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Dose 1 evaluable immunogenicity | <u>For Phase 1 only</u> , all eligible randomized participants who received the vaccine to which they are randomly assigned at the first dose, have at least 1 valid and determinate immunogenicity result from the blood collection within an appropriate window after Dose 1 (same as visit window, ie, within 19-23 days after Dose 1), and have no other important protocol deviations as determined by the clinician. |
| Dose 2 evaluable immunogenicity | All eligible randomized participants who receive 2 doses of the vaccine to which they are randomly assigned, with Dose 2 received within the predefined window (19-42 days after Dose 1), have at least 1 valid and determinate immunogenicity result from the blood collection within an appropriate window after Dose 2 (6-8 days after Dose 2 for Phase 1 and within 28-42 days after Dose 2 for Phase 2/3), and have no other important protocol deviations as determined by the clinician. |
| Dose 1 all-available immunogenicity | <u>For Phase 1 only</u> , all randomized participants who receive at least 1 dose of the study intervention with at least 1 valid and determinate immunogenicity result after Dose 1 but before Dose 2. |
| Dose 2 all-available immunogenicity | All randomized participants who receive at least 1 dose of the study intervention with at least 1 valid and determinate immunogenicity result after Dose 2. |

2.7.3.1.3.4. Statistical Analyses for Immunogenicity

For immunogenicity results of SARS-CoV-2 neutralizing titers and S1- or RBD-binding IgG concentrations, the GMTs and GMCs were calculated as the mean of the assay results after making the logarithm transformation and then exponentiating the mean to express results on the original scale. Two-sided 95% CIs were obtained by taking log transforms of the titers, calculating the 95% CI with reference to Student's t-distribution, and then exponentiating the confidence limits.

GMFRs were defined as the post-vaccination assay result divided by the pre-vaccination result. GMFRs were calculated as the mean of the difference of logarithmically transformed neutralization titers or antibody levels (later result minus earlier result) and exponentiating the mean. The associated 2-sided 95% CIs were obtained by constructing CIs using Student's t-distribution for the mean difference on the natural log scale and exponentiating the confidence limits.

The exact 2-sided 95% CIs for binary endpoints were computed using the F distribution (Clopper-Pearson).⁹

Further details of the analyses are available in the SAPs ([Module 5.3.5.1 C4591001 6-Month Update Interim CSR Appendix 16.1.9 SAP Section 5](#) and [Section 6](#); and [Module 5.3.5.1 BNT162-01 Interim CSR Appendix 16.1.9 SAP Section 6](#)). Titers/concentrations below the lower limit of quantitation (LLOQ) or denoted as below the level of quantitation were set to $0.5 \times$ LLOQ for analysis.

2.7.3.2. Summary of Results of Individual Studies

2.7.3.2.1. Efficacy Against Confirmed COVID-19 - Pivotal Study C4591001 (Phase 2/3)

The efficacy of BNT162b2 in preventing COVID-19 among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen was demonstrated at the first interim analysis, which was conducted after accrual of at least 62 cases (cutoff date

04 November 2020). The results from this analysis, which evaluated the first primary efficacy endpoint only, are provided in Section 2.7.3.2.1.1

The final analysis of efficacy was conducted after accrual of at least 164 cases for the first primary efficacy endpoint (cutoff date, 14 November 2020). The results from these analyses are provided in [Section 2.7.3.2.1.2](#).

Updated descriptive efficacy analyses were performed for COVID-19 cases accrued during blinded placebo-controlled follow-up, up to the cutoff date of 13 March 2021. The results from these analyses are provided in [Section 2.7.3.2.1.3](#).

Details of results from the interim and final efficacy analyses are provided in [Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 11.1](#) and are summarized below. Details of results from the updated efficacy analyses are provided in [Module 5.3.5.1 C4591001 6-Month Update Interim CSR Section 11.1.2](#) and are summarized below.

2.7.3.2.1.1. Interim Analysis of Efficacy in Study C4591001

2.7.3.2.1.1.1. Efficacy Populations – Interim Analysis

For the first primary efficacy endpoint, VE for BNT162b2 against confirmed COVID-19 was evaluated in participants without evidence of prior SARS-CoV-2 infection before and during vaccination regimen. Participants with positive or unknown NAAT results at any illness visit prior to 7 days after Dose 2 were not included in this evaluation for VE. Cases were counted from 7 days after Dose 2.

In the interim analysis, the proportions of participants included in the evaluable efficacy population were similar in the BNT162b2 and placebo groups ([Table 26](#)). Most participants who were excluded from the evaluable efficacy population had not received all vaccinations as randomized or did not receive Dose 2 within the predefined window (ie, 19 to 42 days after Dose 1). There were 302 participants (1.4%) in the BNT162b2 group and 52 participants (0.2%) in the placebo group excluded for having important protocol deviations at or prior to 7 days after Dose 2.

Demographics of participants in the interim analysis evaluable efficacy population for participants without evidence of infection before and during the vaccination regimen were similar between the BNT162b2 and placebo groups ([Table 27](#)). This analysis population had generally similar demographics compared to the safety population. Demographic characteristics for the interim analysis Dose 2 all-available efficacy population were similar to those for the evaluable efficacy population.

2.7.3.2.1.1.2. Primary Efficacy Results – Interim Analysis

2.7.3.2.1.1.2.1. Vaccine Efficacy in Participants Without Prior Evidence of SARS-CoV-2 Infection – 7 Days After Dose 2 – Interim Analysis

Among participants included in the evaluable efficacy population, 32,279 participants overall (16,061 in the BNT162b2 group and 16,218 in the placebo groups) did not have evidence of prior infection with SARS-CoV-2 through 7 days after Dose 2 ([Table 26](#)).

As of the time of the interim analysis, there were 4 confirmed COVID-19 cases in the BNT162b2 group and 90 confirmed COVID-19 cases in the placebo group (Table 2). All evaluable cases were confirmed by tests conducted at the central laboratory.

VE for BNT162b2 against confirmed COVID-19 cases was evaluated in participants without evidence of prior SARS-CoV-2 infection before and during vaccination regimen with cases counted from 7 days after Dose 2.

VE of BNT162b2 was 95.5% with a 99.99% posterior probability for the true VE being >30% conditioning on available data, to overwhelmingly meet the prespecified interim analysis success criterion (>99.5%).

The 95% credible interval for the vaccine efficacy was 88.8% to 98.4%, indicating that given these observed data there was a 95% probability that the true VE lies in this interval. Also, note that the posterior probability that true VE >86.0% is 99.5% and VE >88.8% is 97.5%.

VE of BNT162b2 for the same primary efficacy endpoint based on the all-available efficacy population was 95.7%, with 4 cases in the BNT162b2 group and 93 cases in the placebo group (Table 28).

Table 2. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy Population (7 Days) – Interim Analysis 1

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI) ^e | Pr (VE >30% data) ^f |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|-----------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =16061) | | Placebo (N ^a =16218) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 4 | 1.722 (15899) | 90 | 1.732 (16010) | 95.5 | (88.8, 98.4) | >0.9999 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

Note: Data from subjects who are not confirmed 7 days post dose 2 cases are included in the analysis to comprehensively show all data reported and/or contribute to the total surveillance time calculation but may be subject to change with additional follow-up.

- N = number of subjects in the specified group.
- n1 = Number of subjects meeting the endpoint definition.
- Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- n2 = Number of subjects at risk for the endpoint.
- Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

Table 2. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy Population (7 Days) – Interim Analysis 1

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI) | Pr (VE >30% data) ^f |
|-------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|----------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =16061) | | Placebo (N ^a =16218) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |

f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details. This probability must be at least 99.5% at the interim analysis in order to conclude that the vaccine is efficacious.

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2.7.3.2.1.1.2.2. Vaccine Efficacy by Subgroup – Interim Analysis

VE in participants without prior evidence of SARS-CoV-2 infection was further evaluated by subgroups based on age, sex, race/ethnicity, and country. VE was >90% in all subgroups (Table 3). Results for the Dose 2 all-available population were similar, demonstrating no clinically meaningful differences in VE on the basis of subgroup (Table 29).

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Table 3. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy Population (7 Days) – Interim Analysis 1

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =16061) | | Placebo (N ^a =16218) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | | | | | | |
| Overall | 4 | 1.722 (15899) | 90 | 1.732 (16010) | 95.5 | (88.1, 98.8) |
| Age group (years) | | | | | | |
| 16 to 55 | 2 | 0.954 (8994) | 67 | 0.959 (9040) | 97.0 | (88.7, 99.6) |
| >55 | 2 | 0.767 (6905) | 23 | 0.773 (6970) | 91.2 | (64.6, 99.0) |
| Sex | | | | | | |
| Male | 2 | 0.874 (8115) | 38 | 0.865 (8029) | 94.8 | (79.8, 99.4) |
| Female | 2 | 0.848 (7784) | 52 | 0.867 (7981) | 96.1 | (85.1, 99.5) |
| Race | | | | | | |
| White | 4 | 1.477 (13399) | 85 | 1.491 (13530) | 95.3 | (87.4, 98.7) |
| Black or African American | 0 | 0.124 (1263) | 4 | 0.124 (1277) | 100.0 | (-51.8, 100.0) |
| All others ^f | 0 | 0.121 (1237) | 1 | 0.118 (1203) | 100.0 | (-3690.1, 100.0) |
| Ethnicity | | | | | | |
| Hispanic/Latino | 1 | 0.464 (4389) | 34 | 0.459 (4342) | 97.1 | (82.7, 99.9) |
| Non-Hispanic/non-Latino | 3 | 1.247 (11418) | 56 | 1.262 (11570) | 94.6 | (83.3, 98.9) |
| Country | | | | | | |
| Argentina | 0 | 0.271 (2436) | 28 | 0.266 (2402) | 100.0 | (86.2, 100.0) |
| Brazil | 0 | 0.087 (878) | 2 | 0.087 (879) | 100.0 | (-432.5, 100.0) |
| USA | 4 | 1.360 (12384) | 60 | 1.376 (12530) | 93.3 | (81.8, 98.2) |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

Note: Data from subjects who are not confirmed 7 days post dose 2 cases are included in the analysis to comprehensively show all data reported and/or contribute to the total surveillance time calculation but may be subject to change with additional follow-up.

- N = number of subjects in the specified group.
- n1 = Number of subjects meeting the endpoint definition.
- Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- n2 = Number of subjects at risk for the endpoint.
- Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted to the surveillance time.
- American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, not reported race categories are presented as “All others”.

Table 3. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy Population (7 Days) – Interim Analysis 1

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =16061) | | Placebo (N ^a =16218) | | | |
| | n ^{1b} | Surveillance Time ^c (n ^{2d}) | n ^{1b} | Surveillance Time ^c (n ^{2d}) | | |

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2.7.3.2.1.1.3. Additional Descriptive Efficacy Results – Interim Analysis

2.7.3.2.1.1.3.1. Vaccine Efficacy by Baseline SARS-CoV-2 Status – Interim Analysis

COVID-19 cases evaluable for efficacy after Dose 2 were further evaluated by participant SARS-CoV-2 status at baseline (ie, evidence of prior infection with SARS-CoV-2).

At the time of the interim analysis, there were 2 participants in the evaluable efficacy population who had evaluable COVID-19 and were baseline positive for prior SARS-CoV-2 infection: 1 participant in the BNT162b2 group and 1 participant in the placebo group (Table 30).

Results were similar for the Dose 2 all-available population (ie, 1 participant with COVID-19 in each group was baseline SARS-CoV-2 positive; all others were SARS-CoV-2 negative up to 7 days after Dose 2) (Table 31).

2.7.3.2.1.1.3.2. Vaccine Efficacy for Severe COVID-19 Cases – Interim Analysis

Severe cases of COVID-19 were evaluated from after Dose 1 onwards, and were reported for the Dose 1 all-available efficacy population (see efficacy analysis populations in Section 2.7.3.2.1.1).

As of the time of the interim analysis efficacy, a total of 7 severe cases of COVID-19 were reported as occurring from Dose 1 onwards (Table 4). All of these severe cases were reported in the placebo group. Of these, 5 of 7 severe cases were reported as occurring after Dose 1 and prior to Dose 2; the remaining 2 cases were reported ≥ 7 days after Dose 2.

Of these 7 severe cases reported in the placebo group, all were confirmed as being SARS-CoV-2 negative at baseline.

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Table 4. Severe COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population – Interim Analysis 1

| Efficacy Endpoint | Vaccine Group (as Randomized) | |
|-----------------------------------------|---------------------------------------------|------------------------------------|
| | BNT162b2 (30 µg) (N ^a =21617) | Placebo (N ^a =21633) |
| | n ^b | n ^b |
| Severe COVID-19 occurrence after Dose 1 | 0 | 7 |

Note: Data from subjects who are not confirmed 7 days post dose 2 cases are included in the analysis to comprehensively show all data reported and/or contribute to the total surveillance time calculation but may be subject to change with additional follow-up.

a. N = number of subjects in the specified group.

b. n = Number of subjects meeting the endpoint definition.

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2.7.3.2.1.1.4. Efficacy Conclusions From the Interim Analysis – Study C4591001

The first primary efficacy objective met success criteria at the first interim analysis performed on an accrued 94 cases of COVID-19. BNT162b2 achieved VE of 95.5% with a 95% credible interval of 88.8% to 98.4% among participants without evidence of infection before and during vaccination regimen, and a >99.99% posterior probability for the true VE being >30%, conditioning on available data.

There were no clinically meaningful differences in VE for the first primary efficacy endpoint by participant subgroup, as VE was >90% across age groups, for both male and female participants, across race/ethnic groups, and on the basis of geographic location across study countries.

Evaluation of efficacy among participants who had COVID-19 based on prior SARS-CoV-2 infection status showed 2 participants with COVID-19 cases were SARS-CoV-2 positive at baseline, 1 in each group.

A total of 7 severe cases of COVID-19 were reported in the interim analysis of efficacy, with 5 cases reported after Dose 1 and prior to Dose 2 and the remaining 2 cases reported ≥7 days after Dose 2. All severe cases were reported in placebo recipients and none were reported in BNT162b2 recipients. None were baseline positive for SARS-CoV-2.

The interim analysis efficacy results suggest BNT162b2 at 30 µg provided protection against COVID-19 overall and across subgroups of participants who had no evidence of prior infection with SARS-CoV-2, with severe cases observed exclusively in the placebo group.

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2.7.3.2.1.2. Final Analysis of Efficacy in Study C4591001

Efficacy data for the Phase 3 portion of Study C4591001 were analyzed for all enrolled participants who met the protocol-specified criteria for efficacy evaluation, with a final analysis cutoff date of 14 November 2020.

COVID-19 case evaluation for primary and secondary efficacy endpoints is discussed in [Section 2.7.3.1.2](#).

2.7.3.2.1.2.1. Efficacy Populations – Final Analysis

The proportions of participants included in the final analysis efficacy populations was similar in the BNT162b2 and placebo groups ([Table 32](#)). Most participants who were excluded from the evaluable efficacy population had not received all vaccinations as randomized or did not receive Dose 2 within the predefined window (ie, 19 to 42 days after Dose 1). There were 311 participants in the BNT162b2 group and 60 participants in the placebo group excluded for having important protocol deviations on or prior to 7 days after Dose 2. In the BNT162b2 group, most of these deviations were related to improper administration of the investigational product (263 participants, as compared with 20 participants in the placebo group); among these, most exclusions in the BNT162b2 group were due to dosing/administration errors (105 participants) or administration of investigational product that was deemed not suitable for use by the contractor who distributed the vaccine to study sites (144 participants).

Demographics of participants in the final analysis evaluable efficacy population for participants without evidence of infection prior to 7 days after Dose 2 were similar between BNT162b2 and placebo groups ([Table 33](#)). This analysis population had generally similar demographics compared to the safety population. Demographic characteristics for the final analysis Dose 2 all-available efficacy population and the evaluable population without evidence of infection prior to 14 days after Dose 2 were similar to those for the Dose 2 evaluable efficacy (7 days) population.

2.7.3.2.1.2.2. Signs and Symptoms of COVID-19

The criteria for COVID-19 case determination are described in [Section 2.7.3.1.2.2](#).

The signs and symptoms reported for cases contributing to the analysis for the first primary efficacy endpoint (8 cases in the BNT162b2 group and 162 cases in the placebo group) are summarized in [Table 34](#). These include cases occurring at least 7 days after the second vaccination among participants in the evaluable efficacy population who had no evidence of SARS-CoV-2 infection before or during the vaccination regimen. Most of these participants reported new or increased cough, and other symptoms reported most frequently were new or increased muscle pain, fever, and sore throat. New or increased shortness of breath was reported for 25 participants (15.4%) in the placebo group and for no participants who received BNT162b2.

[Table 35](#) summarizes the signs and symptoms for all cases of COVID-19 occurring at any time after Dose 1 (50 cases in the BNT162b2 group and 275 cases in the placebo group). These include cases occurring among participants in the Dose 1 all-available efficacy population, regardless of evidence of SARS-CoV-2 infection before or during the vaccination

regimen. Most participants reported 2 or more symptoms, and the most frequently reported symptoms were similar to those for the primary efficacy analysis population.

All participants with severe COVID-19 occurring at any time after Dose 1 (1 case in the BNT162b2 group and 9 cases in the placebo group) experienced clinical signs at rest indicative of severe systemic illness (RR \geq 30 breaths per minute, HR \geq 125 beats per minute, SpO₂ \leq 93% on room air at sea level, or PaO₂/FiO₂ <300 mm Hg); respiratory failure and admission to an ICU were each reported for 3 participants (33.3%) in the placebo group (Table 36).

Complete details of signs and symptoms for all efficacy populations and analyses are provided in the CSR.

2.7.3.2.1.2.3. Primary Efficacy Results – Final Analysis

For the first primary efficacy endpoint, VE for BNT162b2 against confirmed COVID-19 was evaluated in participants without evidence of prior SARS-CoV-2 infection before and during vaccination regimen. Cases were counted from 7 days after Dose 2. For the second primary efficacy endpoint, VE for BNT162b2 against confirmed COVID-19 was evaluated in participants with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen. Cases were counted from 7 days after Dose 2.

Secondary efficacy endpoints evaluated confirmed COVID-19 cases in participants either without or with or without evidence of prior SARS-CoV-2 infection before and during vaccination regimen. Cases were counted from 7 days after Dose 2 or from 14 days after Dose 2. Secondary efficacy endpoints are described in Section 2.7.3.1.2.1.

2.7.3.2.1.2.3.1. Vaccine Efficacy Without Prior Evidence of SARS-CoV-2 Infection – 7 Days After Dose 2 – Final Analysis

Among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%, with 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group (Table 5). The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%, indicating that the true VE is at least 90.3% with a 97.5% probability given the observed data.

The vaccine efficacy of BNT162b2 for the same primary efficacy endpoint based on the Dose 2 all-available efficacy population was 95.2%, with 8 and 165 cases in the BNT162b2 and placebo group, respectively (Table 37).

Table 5. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI) | Pr (VE >30% data) ^f |
|----------------------------------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|--------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =18198) | | Placebo (N ^a =18325) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 8 | 2.214 (17411) | 162 | 2.222 (17511) | 95.0 | (90.3, 97.6) | >0.9999 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

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2.7.3.2.1.2.3.2. Vaccine Efficacy With or Without Prior Evidence of SARS-CoV-2 Infection – 7 Days After Dose 2 – Final Analysis

For the second primary efficacy endpoint, VE for BNT162b2 against confirmed COVID-19 was evaluated in participants with or without evidence of prior SARS-CoV-2 infection through 7 days after Dose 2. Cases were counted from 7 days after Dose 2.

Among participants with or without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 94.6%, with 9 and 169 cases in the BNT162b2 and placebo groups respectively. The posterior probability of >99.99% for the true VE greater than 30% met the prespecified success criterion of >98.6% for this endpoint. The 95% credible interval for the vaccine efficacy was 89.9% to 97.3%, indicating that the true VE is at least 89.9% with a 97.5% probability given the available data (Table 6). Note that with a posterior probability of 98.6%, the true vaccine efficacy is at least 89.2% given the available data.

The vaccine efficacy of BNT162b2 for the same primary efficacy endpoint based on the Dose 2 all-available efficacy population was 94.8%, with 9 and 172 cases in the BNT162b2 and placebo group, respectively (Table 38).

Table 6. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) | Pr (VE >30% data) ^f |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =19965) | | Placebo (N ^a =20172) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 9 | 2.332 (18559) | 169 | 2.345 (18708) | 94.6 | (89.9, 97.3) | >0.9999 |

Abbreviations: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

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2.7.3.2.1.2.3.3. Vaccine Efficacy for All Confirmed Cases of COVID-19 After Dose 1 – Dose 1 All-Available Population

A number of confirmed cases of COVID-19 are not captured in the analyses of the first primary endpoint for the evaluable efficacy population because they occurred less than 7 days after Dose 2, or because they occurred in participants who were excluded from the evaluable efficacy population or who had evidence of infection before or during the vaccination regimen.

All reports of COVID-19 with onset at any time after Dose 1 are accounted for in Table 7, which provides a summary of cases for all participants in the Dose 1 all-available efficacy (modified intention-to-treat) population, regardless of evidence of infection before or during the vaccination regimen. Among these participants, 50 cases of COVID-19 occurred after Dose 1 in the BNT162b2 group compared to 275 cases in the placebo group. Notably, in the BNT162b2 group, most cases occurred before Dose 2. The estimated VE against confirmed COVID-19 occurring after Dose 1 was 82% (2-sided 95% CI: 75.6 %, 86.9%), with an

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estimated VE of 52.4% (2-sided 95% CI: 29.5%, 68.4%) against confirmed COVID-19 occurring after Dose 1 but before Dose 2.

Table 7. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =21669) | | Placebo (N ^a =21686) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence after Dose 1 | 50 | 4.015 (21314) | 275 | 3.982 (21258) | 82.0 | (75.6, 86.9) |
| After Dose 1 to before Dose 2 | 39 | | 82 | | 52.4 | (29.5, 68.4) |
| Dose 2 to 7 days after Dose 2 | 2 | | 21 | | 90.5 | (61.0, 98.9) |
| ≥7 Days after Dose 2 | 9 | | 172 | | 94.8 | (89.8, 97.6) |

Abbreviations: VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method (adjusted for surveillance time for overall row).

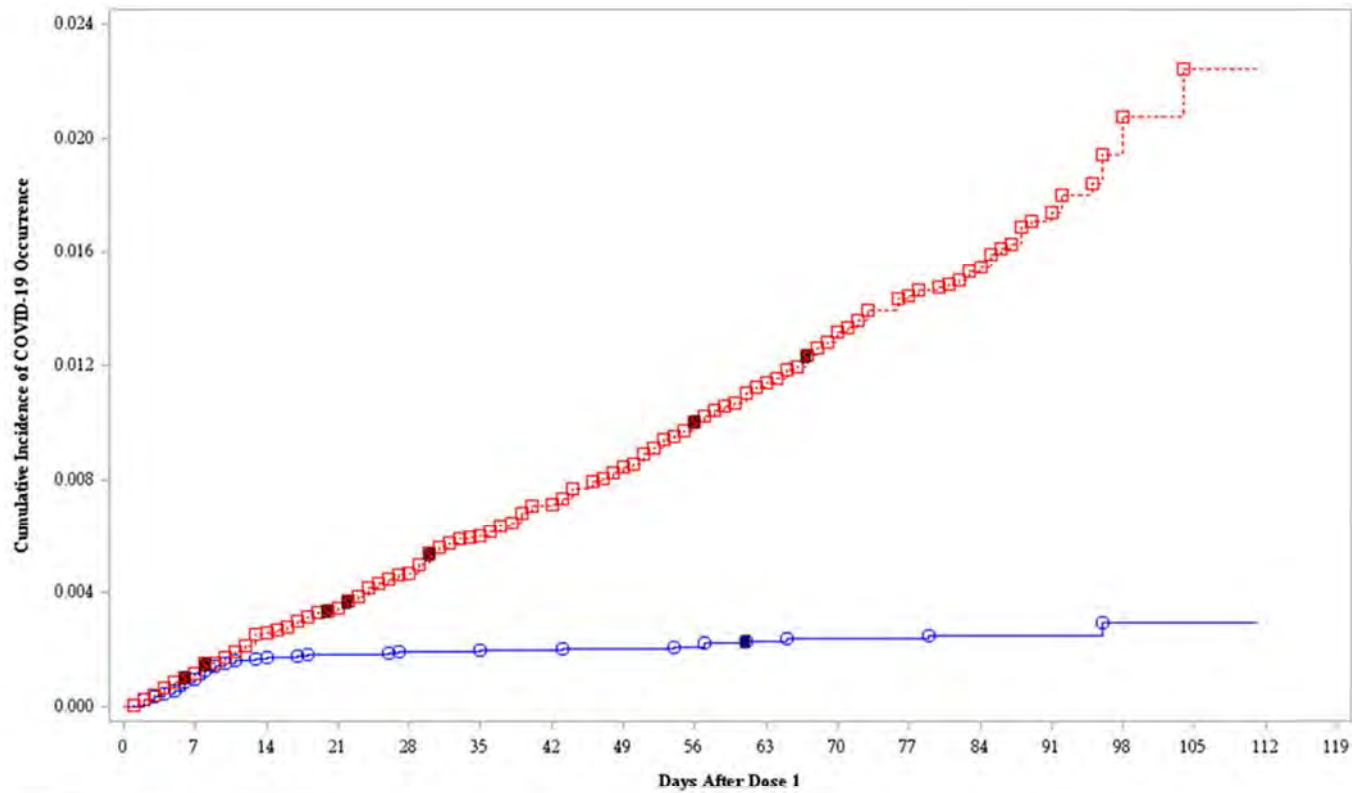
PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 18NOV2020 (17:06)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File:

./nda2_unblinded/C4591001_Efficacy_FA_164/adc19ef_ve_cov_pd1_aai

The early onset of protection is readily apparent in [Figure 1](#), which displays cumulative incidence for the first COVID-19 occurrence after Dose 1 among all vaccinated participants based on Dose 1 all-available efficacy (modified intention-to-treat) population. Disease onset appears to track together for BNT162b2 and placebo until approximately 14 days after Dose 1, at which point the curves diverge, with cases steadily accumulating in the placebo group, while remaining virtually flat in the BNT162b2 group. The darker-appearing symbols for both BNT162b2 (blue circles) and placebo (red squares) curves in [Figure 1](#) have an “S” written inside the open symbol, which denotes severe cases. Severe COVID-19 cases reported in the final analysis are discussed further in [Section 2.7.3.2.1.2.4.2](#).

Figure 1. Cumulative Incidence Curves for the First COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population



No. with events/No. at risk

| | | | | | | | | | | | | | | | | | |
|----|---------|----------|----------|----------|----------|-----------|-----------|-----------|-----------|-----------|-----------|----------|----------|----------|----------|---------|-------|
| A: | 0/21314 | 21/21230 | 37/21054 | 39/20481 | 41/19314 | 42/18377 | 42/17702 | 43/17106 | 44/15464 | 47/14038 | 48/12169 | 48/9591 | 49/8403 | 49/5374 | 50/1463 | 50/398 | 50/0 |
| B: | 0/21258 | 25/21170 | 55/20970 | 73/20366 | 97/19209 | 123/18218 | 143/17578 | 166/17025 | 192/15290 | 212/13876 | 235/11994 | 249/9471 | 257/6294 | 267/3301 | 274/1449 | 275/398 | 275/0 |

—○— A: BNT162b2 (30 µg) - - - □ - - - B: Placebo

Note: "S" indicates subjects with severe COVID-19 or COVID-19 leading to hospitalization.

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2.7.3.2.1.2.3.4. Vaccine Efficacy by Subgroup – Final Analysis

For both primary endpoints, VE was also evaluated for subgroups of participants by age, sex, race/ethnicity, and country for participants without evidence of prior infection and for participants with or without evidence of prior infection.

Among participants without prior evidence of SARS-CoV-2 infection before and during vaccination regimen, VE was >93% in all subgroups, with the exception of “all others” race group (89.3% VE) and Brazil (87.7% VE) (Table 8). VE for additional age subgroups and for all racial groups is provided in Table 39. Notably, in participants ≥65 years of age, VE was 94.7% (1 case in BNT162b2 group vs 19 cases in placebo group; 2-sided 95% CI: 66.7%, 99.9%) (Table 8), and VE in participants ≥75 years of age was 100% (0 cases in BNT162b2 group vs 5 cases in placebo group+; 2-sided 95% CI: -13.1%, 100.0%) (Table 39).

Among participants with or without prior evidence of SARS-CoV-2 infection before and during vaccination regimen, VE was >93% in all subgroups, with the exception of “all others” race group (78.2% VE), Brazil (75.4% VE), and positive prior SARS-CoV-2 infection at baseline (-7.1% VE, 1 case in each vaccine group) (Table 40).

Results for the all-available population were similar; no clinically meaningful differences were observed in VE on the basis of subgroup.

Post Hoc Subgroup Analyses by Risk Status

Post hoc analyses of efficacy by risk status were performed. For these analyses, at-risk participants were defined as those who had at least one Charlson Comorbidity Index condition or who were obese (defined as body mass index ≥ 30 kg/m²). For a summary of Charlson comorbidities among all participants at study entry, see Table 41.

Among participants without prior evidence of SARS-CoV-2 infection before and during the vaccination regimen, VE for participants at risk was 95.3%, as compared with 94.7% for those not at risk (Table 9). VE for participants ≥65 years of age and at risk was 91.7%, as compared with 100% for those ≥65 years of age and not at risk. VE was similar in obese (95.4%) and non-obese (94.8%) participants. A summary of VE for groups of participants by specific co-morbidity is provided in Table 42.

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| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^g) |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =18198) | | Placebo (N ^a =18325) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | | | | | | |
| Overall | 8 | 2.214 (17411) | 162 | 2.222 (17511) | 95.0 | (90.0, 97.9) |
| Age group (years) | | | | | | |
| 16 to 55 | 5 | 1.234 (9897) | 114 | 1.239 (9955) | 95.6 | (89.4, 98.6) |
| >55 | 3 | 0.980 (7500) | 48 | 0.983 (7543) | 93.7 | (80.6, 98.8) |
| ≥65 | 1 | 0.508 (3848) | 19 | 0.511 (3880) | 94.7 | (66.7, 99.9) |
| Sex | | | | | | |
| Male | 3 | 1.124 (8875) | 81 | 1.108 (8762) | 96.4 | (88.9, 99.3) |
| Female | 5 | 1.090 (8536) | 81 | 1.114 (8749) | 93.7 | (84.7, 98.0) |
| Race | | | | | | |
| White | 7 | 1.889 (14504) | 146 | 1.903 (14670) | 95.2 | (89.8, 98.1) |
| Black or African American | 0 | 0.165 (1502) | 7 | 0.164 (1486) | 100.0 | (31.2, 100.0) |
| All others ^f | 1 | 0.160 (1405) | 9 | 0.155 (1355) | 89.3 | (22.6, 99.8) |
| Ethnicity | | | | | | |
| Hispanic/Latino | 3 | 0.605 (4764) | 53 | 0.600 (4746) | 94.4 | (82.7, 98.9) |
| Non-Hispanic/non-Latino | 5 | 1.596 (12548) | 109 | 1.608 (12661) | 95.4 | (88.9, 98.5) |
| Country | | | | | | |
| Argentina | 1 | 0.351 (2545) | 35 | 0.346 (2521) | 97.2 | (83.3, 99.9) |
| Brazil | 1 | 0.119 (1129) | 8 | 0.117 (1121) | 87.7 | (8.1, 99.7) |
| USA | 6 | 1.732 (13359) | 119 | 1.747 (13506) | 94.9 | (88.6, 98.2) |

Table 8. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =18198) | | Placebo (N ^a =18325) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. All others = American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:54) Source Data: adc19ef Table Generation: 18NOV2020 (15:55)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: .nda2_unblinded/C4591001_Efficacy_FA_164/adc19ef_ve_cov_7pd2_wo_sg_eval

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Table 9. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =18198) | | Placebo (N ^a =18325) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | | | | | | |
| Overall | 8 | 2.214 (17411) | 162 | 2.222 (17511) | 95.0 | (90.0, 97.9) |
| At risk ^f | | | | | | |
| Yes | 4 | 1.025 (8030) | 86 | 1.025 (8029) | 95.3 | (87.7, 98.8) |
| No | 4 | 1.189 (9381) | 76 | 1.197 (9482) | 94.7 | (85.9, 98.6) |
| Age group (years) and at risk | | | | | | |
| 16-64 and not at risk | 4 | 0.962 (7671) | 69 | 0.964 (7701) | 94.2 | (84.4, 98.5) |
| 16-64 and at risk | 3 | 0.744 (5878) | 74 | 0.746 (5917) | 95.9 | (87.6, 99.2) |
| ≥65 and not at risk | 0 | 0.227 (1701) | 7 | 0.233 (1771) | 100.0 | (29.0, 100.0) |
| ≥65 and at risk | 1 | 0.281 (2147) | 12 | 0.279 (2109) | 91.7 | (44.2, 99.8) |
| Obese ^g | | | | | | |
| Yes | 3 | 0.763 (6000) | 67 | 0.782 (6103) | 95.4 | (86.0, 99.1) |
| No | 5 | 1.451 (11406) | 95 | 1.439 (11404) | 94.8 | (87.4, 98.3) |
| Age group (years) and obese | | | | | | |
| 16-64 and not obese | 4 | 1.107 (8811) | 83 | 1.101 (8825) | 95.2 | (87.3, 98.7) |
| 16-64 and obese | 3 | 0.598 (4734) | 60 | 0.609 (4789) | 94.9 | (84.4, 99.0) |
| ≥65 and not obese | 1 | 0.343 (2582) | 12 | 0.338 (2567) | 91.8 | (44.5, 99.8) |
| ≥65 and obese | 0 | 0.165 (1265) | 7 | 0.173 (1313) | 100.0 | (27.1, 100.0) |

Table 9. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^g) |
|----------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =18198) | | Placebo (N ^a =18325) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. At risk is defined as having at least one of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m²).
- g. Obese is defined as BMI ≥30 kg/m².

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:54) Source Data: adc19ef Table Generation: 24NOV2020 (17:41)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_EUA_FAEF_RR/adc19ef_ve_cov_7pd2_wo_rg_eval

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2.7.3.2.1.2.4. Secondary Efficacy Results – Final Analysis

2.7.3.2.1.2.4.1. Vaccine Efficacy for COVID-19 (≥14 Days After Dose 2)

Participants Without Evidence of Infection Before and During Vaccination Regimen

For this efficacy endpoint, participants with positive or unknown NAAT results at any illness visit prior to 14 days after Dose 2 were not included in the evaluation for efficacy.

Among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against confirmed COVID-19 occurring at least 14 days after Dose 2 was 94.2%, with 8 and 139 cases in the BNT162b2 and placebo groups respectively (Table 10). The posterior probability of >99.99% for the true VE greater than 30% met the prespecified success criterion of >98.6% for this endpoint. The 95% credible interval for the vaccine efficacy was 88.7% to 97.2%, indicating that the true VE is at least 88.7% with a 97.5% probability given the available data.

Table 10. Vaccine Efficacy – First COVID-19 Occurrence From 14 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 14 Days After Dose 2 – Evaluable Efficacy (14 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI) | Pr (VE >30% data) ^f |
|-----------------------------------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|--------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =18175) | | Placebo (N ^a =18261) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 14 days after Dose 2 | 8 | 1.887 (16612) | 139 | 1.893 (16663) | 94.2 | (88.7, 97.2) | >0.9999 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 14 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 14 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 14 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 17NOV2020 (16:46)

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Participants With or Without Evidence of Infection Before and During Vaccination Regimen

Among participants with or without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against confirmed COVID-19 occurring at least 14 days after Dose 2 was 94.4%, with 8 and 144 cases in the BNT162b2 and placebo groups respectively (Table 11). The posterior probability of >99.99% for the true VE greater than 30% met the prespecified success criterion of >98.6% for this endpoint. The 95% credible interval for the vaccine efficacy was 89.1% to 97.3%, indicating that the true VE is at least 89.1% with a 97.5% probability given the available data.

Table 11. Vaccine Efficacy – First COVID-19 Occurrence From 14 Days After Dose 2 – Subjects With or Without Evidence of Infection Prior to 14 Days After Dose 2 – Evaluable Efficacy (14 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) | Pr (VE >30% data) ^f |
|-----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =19965) | | Placebo (N ^a =20171) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 14 days after Dose 2 | 8 | 1.984 (17645) | 144 | 1.995 (17746) | 94.4 | (89.1, 97.3) | >0.9999 |

Abbreviations: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 14 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

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(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File:

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2.7.3.2.1.2.4.2. Vaccine Efficacy for Severe COVID-19 Cases – Final Analysis Efficacy Against Severe COVID-19 (≥7 Days After Dose 2)

Participants Without Evidence of Infection Before and During Vaccination Regimen

For this efficacy endpoint, participants with positive or unknown NAAT results at any illness visit prior to 7 days after Dose 2 were not included in the evaluation for efficacy.

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Among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, the estimated VE against severe COVID-19 occurring at least 7 days after Dose 2 was 66.4%, with 1 and 3 cases in the BNT162b2 and placebo groups respectively (Table 12). The posterior probability for the true vaccine efficacy greater than 30% is 74.29%, which did not meet the prespecified success criterion of >98.6% for this endpoint due to the small number of severe cases observed after Dose 2 in the study. Consequently, statistical testing of subsequent secondary endpoints (ie, the additional secondary endpoints related to severe disease with pre-specified control of overall type 1 error) ended. However, descriptive summaries for the additional endpoints are provided.

Table 12. Vaccine Efficacy – First Severe COVID-19 Occurrence From 7 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI) ^e | Pr (VE >30% data) ^f |
|-----------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|-----------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =18198) | | Placebo (N ^a =18325) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First severe COVID-19 occurrence from 7 days after Dose 2 | 1 | 2.215 (17411) | 3 | 2.232 (17511) | 66.4 | (-124.8, 96.3) | 0.7429 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 17NOV2020 (16:47)

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Participants With or Without Evidence of Infection Before and During Vaccination Regimen

Among participants with or without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against severe COVID-19 occurring at least 7 days after Dose 2

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was 66.3%, with 1 and 3 cases in the BNT162b2 and placebo groups respectively (Table 13). The posterior probability for the true vaccine efficacy greater than 30% is 74.19%.

Table 13. Vaccine Efficacy – First Severe COVID-19 Occurrence From 7 Days After Dose 2 – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI) ^e | Pr (VE >30% data) ^f |
|-----------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|-----------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =19965) | | Placebo (N ^a =20172) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First severe COVID-19 occurrence from 7 days after Dose 2 | 1 | 2.333 (18566) | 3 | 2.358 (18733) | 66.3 | (-125.5, 96.3) | 0.7419 |

Abbreviations: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
 - b. n1 = Number of subjects meeting the endpoint definition.
 - c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
 - d. n2 = Number of subjects at risk for the endpoint.
 - e. Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
 - f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 17NOV2020 (16:46)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File:
.nda2_unblinded/C4591001 Efficacy FA 164/adc19ef ve sev cov 7pd2 eval

All Confirmed Cases of Severe COVID-19 After Dose 1 – All-Available Population

Among participants in the Dose 1 all-available efficacy population, 1 case of severe COVID-19 occurred after Dose 1 in the BNT162b2 group compared to 9 cases in the placebo group (Table 14). The estimated VE against severe COVID-19 occurring after Dose 1 was 88.9% (2-sided 95% CI: 20.1%, 99.7%), with an estimated VE of 75.0% against severe COVID-19 occurring at least 7 days after Dose 2 (1 case in the BNT162b2 group and 4 cases in the placebo group).

In addition, a post hoc analysis was conducted for efficacy against severe cases of COVID-19 using the CDC definition of severe COVID-19 (hospitalization, admission to the intensive care unit (ICU), intubation or mechanical ventilation, or death).⁶ In this analysis in the Dose 1 all-available efficacy population, 1 case of severe COVID-19 occurred after Dose 1 in the BNT162b2 group compared to 14 cases in the placebo group (Table 43). The estimated VE against severe COVID-19 occurring after Dose 1 was 92.9% (2-sided 95% CI:

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53.2%, 99.8%), with an estimated VE of 100.0% against severe COVID-19 occurring at least 7 days after Dose 2 (no cases in the BNT162b2 group and 5 cases in the placebo group).

Table 14. Vaccine Efficacy – First Severe COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|-----------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =21669) | | Placebo (N ^a =21686) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First severe COVID-19 occurrence after Dose 1 | 1 | 4.021 (21314) | 9 | 4.006 (21259) | 88.9 | (20.1, 99.7) |
| After Dose 1 to before Dose 2 | 0 | | 4 | | 100.0 | (-51.5, 100.0) |
| Dose 2 to 7 days after Dose 2 | 0 | | 1 | | 100.0 | (-3800.0, 100.0) |
| ≥7 Days after Dose 2 | 1 | | 4 | | 75.0 | (-152.6, 99.5) |

Abbreviations: VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method (adjusted for surveillance time for overall row).

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 18NOV2020 (17:43)

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Efficacy Against Severe COVID-19 (≥14 Days After Dose 2)

Participants Without Evidence of Infection Before and During Vaccination Regimen (14 Days) – Severe

For this efficacy endpoint, participants with positive or unknown NAAT results at any illness visit prior to 14 days after Dose 2 were not included in the evaluation for efficacy.

Among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, the estimated VE against severe COVID-19 occurring at least 14 days after Dose 2 was 66.4%, with 1 and 3 cases in the BNT162b2 and placebo groups respectively (Table 15). The posterior probability for the true vaccine efficacy greater than 30% is 74.32%.

Table 15. Vaccine Efficacy – First Severe COVID-19 Occurrence From 14 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 14 Days After Dose 2 – Evaluable Efficacy (14 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI) ^e | Pr (VE >30% data) ^f |
|------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|-----------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =18175) | | Placebo (N ^a =18261) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First severe COVID-19 occurrence from 14 days after Dose 2 | 1 | 1.888 (16612) | 3 | 1.901 (16663) | 66.4 | (-124.7, 96.3) | 0.7432 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 14 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 14 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 14 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

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(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File:

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Participants With or Without Evidence of Infection Before and During Vaccination Regimen (14 Days) – Severe

Among participants with or without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against severe COVID-19 occurring at least 14 days after Dose 2 was 66.3%, with 1 and 3 cases in the BNT162b2 and placebo groups respectively (Table 16). The posterior probability for the true vaccine efficacy greater than 30% is 74.18%.

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Table 16. Vaccine Efficacy – First Severe COVID-19 Occurrence From 14 Days After Dose 2 – Subjects With or Without Evidence of Infection Prior to 14 Days After Dose 2 – Evaluable Efficacy (14 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI) ^e | Pr (VE >30% data) ^f |
|------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|-----------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =19965) | | Placebo (N ^a =20171) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First severe COVID-19 occurrence from 14 days after Dose 2 | 1 | 1.985 (17652) | 3 | 2.007 (17792) | 66.3 | (-125.6, 96.3) | 0.7418 |

Abbreviations: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 14 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

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2.7.3.2.1.2.4.3. Vaccine Efficacy for COVID-19 Cases per CDC Definition – Final Analysis

Efficacy Against COVID-19 Based on CDC-Defined Symptoms (≥7 Days After Dose 2)

Participants Without Evidence of Infection Before and During Vaccination Regimen – CDC Defined – 7 Days

For this efficacy endpoint, participants with positive or unknown NAAT results at any illness visit prior to 7 days after Dose 2 were not included in the evaluation for efficacy.

Among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against CDC-defined COVID-19 occurring at least 7 days after Dose 2 was 95.1% (2-sided 95% CI: 90.2%, 97.9%), with 8 and 165 cases in the BNT162b2 and placebo groups, respectively (Table 44).

Participants With and Without Evidence of Infection Before and During Vaccination Regimen – CDC Defined – 7 Days

Among participants with and without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against CDC-defined COVID-19 occurring at least 7 days after

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Dose 2 was 94.7% (2-sided 95% CI: 89.8%, 97.6%), with 9 and 172 cases in the BNT162b2 and placebo groups, respectively (Table 45).

Efficacy Against COVID-19 Based on CDC-Defined Symptoms (≥ 14 Days After Dose 2)

Among participants without and with or without evidence of SARS-CoV-2 infection before and during vaccination regimen, observed VE results against CDC-defined COVID-19 occurring at least 14 days after Dose 2 were similar to those occurring at least 7 days after Dose 2 (Table 46 and Table 47).

2.7.3.2.1.2.5. Efficacy Conclusions From the Final Analysis – Study C4591001

Evaluable Efficacy Population

In the final efficacy analysis, among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 95.0%, with 8 COVID-19 cases in the BNT162b2 group compared to 162 COVID-19 cases in the placebo group. The 95% credible interval for the vaccine efficacy was 90.3% to 97.6%.

For the second primary endpoint, VE against confirmed COVID-19 occurring at least 7 days after Dose 2 in participants with or without evidence of SARS-CoV-2 infection before and during vaccination regimen was 94.6%, with 9 and 169 cases in the BNT162b2 and placebo groups respectively. The posterior probability of $>99.99\%$ for the true VE greater than 30% met the prespecified success criterion of $>98.6\%$ for this endpoint. The 95% credible interval for the vaccine efficacy was 89.9% to 97.3%.

Observed VE was very high for the first primary efficacy endpoint across subgroups of age, sex, race/ethnicity, and country, as VE was $>93\%$ in all subgroups, with the exception of “all others” race group (89.3% VE) and Brazil (87.7% VE).

For the secondary efficacy endpoints, observed VE against confirmed COVID-19 occurring at least 14 days after Dose 2 in participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, was 94.2%, with 8 and 139 cases in the BNT162b2 and placebo groups, respectively. The posterior probability of $>99.99\%$ for the true VE greater than 30% met the prespecified success criterion of $>98.6\%$ for this endpoint. The 95% credible interval for the vaccine efficacy was 88.7% to 97.2%.

Similarly, among participants with or without evidence of SARS-CoV-2 infection before and during vaccination regimen, VE against confirmed COVID-19 occurring at least 14 days after Dose 2 was 94.4%, with 8 and 144 cases in the BNT162b2 and placebo groups respectively. The posterior probability of $>99.99\%$ for the true VE greater than 30% met the prespecified success criterion of $>98.6\%$ for this endpoint. The 95% credible interval for the vaccine efficacy was 89.1% to 97.3%.

Among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, observed VE of 66.3% against severe COVID-19 occurring at least 7 days after Dose 2 did not meet the prespecified success criterion of the posterior probability

>98.6%, due to the small number of severe cases (1 in the BNT162b2 group, 3 in the placebo group) observed within the prespecified timeframe of ≥ 7 Days after Dose 2 in the study.

The efficacy analyses using CDC defined symptoms to identify COVID-19 cases and severe COVID-19 cases gave similar efficacy results as the analyses using the protocol-defined symptoms.

All-Available Efficacy Population

The early onset of protection is readily apparent from cumulative incidence curves, which show that disease onset tracks conjointly for BNT162b2 and placebo until approximately 14 days after Dose 1, at which point the curves diverge, with cases steadily accumulating in the placebo group, while remaining virtually flat after BNT162b2.

Among all participants (regardless of evidence of infection before or during the vaccination regimen) 50 cases of COVID-19 occurred after Dose 1 in the BNT162b2 group compared with 275 cases in the placebo group, indicating an estimated VE of 82% (2-sided 95% CI: 75.6%, 86.9%) against confirmed COVID-19 occurring after Dose 1, with VE of 52.4% (95% CI: 29.5%, 68.4%) between Dose 1 and Dose 2.

Among the total of 10 severe COVID-19 cases observed after Dose 1, only 1 severe case was seen in BNT162b2 recipients compared to 9 severe COVID-19 cases in placebo recipients; these results, as well as case splits between Dose 1 and Dose 2 and after Dose 2, were consistent with overall efficacy seen against COVID-19.

In conclusion, the final efficacy results show that BNT162b2 at 30 μg provided protection against COVID-19 in participants who had no evidence of prior infection with SARS-CoV-2, including across demographic subgroups, with severe cases observed predominantly in the placebo group.

2.7.3.2.1.3. Updated Efficacy Analyses – Study C4591001

Updated descriptive efficacy analyses were performed using all cases accrued during the blinded placebo-controlled follow-up through the cutoff date of 13 March 2021. Updated efficacy analyses were conducted for the primary efficacy endpoints, including subgroup analyses, and for secondary efficacy endpoints of severe disease and CDC-defined severe disease.

2.7.3.2.1.3.1. Efficacy Populations – Updated Analysis

The proportions of participants included in the updated analysis efficacy populations were similar in the BNT162b2 and placebo groups (Table 48). Most participants who were excluded from the evaluable efficacy population had not received all vaccinations as randomized or did not receive Dose 2 within the predefined window (ie, 19 to 42 days after Dose 1). There were 240 participants in the BNT162b2 group and 60 participants in the placebo group excluded for having important protocol deviations on or prior to 7 days after Dose 2. In the BNT162b2 group, most of these deviations were related to improper administration of the investigational product (203 participants, as compared with 23 participants in the placebo group); among these, most exclusions in the BNT162b2 group

were due to dosing/administration errors (76 participants) or administration of investigational product that was deemed not suitable for use by the contractor who distributed the vaccine to study sites (110 participants) [Table 49](#). These were administration errors that could not have applied to participants who received placebo: eg, errors in dilution of the vaccine or temperature excursions.

Demographic characteristics of participants in the updated analysis evaluable efficacy population for participants without evidence of infection prior to 7 days after Dose 2 were similar in the BNT162b2 and placebo groups ([Table 50](#)). This analysis population had generally similar demographic characteristics compared to the safety population.

2.7.3.2.1.3.2. Efficacy Results – Updated Analyses

As described above, based on results for the first primary efficacy endpoint, overwhelming efficacy was declared at the first (and only) interim analysis ([Section 2.7.3.2.1.1.2.1](#)) and was confirmed at the final analysis ([Section 2.7.3.2.1.2.3.1](#)). A descriptive update based on a total of 927 confirmed cases for the first primary endpoint accrued during blinded placebo-controlled follow-up, up to the data cutoff date of 13 March 2021, is summarized below.

The results presented are for the evaluable efficacy populations, except as noted.

2.7.3.2.1.3.2.1. Vaccine Efficacy Against Confirmed COVID-19 Occurring at Least 7 Days After Dose 2 – Evaluable Efficacy Population - Updated Analysis

Participants Without Evidence of SARS-CoV-2 Infection

Among participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 91.3%, with 77 COVID-19 cases in the BNT162b2 group compared to 850 cases in the placebo group ([Table 17](#)). The 2-sided 95% CI for vaccine efficacy was 89.0% to 93.2%. The posterior probability for the true VE being greater than 30%, given the available data, was >99.99%.

The estimated VE of BNT162b2 for the same efficacy endpoint based on the Dose 2 all-available efficacy population was 91.4% (2-sided 95% CI: 89.1%, 93.3%), with 78 and 866 cases in the BNT162b2 and placebo group, respectively ([Table 51](#)).

Table 17. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | VE (%) | (95% CI) ^e | Pr (VE >30% data) ^f |
|----------------------------------------------------|-------------------------------------------------------------------|-------------------------------------------------------------------|--------|-----------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =20998) | Placebo (N ^a =21096) | | | |
| | n1 ^b Surveillance Time ^c (n2 ^d) | n1 ^b Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 77 6.247 (20712) | 850 6.003 (20713) | 91.3 | (89.0, 93.2) | >0.9999 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 27MAR2021 (01:59)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: /nda2_unblinded/C4591001_BLA/adc19ef_ve_cov_7pd2_wo_eval

Participants With or Without Evidence of SARS-CoV-2 Infection

Among participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen, estimated VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 91.1%, with 81 and 873 cases in the BNT162b2 and placebo groups, respectively (Table 18). The 2-sided 95% CI for vaccine efficacy was 88.8% to 93.0%. The posterior probability for the true VE being greater than 30%, given the available data, was >99.99%.

The estimated VE of BNT162b2 for the same endpoint based on the Dose 2 all-available efficacy population was 91.2% (2-sided 95% CI: 88.9%, 93.0%), with 82 and 889 cases in the BNT162b2 and placebo group, respectively (Table 52).

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Table 18. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | | | Pr (VE >30% data) ^f |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|-----------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =22166) | | Placebo (N ^a =22320) | | VE (%) | (95% CI) ^e | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 81 | 6.509 (21642) | 873 | 6.274 (21689) | 91.1 | (88.8, 93.0) | >0.9999 |

Abbreviation: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 27MAR2021 (01:59)

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2.7.3.2.1.3.2.2. Vaccine Efficacy for All Confirmed Cases of COVID-19 After Dose 1 – Dose 1 All-Available Population – Updated Analysis

A number of confirmed cases of COVID-19 are not captured in the analyses of the primary endpoints for the evaluable efficacy population because they either occurred in participants who were excluded from the evaluable efficacy population, or occurred less than 7 days after Dose 2.

All reports of COVID-19 with onset at any time after Dose 1 are accounted for in [Table 19](#), which provides a summary of VE for confirmed cases for all participants in the Dose 1 all-available efficacy (modified intention-to-treat) population adjusted for surveillance time, regardless of evidence of infection before or during the vaccination regimen. Among these participants, 131 cases of COVID-19 occurred after Dose 1 in the BNT162b2 group compared to 1034 cases in the placebo group. The estimated VE against confirmed COVID-19 occurring at any time after Dose 1 was 87.8% (2-sided 95% CI: 85.3%, 89.9%).

In this population, the estimated VE against all cases occurring ≥ 7 days after Dose 2 was 91.2%. The estimated VE was 91.7% for cases occurring from ≥ 11 days after Dose 1 to before Dose 2, 96.2% for cases occurring from ≥ 7 days after Dose 2 to < 2 months after Dose 2, 90.1% for the period from ≥ 2 months to < 4 months after Dose 2, and 83.7% for the period ≥ 4 months after Dose 2.

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Table 19. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|--------------------------------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =23040) | | Placebo (N ^a =23037) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence after Dose 1 | 131 | 8.412 (22505) | 1034 | 8.124 (22434) | 87.8 | (85.3, 89.9) |
| After Dose 1 to before Dose 2 | 46 | 1.339 (22505) | 110 | 1.331 (22434) | 58.4 | (40.8, 71.2) |
| After Dose 1 to <11 days after Dose 1 | 41 | 0.677 (22505) | 50 | 0.675 (22434) | 18.2 | (-26.1, 47.3) |
| ≥11 Days after Dose 1 to before Dose 2 | 5 | 0.662 (22399) | 60 | 0.656 (22369) | 91.7 | (79.6, 97.4) |
| Dose 2 to 7 days after Dose 2 | 3 | 0.424 (22163) | 35 | 0.422 (22057) | 91.5 | (72.9, 98.3) |
| ≥7 Days after Dose 2 | 82 | 6.649 (22132) | 889 | 6.371 (22001) | 91.2 | (88.9, 93.0) |
| ≥7 days after Dose 2 to <2 Months after Dose 2 | 12 | 2.923 (22132) | 312 | 2.884 (22001) | 96.2 | (93.3, 98.1) |
| ≥2 Months after Dose 2 to <4 Months after Dose 2 | 46 | 2.696 (20814) | 449 | 2.593 (20344) | 90.1 | (86.6, 92.9) |
| ≥4 Months after Dose 2 | 24 | 1.030 (12670) | 128 | 0.895 (11802) | 83.7 | (74.7, 89.9) |

Abbreviation: VE = vaccine efficacy.

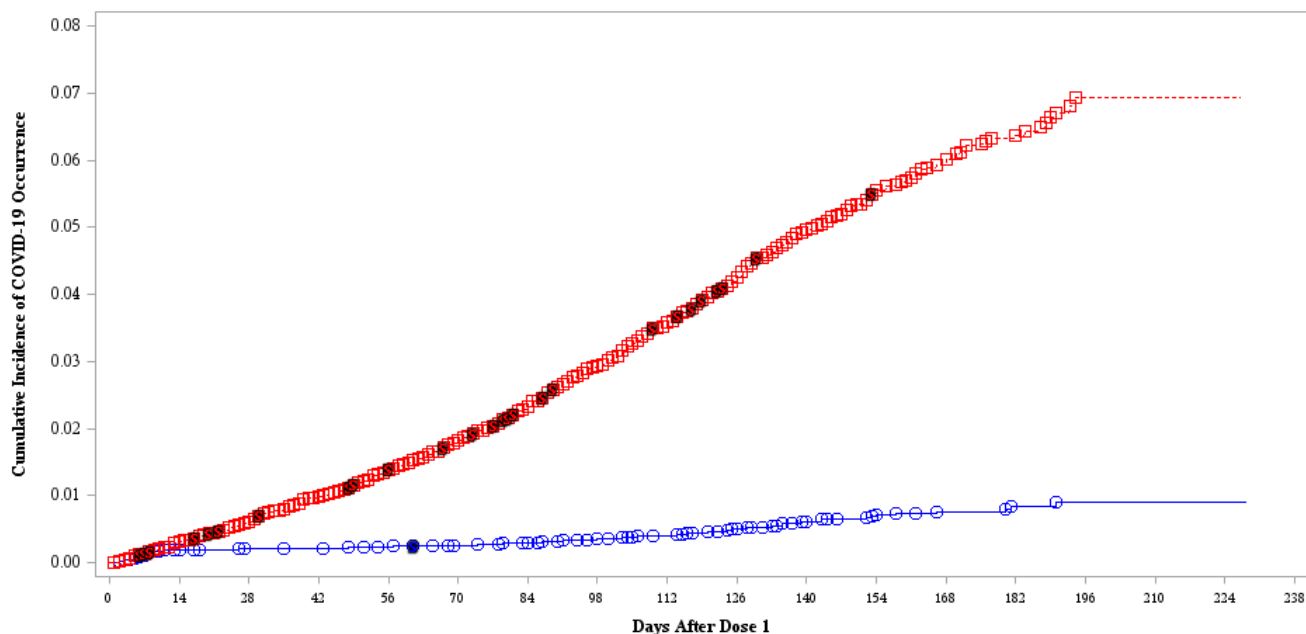
- a. N = number of subjects in the specified group.
 - b. n1 = Number of subjects meeting the endpoint definition.
 - c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
 - d. n2 = Number of subjects at risk for the endpoint.
 - e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 19APR2021 (17:34)
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The early onset of protection is readily apparent in [Figure 2](#), which displays cumulative incidence for the first COVID-19 occurrence after Dose 1 among all vaccinated participants based on Dose 1 all-available efficacy (modified intention-to-treat) population. Disease onset appears to track together for BNT162b2 and placebo until approximately 11 days after Dose 1 (consistent with the data shown in Table 19), at which point the curves diverge, with cases steadily accumulating in the placebo group, while remaining virtually flat in the BNT162b2 group.

The darker-appearing symbols for both BNT162b2 (blue circles) and placebo (red squares) curves in [Figure 2](#) have an “S” written inside the open symbol, which denotes severe cases. Severe COVID-19 cases reported in the updated analysis are discussed further in [Section 2.7.3.2.1.3.2.4](#).

Figure 2. Cumulative Incidence Curves for the First COVID-19 Occurrence After Dose 1– Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

Cumulative Incidence Curves – First COVID-19 Occurrence After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population



Subjects at Risk

| | | | | | | | | | | | | | | | | | |
|-----------------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|------|------|------|------|------|------|
| A: | 22505 | 22398 | 22320 | 22241 | 22037 | 21325 | 20560 | 19085 | 17130 | 14582 | 11376 | 7889 | 4577 | 2463 | 1082 | 158 | 4 |
| B: | 22434 | 22352 | 22193 | 22034 | 21738 | 20889 | 20024 | 18428 | 16401 | 13747 | 10523 | 6997 | 3827 | 1911 | 657 | 38 | 3 |
| Cumulative Number of Events | | | | | | | | | | | | | | | | | |
| A: | 0 | 43 | 47 | 48 | 53 | 59 | 66 | 77 | 87 | 102 | 116 | 125 | 128 | 130 | 131 | 131 | 131 |
| B: | 0 | 70 | 137 | 219 | 309 | 406 | 509 | 630 | 744 | 850 | 939 | 991 | 1016 | 1027 | 1034 | 1034 | 1034 |

○ A: BNT162b2 (30 µg)
□ B: Placebo

Note: "S" indicates subjects with severe COVID-19.
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2.7.3.2.1.3.2.3. Vaccine Efficacy by Subgroup – Updated Analysis

For both primary endpoints, VE was also evaluated for subgroups of participants by age, sex, race/ethnicity, and country, as well as for groups of subjects by risk status and comorbidities. Overall, the results show high rates of VE based on subgroup analyses.

Subgroups of Age, Sex, Race/Ethnicity, and Country

In the evaluable efficacy population, among participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen, estimated VE was $\geq 90\%$ in most subgroups, similar to the 91.3% overall VE (Table 20). High VE was also observed across age groups, with an estimated VE of 100.0% in 12 to 15 year olds, 90.6% in 16 to 64 year olds, 94.5% in those ≥ 65 years, and 96.2% in those ≥ 75 years of age. Estimated VEs were 87.6% among Asian and 88.5% among Hispanic/Latino participants; the estimated VE was 92.6% in the United States, 86.5% in Argentina, 86.2% in Brazil, and 100.0% in South Africa, Germany, and Turkey.

Similar results were observed for subgroup analyses among participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen (Table 53). In analyses for the Dose 1 all-available efficacy population, which included all confirmed cases occurring at any time after Dose 1, no clinically meaningful differences among the subgroups were identified (Table 54).

Subgroup analyses included evaluation of VE by prior SARS-CoV-2 status at baseline. The number of participants with positive prior SARS-CoV-2 status at baseline was relatively small, and the 95% CIs for the estimated VEs in these subgroup analyses were very wide; therefore, the data must be interpreted with caution. However, the results may provide some information regarding the benefits of vaccination for individuals with prior SARS-CoV-2 infection.

Participants with positive prior SARS-CoV-2 status at baseline were defined as those with positive N-binding antibody or NAAT results at Visit 1 or a medical history of COVID-19. In the evaluable efficacy analysis for this subgroup, the estimated VE against cases occurring ≥ 7 days after Dose 2 was 46.9% (3 cases BNT162b2; 6 cases placebo) (Table 53), and in the all-available efficacy analysis the estimated VE against cases occurring at any time after Dose 1 was 19.2% (13 cases BNT162b2, 17 cases placebo) (Table 54).

It is important to note that the subgroup defined above includes participants with both past infections (positive N-binding antibody) and current infections (NAAT positive). Since it is reasonable to expect that vaccination may be less effective in participants currently infected with SARS-CoV-2 at Visit 1, it may be relevant to examine VE specifically in participants who were positive for N-binding only (and were not NAAT-positive) at Visit 1. In the evaluable efficacy analysis for these participants, the estimated VE against cases occurring ≥ 7 days after Dose 2 was 58.9% (2 cases BNT162b2; 5 cases placebo) (Table 53), and in the all-available efficacy analysis the estimated VE against cases occurring at any time after Dose 1 was 70.5% (2 cases BNT162b2, 7 cases placebo) (Table 54). Therefore, estimates of VE are considerably higher in participants who were positive for N-binding antibody only,

suggesting that vaccination provides a benefit for individuals with previous SARS-CoV-infection.

Table 20. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =20998) | | Placebo (N ^a =21096) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | | | | | | |
| Overall | 77 | 6.247 (20712) | 850 | 6.003 (20713) | 91.3 | (89.0, 93.2) |
| Age group (years) | | | | | | |
| 12 to 15 | 0 | 0.154 (1001) | 16 | 0.147 (972) | 100.0 | (75.3, 100.0) |
| 16 to 55 | 52 | 3.593 (11517) | 568 | 3.439 (11533) | 91.2 | (88.3, 93.5) |
| >55 | 25 | 2.499 (8194) | 266 | 2.417 (8208) | 90.9 | (86.3, 94.2) |
| ≥65 | 7 | 1.233 (4192) | 124 | 1.202 (4226) | 94.5 | (88.3, 97.8) |
| 16 to 17 | 0 | 0.061 (342) | 10 | 0.057 (331) | 100.0 | (58.2, 100.0) |
| 16 to 25 | 8 | 0.482 (1629) | 80 | 0.466 (1622) | 90.3 | (80.0, 96.0) |
| 16 to 64 | 70 | 4.859 (15519) | 710 | 4.654 (15515) | 90.6 | (87.9, 92.7) |
| 18 to 64 | 70 | 4.798 (15177) | 700 | 4.597 (15184) | 90.4 | (87.7, 92.6) |
| 55 to 64 | 21 | 1.399 (4426) | 157 | 1.334 (4388) | 87.3 | (79.8, 92.3) |
| 65 to 74 | 6 | 0.994 (3350) | 98 | 0.966 (3379) | 94.1 | (86.6, 97.9) |
| ≥75 | 1 | 0.239 (842) | 26 | 0.237 (847) | 96.2 | (76.9, 99.9) |
| 75 to 85 | 1 | 0.238 (837) | 25 | 0.235 (841) | 96.0 | (75.9, 99.9) |
| >85 | 0 | 0.001 (5) | 1 | 0.001 (6) | 100.0 | (-4055.9, 100.0) |
| Sex | | | | | | |
| Male | 42 | 3.246 (10637) | 399 | 3.047 (10433) | 90.1 | (86.4, 93.0) |
| Female | 35 | 3.001 (10075) | 451 | 2.956 (10280) | 92.4 | (89.2, 94.7) |
| Race | | | | | | |
| White | 67 | 5.208 (17186) | 747 | 5.026 (17256) | 91.3 | (88.9, 93.4) |
| Black or African American | 4 | 0.545 (1737) | 48 | 0.527 (1737) | 91.9 | (78.0, 97.9) |
| American Indian or Alaska Native | 0 | 0.041 (186) | 3 | 0.037 (176) | 100.0 | (-119.0, 100.0) |
| Asian | 3 | 0.260 (946) | 23 | 0.248 (934) | 87.6 | (58.9, 97.6) |
| Native Hawaiian or other Pacific Islander | 0 | 0.015 (54) | 1 | 0.008 (30) | 100.0 | (-1961.2, 100.0) |
| Multiracial | 3 | 0.151 (518) | 22 | 0.128 (476) | 88.5 | (61.6, 97.8) |
| Not reported | 0 | 0.026 (85) | 6 | 0.030 (104) | 100.0 | (2.8, 100.0) |

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Table 20. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =20998) | | Placebo (N ^a =21096) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| All others ^f | 6 | 0.494 (1789) | 55 | 0.451 (1720) | 90.0 | (76.9, 96.5) |
| Ethnicity | | | | | | |
| Hispanic/Latino | 29 | 1.786 (5161) | 241 | 1.711 (5120) | 88.5 | (83.0, 92.4) |
| Non-Hispanic/non-Latino | 47 | 4.429 (15449) | 609 | 4.259 (15484) | 92.6 | (90.0, 94.6) |
| Not reported | 1 | 0.032 (102) | 0 | 0.033 (109) | -∞ | (NA, NA) |
| Country | | | | | | |
| Argentina | 15 | 1.012 (2600) | 108 | 0.986 (2586) | 86.5 | (76.7, 92.7) |
| Brazil | 12 | 0.406 (1311) | 80 | 0.374 (1293) | 86.2 | (74.5, 93.1) |
| Germany | 0 | 0.047 (236) | 1 | 0.048 (242) | 100.0 | (-3874.2, 100.0) |
| South Africa | 0 | 0.080 (291) | 9 | 0.074 (276) | 100.0 | (53.5, 100.0) |
| Turkey | 0 | 0.027 (228) | 5 | 0.025 (222) | 100.0 | (-0.1, 100.0) |
| USA | 50 | 4.674 (16046) | 647 | 4.497 (16094) | 92.6 | (90.1, 94.5) |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- N = number of subjects in the specified group.
- n1 = Number of subjects meeting the endpoint definition.
- Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- n2 = Number of subjects at risk for the endpoint.
- Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- All others = American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.

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(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adc19ef_ve_cov_7pd2_wo_sg_eval

Subgroup Analyses by Risk Status and Comorbidities

Analyses of efficacy by risk status were performed. For these analyses, at-risk participants were defined as those who had at least one Charlson Comorbidity Index condition or who were obese (defined as body mass index ≥ 30 kg/m²). For a summary of Charlson comorbidities among all participants ≥ 16 years of age at study entry, see [Table 55](#).

Among participants without evidence of SARS-CoV-2 infection before and during vaccination regimen, estimated VE was similar for participants at risk (91.6%) and participants not at risk (91.0%) (Table 21). The estimated VE for participants ≥ 65 years of age and at risk was 91.8%, as compared with 98.1% for those ≥ 65 years of age and not at risk. Estimated VE was similar in obese (91.6%) and non-obese (91.1%) participants. When evaluated by type of comorbidity, estimated VE was $>85\%$ for participants with each comorbidity evaluated, including any malignancy, cardiovascular disease, chronic pulmonary disease, diabetes, obesity, and hypertension (Table 56).

Table 21. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =20998) | | Placebo (N ^a =21096) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | | | | | | |
| Overall | 77 | 6.247 (20712) | 850 | 6.003 (20713) | 91.3 | (89.0, 93.2) |
| At risk ^f | | | | | | |
| Yes | 35 | 2.797 (9167) | 401 | 2.681 (9136) | 91.6 | (88.2, 94.3) |
| No | 42 | 3.450 (11545) | 449 | 3.322 (11577) | 91.0 | (87.6, 93.6) |
| Age group (years) and at risk | | | | | | |
| 12-15 and not at risk | 0 | 0.121 (788) | 11 | 0.116 (769) | 100.0 | (61.9, 100.0) |
| 12-15 and at risk | 0 | 0.034 (213) | 5 | 0.032 (203) | 100.0 | (-2.0, 100.0) |
| 16-64 and not at risk | 41 | 2.776 (8887) | 385 | 2.661 (8886) | 89.8 | (85.9, 92.8) |
| 16-64 and at risk | 29 | 2.083 (6632) | 325 | 1.993 (6629) | 91.5 | (87.5, 94.4) |
| ≥ 65 and not at risk | 1 | 0.553 (1870) | 53 | 0.546 (1922) | 98.1 | (89.2, 100.0) |
| ≥ 65 and at risk | 6 | 0.680 (2322) | 71 | 0.656 (2304) | 91.8 | (81.4, 97.1) |
| Obese ^g | | | | | | |
| Yes | 27 | 2.103 (6796) | 314 | 2.050 (6875) | 91.6 | (87.6, 94.6) |
| No | 50 | 4.143 (13911) | 536 | 3.952 (13833) | 91.1 | (88.1, 93.5) |
| Age group (years) and obese | | | | | | |
| 12-15 and not obese | 0 | 0.135 (878) | 13 | 0.131 (867) | 100.0 | (68.3, 100.0) |
| 12-15 and obese | 0 | 0.019 (123) | 3 | 0.016 (105) | 100.0 | (-104.8, 100.0) |
| 16-64 and not obese | 46 | 3.178 (10212) | 444 | 3.028 (10166) | 90.1 | (86.6, 92.9) |
| 16-64 and obese | 24 | 1.680 (5303) | 266 | 1.624 (5344) | 91.3 | (86.7, 94.5) |
| ≥ 65 and not obese | 4 | 0.829 (2821) | 79 | 0.793 (2800) | 95.2 | (87.1, 98.7) |
| ≥ 65 and obese | 3 | 0.404 (1370) | 45 | 0.410 (1426) | 93.2 | (78.9, 98.7) |

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Table 21. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =20998) | | Placebo (N ^a =21096) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
 - b. n1 = Number of subjects meeting the endpoint definition.
 - c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
 - d. n2 = Number of subjects at risk for the endpoint.
 - e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
 - f. Includes subjects who had at least one of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m² [≥16 Years of age] or BMI ≥95th percentile [12-15 Years of age]).
 - g. Subjects (≥16 Years of age) who had BMI ≥30 kg/m². For 12 through 15 years age group, obesity is defined as a BMI at or above the 95th percentile. Refer to the CDC growth charts at https://www.cdc.gov/growthcharts/html_charts/bmiagerev.htm.
- PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adc19ef Table Generation: 30MAR2021 (22:35)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adc19ef_ve_cov_7pd2_wo_rg_eval

2.7.3.2.1.3.2.4. Vaccine Efficacy for Severe COVID-19 Cases – Updated Analysis Efficacy Against Severe COVID-19 (≥7 Days After Dose 2)

Among participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE against severe COVID-19 as defined by FDA occurring at least 7 days after Dose 2 was 95.3% (2-sided 95% CI: 71.0%, 99.9%), with 1 and 21 cases in the BNT162b2 and placebo groups, respectively (Table 22). The posterior probability for the true vaccine efficacy being greater than 30%, given the available data, was >99.99%.

The same number of severe cases were reported among participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen (1 case in the BNT162 group and 21 cases in the placebo group), and the estimated VE was the same (95.3%) (Table 57).

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Table 22. Vaccine Efficacy – First Severe COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | | | Pr (VE >30% data) ^f |
|-----------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|-----------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =20998) | | Placebo (N ^a =21096) | | VE (%) | (95% CI) ^e | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First severe COVID-19 occurrence from 7 days after Dose 2 | 1 | 6.257 (20712) | 21 | 6.120 (20713) | 95.3 | (71.0, 99.9) | >0.9999 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
 - b. n1 = Number of subjects meeting the endpoint definition.
 - c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
 - d. n2 = Number of subjects at risk for the endpoint.
 - e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
 - f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 27MAR2021 (02:26)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2_unblinded/C4591001_BLA/adc19ef_ve_sev_cov_7pd2_wo_eval

All Confirmed Cases of Severe COVID-19 (As Defined by FDA) After Dose 1 – All-Available Efficacy Population

Among participants in the Dose 1 all-available efficacy (modified intention-to-treat) population, 1 case of severe COVID-19 as defined by FDA occurred after Dose 1 in the BNT162b2 group compared to 30 cases in the placebo group (Table 23). The estimated VE against severe COVID-19 occurring after Dose 1 was 96.7% (2-sided 95% CI: 80.3%, 99.9%).

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Table 23. Vaccine Efficacy – First Severe COVID-19 Occurrence After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|-----------------------------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =23040) | | Placebo (N ^a =23037) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First severe COVID-19 occurrence after Dose 1 | 1 | 8.439 (22505) | 30 | 8.288 (22435) | 96.7 | (80.3, 99.9) |
| After Dose 1 to before Dose 2 | 0 | 1.351 (22505) | 6 | 1.360 (22435) | 100.0 | (14.5, 100.0) |
| Dose 2 to 7 days after Dose 2 | 0 | 0.425 (22170) | 1 | 0.423 (22070) | 100.0 | (-3783.5, 100.0) |
| ≥7 Days after Dose 2 | 1 | 6.663 (22142) | 23 | 6.505 (22048) | 95.8 | (73.9, 99.9) |

Abbreviation: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

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2.7.3.2.1.3.2.5. Vaccine Efficacy for Severe COVID-19 Cases per CDC Definition – Updated Analysis

In addition, a supportive analysis was conducted for efficacy against severe cases of COVID-19 using the CDC definition of severe COVID-19 (hospitalization, admission to the intensive care unit (ICU), intubation or mechanical ventilation, or death).⁶

Among efficacy evaluable participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE against CDC-defined severe COVID-19 occurring at least 7 days after Dose 2 was 100.0% (2-sided 95% CI: 88.1%, 100.0%), with 0 and 32 cases in the BNT162b2 and placebo groups, respectively (Table 24).

The same number of CDC-defined severe cases were reported among efficacy evaluable participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen (Table 58).

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Table 24. Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC-Definition From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) (95% CI ^e) | |
|-----------------------------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|-------------------------------|---------------|
| | BNT162b2 (30 µg) (N ^a =20998) | | Placebo (N ^a =21096) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First severe COVID-19 occurrence based on CDC-definition from 7 days after Dose 2 | 0 | 6.250 (20688) | 32 | 6.108 (20680) | 100.0 | (88.1, 100.0) |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
 Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of subjects in the specified group.
 b. n1 = Number of subjects meeting the endpoint definition.
 c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
 d. n2 = Number of subjects at risk for the endpoint.
 e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
 PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 27MAR2021 (02:27)
 (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
 ./nda2_unblinded/C4591001_BLA/adc19ef_ve_sev_7pd2_cdc_wo_eval

All Confirmed Cases of CDC-Defined Severe COVID-19 After Dose 1 – All-Available Efficacy Population

Among participants in the Dose 1 all-available efficacy population, 1 case of CDC-defined severe COVID-19 occurred after Dose 1 (but before Dose 2) in the BNT162b2 group compared to 45 cases in the placebo group (Table 25). The estimated VE against severe CDC-defined COVID-19 occurring after Dose 1 was 97.8% (2-sided 95% CI: 87.2%, 99.9%).

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Table 25. Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC-Definition After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | | |
|-----------------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =23040) | | Placebo (N ^a =23037) | | VE (%) | (95% CI ^e) |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First Severe COVID-19 occurrence based on CDC-definition after Dose 1 | 1 | 8.427 (22473) | 45 | 8.269 (22394) | 97.8 | (87.2, 99.9) |
| After Dose 1 to before Dose 2 | 1 | 1.348 (22473) | 11 | 1.355 (22394) | 90.9 | (37.1, 99.8) |
| Dose 2 to 7 days after Dose 2 | 0 | 0.424 (22141) | 1 | 0.422 (22030) | 100.0 | (-3781.6, 100.0) |
| ≥7 Days after Dose 2 | 0 | 6.654 (22113) | 33 | 6.491 (22008) | 100.0 | (88.5, 100.0) |

Abbreviation: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 19APR2021 (18:26)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:

.nda2 unblinded/C4591001 BLA/adc19ef ve sev cdc pd1 aai

2.7.3.2.1.3.3. Signs and Symptoms of COVID-19

The signs and symptoms reported for cases contributing to the analysis for the first primary efficacy endpoint (77 cases in the BNT162b2 group and 850 cases in the placebo group) are summarized in [Table 59](#). These include cases occurring at least 7 days after the second vaccination among participants in the evaluable efficacy population who had no evidence of SARS-CoV-2 infection before or during the vaccination regimen. In this analysis, the proportions of participants reporting only 1 symptom were 36.4% in the BNT162b2 group, compared with 20.9% in the placebo group; and 15.6% of participants in the BNT162b2 group reported 4 or more symptoms, compared with 30.8% of participants in the placebo group. Most participants reported new or increased cough (63.9% of symptomatic cases overall), and other symptoms reported most frequently were new or increased muscle pain (45.2%), sore throat (38.6%), new loss of taste or smell (36.0%), and fever (35.9%).

[Table 60](#) summarizes the signs and symptoms for all cases of COVID-19 occurring at any time after Dose 1 (131 cases in the BNT162b2 group and 1034 cases in the placebo group). These include cases occurring among participants in the Dose 1 all-available efficacy population, regardless of evidence of SARS-CoV-2 infection before or during the vaccination regimen. The proportions of participants reporting 4 or more symptoms were 19.1% in the BNT162b2 group compared with 30.0% of participants in the placebo group. The most

frequently reported symptoms were similar to those for the analysis of the first primary efficacy endpoint.

The signs and symptoms reported for all confirmed cases of FDA-defined severe COVID-19 reported at any time after Dose 1 (in the all-available population) (1 case in the BNT162b2 group and 30 cases in the placebo group) are summarized in [Table 61](#). The participant who was diagnosed with severe COVID-19 after receiving BNT162b2 had one symptom, SpO₂ ≤93%. Among the 30 severe cases in the placebo group, 63.3% had clinical signs at rest indicative of severe systemic illness (RR ≥30 breaths per minute, HR ≥125 beats per minute, SpO₂ ≤93% on room air at sea level, or PaO₂/FiO₂ <300 mm Hg); 46.7% had respiratory failure (defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation, or ECMO), and 26.7% were admitted to an ICU.

2.7.3.2.1.3.4. Efficacy Conclusions From the Updated Analyses – Study C4591001

Updated Analysis – Efficacy Against Confirmed COVID-19

- In the updated descriptive efficacy analysis (cutoff date 13 March 2021), among participants in the evaluable efficacy population without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 91.3% (95% CI: 89.0%, 93.2%), with 77 cases in the BNT162b2 group and 850 cases in the placebo group. Among participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was 91.1% (95% CI: 88.8%, 93.0%), with 81 and 873 cases in the BNT162b2 and placebo groups, respectively.
- All cases of confirmed COVID-19 are accounted for in the analyses of VE in the all-available (modified intention-to-treat) population (regardless of evidence of infection before or during the vaccination regimen). In this analysis, estimated VE against all cases occurring at any time after Dose 1 was 87.8% (2-sided 95% CI: 85.3%, 89.9%), with 131 cases in the BNT162b2 group and 1034 cases in the placebo group.
- In the all-available (modified intention-to-treat) population, the estimated VE against all cases occurring ≥7 days after Dose 2 was 91.2%. The estimated VE was 91.7% for cases occurring from ≥11 days after Dose 1 to before Dose 2, 96.2% for cases occurring from ≥7 days after Dose 2 to <2 months after Dose 2, 90.1% for the period from ≥2 months to <4 months after Dose 2, and 83.7% for the period ≥4 months after Dose 2.

Efficacy Against Severe Cases of COVID-19

- Among participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen (evaluable efficacy population), the estimated VE against FDA defined severe COVID-19 (protocol definition) occurring at least 7 days after Dose 2 was 95.3% (2-sided 95% CI: 71.0%, 99.9%), with 1 and 21 cases in the BNT162b2 and placebo groups, respectively. Similarly, the estimated VE was also 95.3% (2-sided 95% CI: 70.9%, 99.9%) among participants with or without evidence of SARS-CoV-2 infection, also with 1 and 21 cases in the BNT162b2 and placebo groups, respectively.

- Among participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen (evaluable efficacy population), the estimated VE against CDC-defined severe COVID-19 occurring at least 7 days after Dose 2 was 100.0% (2-sided 95% CI: 88.1%, 100.0%), with 0 and 32 cases in the BNT162b2 and placebo groups, respectively. Similarly, the estimated VE was also 100.0% (2-sided 95% CI: 88.0%, 100.0%) among participants with or without evidence of SARS-CoV-2 infection, also with 0 and 32 cases in the BNT162b2 and placebo groups, respectively
- Among participants in the Dose 1 all-available efficacy population (regardless of evidence of infection before or during the vaccination regimen), estimated VE against severe cases of COVID-19 (as defined by FDA) occurring at any time after Dose 1 was 96.7% (2-sided 95% CI: 80.3%, 99.9%), with 1 case of severe COVID-19 in the BNT162b2 group compared to 30 cases in the placebo group.

Efficacy in Demographic and Risk Subgroups

Among participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen (efficacy evaluable population) VE against COVID-19 occurring at least 7 days after Dose 2 was evaluated, with results as follows:

- Estimated VE was $\geq 90\%$ in most subgroups, similar to the 91.3% overall estimated VE.
- High VE was observed across age subgroups, with an estimated VE of 100.0% in 12 to 15 year olds, 90.6% in 16 to 64 year olds, 94.5% in those ≥ 65 years, and 96.2% in those ≥ 75 years of age.
- The estimated VE was 86.5% in Argentina, 86.2% in Brazil, 92.6% in the United States, and 100.0% in South Africa, Germany, and Turkey.
- The estimated VE was similar for participants at risk (91.6%) and participants not at risk (91.0%). Estimated VE for participants ≥ 65 years of age and at risk was 91.8%, as compared with 98.1% for those ≥ 65 years of age and not at risk. Estimated VE was similar in obese (91.6%) and non-obese (91.1%) participants. When evaluated by type of comorbidity, estimated VE was $>85\%$ for participants with each comorbidity evaluated, including any malignancy, cardiovascular disease, chronic pulmonary disease, diabetes, obesity, and hypertension.

2.7.3.2.2. Immunogenicity Evaluations

In this section, immunogenicity results are first summarized for Phase 1 data from Study BNT162-01 (Section 2.7.3.2.2.1.1) and Study C4591001 (Section 2.7.3.2.2.1.2), including discussion of the rationale for the selection of the vaccine candidate and dose level to take forward into Phase 2/3 of Study C4591001 (Section 2.7.3.2.2.1.3). Subsequently, results from Study C4591001 are presented for the analyses of immunogenicity data for the 360 participants in Phase 2 (Section 2.7.3.2.2.2).

2.7.3.2.2.1. Phase 1 Immunogenicity Results – Candidate and Dose Selection

2.7.3.2.2.1.1. Study BNT162-01 – Phase 1

Study BNT162-01 is currently ongoing, and immunogenicity results reported here are for interim data.

This submission includes serology results (SARS-CoV-2 neutralizing titers and antigen-specific binding IgG levels) through the cutoff date of 23 October 2020. For participants 18 to 55 years of age (younger age group), serology data are available up to Day 43 (21 days after Dose 2) for BNT162b1 recipients and up to Day 85 (63 days after Dose 2) for BNT162b2 recipients. Serology data are also available up to Day 29 (7 days after Dose 2) for individuals 56 to 85 years of age (older age group) who received BNT162b2 at the 20 µg dose level.

This submission also includes T cell response data with cutoff dates as follows:

- ELISpot data: 02 March 2021;
- ICS data: 17 November 2020 for BNT162b1 and 02 March 2021 for BNT162b2.

T cell response data are available for all participants with evaluable data at Day 29 (7 days after Dose 2) and up to Day 184 for a subset of participants who received BNT162b2 at 10, 20, or 30 µg.

2.7.3.2.2.1.1.1. Disposition and Demographics - Study BNT162-01

BNT162b1 – Younger Participants 18 to 55 Years of Age

A total of 84 participants in the 18 to 55 years age group received Dose 1 of BNT162b1, 12 in each of the 7 dose level groups (1, 3, 10, 20, 30, 50, 60 µg), and 69 of these participants received Dose 2 of BNT162b1. Based on the Safety Review Committee's determination, none of the 12 participants in the 60 µg group received the second dose, due to reactogenicity; however, these participants continued in the study. Three participants were withdrawn from the study before the administration of Dose 2 (1 in the 10 µg group due to an adverse event of malaise considered not related to study vaccine by the investigator; 1 in the 20 µg group due to withdrawal by participant; and 1 in the 50 µg group due to private reasons). One additional participant in the 20 µg group was withdrawn from the study after Dose 2 due to private reasons.

Among the 84 younger participants who received at least 1 dose of study vaccine, the mean age was approximately 38 years (range, 19 to 55 years); 52% of participants were male, 96% were white, and 98% were non-Hispanic.

BNT162b1 – Older Participants 56 to 85 Years of Age

A total of 36 participants in the older age group (56 to 85 years of age) received Dose 1 of BNT162b1 (12 at each dose level: 10, 20, and 30 µg). At the time of data cutoff, all of these participants had received Dose 2, except for 1 participant in the 20 µg group, who was continuing in the study. Among the 36 older participants who received at least 1 dose of BNT162b1, the mean age was approximately 66 years (range, 56 to 76); 64% were female, and all were white and non-Hispanic.

BNT162b2 – Younger Participants 18 to 55 Years of Age

A total of 60 younger participants (18 to 55 years of age) received Dose 1 of BNT162b2, 12 in each of the 5 dose level groups (1, 3, 10, 20, 30 µg). All of these participants also received Dose 2 of BNT162b2, except for 2 participants who were withdrawn from the study (one participant in the 1 µg group due to withdrawal by participant, and one participant in the 10 µg group due to an adverse event of nasopharyngitis, considered not related to study vaccine by the investigator).

Among the 60 younger participants who received at least 1 dose of BNT162b2, the mean age was approximately 40 years (range, 19 to 55); 57% of participants were female, and all were white and non-Hispanic.

BNT162b2 – Older Participants 56 to 85 Years of Age

A total of 36 older participants (56 to 85 years of age) received both doses of BNT162b2, 12 in each of the 3 dose level groups (10, 20, and 30 µg). At the time of data cutoff none of these participants had been prematurely discontinued from the study. Among these participants, the mean age was approximately 65 years (range, 56 to 84); 54% were female; and all were white and non-Hispanic.

2.7.3.2.2.1.1.2. T Cell Response Data – Study BNT162-01

T cell mediated immune responses were evaluated using Enzyme-Linked Immuno-Spot (ELISpot) and intracellular cytokine staining (ICS) visualized with fluorescence-activated cell sorting (FACS). Blood samples for evaluation of T cell responses were collected per protocol at baseline (before Dose 1) and at the visit that was to take place approximately 7 days after Dose 2 (Day 29). Cell mediated immune response data were also evaluated in post hoc analyses (not specified in the protocol) using blood collected for general research purposes on approximately Day 43 (21 days after Dose 2) Day 85 (63 days after Dose 2) and Day 184 (162 days after Dose 2). T cell responses were evaluated at these later time points for only a small number of participants who received BNT162b2 at doses of 10, 20, or 30 µg.

Based on the ELISpot and intracellular cytokine staining assay results described below, BNT162b1 and BNT162b2 induced poly-functional and pro-inflammatory CD4+/CD8+

T cell responses in most participants in both the older and younger age groups. Re-stimulation of PBMCs with peptide pools representing the encoded antigens (RBD or full-length S protein) demonstrated a helper response characterized by a robust IFN γ /IL-2 response and only minor IL-4 production. This cytokine profile indicates a favorable Th1 response and only a minimal Th2 immune response.

SARS-CoV-2 specific CD4+ and CD8+ T cell responses - ELISpot

At the ELISpot data cutoff date, evaluable ELISpot data were available for 97 participants who received BNT162b1: 70 in the younger age group (at 1, 3, 10, 20, 30, 50, 60 μ g) and 27 in the older age group (at 10, 20, 30 μ g). For BNT162b2, ELISpot data were available for 76 participants who received BNT162b2: 47 younger participants (at 1, 3, 10, 20, 30 μ g), and 29 older participants (at 10, 20, 30 μ g).

Overall, for both BNT162b1 and BNT162b2, based on data for Day 29, the T cell response rate and the magnitude of the responses as measured by ELISpot were similar across dose levels of 10 μ g and higher and were similar between younger and older participants. Results are shown in [Figure 3](#) (a) for the BNT162b2 group.

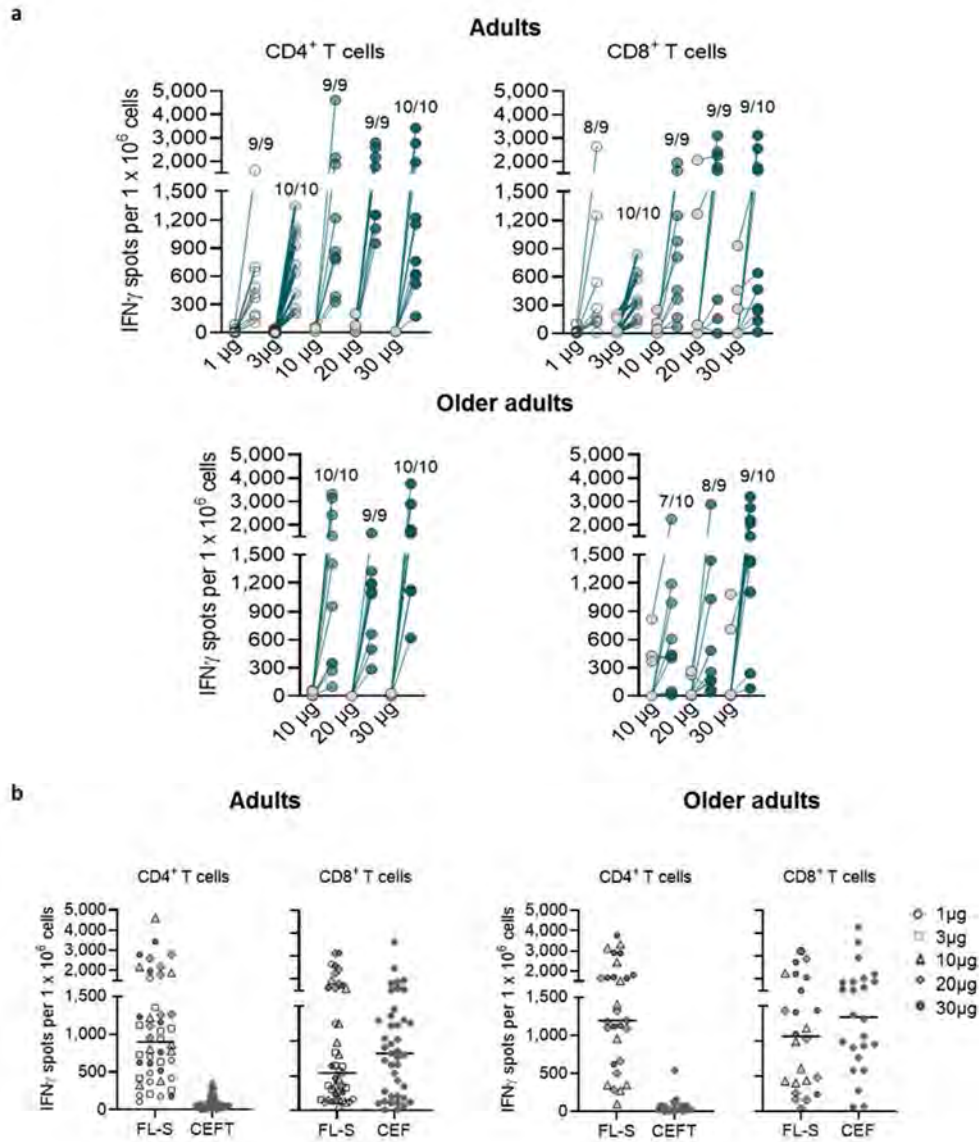
Among participants who received both Dose 1 and Dose 2, BNT162b1 induced strong SARS-CoV-2 RBD-specific CD4⁺ T cell responses in 96.7% (59/61) of younger participants and in 100% (27/27) of older participants; CD8⁺ responses were induced in 77.0% (47/61) of younger participants and in 77.8% (21/27) of older participants. In contrast, T cell responses were detected less often and were lower in magnitude in 9 younger participants who received only Dose 1 in the 60 μ g dose group (55.6% for CD4⁺ and 66.7% for CD8⁺), indicating the importance of a booster dose.

BNT162b2 induced strong SARS-CoV-2 S protein-specific CD4⁺ T cell responses in all participants in both the younger (47/47) and older (29/29) age groups. CD8⁺ T cell responses were induced in 95.7% (45/47) of younger participants and 82.8% (24/29) of older participants. Despite the slightly lower CD8⁺ immunogenicity rate in older participants, the magnitude of the BNT162b2-induced responses was comparable to those induced in younger participants receiving 30 μ g of BNT162b2. These T cell responses were directed against different parts of the antigen, including non-RBD sequences, indicating the induction of multi-epitopic responses by BNT162b2 in both age groups.

For both BNT162b1 and BNT162b2, while the magnitude of the responses varied among individuals, in participants with the strongest responses, post-vaccination CD4⁺ T cell responses to pools of S protein peptides were more than 10-fold the memory responses to peptides of CMV, EBV, influenza virus and tetanus toxoid observed in the same participants, and CD8⁺ T cell responses were comparable with memory responses against the viral antigen peptides in the same participants. Results for BNT162b2 are shown in [Figure 3](#) (b).

Complete results for the ELISpot data are presented in [Module 5.3.5.1 BNT162-01 Interim CSR Appendix 16.1.14 Report R-20-0244 v3.0](#) and [Report GA-RB-022-01A v3.0](#).

Figure 3. Frequency and Magnitude of BNT162b2-Induced CD4+ and CD8+ T cell Responses Against Full-length S protein



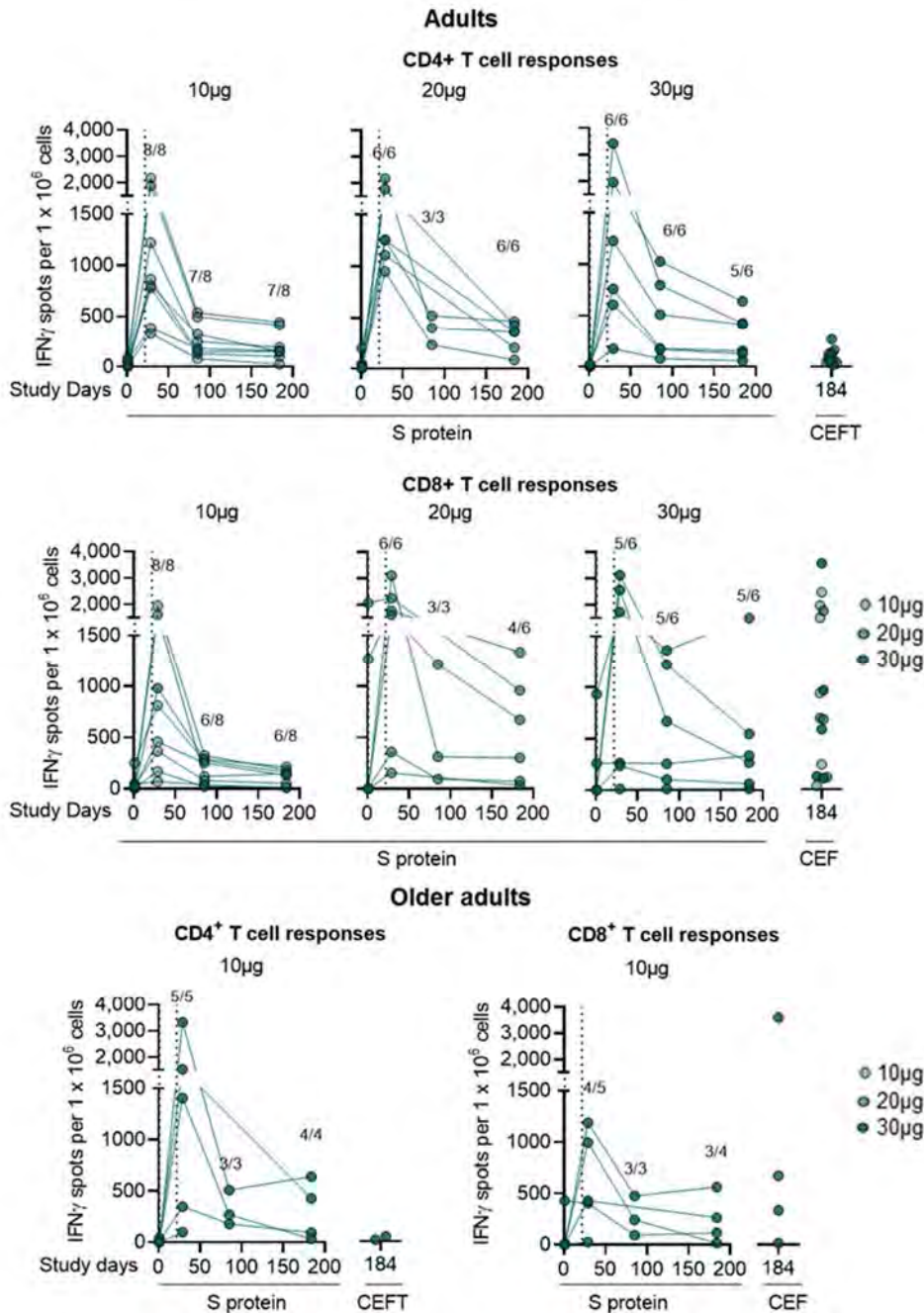
PBMCs obtained on Day 1 (pre-Dose 1) and on Day 29 (7 days post-Dose 2) were analyzed in *ex vivo* IFN γ ELISpot (for details see GA-RB-022-01A). Common pathogen T cell epitope pools CEF (CMV, EBV, and influenza virus HLA class I epitopes) and CEFT (CMV, EBV, influenza virus, and tetanus toxoid HLA class II epitopes) served to assess general T cell reactivity, cell culture medium served as negative control. Each dot represents the sum of normalized mean spot count from duplicate wells stimulated with two peptide pools corresponding to the full-length wt S protein for one study subject, after subtraction of the medium-only control. a, Ratios above post-vaccination data points are the number of subjects with detectable CD4⁺ or CD8⁺ T cell responses within the total number of tested subjects per dose group. b, S protein-specific CD4⁺ and CD8⁺ T cell responses in all subjects with a positive response to S protein (n=46 adults, 29 older adults for CD4⁺ and n=43 adults, 24 older adults for CD8⁺ T cell responses) and their baseline CEFT- and CEF-specific T cell responses. Note: CD4 data from 1 adult subject from the 20 μ g group and CD8 data from two adult subjects from the 20 μ g group could not be normalized and hence have not been included in the plots. Horizontal lines represent the median of each group. Source: Report R-20-0244 v3.0

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Durability of BNT162b2-Induced CD4+ and CD8+ T Cell Responses - ELISpot

Figure 4 illustrates the durability of the CD4+ and CD8+ T cell responses induced by BNT162b2 among younger participants (N = 20) at doses of 10, 20, and 30 µg and among older participants (N=4) receiving 10 µg. T cell responses decreased from Day 29 to Day 85 (63 days after Dose 2), but on Day 184 (162 days after Dose 2) both CD4+ and CD8+ T cell responses were still detectable in the majority of participants at levels higher than, or in the range of, recall antigen memory responses (CEF and CEFT in the figure) (Figure 4).

Figure 4. Durability of BNT162b2-Induced T Cell Responses



PBMCs obtained on Day 1 (before Dose 1), Day 29, Day 85, and Day 184 (7, 63, and 162 days post-Dose 2, respectively), were analyzed in *ex vivo* IFN γ ELISpot (for details see GA-RB-022-01A). Common pathogen T cell epitope pools CEF (CMV, EBV, and influenza virus HLA class I epitopes) and CEFT (CMV, EBV, influenza virus, and tetanus toxoid HLA class II epitopes) served to assess general T cell reactivity, cell culture medium served as negative control. Each dot represents the sum of normalized mean spot count from duplicate wells stimulated with two peptide pools corresponding to the full-length wild-type S protein for one study participant, after subtraction of the medium-only control. Ratios above post-vaccination data points are the number of participants with detectable CD4⁺ or CD8⁺ T cell responses within the total number of tested participants per dose group and time point. Source: Report R-20-0244 v3.0.

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Functional and Pro-inflammatory CD4+/CD8+ T cell Responses – ICS

BNT162b1

ICS/FACS data are available for 95 participants who received any dose level of BNT162b1:

- 68 younger participants (18-55 years): 1 µg (n=10), 3 µg (n=10), 10 µg (n=10), 20 µg (n=6), 30 µg (n=12), 50 µg (n=9), 60 µg (n=11).
- 27 older participants (56-85 years): 10 µg (n=8), 20 µg (n=8), 30 µg (n=11).

Two doses of BNT162b1 (dose range 1 to 50 µg) induced CD4 and CD8 vaccine-specific T cell responses. RBD-specific CD4+ T cell responses had a type 1 helper T (Th1) cell cytokine profile secreting IFN γ , or IL-2, or both. For 81 of the 84 analyzed participants who received both BNT162b1 doses, no production of Th2 cytokine IL-4 in response to RBD peptide pool stimulation was detected. Similarly, RBD-specific CD8+ T cells secreted IFN γ in 54 of the analyzed 84 participants who received both BNT162b1 doses; however, lower levels of IL-2-secreting CD8+ T cells compared to CD4+ T cells were detected.

In the 30 µg dose groups, the fractions of RBD-specific IFN γ + CD8+ T cells reached up to 0.49% (younger participants) and 1.58% (older participants) of total peripheral blood CD8+ T cells. In the 50 µg dose group with younger participants, fractions of up to 3.87% were detected. The mean fraction of both CD4+ and CD8+ cytokine-producing T cells in the BNT162b1 dosed participants (1 to 50 µg) was substantially higher (eg, for participants dosed at 30 µg, 11-fold higher) than that observed in 15 patients who recovered from COVID-19. In the 60 µg group, treated with Dose 1 only, mean fractions of cytokine-producing T cells were lower compared to the other dose level groups, indicating the importance of the booster vaccination. Importantly, the cytokine responses elicited after dosing with BNT162b1 in older participants were similar in response pattern and intensity with those of younger participants.

Complete results of the ICS/FACS analyses for BNT162b1 are provided in [Module 5.3.5.1 BNT162-01 Interim CSR Appendix 16.1.14 Report R-20-0235 v2.0](#).

BNT162b2

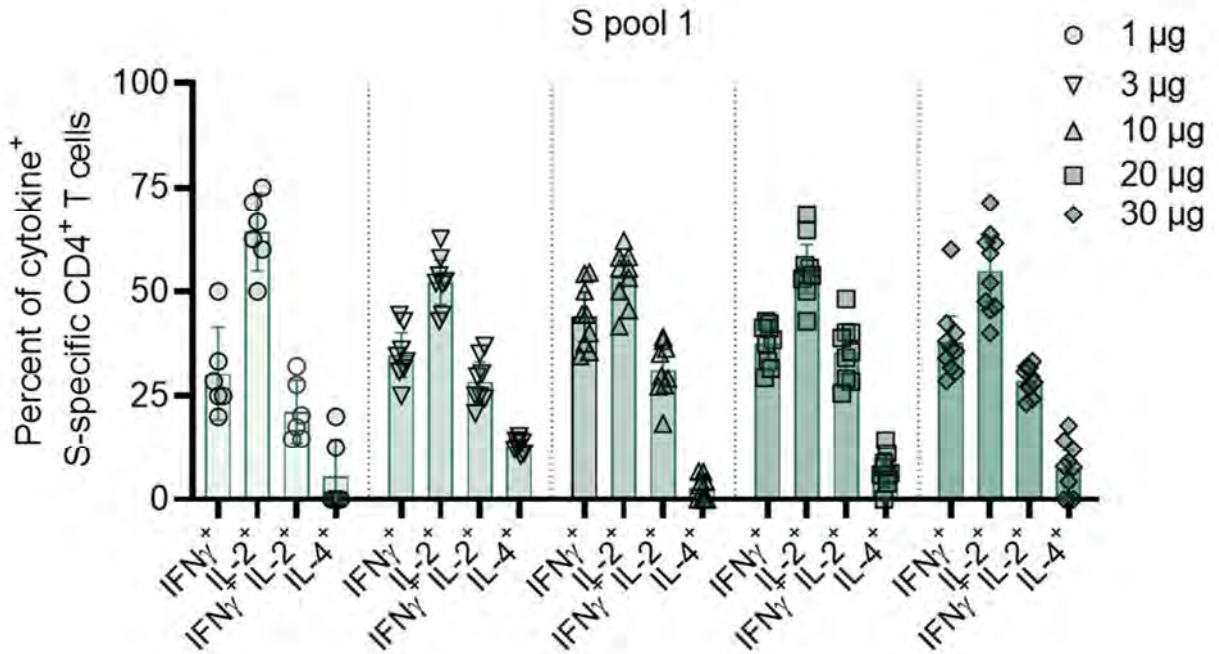
Data are available for 79 participants who received any dose level of BNT162b2:

- 50 younger participants (18-55 years): 1 µg (n=8), 3 µg (n=9), 10 µg (n=11), 20 µg (n=11), 30 µg (n=11).
- 29 older participants (56-85 years): 10 µg (n=11), 20 µg (n=9), 30 µg (n=9).

As evaluated at Day 29, two doses of BNT162b2 (dose range 1 to 30 µg) induced vaccine-specific T cell responses in both age groups analyzed ([Figure 5](#) and [Figure 6](#)). Testing for SARS-CoV-2 S protein-specific T cell responses was performed with two different peptide pools – S pool 1 comprising overlapping peptides from the N-terminal region of the S protein (which is not equivalent to structural domains) and S pool 2 comprising C-terminal regions

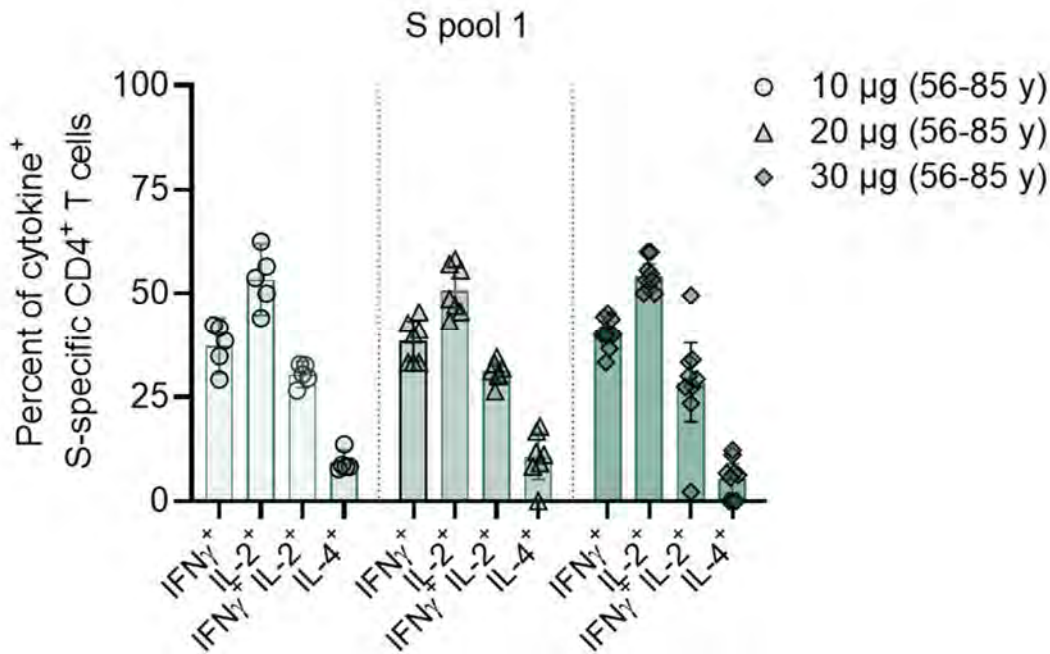
of the S protein. S-specific CD4+ T cell responses analyzed in 79 participants dosed with BNT162b2 are characterized by a Th1 cytokine profile secreting IFN γ , or IL-2, or both.

Figure 5. S-specific CD4+ T Cells Producing the Indicated Cytokines in Response to S Protein Pool 1 as a Fraction of Total Cytokine-Producing S-Specific CD4+ T Cells – BNT162b2, Adults 18-55 Years of Age



Bar charts show arithmetic means with 95% confidence interval at Day 29 (7 days after Dose 2). Cytokine production was calculated by summing up the fractions of all CD4+ T cells positive for either IFN γ , IL-2, or IL-4, setting this sum to 100% and calculating the fraction of each specific cytokine-producing subset thereof. Two participants from the 1 µg dose group, 1 participant from the 3 µg dose group, and 1 participant from the 10 µg dose group were excluded from this analysis (frequency of total cytokine-producing CD4+ T cells <0.03%). Source: Report R-20-0241 v3.0.

Figure 6. S-specific CD4+ T Cells Producing the Indicated Cytokines in Response to S Protein Pool 1 as a Fraction of Total Cytokine-Producing S-Specific CD4+ T Cells (10 to 30 µg BNT162b2 Older Participant Dose Groups)



Bar charts show arithmetic means with 95% CI at Day 29 (7 days after Dose 2). Cytokine production was calculated by summing up the fractions of all CD4+ T cells positive for either IFN γ , IL-2, or IL-4, setting this sum to 100%, and calculating the fraction of each specific cytokine-producing subset thereof. Four participants from the 10 µg dose group and 1 participant from the 20 µg dose group were excluded from this analysis (frequency of total cytokine-producing CD4+ T cells <0.03%).
Source: Report R-20-0241 v3.0.

Almost no Th2 cytokine IL-4 secreting T cells were detectable in response to S peptide sub-pool stimulations (mean fractions: 0.01% and 0.02% of antigen-specific circulating CD4+ T cells in younger participants in the 20 and 30 µg dose level groups, respectively; separate stimulation with S protein sub-pool 1 and sub-pool 2). At Day 29, S-specific CD8+ T cells secreted IFN γ in 65 of the 79 analyzed participants (43/50 younger participants; 22/29 older participants), and IL-2 secreting CD8+ T cells were also detectable. Fractions of S-specific IFN γ + CD8+ T cells targeting the N-terminal domain of the S protein reached up to 1.24% of total peripheral blood CD8+ T cells in the 20 and 30 µg younger participant dose groups and up to 1.57% in the 30 µg older participant dose group. Pre-existing CD8+ T cell responses against the C-terminal region of the S protein were detected in 17 of 79 dosed participants (range: 0.07 to 5.59% IFN γ -producing CD8+ T cells). In 5 of 17 participants, these preexisting responses were slightly amplified upon BNT162b2 dosing.

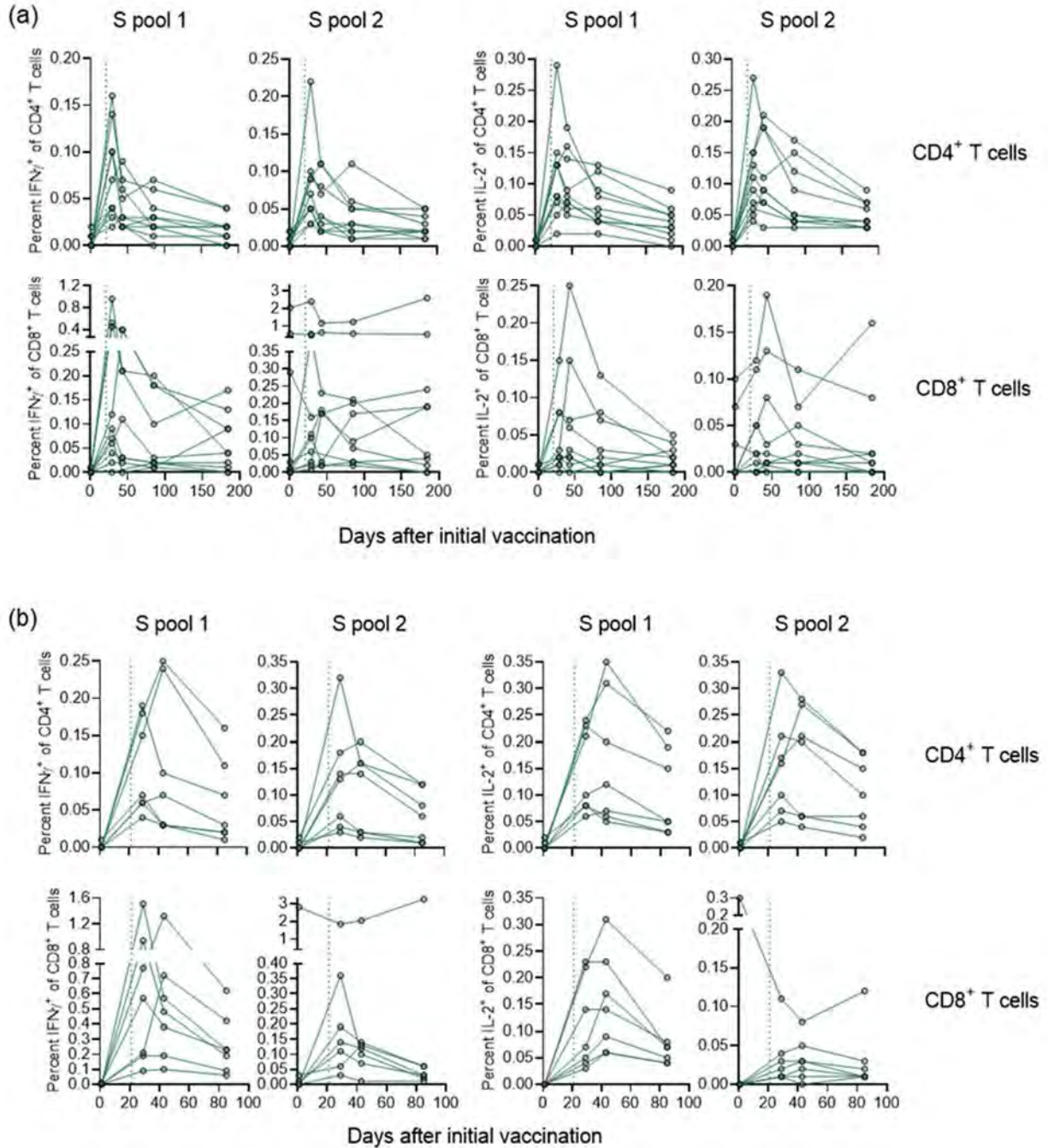
BNT162b2-induced T cell responses, especially for CD8+ T cells, were not limited to the RBD, and pronounced and strong T cell recognition of non-RBD regions of the S protein were observed.

Overall, at Day 29, the mean fractions of S-specific CD4+ and CD8+ T cells were substantially higher (eg, the S protein pool 1 IFN γ CD8+ response of 30 μ g dosed participants was 12.5-fold higher) than that observed in 18 patients who recovered from COVID-19. Importantly, for the clinically targeted 30 μ g dose group, the cytokine responses elicited after vaccination with BNT162b2 in older participants was mostly identical in response pattern and intensity with that of the younger participants.

Persistence of BNT162b2-Induced S-specific CD4+ and CD8+ T Cells - ICS

For the majority of participants, the strong S-specific IFN γ + and IL-2+ CD8+ and Th1 CD4+ T cell responses contracted by Day 43 (3 weeks after Dose 2) and plateaued at a lower level towards Day 85 (9 weeks after Dose 2). This observation held true for all dose level groups analyzed, with varying response magnitudes among individuals. Among the younger participants, the cell-mediated immune responses remained detectable until Day 184 (23 weeks after Dose 2). Day 184 PBMC material from the older adult participants was not yet available at the time of this interim report. [Figure 7](#) shows the data for the 30 μ g BNT162b2 dose group in younger (a, N=10) and older (b, N=7) participants and is considered representative of what is seen for other dose groups.

Figure 7. Persistence of S-specific CD4+ and CD8+ T Cells Producing the Indicated Cytokines (IFN γ and IL-2) as a Fraction of Total Circulating CD4+ and CD8+ T cells – 30 μ g BNT162b2 Dose Group in Younger (a) and Older (b) Participants



Cytokine data are plotted for participants from (a) the 30 μ g dose group in younger participants (aged 18 to 55 yrs, n=10) and (b) 30 μ g dose group in older participants (aged 56 to 85 yrs, n=7) from Day 1 (before Dose 1), Day 29 (7 d post-Dose 2), Day 43 (3 wks post-Dose 2), Day 85 (9 wks post-Dose 2) and Day 184 (23 wks post-Dose 2, (a) only) after Dose 1. Green dotted lines indicate the time point of Dose 2 (Day 21).
 Source: Interim report R-20-0241 v 3.0.

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In summary, BNT162b2 induced poly-functional and pro-inflammatory CD4+/CD8+ T cell responses in almost all participants. The responses persisted in the majority of participants for up to 6 months after Dose 2. The Th1 polarization of the helper T cell response was characterized by a robust IFN γ /IL-2 and only minor IL-4 production upon antigen-specific (wild-type SARS-CoV-2 S protein peptide pools) re-stimulation, which was still observed, although with a reduced magnitude, at later time points.

Complete results of the ICS/FACS analyses for BNT162b2 are provided in [Module 5.3.5.1 BNT162-01 Interim CSR Appendix 16.1.14 Report R-20-0241 v3.0](#).

Conclusion – T Cell Response Data

In conclusion, as analyzed using ELISpot and ICS/FACS, the cytokine responses elicited by both BNT162b1 and BNT162b2 showed no clear dose dependency, and the response pattern and intensity in the older age group were mostly identical to those in the younger age group.

BNT162b1 and BNT162b2 induced poly-functional and pro-inflammatory CD4+/CD8+ T cell responses in almost all participants, with a Th1 polarization of the helper response. The detection of robust IFN γ and IL-2 production but only minor IL-4 production indicates a favorable Th1 profile and the absence of a potentially deleterious Th2 immune response.

2.7.3.2.2.1.1.3. Serological Response Data – Study BNT162-01

At the time of data cutoff for serology, results for serum neutralizing titers and binding antibody concentrations were available for participants in the immunogenicity sets as follows.

BNT162b1:

Younger age group (18-55): 60 participants (12 in each dose level group: 1, 10, 30, 50, and 60 μ g); up to Day 43 for all dose level groups.

BNT162b2:

Younger age group (18-55): 60 participants (12 in each dose level group: 1, 3, 10, 20, 30 μ g); up to Day 50 for 1 μ g and 3 μ g groups, up to Day 85 for 10, 20, 30 μ g groups.

Older age group (56-85): 12 participants in the 20 μ g group; up to Day 29.

Complete data supporting the graphs in the following sections are available in the technical report [Module 5.3.5.1 BNT162-01 Interim CSR Appendix 16.1.14 Report R-20-0253 v2.0](#).

2.7.3.2.2.1.1.3.1. SARS-CoV-2 Serum 50% Neutralizing Titers – Study BNT162-01

For both BNT162b1 and BNT162b2, data for SARS-CoV-2 serum 50% neutralizing titers demonstrated the importance of receiving 2 doses of investigational vaccine. Only modest immune responses were apparent by 21 days after Dose 1, while Dose 2 elicited rapid increases in neutralizing titers, with maximal response levels achieved by 7 days after Dose 2 (Day 29). In the younger age group, results for SARS-CoV-2 serum 50% neutralizing titer

GMTs and GMFRs for the 10 µg and 30 µg dose level groups were similar between BNT162b1 and BNT162b2.

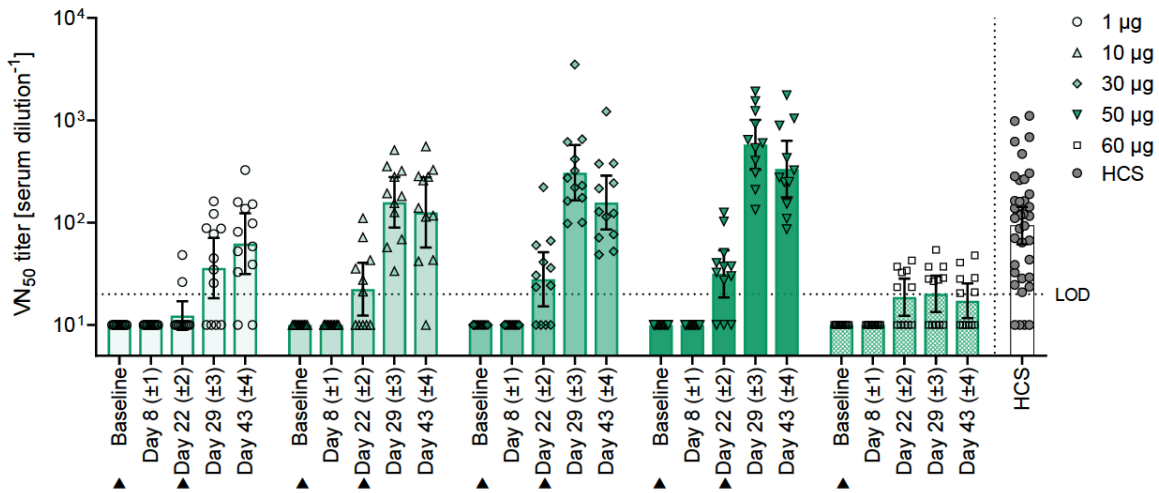
Geometric Mean Titers

For benchmarking, GMTs of the dose level groups were compared with those of a panel of human convalescent sera (HCS) comprising samples obtained from 38 individuals 18 to 85 years of age at least 14 days after confirmed diagnosis of COVID-19.

BNT162b1

Participants in the younger age group who received BNT162b1 showed a strong dose-dependent neutralizing antibody response (Figure 8 and [Report R-20-0253 v2.0 Appendix Table 3](#)). At 21 days after Dose 1 (Day 22), virus neutralizing antibody GMTs (neutralizing GMTs) had increased in a dose-dependent manner for the 1, 10, 30, and 50 µg dose groups. At 7 days after Dose 2 (Day 29), neutralizing GMTs showed a strong, dose level dependent booster response. In the 60 µg dose group, which received Dose 1 but not Dose 2, neutralizing GMTs remained at a lower level, indicating that a booster dose is necessary to increase functional antibody titers. At 21 days after Dose 2 (Day 43), neutralizing GMTs decreased (with exception of the 1 µg dose level). Day 43 virus neutralizing GMTs were 0.7-fold (1 µg) to 3.6-fold (50 µg) those of the COVID-19 HCS panel.

Figure 8. BNT162b1 – Functional 50% SARS-CoV-2 Neutralizing Antibody Titers (VN₅₀) – IMM – Adults 18 to 55 Years of Age



VN₅₀ titers with 95% confidence intervals are shown for younger participants (aged 18 to 55 years) immunized with 1, 10, 30, 50, or 60 µg BNT162b1. Values smaller than the limit of detection (LOD) are plotted as 0.5*LOD. Arrowheads indicate baseline (pre-Dose 1, Day 1) and Dose 2 (Day 22). Dose 2 was not performed in the 60 µg dose group. The dotted horizontal line represents the LOD. IMM = Immunogenicity set; VN₅₀ = 50% SARS-CoV-2 neutralizing antibody titers; HCS = human COVID-19 convalescent serum. Source: Report [R-20-0253](#).

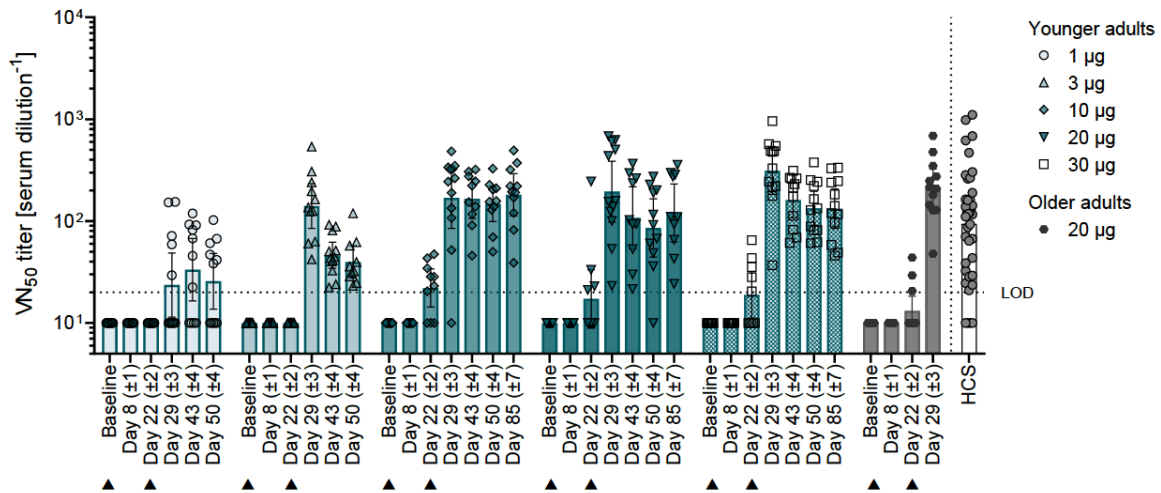
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BNT162b2

Participants who received BNT162b2 showed a strong antibody response (Figure 9 and Report R-20-0253 v2.0 Appendix Table 6). Virus neutralizing GMTs were detected at 21 days after Dose 1 (Day 22), and by 7 days after Dose 2 (Day 29), GMTs had increased substantially in younger participants who received $\geq 3 \mu\text{g}$ BNT162b2 and in older participants who received $20 \mu\text{g}$ BNT162b2. Day 29 virus neutralizing GMTs were comparable between the younger and older adult $20 \mu\text{g}$ dose level groups.

At 21 days after Dose 2 (Day 43), virus neutralizing GMTs in the younger age group decreased for the 3, 20, and $30 \mu\text{g}$ dose levels. Thereafter, neutralizing GMTs remained stable up to 63 days after Dose 2 (Day 85) for younger adult dose groups 10, 20, and $30 \mu\text{g}$ and were 1.3-fold to 1.9-fold those of a COVID-19 HCS panel.

Figure 9. BNT162b2 - Functional 50% SARS-CoV-2 Neutralizing Antibody Titers (VN_{50}) - IMM - Adults 18 to 55 Years of Age and 56 to 85 Years of Age



VN_{50} titers with 95% confidence intervals are shown for younger adults (aged 18 to 55 years) immunized with 1, 3, 10, 20, or $30 \mu\text{g}$ BNT162b2, and older adults (aged 56 to 85 yrs) immunized with $20 \mu\text{g}$ BNT162b2. Values smaller than the limit of detection (LOD) are plotted as $0.5 \times \text{LOD}$. Arrowheads indicate baseline (pre-Dose 1, Day 1) and Dose 2 (Day 22). The dotted horizontal line represents the LOD.

IMM = Immunogenicity set; VN_{50} = 50% SARS-CoV-2 neutralizing antibody titers; HCS = human COVID-19 convalescent serum.
Source: Report R-20-0253.

Geometric Mean Fold-Rise and Seroconversion

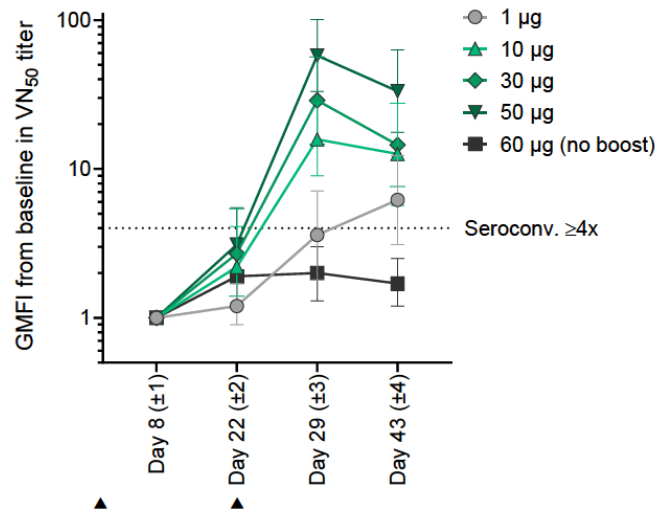
Results for GMFRs in SARS-CoV-2 50% neutralizing titers are consistent with the data described above for GMTs. In the younger age groups, for both vaccines at doses $\geq 3 \mu\text{g}$, GMFRs from before vaccination to 7 days after Dose 2 (Day 29) were substantially higher compared to the respective GMFRs 21 days after Dose 1, and GMFRs declined slightly by Day 43 (Figure 10 and Figure 11; Report R-20-0253 v2.0 Appendix Table 4 and Appendix Table 7).

For BNT162b1 in the younger age group, GMFRs 7 days after Dose 2 were dose dependent, with an observed 15.8 fold-rise after $10 \mu\text{g}$, 28.9 fold-rise after $30 \mu\text{g}$, and 57.8 fold-rise after

the 50 µg dose. For BNT162b2, in the younger age group, GMFRs 7 days after Dose 2 indicated a 16.9 fold-rise after 10 µg, 19.5 fold-rise after 20 µg, and 29.2 fold-rise after the 30 µg dose. For the 30 µg dose of BNT162b2, GMFRs were 15.1 at Day 43, 12.0 at Day 50, and 12.2 at Day 85 (63 days after Dose 2). For the older age group, the GMFR after 20 µg BNT162b2 indicated a 21.7 fold-rise at Day 29.

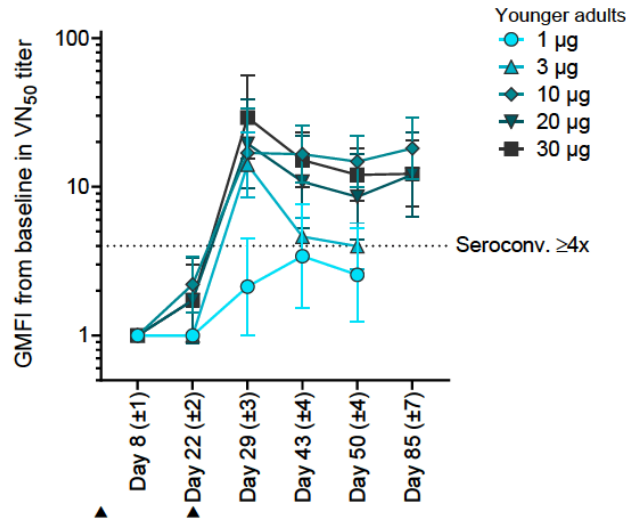
Seroconversion is defined as a ≥ 4 -fold increase in functional antibody titer as compared to baseline. All participants who received the 30 µg or 50 µg dose levels of BNT162b1 were seropositive at 7 days and 21 days after Dose 2 (Day 29 and Day 43) ([Report R-20-0253 v2.0 Appendix Table 5](#)). For the BNT162b2 30 µg dose group in the younger age group, the seroconversion rate was 90.0% at Day 29 and 100% on Days 43, 50, and 85; for the older age group the seroconversion rate after 20 µg BNT162b2 was 100% at Day 29 ([Report R-20-0253 v2.0 Appendix Table 8](#)).

Figure 10. BNT162b1 – Fold Increase From Baseline in Functional 50% SARS-CoV-2 Neutralizing Antibody Titers (VN₅₀) – IMM – Adults 18 to 55 Years of Age



Geometric means fold increase (GMFI) from baseline in VN₅₀ titer with 95% confidence intervals are shown. Arrowheads indicate baseline (pre-Dose 1, Day 1) and Dose 2 (Day 22). Dose 2 was not performed in the 60 µg dose group. The dotted horizontal line represents the threshold for seroconversion (fold increase ≥4). IMM = Immunogenicity set; VN₅₀ = 50% SARS-CoV-2 neutralizing antibody titers. Source: Report R-20-0253 v2.0.

Figure 11. BNT162b2 – Fold Increase from Baseline in Functional 50% SARS-CoV-2 Neutralizing Antibody Titers (VN₅₀) – IMM – Adults 18 to 55 Years of Age



Geometric means fold increase (GMFI) from baseline in VN₅₀ titer with 95% confidence intervals are shown. Arrowheads indicate baseline (pre-Dose 1, Day 1) and Dose 2 (Day 22). The dotted horizontal line represents the threshold for seroconversion (fold increase ≥4). IMM = Immunogenicity set; VN₅₀ = 50% SARS-CoV-2 neutralizing antibody titers. Source: Report R-20-0253 v2.0.

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2.7.3.2.2.1.1.3.2. SARS-CoV-2 Antigen-Specific Binding Antibody Concentrations

As measured by S1- and RBD-binding IgG GMCs, both BNT162b1 and BNT162b2 elicited strong antibody responses. Results for S1- and RBD-binding IgG responses are available in the CSR ([Module 5.3.5.1 BNT162-01 Interim CSR Section 11.2](#) and [Appendix 16.1.14 Report R-20-0253 v2.0 Section 5.1.2](#) and [Section 5.2.2](#)).

2.7.3.2.2.1.1.4. Immunogenicity Conclusions – Study BNT162-01

- **T Cell Responses**

- Based on the ELISpot and ICS assay results, BNT162b1 and BNT162b2 induced poly-functional and pro-inflammatory CD4+/CD8+ T cell responses in most participants. The cytokine responses in older participants were mostly identical in response pattern and intensity with those in younger participants.
- Re-stimulation of PBMCs with peptide pools representing the encoded antigens (RBD or full-length S protein) demonstrated a helper response characterized by a robust IFN γ /IL-2 response and only minor IL-4 production. This cytokine profile indicates a favorable Th1 response and only a minimal Th2 immune response.
- BNT162b2-induced CD4+ and CD8+ T cell responses showed a decrease on Day 85 (63 days after Dose 2), but remained detectable on Day 184 (162 days after Dose 2) in almost all participants vaccinated with >10 μ g at levels higher than or in range of recall antigen memory responses.

- **Serological Responses**

- For both BNT162b1 and BNT162b2, only modest immune responses were apparent by 21 days after Dose 1, while Dose 2 elicited rapid increases in neutralizing titers, with maximal response levels achieved by 7 days after Dose 2 (Day 29). These results demonstrate the importance of receiving 2 doses of investigational vaccine.
- Results for SARS-CoV-2 serum 50% neutralizing titer GMTs and GMFRs for the 10 μ g and 30 μ g dose level groups (younger age group) were similar between BNT162b1 and BNT162b2.
- Results for serum neutralizing titers indicated comparable immune responses between the younger and older age groups receiving the 20 μ g dose level of BNT162b2 at 7 days after Dose 2 (Day 29).
- In the younger age group, after Dose 2 of BNT162b2, GMTs decreased from Day 29 to Day 43 (21 days after Dose 2) and then remained stable up to Day 85 (63 days after Dose 2), when GMTs for the 10, 20, and 30 μ g groups were 1.3-fold to 1.9-fold those of a COVID-19 HCS panel.

2.7.3.2.2.1.2. Study C4591001 – Phase 1

Phase 1 immunogenicity data from Study C4591001 were summarized through 1 month after Dose 2 for all dose levels for both vaccine candidates (BNT162b1 and BNT162b2) (data cutoff date 24 August 2020); these data are reported in full in [Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 11.2.1](#) and are summarized briefly in this SCE, [Section 2.7.3.2.2.1.2.2](#).

Immunogenicity results are also available for the 6-month post Dose 2 time point for participants who received BNT162b2 30 µg (data cutoff date 13 March 2021); these results are reported in [Module 5.3.5.1 C4591001 6-Month Update Interim CSR Section 11.2.1](#) and in this SCE, [Section 2.7.3.2.2.1.2.3](#).

All immunogenicity results for C4591001 presented in the SCE are for the evaluable immunogenicity populations; results for the all-available immunogenicity populations are available in the CSRs.

2.7.3.2.2.1.2.1. Disposition, Data Sets Analyzed, and Demographics - Study C4591001, Phase 1

Disposition – Phase 1

A total of 195 participants were randomized in 2 age groups (18-55 or 65-85 years of age) to receive 2 doses of BNT162b1 or placebo (N=105) or BNT162b2 or placebo (N=90).

In each age group, 15 participants were randomized at each successive dose level (eg, 10 µg, 20 µg, 30 µg) to receive either active vaccine (N=12) or placebo (N=3). In both the younger and older age groups, all participants randomized to the BNT162b1 and BNT162b2 10-µg, 20-µg, and 30-µg dose groups and the corresponding placebo groups received both doses of active vaccine or placebo.

In the BNT162b1 100-µg dose group, all 12 participants in the younger age group who were randomized received Dose 1. However, based on observed reactogenicity after Dose 1, the IRC recommended that a second dose of 100-µg BNT162b1 not be administered. Because dosing of 100 µg BNT162b1 could not be completed, results for this group and the corresponding placebo group will not be discussed further in this SCE, but are available in the C4591001 Final Analysis CSR.

Data Sets Analyzed – Phase 1

Exclusions from the evaluable immunogenicity populations are detailed in [Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 10.4.1](#).

Demographics Phase 1

BNT162b1

Overall, in the Dose 1 evaluable immunogenicity population, most participants were white in both the younger age group (82.2%) and older age group (93.2%). Median age was 35.0

years in the younger age group and 68.5 years in the older age group. In the younger age group, 62.2% of participants were male; and in the older age group, 70.5% were female.

BNT162b2

Overall, in the Dose 1 evaluable immunogenicity population, most participants were white in the younger age group (85.7%), and all participants were white in the older age group (100%). Median age was 36.0 years in the younger age group and 68.0 years in the older age group. In the younger age group, 61.9% of participants were female, and in the older age group, 61.4% were female.

2.7.3.2.2.1.2.2. Immunogenicity Results Through 1 Month After Dose 2

2.7.3.2.2.1.2.2.1. SARS-CoV-2 Neutralizing Titers – Study C4591001, Phase 1

Overall, both BNT162b1 and BNT162b2 elicited robust SARS-CoV-2 neutralization responses 7 days after Dose 2 in both younger and older adults, based on GMTs, GMFRs, and proportions of participants achieving a ≥ 4 -fold rise in neutralizing titers, and high response levels were maintained through 1 month after Dose 2. In general, SARS-CoV-2 neutralization responses in older participants (65-85 years of age) tended to be lower than those in younger participants (18-55 years of age).

Geometric Mean Titers

For both BNT162b1 and BNT162b2 recipients in both age groups, SARS-CoV-2 50% neutralizing GMTs modestly increased by Day 21 after Dose 1 and were substantially increased 7 days after Dose 2. At most time points, for both BNT162b1 and BNT162b2 recipients, GMTs in the older age group tended to be lower than GMTs in the younger age group at the same dose level.

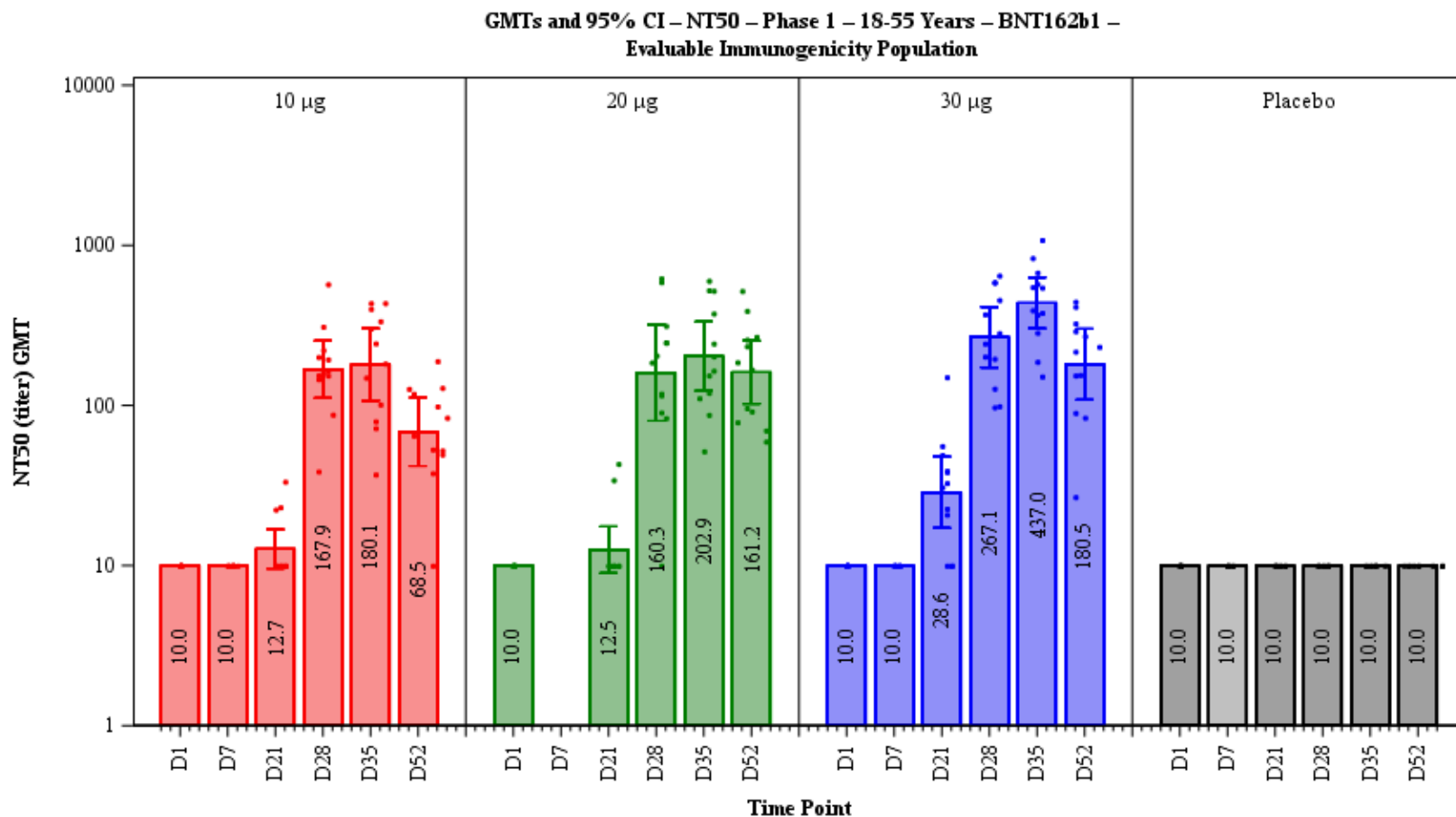
BNT162b1

In the younger age group, SARS-CoV-2 50% neutralizing GMTs modestly increased by Day 21 after Dose 1 of BNT162b1 and were substantially increased 7 days after Dose 2 (Day 28), with higher GMTs observed in the 30- μ g dose group compared to the 10- μ g and 20- μ g dose groups (Figure 12). For all dose groups, GMTs increased further at 14 days after Dose 2 (Day 35) and then decreased at 1 month after Dose 2 (Day 52); however, the Day 52 GMTs remained substantially higher than those at Day 21 after Dose 1.

In the older age group, generally similar trends were observed, in that substantial SARS-CoV-2 50% neutralizing responses (GMTs) were observed by 7 days after Dose 2 (Day 28) and at later time points in the 20- μ g and 30- μ g dose groups (Figure 13). However, only modest responses were observed at any time point in the 10- μ g dose group.

SARS-CoV-2 50% neutralizing GMTs were generally lower in the older age group than in the younger age group at the same dose level.

Figure 12. Geometric Mean Titers and 95% CI: SARS-CoV-2 Neutralization Assay - NT50 – Phase 1, 2 Doses, 21 Days Apart – 18-55 Years of Age – BNT162b1 – Evaluable Immunogenicity Population



Abbreviations: GMT = geometric mean titer; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Dots present individual antibody levels.

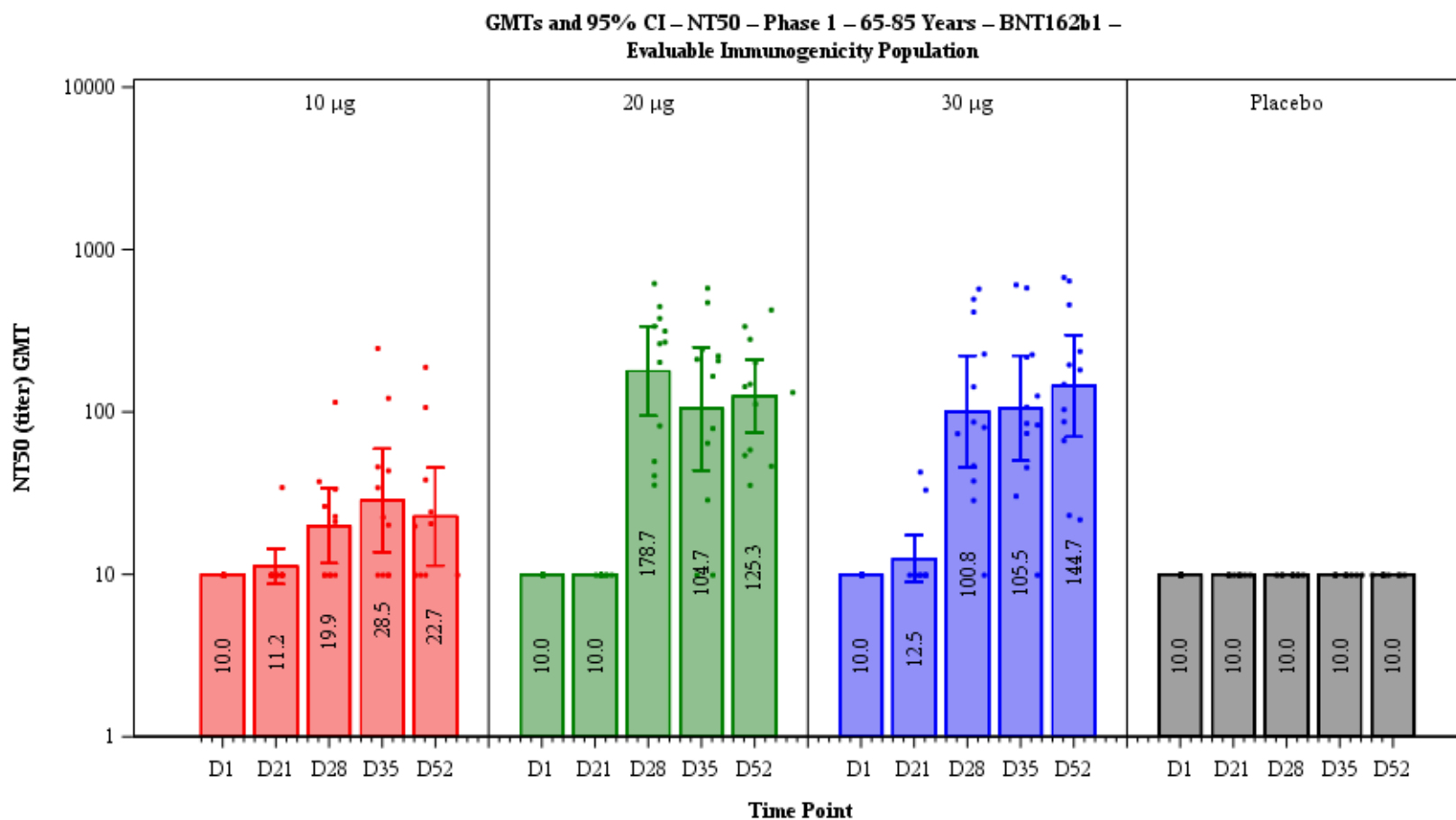
Note: Number within each bar denotes geometric mean.

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Figure 13. Geometric Mean Titers and 95% CI: SARS-CoV-2 Neutralization Assay - NT50 – Phase 1, 2 Doses, 21 Days Apart – 65-85 Years of Age – BNT162b1 – Evaluable Immunogenicity Population



Abbreviations: GMT = geometric mean titer; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Dots present individual antibody levels.

Note: Number within each bar denotes geometric mean.

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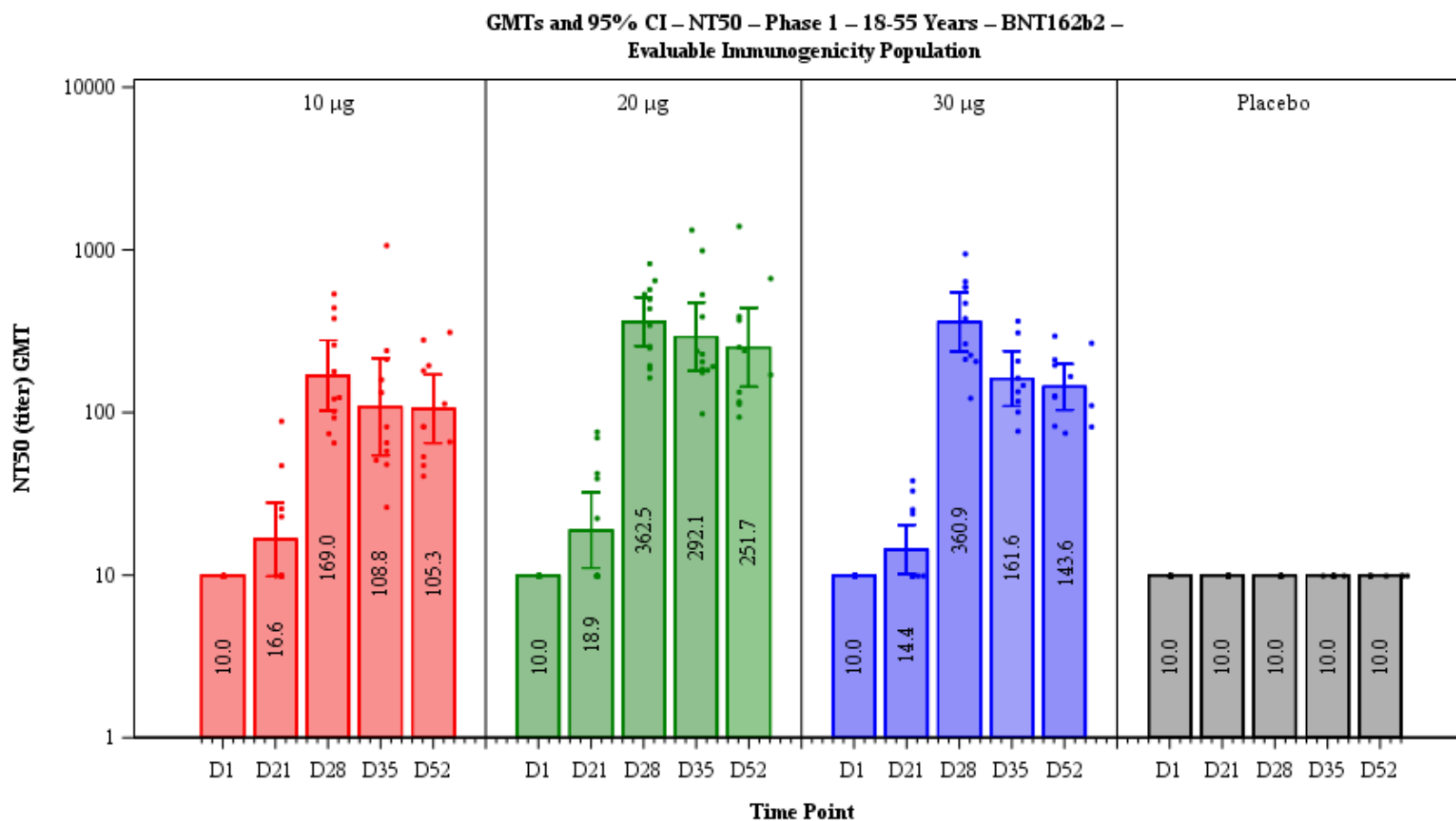
BNT162b2

In the younger age group, SARS-CoV-2 50% neutralizing GMTs modestly increased by Day 21 after Dose 1 of BNT162b2 and were substantially increased 7 days after Dose 2 (Day 28), with higher GMTs observed in the 20- μ g and 30- μ g dose groups compared to the 10- μ g dose group (Figure 14). The GMTs decreased at 14 days after Dose 2 (Day 35) and 1 month after Dose 2 (Day 52) of BNT162b2; however, the GMTs remained substantially higher than those at 21 days after Dose 1.

In the older age group, SARS-CoV-2 50% neutralizing GMTs were substantially increased 7 days after Dose 2 (Day 28) and were similar in the 10- μ g and 20- μ g dose groups and higher in the 30- μ g dose group (Figure 15). At 1 month after Dose 2 (Day 52), GMTs had decreased in all dose groups; however, the Day 52 GMTs remained higher than those at 21 days after Dose 1.

Among participants who received 20 μ g BNT162b2, SARS-CoV-2 50% neutralizing GMTs were substantially lower in the older age group than in the younger age group; however, among those receiving 30 μ g BNT162b2, GMTs were similar or higher in the older age group than in the younger age group at 14 days and 1 month after Dose 2 (Days 35 and 52).

Figure 14. Geometric Mean Titers and 95% CI: SARS-CoV-2 Neutralization Assay - NT50 – Phase 1, 2 Doses, 21 Days Apart – 18-55 Years of Age – BNT162b2 – Evaluable Immunogenicity Population



Abbreviations: GMT = geometric mean titer; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Dots present individual antibody levels.

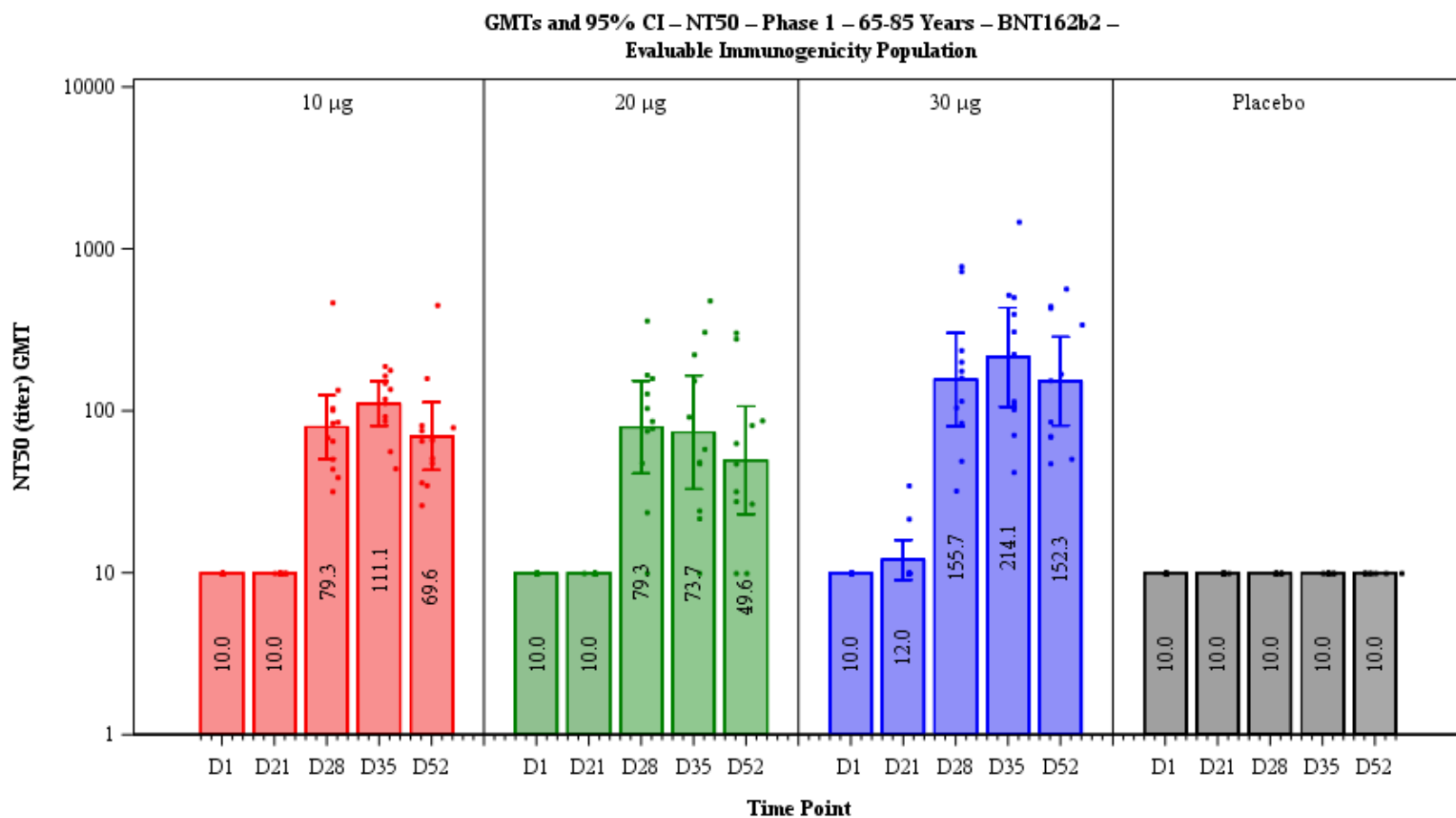
Note: Number within each bar denotes geometric mean.

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Figure 15. Geometric Mean Titers and 95% CI: SARS-CoV-2 Neutralization Assay - NT50 – Phase 1, 2 Doses, 21 Days Apart – 65-85 Years of Age – BNT162b2 – Evaluable Immunogenicity Population



Abbreviations: GMT = geometric mean titer; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Dots present individual antibody levels.

Note: Number within each bar denotes geometric mean.

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Geometric Mean Fold-Rise (GMFR)

For the BNT162b1 and the BNT162b2 recipients, across dose level groups and in both age groups, GMFRs of SARS-CoV-2 50% neutralizing titers from before vaccination to 7 days after Dose 2 (Day 28) were substantially higher compared to GMFRs 21 days after Dose 1. Among both BNT162b1 and BNT162b2 recipients, GMFRs in the older age group were generally lower than those in the younger age group at the same dose level. Results for GMFR are available in [Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 11.2.1.1.2](#).

Proportion of Participants Achieving ≥ 4 -Fold Rise

Overall, for both BNT162b1 and BNT162b2 recipients, across dose level groups and in both age groups, most participants achieved a ≥ 4 -fold rise in SARS-CoV-2 50% neutralizing titers from before vaccination to 7 days after Dose 2, except for participants in the older age group receiving the 10- μ g BNT162b1 dose. Results for the proportion of participants achieving a ≥ 4 -fold rise are available in [Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 11.2.1.1.3](#).

2.7.3.2.2.1.2.2.2. SARS-CoV-2 Antigen-Specific Binding IgG Levels – Study C4591001, Phase 1

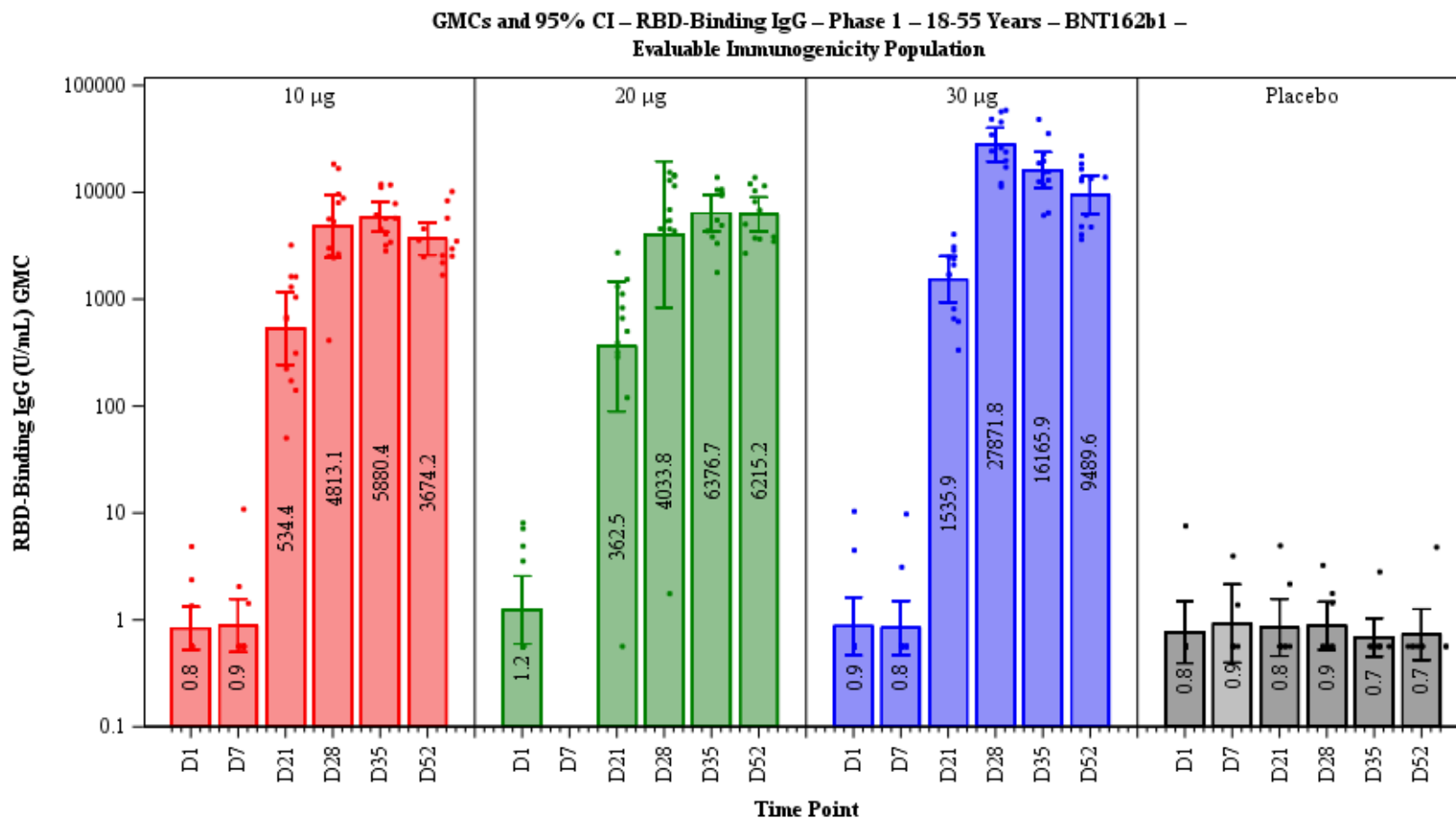
Vaccine candidate BNT162b1 encodes the RBD of SARS-CoV-2, and BNT162b2 encodes the P2 S. In this section, RBD-binding IgG responses are described for BNT162b1, and S1-binding IgG responses are described for BNT162b2.

Both BNT162b1 and BNT162b2 elicited substantial rises in antigen binding IgG levels 7 days after Dose 2, based on GMCs, GMFRs, and proportions of participants achieving a ≥ 4 -fold rise in IgG-antigen specific binding. Responses were maintained through Day 52.

Geometric Mean Concentrations

Overall, for both BNT162b1 and BNT162b2 recipients, and in both age groups, RBD- and S1-binding GMCs increased substantially by Day 21 after Dose 1 and were further increased 7 days after Dose 2 (see [Figure 16](#) through [Figure 19](#)). At 1 month after Dose 2 (Day 52), the GMCs remained higher than at Day 21 after Dose 1. GMCs in the older age group were generally lower than the GMCs in the younger age group at the same dose level.

Figure 16. Geometric Mean Concentrations and 95% CI: SARS-CoV-2 RBD-binding IgG Level Assay – Phase 1, 2 Doses, 21 Days Apart – 18-55 Years of Age – BNT162b1 – Evaluable Immunogenicity Population



Abbreviations: GMC = geometric mean concentration; IgG = immunoglobulin G; RBD = receptor-binding domain.

Note: Dots present individual antibody levels.

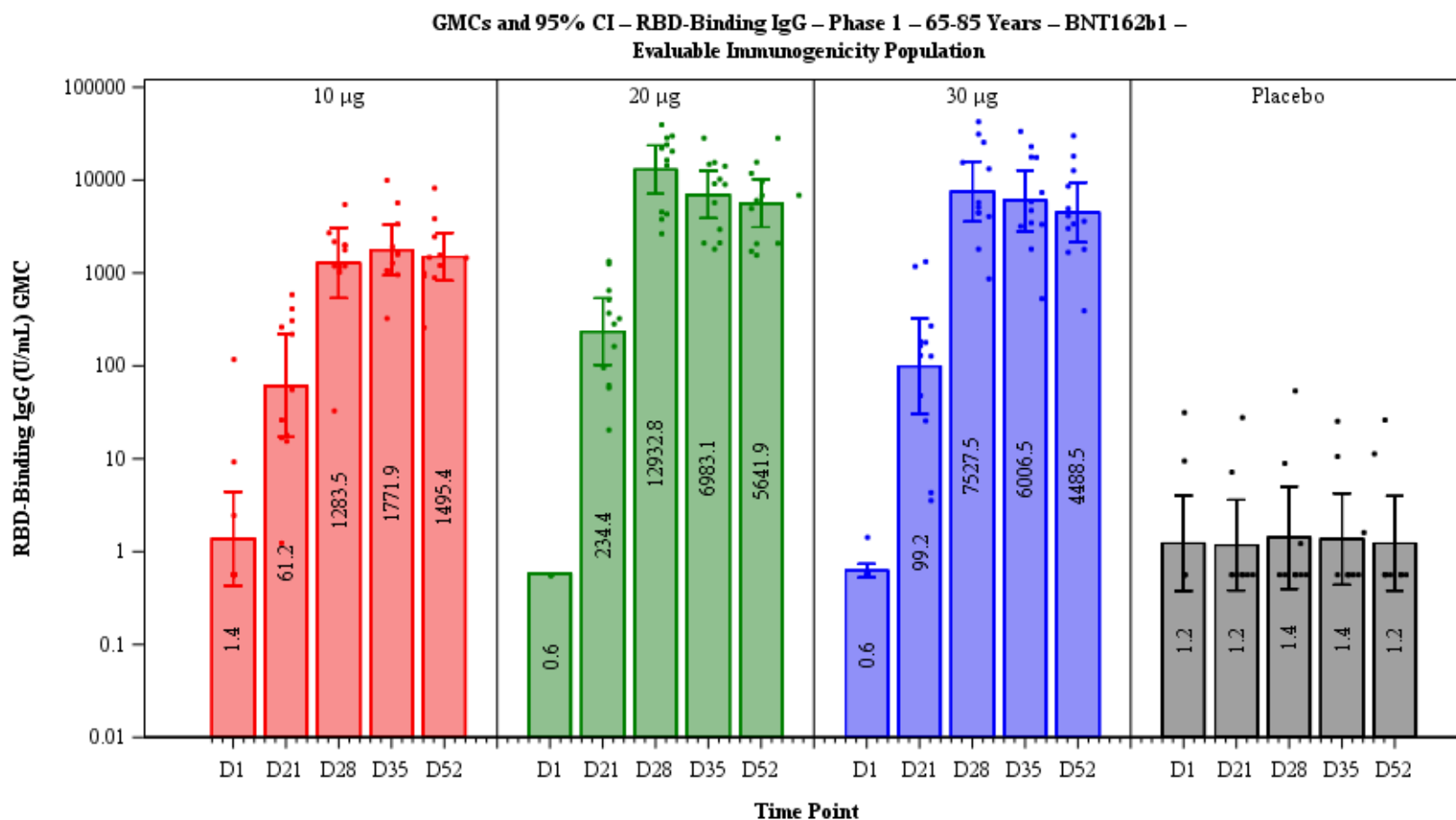
Note: Number within each bar denotes geometric mean.

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Figure 17. Geometric Mean Concentrations and 95% CI: SARS-CoV-2 RBD-binding IgG Level Assay – Phase 1, 2 Doses, 21 Days Apart – 65-85 Years of Age, BNT162b1 – Evaluable Immunogenicity Population



Abbreviations: GMC = geometric mean concentration; IgG = immunoglobulin G; RBD = receptor-binding domain.

Note: Dots present individual antibody levels.

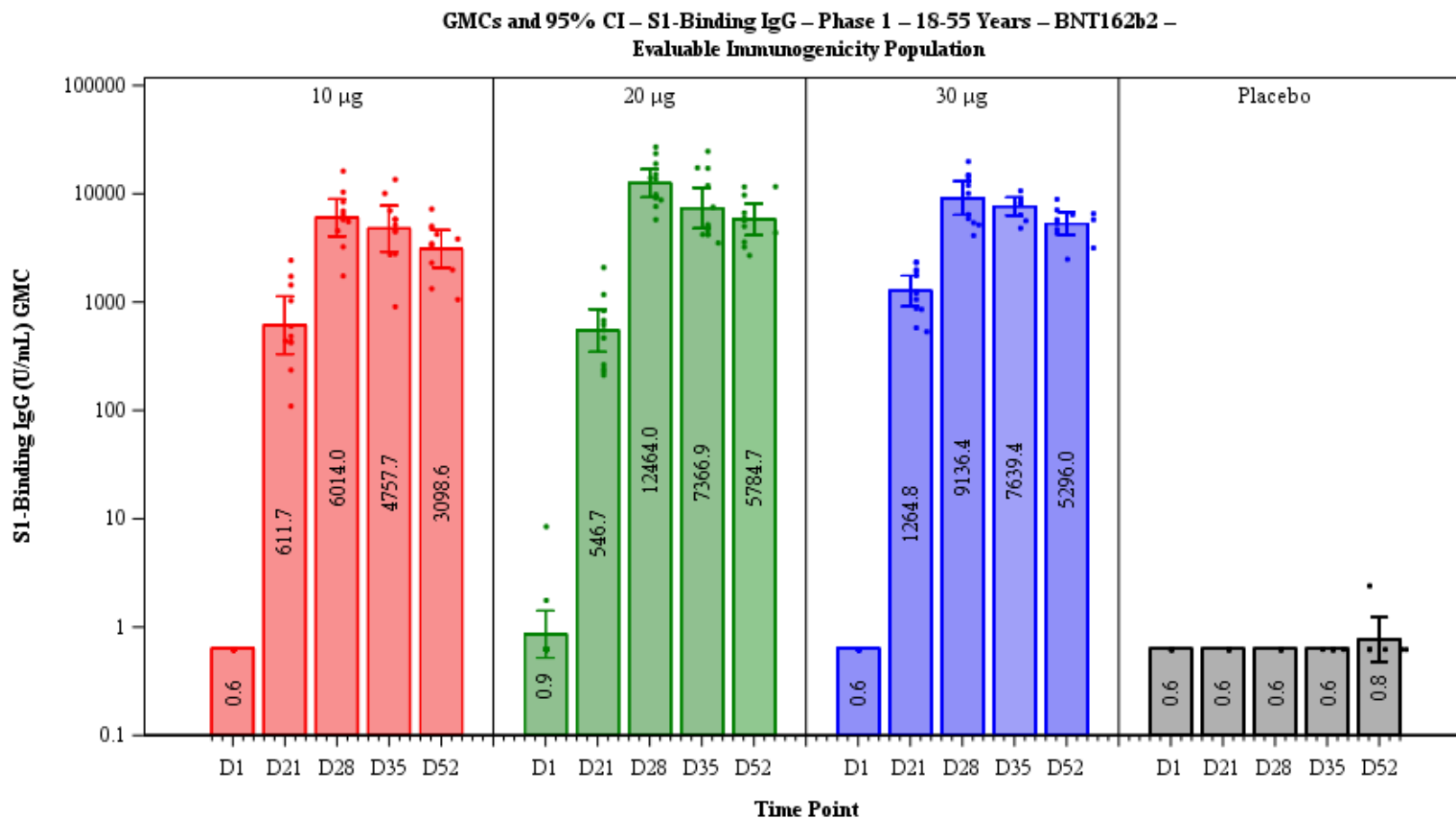
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Figure 18. Geometric Mean Concentrations and 95% CI: SARS-CoV-2 S1-binding IgG Level Assay – Phase 1, 2 Doses, 21 Days Apart – 18-55 Years of Age – BNT162b2 – Evaluable Immunogenicity Population



Abbreviations: GMC = geometric mean concentration; IgG = immunoglobulin G; S1 = spike protein S1 subunit.

Note: Dots present individual antibody levels.

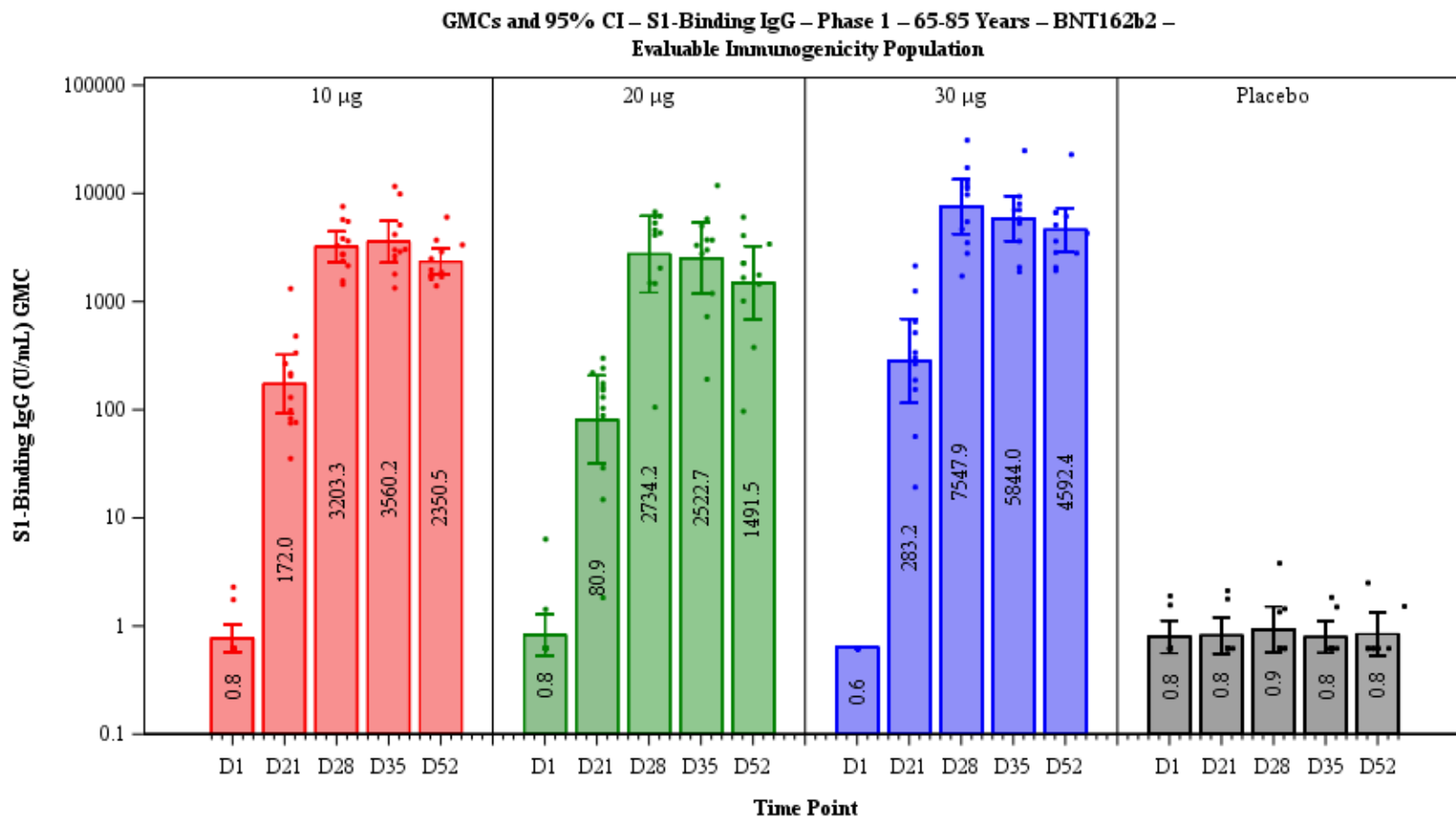
Note: Number within each bar denotes geometric mean.

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Figure 19. Geometric Mean Concentrations and 95% CI: SARS-CoV-2 S1-binding IgG Level Assay – Phase 1, 2 Doses, 21 Days Apart – 65-85 Years of Age – BNT162b2 – Evaluable Immunogenicity Population



Abbreviations: GMC = geometric mean concentration; IgG = immunoglobulin G; S1 = spike protein S1 subunit.

Note: Dots present individual antibody levels.

Note: Number within each bar denotes geometric mean.

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Geometric Mean Fold-Rise (GMFR)

For BNT162b1 and BNT162b2 recipients, and in both age groups, GMFRs of SARS-CoV-2 antigen-specific binding IgG were substantially higher 7 days after Dose 2 (Day 28) than 21 days after Dose 1. GMFRs peaked by 7 days or 14 days after Dose 2, and although decreased by 1 month after Dose 2, GMFRs at this time point were still substantially higher than at Day 21 after Dose 1. Results for GMFR are available in [Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 11.2.1.2.2](#).

Proportion of Participants Achieving a ≥ 4 -Fold Rise

BNT162b1

In both age groups, 100% of participants in each dose level group achieved a ≥ 4 -fold rise in RBD-binding IgG levels at all time points after Dose 2 of BNT162b1, except for the 20- μg dose group at Day 7 after Dose 2 (91.7% in the younger age group).

BNT162b2

In both age groups, 100% of participants in each dose level group achieved a ≥ 4 -fold rise in S1-binding IgG levels at all time points after Dose 2 of BNT162b2.

Results for the proportion of participants achieving a ≥ 4 -fold rise are available in [Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 11.2.1.2.3](#).

2.7.3.2.2.1.2.3. Persistence of the Immune Response Through 6 Months After Dose 2 of 30 μg BNT162b2 – Study C4591001, Phase 1

For participants who received the 30 μg dose level of BNT162b2 (and corresponding placebo), blood samples collected approximately 6 months after Dose 2 were assayed for SARS-CoV-2 neutralizing activity and for S1-binding IgG concentrations. Blood samples from some earlier time points for these participants were re-analyzed with the 6-month post Dose 2 samples to assure assay comparability between time points.

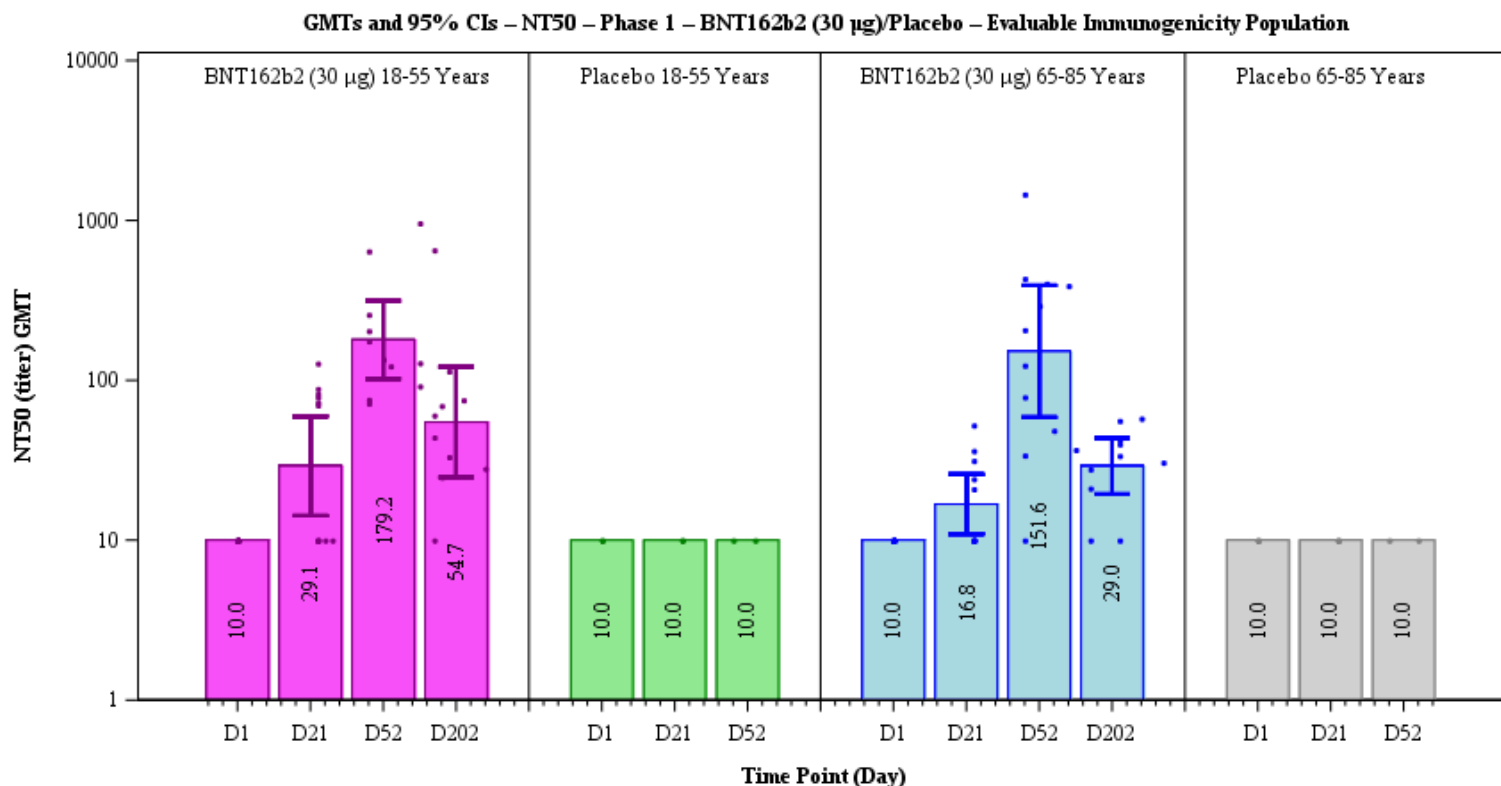
GMTs, GMCs, and GMFRs

Among participants who received the 30 μg dose level of BNT162b2, in both age groups, the observed SARS-CoV-2 serum 50% neutralizing GMTs declined from 1 month after Dose 2 (Day 52) to 6 months after Dose 2 (Day 202). In the younger age group, GMTs were 179.2 at 1 month after Dose 2 and 54.7 at 6 months after Dose 2; in the older age group GMTs declined from 151.6 to 29.0 ([Figure 20](#) and [Table 62](#)). While GMTs at 6 months after Dose 2 of BNT162b2 were lower than those at 1 month after Dose 2, they were numerically higher than those observed before vaccination. Observed S1-binding IgG GMCs demonstrated similar trends ([Figure 21](#) and [Table 62](#)).

In the younger and older age groups, respectively, GMFRs of SARS-CoV-2 serum 50% neutralizing titers from before BNT162b2 to each subsequent time point were 2.9 and 1.7 at Day 21 (immediately before Dose 2), 17.9 and 15.2 at 1 month after Dose 2; and 5.5 and

2.9 at 6 months after Dose 2. Results for GMFRs of S1-binding IgG concentrations reflected similar trends ([Table 63](#)).

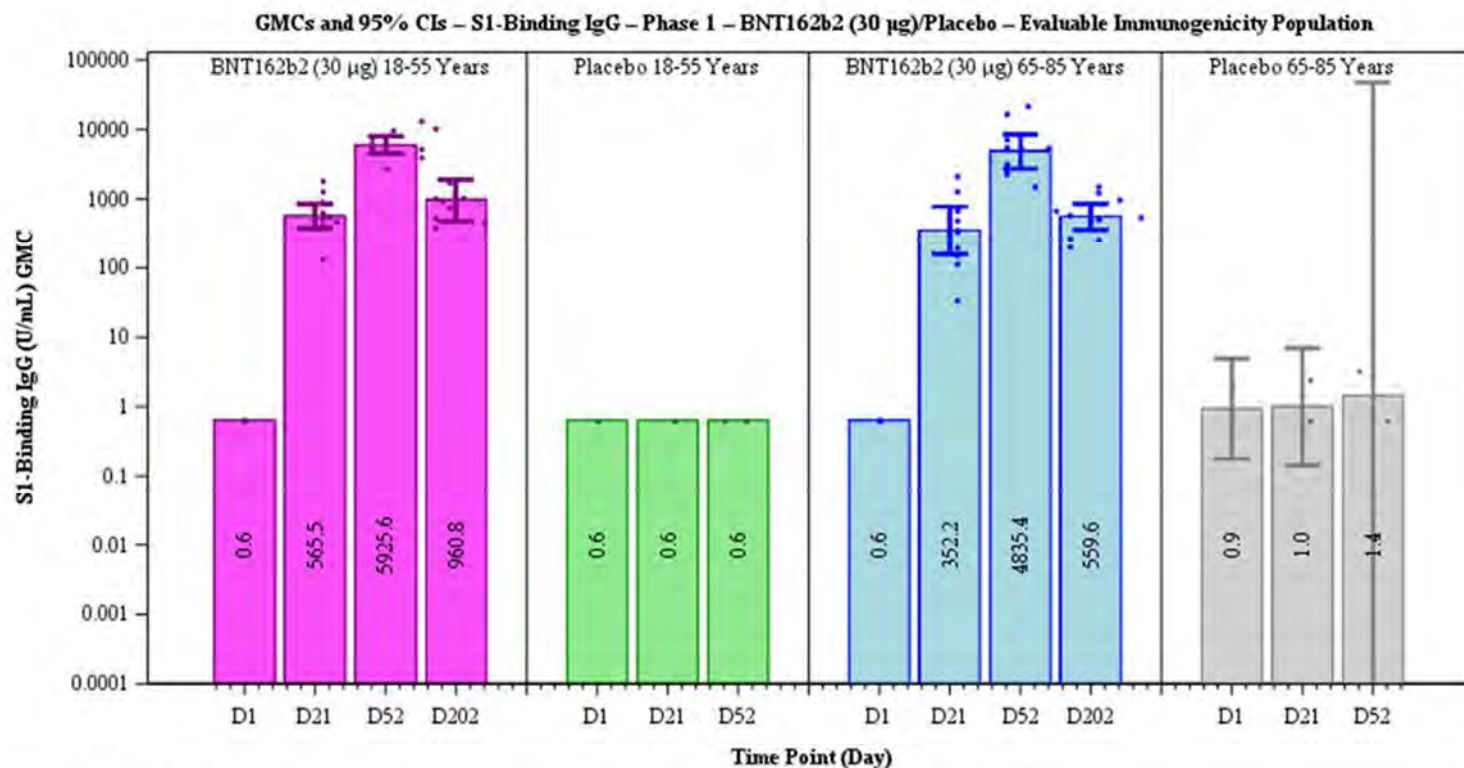
Figure 20. **Geometric Mean Titers and 95% CIs: SARS-CoV-2 Neutralization Assay – NT50 – Phase 1, 2 Doses, 21 Days Apart – BNT162b2 (30 µg)/Placebo – Evaluable Immunogenicity Population**



Abbreviations: D = day; GMT = geometric mean titer; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
 Note: Blood samples from the Day 7 and Day 14 post-Dose 2 visits are not included since these samples were not retested with the 6-month post-Dose 2 samples.
 Note: Dots represent individual antibody levels.
 Note: Number within each bar denotes geometric mean titer.
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Figure 21. Geometric Mean Concentrations and 95% CIs: S1-Binding IgG Level Assay – Phase 1, 2 Doses, 21 Days Apart – BNT162b2 (30 µg)/Placebo – Evaluable Immunogenicity Population



Abbreviations: D = day; GMC = geometric mean concentration; IgG = immunoglobulin G; S1 = spike protein S1 subunit.

Note: Blood samples from the Day 7 and Day 14 post-Dose 2 visits are not included since these samples were not retested with the 6-month post-Dose 2 samples.

Note: Dots represent individual antibody levels.

Note: Number within each bar denotes geometric mean titer.

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Proportion of Participants Achieving \geq 4-Fold Rise

In the younger age group receiving BNT162b2, the proportions of participants who achieved a \geq 4-fold increase in SARS-CoV-2 50% neutralizing titers from before vaccination to each time point were: 50.0% (6/12) at Day 21; 100.0% (11/11) at 1 month after Dose 2; and 60.0% (6/10) at 6 months after Dose 2. In the older age group receiving BNT162b2, these proportions were 9.1% (1/11) at Day 21; 81.8% (9/11) at 1 month after Dose 2; and 27.3% (3/11) at 6 months after Dose 2 (Table 64). With respect to S1-binding IgG concentrations, 100% of participants in both age groups had a \geq 4-fold increase from baseline at each of these time points.

2.7.3.2.2.1.2.4. Immunogenicity Conclusions – Study C4591001 Phase 1

- Both BNT162b1 and BNT162b2 elicited robust SARS-CoV-2 neutralizing titers. GMTs were modestly increased by Day 21 after the first dose and were substantially increased by 7 days after the second dose, with high response levels maintained through 1 month after Dose 2.
- Antigen binding IgG levels increased substantially by Day 21 after the first dose and were further increased by 7 days after the second dose, with high response levels maintained through 1 month after Dose 2.
- GMTs and GMCs in the older age group were generally lower than in the younger age group at the same dose level.
- For Phase 1 participants who received BNT162b2 30 μ g, SARS-CoV-2 serum neutralizing titers and serum S1-binding IgG concentrations at 6 months after dose 2 had decreased relative to those observed at 1 month after Dose 2 but remained higher than values observed before vaccination.

2.7.3.2.2.1.3. Phase 1 Conclusions – Rationale for Candidate and Dose Level Selection

The Phase 1 immunogenicity data from both Studies C4591001 and BNT162-01 collectively showed robust immunogenicity elicited by both candidate vaccines. Overall, the immunogenicity responses were similar between the 2 candidates. When selecting the dose level for Phase 2/3, the major driver was maximizing SARS-CoV-2 neutralizing antibody responses in the older age group, who are at highest risk of severe disease. A robust immune response was elicited in both younger and older adults by BNT162b2 at the 30 μ g dose level, which was ultimately selected to proceed to Phase 2/3 development.

- In Phase 1 of Study C4591001, both BNT162b1 and BNT162b2 elicited robust SARS-CoV-2 neutralization and antigen-specific IgG binding in younger and older adults as shown by GMTs/GMCs, GMFRs, and proportions of participants achieving a \geq 4-fold rise in neutralizing titers and antigen-binding IgG levels.

- Both BNT162b1 and BNT162b2 vaccine candidates demonstrated robust SARS-CoV-2 neutralization and substantial rises in IgG-antigen binding levels following the second dose across dose levels and age groups.
- In older adults, who are at higher risk of severe COVID-19 disease, the neutralizing response to BNT162b2 was highest at the 30 µg dose level compared to the 20 µg dose level, favoring the 30 µg dose level for Phase 2/3 development.
- Study BNT162-01 provides evidence for robust T cell-mediated immunity, with both BNT162b1 and BNT162 inducing poly-functional and pro-inflammatory CD4+/CD8+ T cell responses in almost all participants. The detection of robust IFN γ and IL-2 production but only minimal IL-4 production indicates a favorable Th1 profile and the absence of a potentially deleterious Th2 immune response.
- Immunogenicity data from Study BNT162-01 were generally concordant with results in pivotal Study C4591001, showing robust SARS CoV-2 neutralization and substantial rises in IgG-antigen binding levels following the second dose, and complimentary T cell immune response data.

2.7.3.2.2.2. Phase 2 Immunogenicity Results – Study C4591001

2.7.3.2.2.2.1. Disposition, Data Sets Analyzed, and Demographics – Study C4591001 Phase 2

Disposition

The 360 participants enrolled as part of Phase 2 were randomized equally to the BNT162b2 (30 µg) and placebo groups (180 participants each). Among participants randomized to the BNT162b2 group, 88 participants were in the younger age group (18 to 55 years of age) and 92 participants were in the older age group (56 to 85 years of age) ([Table 65](#)).

All 360 participants received both doses of study vaccine, except for 1 participant in the younger age group who was withdrawn from the study after Dose 1 of BNT162b2 but before Dose 2 because of an SAE of gastric adenocarcinoma 23 days after receiving Dose 1.

Data Sets Analyzed

Immunogenicity results are currently available for the prevaccination and 1 month post Dose 2 time point; results for later time points will be reported when available.

A total of 7 participants (3 in the BNT162b2 group and 4 in the placebo group) were excluded from the Dose 2 all-available immunogenicity population because they did not have at least 1 valid and determinate immunogenicity result after Dose 2. The Dose 2 evaluable immunogenicity population included 93.9% of participants who received BNT162b2 and 92.8% of participants who received placebo. The reasons for data exclusion are shown in [Table 65](#). Serology data at 1 month after Dose 2 from 2 participants who had a postbaseline positive SARS-CoV-2 test result were excluded in the analysis based on the Dose 2 evaluable immunogenicity populations, following the study protocol and SAP.

Demographics

In the Dose 2 evaluable immunogenicity population, 52.1% of participants were male; 84.8% were White and 10.1% were Black or African American; 10.7% were Hispanic; and the median age was 56 years (range 18 to 85) (Table 66).

2.7.3.2.2.2. SARS-CoV-2 Neutralizing Titers and S1-Binding IgG Concentrations – Study C4591001, Phase 2

Results of immunogenicity analyses reported here are those for the Dose 2 evaluable immunogenicity population; note that baseline positive participants (by SARS-CoV-2 N-binding antibody or positive NAAT at Visit 1) were not excluded from these analyses. Immunogenicity results for the Dose 2 all-available immunogenicity population were similar to those for the evaluable population.

Geometric Mean Titers/Concentrations (GMTs/GMCs)

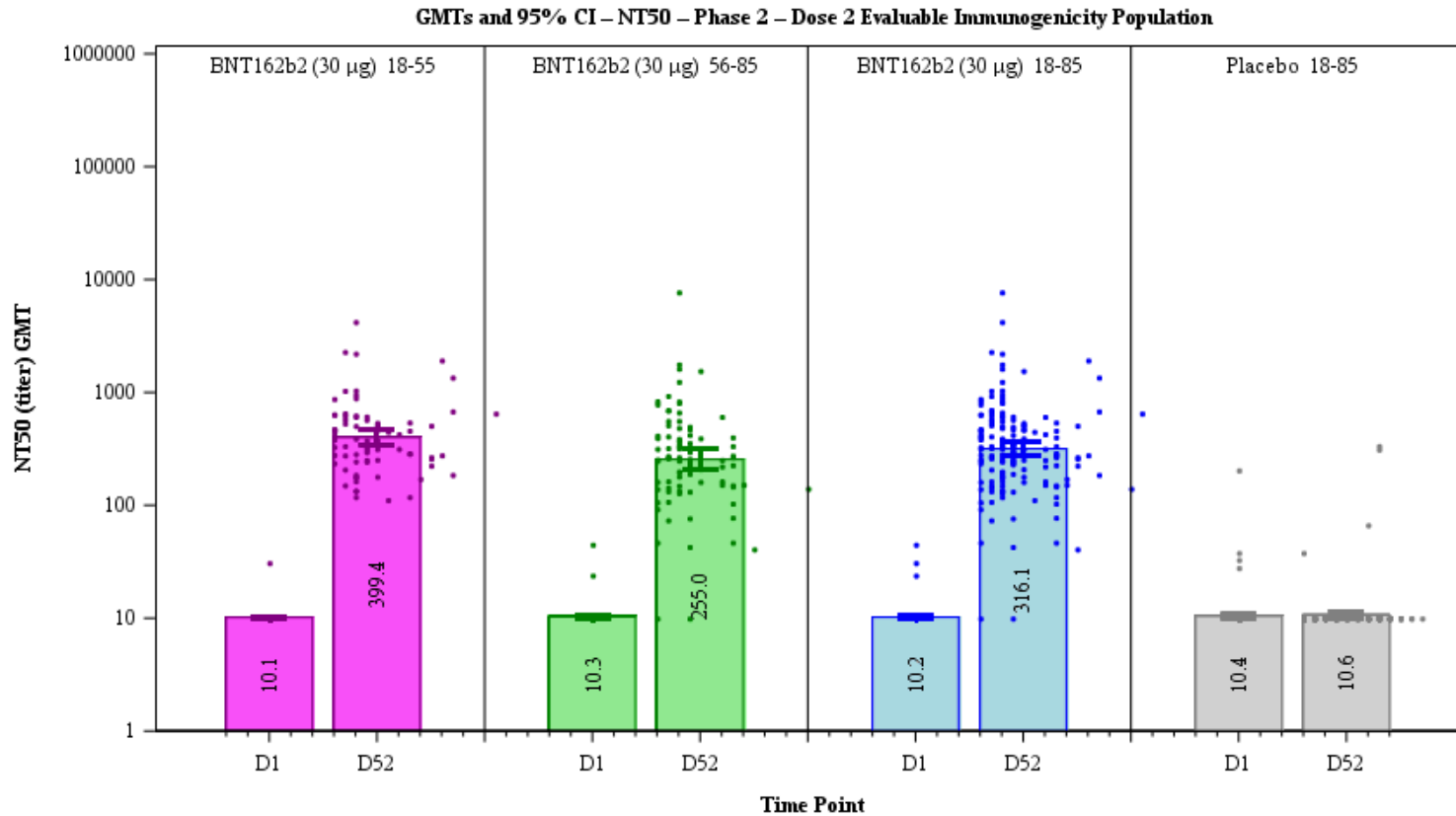
BNT162b2 elicited robust SARS-CoV-2 immune responses at 1 month after Dose 2 as measured by both SARS-CoV-2 50% neutralizing titers (GMTs) (Figure 22) and S1-binding IgG concentrations (GMCs) (Figure 23). GMTs and GMCs were higher in younger participants (18-55 years of age) than in older participants (56-85 years of age) (Table 67).

Of note, 50% neutralizing GMTs at 1-month post Dose 2 for both younger (GMT = 399.4) and older participants (GMT = 255.0) in the evaluable immunogenicity population were similar to the GMTs of a comparative panel of HCS (GMT = 319).⁸ The HCS is the same panel described in Section 2.7.3.1.3.4 except that 5 sera from the N=38 serum panel had been depleted.

Geometric Mean Fold-Rise (GMFR) in Titers/Concentrations

Results for GMFRs in SARS-CoV-2 50% neutralizing titers and S1-binding IgG concentrations were robust at 1 month after Dose 2 of BNT162b2, with higher GMFRs observed in younger participants than in older participants (Table 68).

Figure 22. **Geometric Mean Titers: SARS-CoV-2 Neutralization Assay - NT50 – Evaluable Immunogenicity Population (Study C4591001, Phase 2)**



Abbreviations: GMT = geometric mean titer; NT50 = 50% neutralizing titer; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Dots present individual antibody levels.

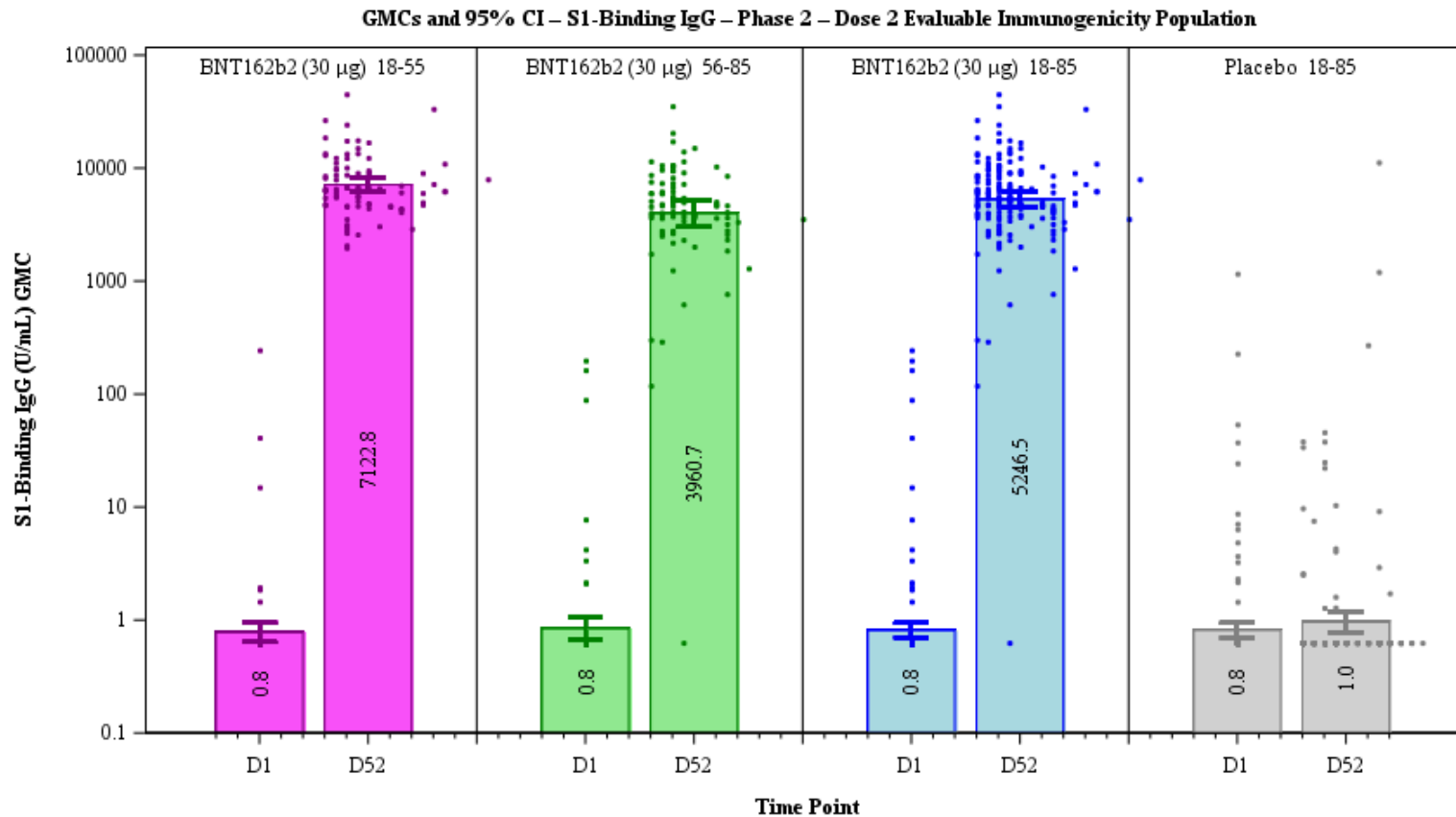
Note: Number within each bar denotes geometric mean.

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Figure 23. Geometric Mean Concentrations: SARS-CoV-2 S1-binding IgG Level Assay – Evaluable Immunogenicity Population (Study C4591001, Phase 2)



Abbreviations: GMC = geometric mean concentration; IgG = immunoglobulin G; S1 = spike protein S1 subunit.

Note: Dots present individual antibody levels.

Note: Number within each bar denotes geometric mean.

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2.7.3.2.2.3. SARS-CoV-2 Neutralizing Titers and S1-Binding IgG Concentrations by Baseline SARS-CoV-2 Status – Study C4591001, Phase 2

Immunogenicity results were summarized by baseline SARS-CoV-2 status (positive or negative; ie, participants with or without serological or virological evidence of SARS-CoV-2 infection before vaccination). Positive baseline SARS-CoV-2 status was defined as positive by N-binding antibody at Visit 1, or positive NAAT at Visit 1, or a medical history of COVID-19; negative baseline SARS-CoV-2 status was defined as negative by N-binding antibody and negative NAAT at Visit 1.

Geometric Mean Titers/Concentrations (GMTs/GMCs)

A few participants in the Dose 2 evaluable immunogenicity population had a positive baseline SARS-CoV-2 status: a total of 9 participants with immunogenicity data at the pre-vaccination time point (5 who received BNT162b2 and 4 who received placebo) and 7 participants (3 who received BNT162b2 and 4 who received placebo) with immunogenicity data at the 1 month post Dose 2 time point. These SARS-CoV-2 status positive participants were analyzed separately from the baseline negative participants. In general, at 1 month post Dose 2 among BNT162b2 recipients, observed SARS-CoV-2 50% neutralizing GMTs and S1-binding IgG GMCs were numerically higher in participants with a positive baseline SARS-CoV-2 status (n=3) than in those with a negative baseline SARS-CoV-2 status (n=163) (Table 69).

Geometric Mean Fold-Rise (GMFR) in Titers/Concentrations

When analyzing GMFRs stratified by SARS-CoV-2 status at 1 month post Dose 2, among BNT162b2 recipients (Table 70), the GMFRs for SARS-CoV-2 50% neutralizing titers and S1-binding IgG were similar to those in the combined baseline positive and negative participant group (Table 68).

2.7.3.2.2.4. Phase 2 Immunogenicity Conclusions – Study C4591001

Immunogenicity results from 360 participants in Phase 2 of Study C4591001 demonstrated that BNT162b2 at 30 µg elicited robust SARS-CoV-2 neutralization and S1-binding IgG antibody responses at 1 month after Dose 2 similar to those previously observed in Phase 1 of the study. Notably, SARS-CoV-2 neutralizing titers were higher in the younger age group compared to the older age group. Of note, GMTs for younger and older participants at 1 month after Dose 2 were similar to the GMTs of a comparative panel of HCS.⁸ S1-binding GMCs were generally higher in the younger age group compared to the older age group, again concordant with observations in the Phase 1 portion of the study.

2.7.3.2.2.3. Immunogenicity Conclusions for BNT162b2

- Two doses of BNT162b2 (30 µg) administered 21 days apart elicited robust SARS-CoV-2 neutralization responses and substantial rises in SARS-CoV-2 antigen-specific binding IgG levels in younger (18-55 years) and older (56-85 years) adults.
- SARS-CoV-2 50% neutralizing titers were modestly increased from baseline by 21 days after Dose 1, with substantial increases observed by 7 Days after Dose 2.

- S1-binding GMCs increased substantially from baseline by Day 21 after Dose 1 and were further increased 7 days after Dose 2.
- High response levels were maintained through 1 month after Dose 2 as measured by both SARS-CoV-2 neutralizing titers and S1-binding IgG.
- In Phase 1 of Study C4591001, at 6 months after Dose 2 of BNT162b2 30 µg, neutralizing titers and S1-binding IgG concentrations had decreased relative to levels observed at 1 month after Dose 2 but were above prevaccination levels.
- SARS-CoV-2 neutralizing GMTs and S1-binding GMCs were generally higher in the younger participants than older participants.
- Of note, SARS-CoV-2 neutralizing GMTs for younger and older participants were similar to or greater than the GMTs for a comparative panel of human convalescent sera.
- Participants who had evidence of prior SARS-CoV-2 infection had modestly elevated GMTs and GMCs detected at study baseline compared with baseline negative participants. Both baseline SARS-CoV-2 positive and negative participants had substantial increases in GMTs and GMCs from baseline to 1 month after Dose 2. The increases were more pronounced for those who were baseline positive, which suggests that immune responses from prior infection were further boosted by BNT162b2 immunization.
- BNT162 induces poly-functional and pro-inflammatory CD4+/CD8+ T cell responses in almost all participants. The detection of robust IFN γ and IL-2 production but only minimal IL-4 production indicates a favorable Th1 profile and the absence of a potentially deleterious Th2 immune response.

2.7.3.3. Comparison and Analyses of Results Across Studies

Not applicable.

2.7.3.4. Analysis of Clinical Information Relevant to Dosing Recommendations

The immunogenicity data supporting the selection of the SARS-CoV-2 mRNA vaccine candidate, regimen, and dose level are from Study BNT162-01 and Phase 1 of Study C4591001, which are described in [Section 2.7.3.2.1](#).

2.7.3.5. Persistence of Efficacy and/or Tolerance Effects

Following demonstration of VE of $\geq 95\%$ in the prespecified interim and final efficacy analyses (data cutoff dates of 04 November 2020 and 14 November 2020, respectively), updated analyses were conducted for COVID-19 cases accrued over a longer period during blinded placebo-controlled follow-up after Dose 2 (updated analysis data cutoff date: 13 March 2021).

In the updated analyses in the evaluable efficacy populations, both among participants without, and among those with and without, evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE against confirmed COVID-19 occurring at least 7 days after Dose 2 was approximately 91% and the estimated VE against FDA-defined severe COVID-19 (as defined by FDA) occurring at least 7 days after Dose 2 was approximately 95%. In the all-available efficacy population, estimated VE against severe COVID-19 occurring at any time after Dose 1 was 96.7%. The total duration of protection BNT162b2 provides against symptomatic COVID-19 is not yet known.

Phase 1 immunogenicity data indicate that the functional antibody and T cell responses induced by 30 µg BNT162b2 persist for at least 6 months after Dose 2. SARS-CoV-2 serum neutralizing titers and serum S1-binding IgG concentrations at 6 months after dose 2 had decreased relative to those observed at 1 month after Dose 2 but remained higher than values observed before vaccination. The total duration of antibody persistence is not yet known. Results for antibody persistence at 6 months after Dose 2 are not yet available for participants vaccinated in Phase 2. Those results, as well as data for 12 and 24 months after Dose 2 in both Phase 1 and Phase 2, will be provided in future submissions.

Despite the decrease in SARS-CoV-2 serum neutralizing titers and serum S1-binding IgG concentrations from 1 month to 6 months after dose 2 that was observed in Phase 1 participants who received 30 µg BNT162b2, VE remained high (>90%) in updated efficacy analyses for Phase 2/3 participants. Data are insufficient to allow estimation of an immunological correlate of protection.

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2.7.3.6. Appendix

Study C4591001 – Efficacy – Interim Analysis

Table 26. Efficacy Populations – Interim Analysis 1

| | Vaccine Group (as Randomized) | | |
|-----------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|-------------------------------|-----------------------------|
| | BNT162b2 (30 µg) n ^a (%) | Placebo n ^a (%) | Total n ^a (%) |
| Randomized ^b | 21653 (100.0) | 21672 (100.0) | 43325 (100.0) |
| Dose 1 all-available efficacy population | 21617 (99.8) | 21633 (99.8) | 43250 (99.8) |
| Subjects without evidence of infection before Dose 1 | 17237 (79.6) | 17221 (79.5) | 34458 (79.5) |
| Subjects excluded from Dose 1 all-available efficacy population | 36 (0.2) | 39 (0.2) | 75 (0.2) |
| Reason for exclusion ^c | | | |
| Did not receive at least 1 vaccination | 35 (0.2) | 39 (0.2) | 74 (0.2) |
| Did not provide informed consent | 1 (0.0) | 0 | 1 (0.0) |
| Dose 2 all-available efficacy population | 18868 (87.1) | 18877 (87.1) | 37745 (87.1) |
| Subjects without evidence of infection prior to 7 days after Dose 2 | 16463 (76.0) | 16426 (75.8) | 32889 (75.9) |
| Subjects excluded from Dose 2 all-available efficacy population | 2785 (12.9) | 2795 (12.9) | 5580 (12.9) |
| Reason for exclusion ^c | | | |
| Did not complete 2 vaccination doses | 2784 (12.9) | 2795 (12.9) | 5579 (12.9) |
| Did not provide informed consent | 1 (0.0) | 0 | 1 (0.0) |
| Evaluable efficacy population (7 Days) | 18380 (84.9) | 18618 (85.9) | 36998 (85.4) |
| Subjects without evidence of infection prior to 7 days after Dose 2 | 16061 (74.2) | 16218 (74.8) | 32279 (74.5) |
| Subjects excluded from evaluable efficacy population (7 Days) | 3273 (15.1) | 3054 (14.1) | 6327 (14.6) |
| Reason for exclusion ^c | | | |
| Randomized but did not meet all eligibility criteria | 15 (0.1) | 16 (0.1) | 31 (0.1) |
| Did not provide informed consent | 1 (0.0) | 0 | 1 (0.0) |
| Did not receive all vaccination(s) as randomized or did not receive Dose 2 within the predefined window (19-42 days after Dose 1) | 3038 (14.0) | 3035 (14.0) | 6073 (14.0) |
| Had other important protocol deviations on or prior to 7 days after Dose 2 | 302 (1.4) | 52 (0.2) | 354 (0.8) |

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Table 26. Efficacy Populations – Interim Analysis 1

| | Vaccine Group (as Randomized) | | |
|--|----------------------------------------|-------------------------------|-----------------------------|
| | BNT162b2 (30 µg) n ^a (%) | Placebo n ^a (%) | Total n ^a (%) |

Note: Data from subjects who are not confirmed 7 days post dose 2 cases are included in the analysis to comprehensively show all data reported and/or contribute to the total surveillance time calculation but may be subject to change with additional follow-up.

- a. n = Number of subjects with the specified characteristic.
- b. These values are the denominators for the percentage calculations.
- c. Subjects may have been excluded for more than 1 reason.

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Table 27. Demographic Characteristics – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy Population (7 Days) – Interim Analysis 1

| | Vaccine Group (as Randomized) | | |
|-------------------------------------------|-------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =16061) n ^b (%) | Placebo (N ^a =16218) n ^b (%) | Total (N ^a =32279) n ^b (%) |
| Sex | | | |
| Male | 8197 (51.0) | 8144 (50.2) | 16341 (50.6) |
| Female | 7864 (49.0) | 8074 (49.8) | 15938 (49.4) |
| Race | | | |
| White | 13502 (84.1) | 13692 (84.4) | 27194 (84.2) |
| Black or African American | 1298 (8.1) | 1303 (8.0) | 2601 (8.1) |
| American Indian or Alaska native | 88 (0.5) | 82 (0.5) | 170 (0.5) |
| Asian | 712 (4.4) | 716 (4.4) | 1428 (4.4) |
| Native Hawaiian or other Pacific Islander | 40 (0.2) | 26 (0.2) | 66 (0.2) |
| Multiracial | 341 (2.1) | 297 (1.8) | 638 (2.0) |
| Not reported | 80 (0.5) | 102 (0.6) | 182 (0.6) |
| Ethnicity | | | |
| Hispanic/Latino | 4415 (27.5) | 4383 (27.0) | 8798 (27.3) |
| Non-Hispanic/non-Latino | 11553 (71.9) | 11736 (72.4) | 23289 (72.1) |
| Not reported | 93 (0.6) | 99 (0.6) | 192 (0.6) |
| Country | | | |
| Argentina | 2445 (15.2) | 2415 (14.9) | 4860 (15.1) |
| Brazil | 889 (5.5) | 889 (5.5) | 1778 (5.5) |
| South Africa | 215 (1.3) | 218 (1.3) | 433 (1.3) |
| USA | 12512 (77.9) | 12696 (78.3) | 25208 (78.1) |
| Age group | | | |
| 16-55 Years | 9093 (56.6) | 9172 (56.6) | 18265 (56.6) |
| >55 Years | 6968 (43.4) | 7046 (43.4) | 14014 (43.4) |
| Age at vaccination (years) | | | |

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Table 27. Demographic Characteristics – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy Population (7 Days) – Interim Analysis 1

| | Vaccine Group (as Randomized) | | |
|-----------|-------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =16061) n ^b (%) | Placebo (N ^a =16218) n ^b (%) | Total (N ^a =32279) n ^b (%) |
| Mean (SD) | 50.9 (15.58) | 50.7 (15.68) | 50.8 (15.63) |
| Median | 52.0 | 52.0 | 52.0 |
| Min, max | (16, 89) | (16, 91) | (16, 91) |

Note: Data from subjects who are not confirmed 7 days post dose 2 cases are included in the analysis to comprehensively show all data reported and/or contribute to the total surveillance time calculation but may be subject to change with additional follow-up.

- a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.
- b. n = Number of subjects with the specified characteristic.

PFIZER CONFIDENTIAL SDTM Creation: 06NOV2020 (01:29) Source Data: adsl Table Generation: 06NOV2020 (16:35)

(Cutoff Date: 04Nov2020, Snapshot Date: 04Nov2020) Output File: ./nda2_unblinded_ia/C4591001_IA_62/adsl_demo_7d_eval_eff

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Table 28. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Dose 2 All-Available Efficacy Population – Interim Analysis 1

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI) ^e | Pr (VE >30% data) ^f |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|-----------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =16463) | | Placebo (N ^a =16426) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 4 | 1.761 (16298) | 93 | 1.748 (16213) | 95.7 | (89.3, 98.5) | >0.9999 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

Note: Data from subjects who are not confirmed 7 days post dose 2 cases are included in the analysis to comprehensively show all data reported and/or contribute to the total surveillance time calculation but may be subject to change with additional follow-up.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102,1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details. This probability must be at least 99.5% at the interim analysis in order to conclude that the vaccine is efficacious.

PFIZER CONFIDENTIAL SDTM Creation: 05NOV2020 (20:48) Source Data: adc19ef Table Generation: 09NOV2020 (16:43)

(Cutoff Date: 04Nov2020, Snapshot Date: 04Nov2020) Output File: /nda2_unblinded_ia/C4591001_IA_62/adc19ef_ve_cov_7pd2_wo_aai

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Table 29. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Dose 2 All-Available Efficacy Population – Interim Analysis 1

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =16463) | | Placebo (N ^a =16426) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | | | | | | |
| Overall | 4 | 1.761 (16298) | 93 | 1.748 (16213) | 95.7 | (88.7, 98.9) |
| Age group (years) | | | | | | |
| 16 to 55 | 2 | 0.975 (9217) | 70 | 0.968 (9156) | 97.2 | (89.4, 99.7) |
| >55 | 2 | 0.785 (7081) | 23 | 0.780 (7057) | 91.4 | (65.0, 99.0) |
| Sex | | | | | | |
| Male | 2 | 0.893 (8320) | 41 | 0.874 (8138) | 95.2 | (81.6, 99.4) |
| Female | 2 | 0.867 (7978) | 52 | 0.874 (8075) | 96.1 | (85.3, 99.5) |
| Race | | | | | | |
| White | 4 | 1.513 (13771) | 88 | 1.505 (13708) | 95.5 | (88.0, 98.8) |
| Black or African American | 0 | 0.125 (1281) | 4 | 0.125 (1285) | 100.0 | (-50.8, 100.0) |
| All others ^f | 0 | 0.122 (1246) | 1 | 0.119 (1220) | 100.0 | (-3708.9, 100.0) |
| Ethnicity | | | | | | |
| Hispanic/Latino | 1 | 0.471 (4499) | 35 | 0.464 (4437) | 97.2 | (83.3, 99.9) |
| Non-Hispanic/non-Latino | 3 | 1.279 (11702) | 58 | 1.274 (11678) | 94.8 | (84.2, 99.0) |
| Country | | | | | | |
| Argentina | 0 | 0.275 (2516) | 29 | 0.269 (2477) | 100.0 | (86.7, 100.0) |
| Brazil | 0 | 0.087 (878) | 2 | 0.087 (881) | 100.0 | (-433.0, 100.0) |
| USA | 4 | 1.395 (12702) | 62 | 1.389 (12656) | 93.6 | (82.7, 98.3) |

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Table 29. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Dose 2 All-Available Efficacy Population – Interim Analysis 1

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =16463) | | Placebo (N ^a =16426) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

Note: Data from subjects who are not confirmed 7 days post dose 2 cases are included in the analysis to comprehensively show all data reported and/or contribute to the total surveillance time calculation but may be subject to change with additional follow-up.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted to the surveillance time.
- f. American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, not reported race categories are presented as “All others”.

PFIZER CONFIDENTIAL SDTM Creation: 05NOV2020 (20:53) Source Data: adc19ef Table Generation: 09NOV2020 (16:43)

(Cutoff Date: 04Nov2020, Snapshot Date: 04Nov2020) Output File: ./nda2_unblinded_ia/C4591001_IA_62/adc19ef_ve_cov_7pd2_wo_sg_aai

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Table 30. COVID-19 Occurrence From 7 Days After Dose 2, by Prior SARS-CoV-2 Status – Evaluable Efficacy Population (7 Days) – Interim Analysis 1

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | |
|-----------------------------------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =18380) n ^b | Placebo (N ^a =18618) n ^b |
| COVID-19 occurrence from 7 days after Dose 2 | | |
| Prior SARS-CoV-2 Status | | |
| Positive at baseline ^c | 1 | 1 |
| Negative at baseline but positive on or prior to 7 days after Dose 2 ^d | 0 | 0 |
| Negative prior to 7 days after Dose 2 ^e | 4 | 90 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Subjects whose prior SARS-CoV-2 status cannot be determined due to missing N-binding antibody or NAAT at Visit 1 or Visit 2 were not included in the analysis.

- a. N = number of subjects in the specified group.
- b. n = Number of subjects meeting the endpoint definition.
- c. Positive N-binding antibody at Visit 1, or positive NAAT at Visit 1, or had medical history of COVID-19.
- d. Negative N-binding antibody at Visit 1 and negative NAAT at Visit 1, positive NAAT at Visit 2 or at unscheduled visit, if any, prior to 7 days after Dose 2.
- e. Negative N-binding antibody at Visit 1, negative NAAT at Visit 1 and Visit 2, and negative at unscheduled visit, if any, prior to 7 days after Dose 2.

PFIZER CONFIDENTIAL SDTM Creation: 05NOV2020 (20:48) Source Data: adc19ef Table Generation: 06NOV2020 (16:32)

(Cutoff Date: 04Nov2020, Snapshot Date: 04Nov2020) Output File: ./nda2_unblinded_ia/C4591001_IA_62/adc19ef_cov_bl_7dpd2_eval

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Table 31. COVID-19 Occurrence From 7 Days After Dose 2, by Prior SARS-CoV-2 Status – Dose 2 All-Available Efficacy Population – Interim Analysis 1

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | |
|-----------------------------------------------------------------------------------|---------------------------------------------------------------|------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =18868) n ^b | Placebo (N ^a =18877) n ^b |
| COVID-19 occurrence from 7 days after Dose 2 | | |
| Prior SARS-CoV-2 Status | | |
| Positive at baseline ^c | 1 | 1 |
| Negative at baseline but positive on or prior to 7 days after Dose 2 ^d | 0 | 0 |
| Negative prior to 7 days after Dose 2 ^e | 4 | 93 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Subjects whose prior SARS-CoV-2 status cannot be determined due to missing N-binding antibody or NAAT at Visit 1 or Visit 2 were not included in the analysis.

- a. N = number of subjects in the specified group.
- b. n = Number of subjects meeting the endpoint definition.
- c. Positive N-binding antibody at Visit 1, or positive NAAT at Visit 1, or had medical history of COVID-19.
- d. Negative N-binding antibody at Visit 1 and negative NAAT at Visit 1, positive NAAT at Visit 2 or at unscheduled visit, if any, prior to 7 days after Dose 2.
- e. Negative N-binding antibody at Visit 1, negative NAAT at Visit 1 and Visit 2, and negative at unscheduled visit, if any, prior to 7 days after Dose 2.

PFIZER CONFIDENTIAL SDTM Creation: 05NOV2020 (20:48) Source Data: adc19ef Table Generation: 06NOV2020 (16:32)

(Cutoff Date: 04Nov2020, Snapshot Date: 04Nov2020) Output File: ./nda2_unblinded_ia/C4591001_IA_62/adc19ef_cov_bl_7dpd2_aai

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Table 32. Efficacy Populations

| | Vaccine Group (as Randomized) | | Total n ^a (%) |
|---------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|-------------------------------|-----------------------------|
| | BNT162b2 (30 µg) n ^a (%) | Placebo n ^a (%) | |
| Randomized ^b | 21823 (100.0) | 21828 (100.0) | 43651 (100.0) |
| Dose 1 all-available efficacy population | 21768 (99.7) | 21783 (99.8) | 43551 (99.8) |
| Subjects without evidence of infection before Dose 1 | 20314 (93.1) | 20296 (93.0) | 40610 (93.0) |
| Subjects excluded from Dose 1 all-available efficacy population | 55 (0.3) | 45 (0.2) | 100 (0.2) |
| Reason for exclusion ^c | | | |
| Did not receive at least 1 vaccination | 54 (0.2) | 45 (0.2) | 99 (0.2) |
| Did not provide informed consent | 1 (0.0) | 0 | 1 (0.0) |
| Dose 2 all-available efficacy population | 20566 (94.2) | 20536 (94.1) | 41102 (94.2) |
| Subjects without evidence of infection prior to 7 days after Dose 2 | 18701 (85.7) | 18627 (85.3) | 37328 (85.5) |
| Subjects without evidence of infection prior to 14 days after Dose 2 | 18678 (85.6) | 18563 (85.0) | 37241 (85.3) |
| Subjects excluded from Dose 2 all-available efficacy population | 1257 (5.8) | 1292 (5.9) | 2549 (5.8) |
| Reason for exclusion ^c | | | |
| Did not receive 2 vaccinations | 1256 (5.8) | 1292 (5.9) | 2548 (5.8) |
| Did not provide informed consent | 1 (0.0) | 0 | 1 (0.0) |
| Evaluable efficacy (7 days) population | 20033 (91.8) | 20244 (92.7) | 40277 (92.3) |
| Subjects without evidence of infection prior to 7 days after Dose 2 | 18242 (83.6) | 18379 (84.2) | 36621 (83.9) |
| Evaluable efficacy (14 days) population | 20033 (91.8) | 20243 (92.7) | 40276 (92.3) |
| Subjects without evidence of infection prior to 14 days after Dose 2 | 18219 (83.5) | 18315 (83.9) | 36534 (83.7) |
| Subjects excluded from evaluable efficacy (7 days) population | 1790 (8.2) | 1584 (7.3) | 3374 (7.7) |
| Subjects excluded from evaluable efficacy (14 days) population | 1790 (8.2) | 1585 (7.3) | 3375 (7.7) |
| Reason for exclusion ^c | | | |
| Randomized but did not meet all eligibility criteria | 36 (0.2) | 26 (0.1) | 62 (0.1) |
| Did not provide informed consent | 1 (0.0) | 0 | 1 (0.0) |
| Did not receive all vaccinations as randomized or did not receive Dose 2 within the predefined window (19-42 days after Dose 1) | 1550 (7.1) | 1561 (7.2) | 3111 (7.1) |

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Table 32. Efficacy Populations

| | Vaccine Group (as Randomized) | | |
|-----------------------------------------------------------------------------|----------------------------------------|-------------------------------|-----------------------------|
| | BNT162b2 (30 µg) n ^a (%) | Placebo n ^a (%) | Total n ^a (%) |
| Had other important protocol deviations on or prior to 7 days after Dose 2 | 311 (1.4) | 60 (0.3) | 371 (0.8) |
| Had other important protocol deviations on or prior to 14 days after Dose 2 | 311 (1.4) | 61 (0.3) | 372 (0.9) |

Note: HIV-positive subjects are included in this summary but not included in the analyses of the overall study objectives.

- a. n = Number of subjects with the specified characteristic.
- b. These values are the denominators for the percentage calculations.
- c. Subjects may have been excluded for more than 1 reason.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (10:49) Source Data: adsl Table Generation: 17NOV2020 (18:29)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adsl_eff_pop

Table 33. Demographic Characteristics – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| | Vaccine Group (as Randomized) | | |
|-------------------------------------------|-------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =18242) n ^b (%) | Placebo (N ^a =18379) n ^b (%) | Total (N ^a =36621) n ^b (%) |
| Sex | | | |
| Male | 9318 (51.1) | 9225 (50.2) | 18543 (50.6) |
| Female | 8924 (48.9) | 9154 (49.8) | 18078 (49.4) |
| Race | | | |
| White | 15110 (82.8) | 15301 (83.3) | 30411 (83.0) |
| Black or African American | 1617 (8.9) | 1617 (8.8) | 3234 (8.8) |
| American Indian or Alaska native | 118 (0.6) | 106 (0.6) | 224 (0.6) |
| Asian | 815 (4.5) | 810 (4.4) | 1625 (4.4) |
| Native Hawaiian or other Pacific Islander | 48 (0.3) | 29 (0.2) | 77 (0.2) |
| Multiracial | 448 (2.5) | 402 (2.2) | 850 (2.3) |
| Not reported | 86 (0.5) | 114 (0.6) | 200 (0.5) |
| Ethnicity | | | |
| Hispanic/Latino | 4886 (26.8) | 4857 (26.4) | 9743 (26.6) |
| Non-Hispanic/non-Latino | 13253 (72.7) | 13412 (73.0) | 26665 (72.8) |
| Not reported | 103 (0.6) | 110 (0.6) | 213 (0.6) |
| Country | | | |
| Argentina | 2561 (14.0) | 2539 (13.8) | 5100 (13.9) |
| Brazil | 1232 (6.8) | 1223 (6.7) | 2455 (6.7) |
| Germany | 121 (0.7) | 126 (0.7) | 247 (0.7) |
| South Africa | 287 (1.6) | 279 (1.5) | 566 (1.5) |
| USA | 14041 (77.0) | 14212 (77.3) | 28253 (77.1) |
| Age group | | | |
| 12-15 Years | 46 (0.3) | 42 (0.2) | 88 (0.2) |
| 16-55 Years | 10428 (57.2) | 10507 (57.2) | 20935 (57.2) |

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Table 33. Demographic Characteristics – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| | Vaccine Group (as Randomized) | | |
|----------------------------|-------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =18242) n ^b (%) | Placebo (N ^a =18379) n ^b (%) | Total (N ^a =36621) n ^b (%) |
| >55 Years | 7768 (42.6) | 7830 (42.6) | 15598 (42.6) |
| ≥65 Years | 3980 (21.8) | 4038 (22.0) | 8018 (21.9) |
| Age at vaccination (years) | | | |
| Mean (SD) | 50.6 (15.70) | 50.4 (15.81) | 50.5 (15.76) |
| Median | 52.0 | 52.0 | 52.0 |
| Min, max | (12, 89) | (12, 91) | (12, 91) |

Note: HIV-positive subjects are included in this summary but not included in the analyses of the overall study objectives.
 a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.
 b. n = Number of subjects with the specified characteristic.
 PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (10:49) Source Data: adsl Table Generation: 17NOV2020 (18:29)
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Table 34. Summary of Signs and Symptoms for COVID-19 Occurrence From 7 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| | Vaccine Group (as Randomized) | | |
|-------------------------------------------------------|-----------------------------------------|----------------------------------|--------------------------------|
| | BNT162b2 (30 µg) (N ^a =8) | Placebo (N ^a =162) | Total (N ^a =170) |
| Signs and Symptoms | n ^b (%) | n ^b (%) | n ^b (%) |
| Subjects with specific signs and symptoms of COVID-19 | | | |
| Fever | 2 (25.0) | 76 (46.9) | 78 (45.9) |
| New or increased cough | 3 (37.5) | 114 (70.4) | 117 (68.8) |
| New or increased shortness of breath | 0 (0.0) | 25 (15.4) | 25 (14.7) |
| Chills | 2 (25.0) | 57 (35.2) | 59 (34.7) |
| New or increased muscle pain | 1 (12.5) | 81 (50.0) | 82 (48.2) |
| New loss of taste or smell | 5 (62.5) | 43 (26.5) | 48 (28.2) |
| Sore throat | 3 (37.5) | 68 (42.0) | 71 (41.8) |
| Diarrhea | 1 (12.5) | 18 (11.1) | 19 (11.2) |
| Vomiting | 2 (25.0) | 6 (3.7) | 8 (4.7) |
| Subjects with specific number of signs and symptoms | | | |
| 1 | 1 (12.5) | 24 (14.8) | 25 (14.7) |
| 2 | 3 (37.5) | 46 (28.4) | 49 (28.8) |
| 3 | 4 (50.0) | 34 (21.0) | 38 (22.4) |
| 4 | 0 (0.0) | 33 (20.4) | 33 (19.4) |
| 5 | 0 (0.0) | 16 (9.9) | 16 (9.4) |
| >5 | 0 (0.0) | 9 (5.6) | 9 (5.3) |

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Table 34. Summary of Signs and Symptoms for COVID-19 Occurrence From 7 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Signs and Symptoms | Vaccine Group (as Randomized) | | |
|--------------------|-----------------------------------------|----------------------------------|--------------------------------|
| | BNT162b2 (30 µg) (N ^a =8) | Placebo (N ^a =162) | Total (N ^a =170) |
| | n ^b (%) | n ^b (%) | n ^b (%) |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-COV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of subjects with COVID-19 occurrence from 7 days after dose 2 in the specified group. This value is used as the denominator for the percentage calculations.

b. n = Number of subjects with the specific criteria meeting the definition. A subject can have more than 1 symptom.

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Table 35. Summary of Signs and Symptoms for COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

| Signs and Symptoms | Vaccine Group (as Randomized) | | |
|-------------------------------------------------------|------------------------------------------|----------------------------------|--------------------------------|
| | BNT162b2 (30 µg) (N ^a =50) | Placebo (N ^a =275) | Total (N ^a =325) |
| | n ^b (%) | n ^b (%) | n ^b (%) |
| Subjects with specific signs and symptoms of COVID-19 | | | |
| Fever | 20 (40.0) | 122 (44.4) | 142 (43.7) |
| New or increased cough | 22 (44.0) | 186 (67.6) | 208 (64.0) |
| New or increased shortness of breath | 4 (8.0) | 44 (16.0) | 48 (14.8) |
| Chills | 10 (20.0) | 86 (31.3) | 96 (29.5) |
| New or increased muscle pain | 12 (24.0) | 121 (44.0) | 133 (40.9) |
| New loss of taste or smell | 24 (48.0) | 91 (33.1) | 115 (35.4) |
| Sore throat | 18 (36.0) | 111 (40.4) | 129 (39.7) |
| Diarrhea | 4 (8.0) | 35 (12.7) | 39 (12.0) |
| Vomiting | 5 (10.0) | 11 (4.0) | 16 (4.9) |
| Subjects with specific number of signs and symptoms | | | |
| 1 | 16 (32.0) | 44 (16.0) | 60 (18.5) |
| 2 | 14 (28.0) | 82 (29.8) | 96 (29.5) |
| 3 | 11 (22.0) | 63 (22.9) | 74 (22.8) |
| 4 | 5 (10.0) | 40 (14.5) | 45 (13.8) |
| 5 | 2 (4.0) | 31 (11.3) | 33 (10.2) |
| >5 | 2 (4.0) | 15 (5.5) | 17 (5.2) |

a. N = number of subjects with COVID-19 occurrence after dose 1 in the specified group. This value is used as the denominator for the percentage calculations.

b. n = Number of subjects with the specific criteria meeting the definition. A subject can have more than 1 symptom.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:54) Source Data: adc19ef Table Generation: 17NOV2020 (16:47)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adsympt_symp_cov_d1_aai

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Table 36. Summary of Signs and Symptoms for Severe COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

| Signs and Symptoms | Vaccine Group (as Randomized) | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------|--------------------------------|-------------------------------|
| | BNT162b2 (30 µg) (N ^a =1) | Placebo (N ^a =9) | Total (N ^a =10) |
| | n ^b (%) | n ^b (%) | n ^b (%) |
| Subjects with specific signs and symptoms of severe COVID-19 | | | |
| Clinical signs at rest indicative of severe systemic illness (RR ≥30 breaths per minute, HR ≥125 beats per minute, SpO ₂ ≤93% on room air at sea level, or PaO ₂ /FiO ₂ <300 mm Hg) | 1 (100.0) | 9 (100.0) | 10 (100.0) |
| Respiratory failure (defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation, or ECMO) | 0 (0.0) | 3 (33.3) | 3 (30.0) |
| Significant acute renal, hepatic, or neurologic dysfunction | 0 (0.0) | 1 (11.1) | 1 (10.0) |
| Admission to an ICU | 0 (0.0) | 3 (33.3) | 3 (30.0) |
| Subjects with specific number of signs and symptoms | | | |
| 1 | 1 (100.0) | 5 (55.6) | 6 (60.0) |
| 2 | 0 (0.0) | 2 (22.2) | 2 (20.0) |
| 3 | 0 (0.0) | 1 (11.1) | 1 (10.0) |
| 5 | 0 (0.0) | 1 (11.1) | 1 (10.0) |

Abbreviations: DBP = diastolic blood pressure; ECMO = extracorporeal membrane oxygenation; FiO₂ = fraction of inspired oxygen; HR = heart rate; ICU = intensive care unit; PaO₂ = partial pressure of oxygen, arterial; RR = respiratory rate; SBP = systolic blood pressure; SpO₂ = oxygen saturation as measured by pulse oximetry.

a. N = number of subjects with severe COVID-19 occurrence after dose 1 in the specified group. This value is used as the denominator for the percentage calculations.

b. n = Number of subjects with the specific criteria meeting the definition. A subject can have more than 1 symptom.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:54) Source Data: adc19ef Table Generation: 17NOV2020 (16:49)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adsympt_symp_sev_cov_d1_aai

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Table 37. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Dose 2 All-Available Efficacy Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) | Pr (VE >30% data) ^f |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =18650) | | Placebo (N ^a =18570) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 8 | 2.266 (17852) | 165 | 2.244 (17746) | 95.2 | (90.6, 97.7) | >0.9999 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102,1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 17NOV2020 (16:46)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adc19ef_ve_cov_7pd2_wo_aai

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Table 38. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Dose 2 All-Available Efficacy Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) | Pr (VE >30% data) ^f |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =20488) | | Placebo (N ^a =20459) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 9 | 2.389 (19049) | 172 | 2.370 (18971) | 94.8 | (90.2, 97.4) | >0.9999 |

Abbreviations: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Credible interval for VE was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 17NOV2020 (16:46)
 (Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adc19ef_ve_cov_7pd2_aai

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Table 39. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Requested Subgroup – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =18198) | | Placebo (N ^a =18325) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | | | | | | |
| Overall | 8 | 2.214 (17411) | 162 | 2.222 (17511) | 95.0 | (90.0, 97.9) |
| Age group (years) | | | | | | |
| 12 to 15 | 0 | 0.000 (14) | 0 | 0.000 (13) | NE | (NE, NE) |
| 16 to 17 | 0 | 0.002 (52) | 0 | 0.003 (55) | NE | (NE, NE) |
| 18 to 64 | 7 | 1.703 (13497) | 143 | 1.708 (13563) | 95.1 | (89.6, 98.1) |
| 65 to 74 | 1 | 0.406 (3074) | 14 | 0.406 (3095) | 92.9 | (53.1, 99.8) |
| ≥75 | 0 | 0.102 (774) | 5 | 0.106 (785) | 100.0 | (-13.1, 100.0) |
| Race | | | | | | |
| White | 7 | 1.889 (14504) | 146 | 1.903 (14670) | 95.2 | (89.8, 98.1) |
| Black or African American | 0 | 0.165 (1502) | 7 | 0.164 (1486) | 100.0 | (31.2, 100.0) |
| American Indian or Alaska native | 0 | 0.011 (100) | 1 | 0.010 (96) | 100.0 | (-3429.0, 100.0) |
| Asian | 1 | 0.092 (764) | 4 | 0.093 (769) | 74.6 | (-156.6, 99.5) |
| Native Hawaiian or other Pacific Islander | 0 | 0.006 (46) | 1 | 0.003 (29) | 100.0 | (-2266.9, 100.0) |
| Multiracial | 0 | 0.042 (414) | 1 | 0.036 (359) | 100.0 | (-3231.3, 100.0) |
| Not reported | 0 | 0.010 (81) | 2 | 0.012 (102) | 100.0 | (-563.3, 100.0) |

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Table 39. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Requested Subgroup – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =18198) | | Placebo (N ^a =18325) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:54) Source Data: adc19ef Table Generation: 23NOV2020 (16:38)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_EUA_FAEF_RR/adc19ef_ve_cov_7pd2_worq_sg_eval

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Table 40. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =19965) | | Placebo (N ^a =20172) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | | | | | | |
| Overall | 9 | 2.332 (18559) | 169 | 2.345 (18708) | 94.6 | (89.6, 97.6) |
| Age group (years) | | | | | | |
| 16 to 55 | 6 | 1.309 (10653) | 120 | 1.317 (10738) | 95.0 | (88.7, 98.2) |
| >55 | 3 | 1.022 (7892) | 49 | 1.028 (7956) | 93.8 | (80.9, 98.8) |
| ≥65 | 1 | 0.530 (4044) | 19 | 0.532 (4067) | 94.7 | (66.8, 99.9) |
| Sex | | | | | | |
| Male | 4 | 1.183 (9457) | 85 | 1.170 (9342) | 95.3 | (87.6, 98.8) |
| Female | 5 | 1.149 (9102) | 84 | 1.176 (9366) | 93.9 | (85.2, 98.1) |
| Race | | | | | | |
| White | 7 | 1.975 (15294) | 153 | 1.990 (15473) | 95.4 | (90.3, 98.2) |
| Black or African American | 0 | 0.187 (1758) | 7 | 0.188 (1758) | 100.0 | (30.4, 100.0) |
| All others ^f | 2 | 0.170 (1507) | 9 | 0.167 (1477) | 78.2 | (-5.4, 97.7) |
| Ethnicity | | | | | | |
| Hispanic/Latino | 3 | 0.637 (5074) | 55 | 0.638 (5090) | 94.5 | (83.2, 98.9) |
| Non-Hispanic/non-Latino | 6 | 1.681 (13380) | 114 | 1.693 (13509) | 94.7 | (88.1, 98.1) |
| Country | | | | | | |
| Argentina | 1 | 0.366 (2664) | 36 | 0.367 (2684) | 97.2 | (83.5, 99.9) |
| Brazil | 2 | 0.134 (1274) | 8 | 0.132 (1257) | 75.4 | (-23.5, 97.5) |
| USA | 6 | 1.816 (14141) | 124 | 1.830 (14287) | 95.1 | (89.1, 98.2) |
| South Africa | 0 | 0.015 (362) | 1 | 0.015 (363) | 100.0 | (-3818.9, 100.0) |

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Table 40. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|-----------------------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =19965) | | Placebo (N ^a =20172) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| Prior SARS-CoV-2 Status | | | | | | |
| Positive at baseline ^g | 1 | 0.056 (526) | 1 | 0.060 (567) | -7.1 | (-8309.9, 98.6) |
| Negative at baseline but positive prior to 7 days after Dose 2 ^h | 0 | 0.003 (27) | 1 | 0.004 (34) | 100.0 | (-6004.9, 100.0) |
| Negative prior to 7 days after Dose 2 ⁱ | 8 | 2.214 (17411) | 162 | 2.222 (17511) | 95.0 | (90.0, 97.9) |
| Unknown | 0 | 0.059 (595) | 5 | 0.060 (596) | 100.0 | (-9.6, 100.0) |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. All others = American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
- g. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
- h. Negative N-binding antibody result and negative NAAT result at Visit 1, positive NAAT result at Visit 2 or at unscheduled visit, if any, prior to 7 days after Dose 2.
- i. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1 and Visit 2, and negative NAAT result at unscheduled visit, if any, prior to 7 days after Dose 2.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:54) Source Data: adc19ef Table Generation: 18NOV2020 (15:55)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adc19ef_ve_cov_7pd2_sg_eval

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Table 41. Baseline Charlson Comorbidities – Phase 2/3 (All Subjects) – Safety Population

| Charlson Comorbidity Index Category | Vaccine Group (as Administered) | | Total (N ^a =43448) n ^b (%) |
|----------------------------------------|-------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =21720) n ^b (%) | Placebo (N ^a =21728) n ^b (%) | |
| Subjects with any Charlson comorbidity | 4559 (21.0) | 4419 (20.3) | 8978 (20.7) |
| AIDS/HIV | 99 (0.5) | 98 (0.5) | 197 (0.5) |
| Any Malignancy | 808 (3.7) | 753 (3.5) | 1561 (3.6) |
| Cerebrovascular Disease | 227 (1.0) | 194 (0.9) | 421 (1.0) |
| Chronic Pulmonary Disease | 1730 (8.0) | 1713 (7.9) | 3443 (7.9) |
| Congestive Heart Failure | 108 (0.5) | 97 (0.4) | 205 (0.5) |
| Dementia | 7 (0.0) | 11 (0.1) | 18 (0.0) |
| Diabetes With Chronic Complication | 112 (0.5) | 125 (0.6) | 237 (0.5) |
| Diabetes Without Chronic Complication | 1692 (7.8) | 1676 (7.7) | 3368 (7.8) |
| Hemiplegia or Paraplegia | 15 (0.1) | 22 (0.1) | 37 (0.1) |
| Leukemia | 14 (0.1) | 10 (0.0) | 24 (0.1) |
| Lymphoma | 25 (0.1) | 36 (0.2) | 61 (0.1) |
| Metastatic Solid Tumor | 4 (0.0) | 3 (0.0) | 7 (0.0) |
| Mild Liver Disease | 145 (0.7) | 112 (0.5) | 257 (0.6) |
| Moderate or Severe Liver Disease | 1 (0.0) | 2 (0.0) | 3 (0.0) |
| Myocardial Infarction | 220 (1.0) | 216 (1.0) | 436 (1.0) |
| Peptic Ulcer Disease | 62 (0.3) | 81 (0.4) | 143 (0.3) |
| Peripheral Vascular Disease | 144 (0.7) | 132 (0.6) | 276 (0.6) |
| Renal Disease | 139 (0.6) | 145 (0.7) | 284 (0.7) |
| Rheumatic Disease | 75 (0.3) | 65 (0.3) | 140 (0.3) |

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Table 41. Baseline Charlson Comorbidities – Phase 2/3 (All Subjects) – Safety Population

| Charlson Comorbidity Index Category | Vaccine Group (as Administered) | | Total (N ^a =43448) n ^b (%) |
|-------------------------------------|-------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =21720) n ^b (%) | Placebo (N ^a =21728) n ^b (%) | |

Note: MedDRA (v23.1) coding dictionary applied.

Note: HIV-positive subjects are included in this summary but not included in the analyses of the overall study objectives.

Note: Data for subjects randomized on or after 10OCT2020 are included to comprehensively show all data reported but are subject to change with additional follow-up.

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.

b. n = Number of subjects with the specified characteristic. Subjects with multiple occurrences within each category are counted only once. For 'Subjects with any Charlson comorbidity', n = number of subjects reporting at least 1 occurrence of any Charlson comorbidity.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (10:04) Source Data: admh Table Generation: 17NOV2020 (16:25)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_IA_P3_2MPD2/admh_s002_risk_all_p3_saf

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Table 42. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Comorbidity Status – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =18198) | | Placebo (N ^a =18325) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | | | | | | |
| Overall | 8 | 2.214 (17411) | 162 | 2.222 (17511) | 95.0 | (90.0, 97.9) |
| Comorbidity | | | | | | |
| No comorbidity | 4 | 1.189 (9381) | 76 | 1.197 (9482) | 94.7 | (85.9, 98.6) |
| Any comorbidity ^f | 4 | 1.025 (8030) | 86 | 1.025 (8029) | 95.3 | (87.7, 98.8) |
| Any malignancy | 1 | 0.092 (704) | 4 | 0.090 (681) | 75.7 | (-145.8, 99.5) |
| Cardiovascular | 0 | 0.067 (534) | 5 | 0.062 (492) | 100.0 | (-0.8, 100.0) |
| Chronic pulmonary disease | 1 | 0.175 (1374) | 14 | 0.171 (1358) | 93.0 | (54.1, 99.8) |
| Diabetes | 1 | 0.176 (1372) | 19 | 0.176 (1374) | 94.7 | (66.8, 99.9) |
| Obese (≥30.0 kg/m ²) | 3 | 0.763 (6000) | 67 | 0.782 (6103) | 95.4 | (86.0, 99.1) |
| Hypertension | 2 | 0.567 (4413) | 44 | 0.567 (4437) | 95.4 | (82.6, 99.5) |
| Diabetes (including gestational diabetes) | 1 | 0.177 (1381) | 20 | 0.178 (1384) | 95.0 | (68.7, 99.9) |

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Table 42. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Comorbidity Status – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =18198) | | Placebo (N ^a =18325) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. Subject who had 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥30 kg/m².

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:54) Source Data: adc19ef Table Generation: 29NOV2020 (21:33)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_EUA_FAEF_RR/adc19ef_ve_cov_7pd2_wo_cg_eval

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Table 43. Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC-Definition After Dose 1 – Dose 1 All-Available Efficacy Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | | |
|-----------------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =21669) | | Placebo (N ^a =21686) | | VE (%) | (95% CI ^e) |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First Severe COVID-19 occurrence based on CDC-definition after Dose 1 | 1 | 4.018 (21299) | 14 | 4.001 (21238) | 92.9 | (53.2, 99.8) |
| After Dose 1 to before Dose 2 | 1 | | 8 | | 87.5 | (6.8, 99.7) |
| Dose 2 to 7 days after Dose 2 | 0 | | 1 | | 100.0 | (-3800.0, 100.0) |
| ≥7 Days after Dose 2 | 0 | | 5 | | 100.0 | (-9.1, 100.0) |

Abbreviations: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method (adjusted for surveillance time for overall row).

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 03DEC2020 (22:53)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_VRBPA/adc19ef_ve_sev_cdc_pd1_aai

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Table 44. Vaccine Efficacy – First COVID-19 Occurrence Based on CDC-Defined Symptoms From 7 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =18198) | | Placebo (N ^a =18325) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence based on CDC-defined symptoms from 7 days after Dose 2 | 8 | 2.213 (17399) | 165 | 2.220 (17495) | 95.1 | (90.2, 97.9) |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 18NOV2020 (07:39)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adc19ef_ve_cov_7pd2_wo_cdc_eval

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Table 45. Vaccine Efficacy – First COVID-19 Occurrence Based on CDC-Defined Symptoms From 7 Days After Dose 2 – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =19965) | | Placebo (N ^a =20172) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence based on CDC-defined symptoms from 7 days after Dose 2 | 9 | 2.330 (18544) | 172 | 2.343 (18690) | 94.7 | (89.8, 97.6) |

Abbreviations: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 18NOV2020 (07:39)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001 Efficacy FA 164/adc19ef ve cov 7pd2 cdc eval

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Table 46. Vaccine Efficacy – First COVID-19 Occurrence Based on CDC-Defined Symptoms From 14 Days After Dose 2 – Subjects Without Evidence of Infection Prior to 14 Days After Dose 2 – Evaluable Efficacy (14 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|-----------------------------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =18175) | | Placebo (N ^a =18261) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence based on CDC-defined symptoms from 14 days after Dose 2 | 8 | 1.886 (16600) | 141 | 1.891 (16647) | 94.3 | (88.5, 97.6) |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 14 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 14 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 14 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 18NOV2020 (07:39)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adc19ef_ve_cov_14pd2_wo_cdc_eval

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Table 47. Vaccine Efficacy – First COVID-19 Occurrence Based on CDC-Defined Symptoms From 14 Days After Dose 2 – Subjects With or Without Evidence of Infection Prior to 14 Days After Dose 2 – Evaluable Efficacy (14 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|-----------------------------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =19965) | | Placebo (N ^a =20171) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence based on CDC-defined symptoms from 14 days after Dose 2 | 8 | 1.983 (17630) | 146 | 1.993 (17727) | 94.5 | (88.9, 97.7) |

Abbreviations: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 14 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 18NOV2020 (07:39)

(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001 Efficacy FA 164/adc19ef ve cov 14pd2 cdc eval

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Study C4591001 – Efficacy – Updated Analysis

Table 48. Efficacy Populations – Blinded Placebo-Controlled Follow-up Period

| | Vaccine Group (as Randomized) | | |
|------------------------------------------------------------------------------------------------------------|----------------------------------------|-------------------------------|-----------------------------|
| | BNT162b2 (30 µg) n ^a (%) | Placebo n ^a (%) | Total n ^a (%) |
| Randomized ^b | 23219 (100.0) | 23210 (100.0) | 46429 (100.0) |
| Dose 1 all-available efficacy population | 23140 (99.7) | 23137 (99.7) | 46277 (99.7) |
| Subjects without evidence of infection before Dose 1 | 22200 (95.6) | 22191 (95.6) | 44391 (95.6) |
| Subjects excluded from Dose 1 all-available efficacy population | 79 (0.3) | 73 (0.3) | 152 (0.3) |
| Reason for exclusion ^c | | | |
| Did not receive at least 1 vaccination | 58 (0.2) | 51 (0.2) | 109 (0.2) |
| Data considered potentially unreliable due to lack of PI oversight identified as significant quality event | 21 (0.1) | 22 (0.1) | 43 (0.1) |
| Dose 2 all-available efficacy population | 22771 (98.1) | 22741 (98.0) | 45512 (98.0) |
| Subjects without evidence of infection prior to 7 days after Dose 2 | 21544 (92.8) | 21470 (92.5) | 43014 (92.6) |
| Subjects excluded from Dose 2 all-available efficacy population | 448 (1.9) | 469 (2.0) | 917 (2.0) |
| Reason for exclusion ^c | | | |
| Did not receive 2 vaccinations | 384 (1.7) | 443 (1.9) | 827 (1.8) |
| Data considered potentially unreliable due to lack of PI oversight identified as significant quality event | 21 (0.1) | 22 (0.1) | 43 (0.1) |
| Unblinded prior to 7 days after Dose 2 | 45 (0.2) | 11 (0.0) | 56 (0.1) |
| Evaluable efficacy (7 days) population | 22255 (95.8) | 22410 (96.6) | 44665 (96.2) |
| Subjects without evidence of infection prior to 7 days after Dose 2 | 21069 (90.7) | 21175 (91.2) | 42244 (91.0) |
| Subjects excluded from evaluable efficacy (7 days) population | 964 (4.2) | 800 (3.4) | 1764 (3.8) |
| Reason for exclusion ^c | | | |
| Randomized but did not meet all eligibility criteria | 33 (0.1) | 30 (0.1) | 63 (0.1) |
| Data considered potentially unreliable due to lack of PI oversight identified as significant quality event | 21 (0.1) | 22 (0.1) | 43 (0.1) |

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Table 48. Efficacy Populations – Blinded Placebo-Controlled Follow-up Period

| | Vaccine Group (as Randomized) | | Total n ^a (%) |
|---------------------------------------------------------------------------------------------------------------------------------|----------------------------------------|-------------------------------|-----------------------------|
| | BNT162b2 (30 µg) n ^a (%) | Placebo n ^a (%) | |
| Did not receive all vaccinations as randomized or did not receive Dose 2 within the predefined window (19-42 days after Dose 1) | 732 (3.2) | 748 (3.2) | 1480 (3.2) |
| Unblinded prior to 7 days after Dose 2 | 45 (0.2) | 11 (0.0) | 56 (0.1) |
| Had other important protocol deviations on or prior to 7 days after Dose 2 | 240 (1.0) | 60 (0.3) | 300 (0.6) |

Note: HIV-positive subjects are included in this summary but not included in the analyses of the overall study objectives.

a. n = Number of subjects with the specified characteristic.
 b. These values are the denominators for the percentage calculations.
 c. Subjects may have been excluded for more than 1 reason.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (02:27)
 (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adsl_eff_pop

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Table 49. Subjects Excluded From Evaluable Efficacy Population Due to Important Protocol Deviations on or Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period

| | Vaccine Group (as Randomized) | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------|----------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =240) n ^b (%) | Placebo (N ^a =60) n ^b (%) |
| Concomitant Medications | 3 (1.3) | 7 (11.7) |
| Receipt of any other nonstudy coronavirus vaccine at any time prior to or during the study. | 0 (0.0) | 1 (1.7) |
| Subject received chronic systemic treatment with known immunosuppressant medication, or radiotherapy, within 60 days before enrollment through conclusion of the study. | 1 (0.4) | 1 (1.7) |
| Subject received systemic corticosteroids (>=20mg/day of prednisone or equivalent) for >=14 days is prohibited from 28 days prior to enrollment to specified visits/cohorts per protocol. | 2 (0.8) | 5 (8.3) |
| Inclusion/Exclusion | 16 (6.7) | 15 (25.0) |
| Participant failed to meet inclusion criterion #01 (Male or female participants between the ages of 18 and 55 years, inclusive, 65 and 85 years, inclusive, or 18 and 85 years, inclusive, at randomization (dependent upon study phase). | 1 (0.4) | 0 (0.0) |
| Participant failed to meet inclusion criterion #03 (Healthy participants who are determined by medical history, physical examination and clinical judgement of the investigator to be eligible for inclusion in the study) | 1 (0.4) | 5 (8.3) |
| Participant met exclusion criterion #01 (participant having other medical or psychiatric condition) | 0 (0.0) | 2 (3.3) |
| Participant met exclusion criterion #02 (participant having known infection with HIV, HCV or HBV) | 4 (1.7) | 3 (5.0) |
| Participant met exclusion criterion #11 (women who are pregnant or breastfeeding) | 4 (1.7) | 3 (5.0) |
| Participant met exclusion criterion #13 (participant receiving treatment with immunosuppressive therapy as specified in protocol) | 4 (1.7) | 1 (1.7) |
| Participant met exclusion criterion #16 (Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation) | 0 (0.0) | 1 (1.7) |
| Participant met exclusion criterion #22 (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) | 2 (0.8) | 0 (0.0) |
| Investigational Product | 203 (84.6) | 23 (38.3) |
| Dosing/administration error, subject did not receive correct dose of vaccine | 76 (31.7) | 3 (5.0) |
| IP administered that was deemed not suitable for use by Almac | 110 (45.8) | 0 (0.0) |

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Table 49. Subjects Excluded From Evaluable Efficacy Population Due to Important Protocol Deviations on or Prior to 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period

| | Vaccine Group (as Randomized) | |
|---------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------|---------------------------------|
| | BNT162b2 (30 µg) (N ^a =240) | Placebo (N ^a =60) |
| | n ^b (%) | n ^b (%) |
| Incorrect IP assigned to subject due to IRT not being utilized | 1 (0.4) | 0 (0.0) |
| Incorrect vaccine allocation/assigned to subject | 5 (2.1) | 5 (8.3) |
| Other IP deviation | 9 (3.8) | 11 (18.3) |
| Subject was vaccinated despite being ineligible | 1 (0.4) | 2 (3.3) |
| Subject was vaccinated despite meeting temporary delay criterion #4 (receiving short-term (| 2 (0.8) | 2 (3.3) |
| Laboratory | 2 (0.8) | 1 (1.7) |
| Nasal swab can't be analyzed due to incorrect shipping procedure | 2 (0.8) | 1 (1.7) |
| Other | 19 (7.9) | 15 (25.0) |
| Efficacy data considered potentially unreliable due to lack of PI oversight identified as significant quality event | 15 (6.3) | 13 (21.7) |
| Safety and efficacy data considered potentially unreliable due to lack of PI oversight identified as significant quality event. | 4 (1.7) | 2 (3.3) |

Note: HIV-positive subjects are included in this summary but not included in the analyses of the overall study objectives.

a. N = number of subjects excluded from evaluable efficacy population due to important protocol deviations in the specified group. This value is used as the denominator for the percentage calculations.

b. n = Number of subjects with the specific characteristic.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (15:56)
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Table 50. Demographic Characteristics – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| | Vaccine Group (as Randomized) | | |
|-------------------------------------------|-------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =21069) n ^b (%) | Placebo (N ^a =21175) n ^b (%) | Total (N ^a =42244) n ^b (%) |
| Sex | | | |
| Male | 10824 (51.4) | 10689 (50.5) | 21513 (50.9) |
| Female | 10245 (48.6) | 10486 (49.5) | 20731 (49.1) |
| Race | | | |
| White | 17458 (82.9) | 17604 (83.1) | 35062 (83.0) |
| Black or African American | 1799 (8.5) | 1812 (8.6) | 3611 (8.5) |
| American Indian or Alaska Native | 188 (0.9) | 182 (0.9) | 370 (0.9) |
| Asian | 959 (4.6) | 949 (4.5) | 1908 (4.5) |
| Native Hawaiian or other Pacific Islander | 55 (0.3) | 31 (0.1) | 86 (0.2) |
| Multiracial | 522 (2.5) | 489 (2.3) | 1011 (2.4) |
| Not reported | 88 (0.4) | 108 (0.5) | 196 (0.5) |
| All others ^c | 1812 (8.6) | 1759 (8.3) | 3571 (8.5) |
| Racial Designation | | | |
| Japanese | 78 (0.4) | 74 (0.3) | 152 (0.4) |
| Ethnicity | | | |
| Hispanic/Latino | 5241 (24.9) | 5217 (24.6) | 10458 (24.8) |
| Non-Hispanic/non-Latino | 15725 (74.6) | 15846 (74.8) | 31571 (74.7) |
| Not reported | 103 (0.5) | 112 (0.5) | 215 (0.5) |
| Country | | | |
| Argentina | 2624 (12.5) | 2617 (12.4) | 5241 (12.4) |
| Brazil | 1326 (6.3) | 1314 (6.2) | 2640 (6.2) |
| Germany | 238 (1.1) | 242 (1.1) | 480 (1.1) |
| South Africa | 307 (1.5) | 297 (1.4) | 604 (1.4) |
| Turkey | 231 (1.1) | 226 (1.1) | 457 (1.1) |

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Table 50. Demographic Characteristics – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| | Vaccine Group (as Randomized) | | |
|----------------------------|-------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =21069) n ^b (%) | Placebo (N ^a =21175) n ^b (%) | Total (N ^a =42244) n ^b (%) |
| USA | 16343 (77.6) | 16479 (77.8) | 32822 (77.7) |
| Age group (years) | | | |
| 12 to 15 | 1005 (4.8) | 978 (4.6) | 1983 (4.7) |
| 16 to 55 | 11753 (55.8) | 11824 (55.8) | 23577 (55.8) |
| >55 | 8311 (39.4) | 8373 (39.5) | 16684 (39.5) |
| ≥65 | 4245 (20.1) | 4296 (20.3) | 8541 (20.2) |
| 16 to 17 | 344 (1.6) | 334 (1.6) | 678 (1.6) |
| 16 to 25 | 1657 (7.9) | 1668 (7.9) | 3325 (7.9) |
| 16 to 64 | 15819 (75.1) | 15901 (75.1) | 31720 (75.1) |
| 18 to 64 | 15475 (73.4) | 15567 (73.5) | 31042 (73.5) |
| 55 to 64 | 4499 (21.4) | 4493 (21.2) | 8992 (21.3) |
| 65 to 74 | 3392 (16.1) | 3442 (16.3) | 6834 (16.2) |
| ≥75 | 853 (4.0) | 854 (4.0) | 1707 (4.0) |
| 75 to 85 | 848 (4.0) | 848 (4.0) | 1696 (4.0) |
| >85 | 5 (0.0) | 6 (0.0) | 11 (0.0) |
| Comorbidities ^d | | | |
| Yes | 9390 (44.6) | 9411 (44.4) | 18801 (44.5) |
| No | 11679 (55.4) | 11764 (55.6) | 23443 (55.5) |
| Age at vaccination (years) | | | |
| Mean (SD) | 48.3 (17.41) | 48.2 (17.41) | 48.3 (17.41) |
| Median | 50.0 | 50.0 | 50.0 |
| Min, max | (12, 89) | (12, 91) | (12, 91) |

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Table 50. Demographic Characteristics – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Vaccine Group (as Randomized) | | |
|-------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
| BNT162b2 (30 µg) (N ^a =21069) n ^b (%) | Placebo (N ^a =21175) n ^b (%) | Total (N ^a =42244) n ^b (%) |

Note: HIV-positive subjects are included in this summary but not included in the analyses of the overall study objectives.

- a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.
- b. n = Number of subjects with the specified characteristic.
- c. All others = American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
- d. Number of subjects who have 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥30 kg/m² (≥16 Years of age) or BMI ≥95th percentile (12-15 Years of age).

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 19APR2021 (17:13)

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Table 51. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Dose 2 All-Available Efficacy Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) | Pr (VE >30% data) ^f |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =21467) | | Placebo (N ^a =21387) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 78 | 6.380 (21177) | 866 | 6.094 (20999) | 91.4 | (89.1, 93.3) | >0.9999 |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102,1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 27MAR2021 (01:59)

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Table 52. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Dose 2 All-Available Efficacy Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI) ^e | Pr (VE >30% data) ^f |
|----------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|-----------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =22675) | | Placebo (N ^a =22645) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First COVID-19 occurrence from 7 days after Dose 2 | 82 | 6.649 (22132) | 889 | 6.371 (22001) | 91.2 | (88.9, 93.0) | >0.9999 |

Abbreviation: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 27MAR2021 (02:26)
 (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adc19ef_ve_cov_7pd2_aai

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Table 53. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^a) |
|----------------------------------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =22166) | | Placebo (N ^a =22320) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | | | | | | |
| Overall | 81 | 6.509 (21642) | 873 | 6.274 (21689) | 91.1 | (88.8, 93.0) |
| Age group (years) | | | | | | |
| 12 to 15 | 0 | 0.170 (1109) | 18 | 0.163 (1094) | 100.0 | (78.1, 100.0) |
| 16 to 55 | 56 | 3.766 (12088) | 584 | 3.619 (12142) | 90.8 | (87.9, 93.1) |
| >55 | 25 | 2.573 (8445) | 271 | 2.491 (8453) | 91.1 | (86.5, 94.3) |
| ≥65 | 7 | 1.267 (4315) | 128 | 1.232 (4326) | 94.7 | (88.7, 97.9) |
| 16 to 17 | 0 | 0.065 (365) | 11 | 0.061 (355) | 100.0 | (62.4, 100.0) |
| 16 to 25 | 10 | 0.511 (1734) | 84 | 0.498 (1740) | 88.4 | (77.6, 94.6) |
| 16 to 64 | 74 | 5.073 (16218) | 727 | 4.879 (16269) | 90.2 | (87.6, 92.4) |
| 18 to 64 | 74 | 5.008 (15853) | 716 | 4.817 (15914) | 90.1 | (87.4, 92.3) |
| 55 to 64 | 21 | 1.442 (4563) | 159 | 1.386 (4559) | 87.3 | (79.9, 92.4) |
| 65 to 74 | 6 | 1.021 (3450) | 102 | 0.992 (3468) | 94.3 | (87.1, 98.0) |
| ≥75 | 1 | 0.246 (865) | 26 | 0.240 (858) | 96.2 | (77.2, 99.9) |
| 75 to 85 | 1 | 0.244 (860) | 25 | 0.238 (852) | 96.1 | (76.2, 99.9) |
| >85 | 0 | 0.001 (5) | 1 | 0.001 (6) | 100.0 | (-4055.9, 100.0) |
| Sex | | | | | | |
| Male | 44 | 3.376 (11103) | 411 | 3.181 (10920) | 89.9 | (86.2, 92.8) |
| Female | 37 | 3.133 (10539) | 462 | 3.093 (10769) | 92.1 | (88.9, 94.5) |
| Race | | | | | | |

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Table 53. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^g) |
|-------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =22166) | | Placebo (N ^a =22320) | | | |
| | n ^{1b} | Surveillance Time ^c (n ^{2d}) | n ^{1b} | Surveillance Time ^c (n ^{2d}) | | |
| White | 69 | 5.379 (17801) | 768 | 5.191 (17880) | 91.3 | (88.9, 93.3) |
| Black or African American | 4 | 0.611 (1958) | 49 | 0.601 (1985) | 92.0 | (78.1, 97.9) |
| American Indian or Alaska Native | 0 | 0.044 (200) | 3 | 0.039 (182) | 100.0 | (-114.5, 100.0) |
| Asian | 3 | 0.268 (976) | 24 | 0.257 (967) | 88.0 | (60.5, 97.7) |
| Native Hawaiian or other Pacific Islander | 0 | 0.016 (57) | 1 | 0.008 (31) | 100.0 | (-1896.2, 100.0) |
| Multiracial | 5 | 0.164 (561) | 22 | 0.145 (532) | 79.9 | (45.7, 94.1) |
| Not reported | 0 | 0.028 (89) | 6 | 0.033 (112) | 100.0 | (-0.0, 100.0) |
| All others ^f | 8 | 0.519 (1883) | 56 | 0.481 (1824) | 86.8 | (72.1, 94.5) |
| Ethnicity | | | | | | |
| Hispanic/Latino | 32 | 1.862 (5408) | 245 | 1.794 (5391) | 87.4 | (81.8, 91.6) |
| Non-Hispanic/non-Latino | 48 | 4.615 (16128) | 628 | 4.445 (16186) | 92.6 | (90.1, 94.6) |
| Not reported | 1 | 0.033 (106) | 0 | 0.034 (112) | -∞ | (NA, NA) |
| Country | | | | | | |
| Argentina | 16 | 1.033 (2655) | 110 | 1.017 (2670) | 85.7 | (75.7, 92.1) |
| Brazil | 14 | 0.441 (1419) | 82 | 0.408 (1401) | 84.2 | (71.9, 91.7) |
| Germany | 0 | 0.047 (237) | 1 | 0.048 (243) | 100.0 | (-3868.6, 100.0) |
| South Africa | 0 | 0.099 (358) | 10 | 0.096 (358) | 100.0 | (56.6, 100.0) |
| Turkey | 0 | 0.029 (238) | 6 | 0.026 (232) | 100.0 | (22.2, 100.0) |
| USA | 51 | 4.861 (16735) | 664 | 4.678 (16785) | 92.6 | (90.2, 94.6) |
| Prior SARS-CoV-2 Status | | | | | | |
| Positive at baseline ^g | 3 | 0.190 (639) | 6 | 0.201 (689) | 46.9 | (-148.7, 91.4) |

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Table 53. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^g) |
|-----------------------------------------------------------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =22166) | | Placebo (N ^a =22320) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| Positive N-binding only | 2 | 0.147 (494) | 5 | 0.151 (516) | 58.9 | (-151.3, 96.1) |
| Positive NAAT only | 0 | 0.014 (50) | 1 | 0.015 (58) | 100.0 | (-3996.1, 100.0) |
| Positive NAAT and N-binding | 1 | 0.028 (95) | 0 | 0.035 (114) | -∞ | (NA, NA) |
| Negative at baseline but positive prior to 7 days after Dose 2 ^h | 0 | 0.011 (43) | 3 | 0.014 (60) | 100.0 | (-211.3, 100.0) |
| Negative prior to 7 days after Dose 2 ⁱ | 77 | 6.247 (20712) | 850 | 6.003 (20712) | 91.3 | (89.0, 93.2) |
| Unknown | 1 | 0.062 (248) | 14 | 0.055 (228) | 93.7 | (58.3, 99.9) |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. All others = American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
- g. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
- h. Negative N-binding antibody result and negative NAAT result at Visit 1, positive NAAT result at Visit 2 or at unscheduled visit, if any, prior to 7 days after Dose 2.
- i. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1 and Visit 2, and negative NAAT result at unscheduled visit, if any, prior to 7 days after Dose 2.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adc19ef Table Generation: 30MAR2021 (22:37)
 (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adc19ef_ve_cov_7pd2_sg_eval

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Table 54. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =23040) | | Placebo (N ^a =23037) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence after Dose 1 | | | | | | |
| Overall | 131 | 8.412 (22505) | 1034 | 8.124 (22434) | 87.8 | (85.3, 89.9) |
| Age group (years) | | | | | | |
| 12 to 15 | 3 | 0.257 (1120) | 35 | 0.250 (1119) | 91.6 | (73.5, 98.4) |
| 16 to 55 | 95 | 4.845 (12645) | 693 | 4.669 (12626) | 86.8 | (83.6, 89.5) |
| >55 | 33 | 3.310 (8740) | 306 | 3.204 (8689) | 89.6 | (85.0, 92.9) |
| ≥65 | 12 | 1.645 (4455) | 138 | 1.596 (4437) | 91.6 | (84.8, 95.7) |
| 16 to 17 | 3 | 0.094 (373) | 19 | 0.090 (370) | 84.8 | (48.4, 97.1) |
| 16 to 25 | 18 | 0.661 (1811) | 114 | 0.651 (1836) | 84.4 | (74.3, 91.1) |
| 16 to 64 | 116 | 6.511 (16930) | 861 | 6.278 (16878) | 87.0 | (84.2, 89.4) |
| 18 to 64 | 113 | 6.417 (16557) | 842 | 6.188 (16508) | 87.1 | (84.2, 89.5) |
| 55 to 64 | 25 | 1.840 (4738) | 185 | 1.772 (4697) | 87.0 | (80.2, 91.8) |
| 65 to 74 | 10 | 1.319 (3550) | 112 | 1.285 (3560) | 91.3 | (83.4, 95.9) |
| ≥75 | 2 | 0.326 (905) | 26 | 0.310 (877) | 92.7 | (70.7, 99.2) |
| 75 to 85 | 2 | 0.324 (899) | 25 | 0.309 (871) | 92.4 | (69.4, 99.1) |
| >85 | 0 | 0.002 (6) | 1 | 0.002 (6) | 100.0 | (-3408.8, 100.0) |
| Sex | | | | | | |
| Male | 70 | 4.355 (11560) | 500 | 4.115 (11312) | 86.8 | (83.0, 89.9) |
| Female | 61 | 4.057 (10945) | 534 | 4.009 (11122) | 88.7 | (85.3, 91.5) |
| Race | | | | | | |

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Table 54. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|-------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =23040) | | Placebo (N ^a =23037) | | | |
| | n ^{1b} | Surveillance Time ^c (n2 ^d) | n ^{1b} | Surveillance Time ^c (n2 ^d) | | |
| White | 115 | 6.957 (18538) | 916 | 6.719 (18479) | 87.9 | (85.3, 90.1) |
| Black or African American | 6 | 0.783 (2042) | 53 | 0.770 (2063) | 88.9 | (74.1, 96.1) |
| American Indian or Alaska Native | 1 | 0.061 (216) | 7 | 0.055 (209) | 86.9 | (-1.6, 99.7) |
| Asian | 4 | 0.348 (995) | 26 | 0.337 (990) | 85.1 | (57.0, 96.2) |
| Native Hawaiian or other Pacific Islander | 0 | 0.021 (58) | 1 | 0.011 (32) | 100.0 | (-2000.0, 100.0) |
| Multiracial | 5 | 0.208 (565) | 25 | 0.190 (546) | 81.8 | (51.6, 94.6) |
| Not reported | 0 | 0.035 (91) | 6 | 0.042 (115) | 100.0 | (-0.7, 100.0) |
| All others ^f | 10 | 0.672 (1925) | 65 | 0.635 (1892) | 85.5 | (71.5, 93.3) |
| Ethnicity | | | | | | |
| Hispanic/Latino | 52 | 2.351 (5701) | 302 | 2.282 (5673) | 83.3 | (77.5, 87.8) |
| Non-Hispanic/non-Latino | 78 | 6.018 (16692) | 730 | 5.799 (16647) | 89.7 | (87.0, 92.0) |
| Not reported | 1 | 0.043 (112) | 2 | 0.043 (114) | 49.4 | (-872.9, 99.1) |
| Country | | | | | | |
| Argentina | 32 | 1.282 (2846) | 146 | 1.269 (2840) | 78.3 | (68.0, 85.7) |
| Brazil | 14 | 0.554 (1430) | 95 | 0.520 (1420) | 86.1 | (75.6, 92.7) |
| Germany | 2 | 0.067 (246) | 1 | 0.069 (250) | -104.5 | (-11965.9, 89.4) |
| South Africa | 0 | 0.128 (367) | 11 | 0.125 (365) | 100.0 | (61.1, 100.0) |
| Turkey | 3 | 0.048 (246) | 12 | 0.045 (244) | 76.4 | (12.4, 95.7) |
| USA | 80 | 6.333 (17370) | 769 | 6.095 (17315) | 90.0 | (87.4, 92.1) |
| Baseline SARS-CoV-2 status | | | | | | |
| Positive ^g | 13 | 0.250 (692) | 17 | 0.265 (736) | 19.2 | (-76.6, 63.9) |
| Positive N-binding only | 2 | 0.192 (521) | 7 | 0.198 (542) | 70.5 | (-54.7, 97.0) |
| Positive NAAT only | 10 | 0.020 (66) | 9 | 0.020 (69) | -10.5 | (-207.3, 59.7) |

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Table 54. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|-----------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =23040) | | Placebo (N ^a =23037) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| Positive NAAT and N-binding | 1 | 0.038 (105) | 1 | 0.046 (124) | -20.5 | (-9359.2, 98.5) |
| Negative ^h | 116 | 8.101 (21615) | 1015 | 7.804 (21521) | 89.0 | (86.6, 91.0) |
| Unknown | 2 | 0.061 (198) | 2 | 0.055 (177) | 9.7 | (-1145.4, 93.5) |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from Dose 1 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. All others = American Indian or Alaska native, Asian, Native Hawaiian or other Pacific Islander, multiracial, and not reported race categories.
- g. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
- h. Negative N-binding antibody result at Visit 1, negative NAAT result at Visit 1, and no medical history of COVID-19.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adc19ef Table Generation: 30MAR2021 (22:32)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adc19ef_ve_cov_pd1_sg_aai

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Table 55. Baseline Charlson Comorbidities - Phase 2/3 Subjects \geq 16 Years of Age - Safety Population

| Charlson Comorbidity Index Category | Vaccine Group (as Administered) | | Total (N ^a =44047) n ^b (%) |
|----------------------------------------|-------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =22026) n ^b (%) | Placebo (N ^a =22021) n ^b (%) | |
| Subjects with any Charlson comorbidity | 4628 (21.0) | 4511 (20.5) | 9139 (20.7) |
| AIDS/HIV | 100 (0.5) | 100 (0.5) | 200 (0.5) |
| Any malignancy | 812 (3.7) | 757 (3.4) | 1569 (3.6) |
| Cerebrovascular disease | 227 (1.0) | 198 (0.9) | 425 (1.0) |
| Chronic pulmonary disease | 1783 (8.1) | 1775 (8.1) | 3558 (8.1) |
| Congestive heart failure | 109 (0.5) | 102 (0.5) | 211 (0.5) |
| Dementia | 7 (0.0) | 11 (0.0) | 18 (0.0) |
| Diabetes with chronic complication | 116 (0.5) | 130 (0.6) | 246 (0.6) |
| Diabetes without chronic complication | 1700 (7.7) | 1699 (7.7) | 3399 (7.7) |
| Hemiplegia or paraplegia | 15 (0.1) | 25 (0.1) | 40 (0.1) |
| Leukemia | 14 (0.1) | 11 (0.0) | 25 (0.1) |
| Lymphoma | 26 (0.1) | 36 (0.2) | 62 (0.1) |
| Metastatic solid tumor | 4 (0.0) | 3 (0.0) | 7 (0.0) |
| Mild liver disease | 152 (0.7) | 115 (0.5) | 267 (0.6) |
| Moderate or severe liver disease | 2 (0.0) | 3 (0.0) | 5 (0.0) |
| Myocardial infarction | 225 (1.0) | 218 (1.0) | 443 (1.0) |
| Peptic ulcer disease | 63 (0.3) | 84 (0.4) | 147 (0.3) |
| Peripheral vascular disease | 144 (0.7) | 139 (0.6) | 283 (0.6) |
| Renal disease | 140 (0.6) | 153 (0.7) | 293 (0.7) |
| Rheumatic disease | 75 (0.3) | 71 (0.3) | 146 (0.3) |

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Table 55. Baseline Charlson Comorbidities - Phase 2/3 Subjects ≥16 Years of Age - Safety Population

| Charlson Comorbidity Index Category | Vaccine Group (as Administered) | | |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|----------------------------------------------------------|--------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =22026) n ^b (%) | Placebo (N ^a =22021) n ^b (%) | Total (N ^a =44047) n ^b (%) |
| Abbreviation: AIDS = acquired immunodeficiency syndrome. Note: MedDRA (v23.1) coding dictionary applied. Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately. a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations. b. n = Number of subjects with the specified characteristic. Subjects with multiple occurrences within each category are counted only once. For "Subjects with any Charlson comorbidity," n = number of subjects reporting at least 1 occurrence of any Charlson comorbidity. PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:25) Source Data: admh Table Generation: 27MAR2021 (01:28) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/admh_s002_risk_all_p3_saf | | | |

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Table 56. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Comorbidity Status – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|-----------------------------------------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =20998) | | Placebo (N ^a =21096) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First COVID-19 occurrence from 7 days after Dose 2 | | | | | | |
| Overall | 77 | 6.247 (20712) | 850 | 6.003 (20713) | 91.3 | (89.0, 93.2) |
| Comorbidity | | | | | | |
| No comorbidity | 42 | 3.450 (11545) | 449 | 3.322 (11577) | 91.0 | (87.6, 93.6) |
| Any comorbidity ^f | 35 | 2.797 (9167) | 401 | 2.681 (9136) | 91.6 | (88.2, 94.3) |
| Any malignancy | 3 | 0.228 (770) | 27 | 0.214 (748) | 89.6 | (66.2, 98.0) |
| Cardiovascular | 3 | 0.172 (584) | 23 | 0.159 (555) | 88.0 | (60.2, 97.7) |
| Chronic pulmonary disease | 8 | 0.490 (1684) | 69 | 0.460 (1671) | 89.1 | (77.3, 95.5) |
| Diabetes | 9 | 0.465 (1529) | 61 | 0.444 (1517) | 85.9 | (71.4, 93.8) |
| Obese (≥30.0 kg/m ² [≥16 Years of age]) | 27 | 2.083 (6673) | 311 | 2.034 (6770) | 91.5 | (87.4, 94.5) |
| Obese (≥95 th percentile [12-15 Years of age]) | 0 | 0.019 (123) | 3 | 0.016 (105) | 100.0 | (-104.8, 100.0) |
| Hypertension | 15 | 1.481 (4900) | 191 | 1.427 (4896) | 92.4 | (87.2, 95.8) |
| Diabetes (including gestational diabetes) | 9 | 0.468 (1538) | 63 | 0.447 (1531) | 86.3 | (72.4, 94.0) |

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Table 56. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Comorbidity Status – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint Subgroup | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|----------------------------|------------------------------------------|---------------------------------------------------|---------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =20998) | | Placebo (N ^a =21096) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2; VE = vaccine efficacy.
 Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of subjects in the specified group.
 b. n1 = Number of subjects meeting the endpoint definition.
 c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
 d. n2 = Number of subjects at risk for the endpoint.
 e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
 f. Subject who had 1 or more comorbidities that increase the risk of severe COVID-19 disease: defined as subjects who had at least one of the Charlson comorbidity index category or BMI ≥30 kg/m² (≥16 Years of age) or BMI ≥95th percentile (12-15 Years of age).

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adc19ef Table Generation: 30MAR2021 (22:39)
 (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adc19ef_ve_cov_7pd2_wo_cg_eval

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Table 57. Vaccine Efficacy – First Severe COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI) ^e | Pr (VE >30% data) ^f |
|-----------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|-----------------------|----------------------------------|
| | BNT162b2 (30 µg) (N ^a =22166) | | Placebo (N ^a =22320) | | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | | |
| First severe COVID-19 occurrence from 7 days after Dose 2 | 1 | 6.522 (21649) | 21 | 6.404 (21730) | 95.3 | (70.9, 99.9) | >0.9999 |

Abbreviation: VE = vaccine efficacy.

- a. N = number of subjects in the specified group.
- b. n1 = Number of subjects meeting the endpoint definition.
- c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.
- d. n2 = Number of subjects at risk for the endpoint.
- e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.
- f. Posterior probability (Pr) was calculated using a beta-binomial model with prior beta (0.700102, 1) adjusted for surveillance time. Refer to the statistical analysis plan, Appendix 2, for more details.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:19) Source Data: adc19ef Table Generation: 27MAR2021 (02:26)
 (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adc19ef_ve_sev_cov_7pd2_eval

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Table 58. Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC-Definition From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects With or Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Efficacy Endpoint | Vaccine Group (as Randomized) | | | | VE (%) | (95% CI ^e) |
|-----------------------------------------------------------------------------------|---------------------------------------------|---------------------------------------------------|------------------------------------|---------------------------------------------------|--------|------------------------|
| | BNT162b2 (30 µg) (N ^a =22166) | | Placebo (N ^a =22320) | | | |
| | n1 ^b | Surveillance Time ^c (n2 ^d) | n1 ^b | Surveillance Time ^c (n2 ^d) | | |
| First severe COVID-19 occurrence based on CDC-definition from 7 days after Dose 2 | 0 | 6.514 (21620) | 32 | 6.391 (21693) | 100.0 | (88.0, 100.0) |

Abbreviation: VE = vaccine efficacy.

a. N = number of subjects in the specified group.

b. n1 = Number of subjects meeting the endpoint definition.

c. Total surveillance time in 1000 person-years for the given endpoint across all subjects within each group at risk for the endpoint. Time period for COVID-19 case accrual is from 7 days after Dose 2 to the end of the surveillance period.

d. n2 = Number of subjects at risk for the endpoint.

e. Confidence interval (CI) for VE is derived based on the Clopper and Pearson method adjusted for surveillance time.

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(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adc19ef_ve_sev_7pd2_cdc_eval

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Table 59. Summary of Signs and Symptoms for First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| Signs and Symptoms | Vaccine Group (as Randomized) | | |
|-------------------------------------------------------|----------------------------------------------------------------|--------------------------------------------------------|------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =77) n ^b (%) | Placebo (N ^a =850) n ^b (%) | Total (N ^a =927) n ^b (%) |
| Subjects with specific signs and symptoms of COVID-19 | | | |
| Fever | 14 (18.2) | 319 (37.5) | 333 (35.9) |
| New or increased cough | 36 (46.8) | 556 (65.4) | 592 (63.9) |
| New or increased shortness of breath | 8 (10.4) | 121 (14.2) | 129 (13.9) |
| Chills | 15 (19.5) | 262 (30.8) | 277 (29.9) |
| New or increased muscle pain | 24 (31.2) | 395 (46.5) | 419 (45.2) |
| New loss of taste or smell | 37 (48.1) | 297 (34.9) | 334 (36.0) |
| Sore throat | 29 (37.7) | 329 (38.7) | 358 (38.6) |
| Diarrhea | 11 (14.3) | 136 (16.0) | 147 (15.9) |
| Vomiting | 3 (3.9) | 32 (3.8) | 35 (3.8) |
| Subjects with specific number of signs and symptoms | | | |
| 1 | 28 (36.4) | 178 (20.9) | 206 (22.2) |
| 2 | 22 (28.6) | 233 (27.4) | 255 (27.5) |
| 3 | 15 (19.5) | 177 (20.8) | 192 (20.7) |
| 4 | 6 (7.8) | 132 (15.5) | 138 (14.9) |
| 5 | 2 (2.6) | 70 (8.2) | 72 (7.8) |
| >5 | 4 (5.2) | 60 (7.1) | 64 (6.9) |

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Table 59. Summary of Signs and Symptoms for First COVID-19 Occurrence From 7 Days After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Subjects Without Evidence of Infection Prior to 7 Days After Dose 2 – Evaluable Efficacy (7 Days) Population

| | Vaccine Group (as Randomized) | | |
|--------------------|------------------------------------------|----------------------------------|--------------------------------|
| | BNT162b2 (30 µg) (N ^a =77) | Placebo (N ^a =850) | Total (N ^a =927) |
| Signs and Symptoms | n ^b (%) | n ^b (%) | n ^b (%) |

Abbreviations: N-binding = SARS-CoV-2 nucleoprotein-binding; NAAT = nucleic acid amplification test; SARS-COV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Subjects who had no serological or virological evidence (prior to 7 days after receipt of the last dose) of past SARS-CoV-2 infection (ie, N-binding antibody [serum] negative at Visit 1 and SARS-CoV-2 not detected by NAAT [nasal swab] at Visits 1 and 2), and had negative NAAT (nasal swab) at any unscheduled visit prior to 7 days after Dose 2 were included in the analysis.

a. N = number of subjects with first COVID-19 occurrence from 7 days after dose 2 in the specified group. This value is used as the denominator for the percentage calculations.

b. n = Number of subjects with the specific criteria meeting the definition. A subject can have more than 1 symptom.

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Table 60. Summary of Signs and Symptoms for First COVID-19 Occurrence After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

| Signs and Symptoms | Vaccine Group (as Randomized) | | |
|-------------------------------------------------------|-----------------------------------------------------------------|---------------------------------------------------------|-------------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =131) n ^b (%) | Placebo (N ^a =1034) n ^b (%) | Total (N ^a =1165) n ^b (%) |
| Subjects with specific signs and symptoms of COVID-19 | | | |
| Fever | 33 (25.2) | 393 (38.0) | 426 (36.6) |
| New or increased cough | 61 (46.6) | 668 (64.6) | 729 (62.6) |
| New or increased shortness of breath | 15 (11.5) | 150 (14.5) | 165 (14.2) |
| Chills | 25 (19.1) | 311 (30.1) | 336 (28.8) |
| New or increased muscle pain | 42 (32.1) | 468 (45.3) | 510 (43.8) |
| New loss of taste or smell | 58 (44.3) | 370 (35.8) | 428 (36.7) |
| Sore throat | 50 (38.2) | 403 (39.0) | 453 (38.9) |
| Diarrhea | 16 (12.2) | 157 (15.2) | 173 (14.8) |
| Vomiting | 7 (5.3) | 38 (3.7) | 45 (3.9) |
| Subjects with specific number of signs and symptoms | | | |
| 1 | 47 (35.9) | 215 (20.8) | 262 (22.5) |
| 2 | 36 (27.5) | 288 (27.9) | 324 (27.8) |
| 3 | 23 (17.6) | 221 (21.4) | 244 (20.9) |
| 4 | 14 (10.7) | 149 (14.4) | 163 (14.0) |
| 5 | 5 (3.8) | 93 (9.0) | 98 (8.4) |
| >5 | 6 (4.6) | 68 (6.6) | 74 (6.4) |

a. N = number of subjects with first COVID-19 occurrence after dose 1 in the specified group. This value is used as the denominator for the percentage calculations.

b. n = Number of subjects with the specific criteria meeting the definition. A subject can have more than 1 symptom.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adc19ef Table Generation: 27MAR2021 (02:27)

(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adsympt symp cov d1 aai

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Table 61. Summary of Signs and Symptoms for First Severe COVID-19 Occurrence After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

| Signs and Symptoms | Vaccine Group (as Randomized) | | |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------|-------------------------------------------------------|-----------------------------------------------------|
| | BNT162b2 (30 µg) (N ^a =1) n ^b (%) | Placebo (N ^a =30) n ^b (%) | Total (N ^a =31) n ^b (%) |
| Subjects with specific signs and symptoms of severe COVID-19 | | | |
| Clinical signs at rest indicative of severe systemic illness (RR ≥30 breaths per minute, HR ≥125 beats per minute, SpO ₂ ≤93% on room air at sea level, or PaO ₂ /FiO ₂ <300 mm Hg) | 1 (100.0) | 19 (63.3) | 20 (64.5) |
| Respiratory failure (defined as needing high-flow oxygen, noninvasive ventilation, mechanical ventilation, or ECMO) | 0 (0.0) | 14 (46.7) | 14 (45.2) |
| Evidence of shock (SBP <90 mm Hg, DBP <60 mm Hg, or requiring vasopressors) | 0 (0.0) | 3 (10.0) | 3 (9.7) |
| Significant acute renal, hepatic, or neurologic dysfunction | 0 (0.0) | 2 (6.7) | 2 (6.5) |
| Admission to an ICU | 0 (0.0) | 8 (26.7) | 8 (25.8) |
| Subjects with specific number of signs and symptoms | | | |
| 1 | 1 (100.0) | 20 (66.7) | 21 (67.7) |
| 2 | 0 (0.0) | 4 (13.3) | 4 (12.9) |
| 3 | 0 (0.0) | 5 (16.7) | 5 (16.1) |
| 5 | 0 (0.0) | 1 (3.3) | 1 (3.2) |

Abbreviations: DBP = diastolic blood pressure; ECMO = extracorporeal membrane oxygenation; FiO₂ = fraction of inspired oxygen; HR = heart rate; ICU = intensive care unit; PaO₂ = partial pressure of oxygen, arterial; RR = respiratory rate; SBP = systolic blood pressure; SpO₂ = oxygen saturation as measured by pulse oximetry.

a. N = number of subjects with first severe COVID-19 occurrence after dose 1 in the specified group. This value is used as the denominator for the percentage calculations.

b. n = Number of subjects with the specific criteria meeting the definition. A subject can have more than 1 symptom.

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Study C4591001 – Phase 1 Immunogenicity

Table 62. Summary of Geometric Mean Titers/Concentrations – Phase 1, 2 Doses, 21 Days Apart – BNT162b2 (30 µg)/Placebo – Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Vaccine Group (as Randomized) | | | | | | | |
|------------------------------------------------|------------------------------------------------|-------------------------------|------------------------------------------------|----------------|------------------------------------------------|--------------------|------------------------------------------------|---------|-----------------------|
| | | 18-55 Years of Age | | | | 65-85 Years of Age | | | |
| | | BNT162b2 (30 µg) | | Placebo | | BNT162b2 (30 µg) | | Placebo | |
| n ^b | GMT/GMC ^c (95% CI ^c) | n ^b | GMT/GMC ^c (95% CI ^c) | n ^b | GMT/GMC ^c (95% CI ^c) | n ^b | GMT/GMC ^c (95% CI ^c) | | |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 1/Prevax | 12 | 10.0 (10.0, 10.0) | 2 | 10.0 (10.0, 10.0) | 11 | 10.0 (10.0, 10.0) | 3 | 10.0 (10.0, 10.0) |
| | 1/Day 21 | 12 | 29.1 (14.2, 59.6) | 2 | 10.0 (10.0, 10.0) | 11 | 16.8 (10.9, 25.8) | 3 | 10.0 (10.0, 10.0) |
| | 2/1 Month | 11 | 179.2 (102.3, 313.8) | 2 | 10.0 (10.0, 10.0) | 11 | 151.6 (58.6, 392.1) | 2 | 10.0 (10.0, 10.0) |
| | 2/6 Months | 10 | 54.7 (24.7, 121.1) | 0 | NE (NE, NE) | 11 | 29.0 (19.4, 43.5) | 0 | NE (NE, NE) |
| S1-binding IgG level assay (U/mL) | 1/Prevax | 12 | 0.6 (0.6, 0.6) | 2 | 0.6 (0.6, 0.6) | 11 | 0.6 (0.6, 0.6) | 3 | 0.9 (0.2, 4.9) |
| | 1/Day 21 | 12 | 565.5 (372.5, 858.5) | 2 | 0.6 (0.6, 0.6) | 11 | 352.2 (160.1, 775.2) | 3 | 1.0 (0.1, 6.9) |
| | 2/1 Month | 11 | 5925.6 (4457.2, 7877.7) | 2 | 0.6 (0.6, 0.6) | 11 | 4835.4 (2756.1, 8483.3) | 2 | 1.4 (0.0, 47501.5) |
| | 2/6 Months | 10 | 960.8 (483.8, 1908.1) | 0 | NE (NE, NE) | 11 | 559.6 (363.0, 862.8) | 0 | NE (NE, NE) |

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Table 62. Summary of Geometric Mean Titers/Concentrations – Phase 1, 2 Doses, 21 Days Apart – BNT162b2 (30 µg)/Placebo – Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Vaccine Group (as Randomized) | | | | | | | |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|-------------------------------|------------------------------------------------|----------------|------------------------------------------------|--------------------|------------------------------------------------|---------|--|
| | | 18-55 Years of Age | | | | 65-85 Years of Age | | | |
| | | BNT162b2 (30 µg) | | Placebo | | BNT162b2 (30 µg) | | Placebo | |
| n ^b | GMT/GMC ^c (95% CI ^c) | n ^b | GMT/GMC ^c (95% CI ^c) | n ^b | GMT/GMC ^c (95% CI ^c) | n ^b | GMT/GMC ^c (95% CI ^c) | | |
| <p>Abbreviations: GMC = geometric mean concentration; GMT = geometric mean titer; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; NE = not estimable; NT50 = 50% neutralizing titer; S1 = spike protein S1 subunit; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.</p> <p>Note: The Dose 1 evaluable population was used for time points after Dose 1 and before Dose 2 and the Dose 2 evaluable population was used for time points after Dose 2.</p> <p>Note: Blood samples from the Day 7 and Day 14 post-Dose 2 visits are not included since these samples were not retested with the 6-month post-Dose 2 samples.</p> <p>a. Protocol-specified timing for blood sample collection.</p> <p>b. n = Number of subjects with valid and determinate assay results for the specified assay at the given dose/sampling time point.</p> <p>c. GMTs, GMCs, and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers or concentrations and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.</p> <p>PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:25) Source Data: adva Table Generation: 27MAR2021 (04:57) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adva_s001_gm_b2_eval_p1</p> | | | | | | | | | |

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Table 63. Summary of Geometric Mean Fold Rises From Before Vaccination to Each Subsequent Time Point – Phase 1, 2 Doses, 21 Days Apart – BNT162b2 (30 µg)/Placebo – Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Vaccine Group (as Randomized) | | | | | | | |
|------------------------------------------------|----------------------------------------------|-------------------------------|-----------------------------------------------------------------|----------------|--------------------------------------------------------|--------------------|-----------------------------------------------------------------|----------------|--------------------------------------------------------|
| | | 18-55 Years of Age | | | | 65-85 Years of Age | | | |
| | | n ^b | BNT162b2 (30 µg) GMFR ^c (95% CI ^c) | n ^b | Placebo GMFR ^c (95% CI ^c) | n ^b | BNT162b2 (30 µg) GMFR ^c (95% CI ^c) | n ^b | Placebo GMFR ^c (95% CI ^c) |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 1/Day 21 | 12 | 2.9 (1.4, 6.0) | 2 | 1.0 (1.0, 1.0) | 11 | 1.7 (1.1, 2.6) | 3 | 1.0 (1.0, 1.0) |
| | 2/1 Month | 11 | 17.9 (10.2, 31.4) | 2 | 1.0 (1.0, 1.0) | 11 | 15.2 (5.9, 39.2) | 2 | 1.0 (1.0, 1.0) |
| | 2/6 Months | 10 | 5.5 (2.5, 12.1) | 0 | NE (NE, NE) | 11 | 2.9 (1.9, 4.3) | 0 | NE (NE, NE) |
| S1-binding IgG level assay (U/mL) | 1/Day 21 | 12 | 893.0 (588.2, 1355.7) | 2 | 1.0 (1.0, 1.0) | 11 | 556.3 (252.7, 1224.2) | 3 | 1.1 (0.8, 1.4) |
| | 2/1 Month | 11 | 9357.4 (7038.6, 12440.1) | 2 | 1.0 (1.0, 1.0) | 11 | 7635.8 (4352.3, 13396.5) | 2 | 1.3 (0.1, 26.9) |
| | 2/6 Months | 10 | 1517.2 (764.0, 3013.2) | 0 | NE (NE, NE) | 11 | 883.7 (573.2, 1362.5) | 0 | NE (NE, NE) |

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Table 63. Summary of Geometric Mean Fold Rises From Before Vaccination to Each Subsequent Time Point – Phase 1, 2 Doses, 21 Days Apart – BNT162b2 (30 µg)/Placebo – Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Vaccine Group (as Randomized) | | | | | | | |
|----------------|----------------------------------------------|-------------------------------|---------------------------------------------|----------------|---------------------------------------------|--------------------|---------------------------------------------|---------|--|
| | | 18-55 Years of Age | | | | 65-85 Years of Age | | | |
| | | BNT162b2 (30 µg) | | Placebo | | BNT162b2 (30 µg) | | Placebo | |
| n ^b | GMFR ^c (95% CI ^c) | n ^b | GMFR ^c (95% CI ^c) | n ^b | GMFR ^c (95% CI ^c) | n ^b | GMFR ^c (95% CI ^c) | | |

Abbreviations: GMFR = geometric mean fold rise; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; NE = not estimable;

NT50 = 50% neutralizing titer; S1 = spike protein S1 subunit; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: The Dose 1 evaluable population was used for time points after Dose 1 and before Dose 2 and the Dose 2 evaluable population was used for time points after Dose 2.

Note: Blood samples from the Day 7 and Day 14 post-Dose 2 visits are not included since these samples were not retested with the 6-month post-Dose 2 samples.

a. Protocol-specified timing for blood sample collection.

b. n = Number of subjects with valid and determinate assay results for the specified assay both before vaccination and at the given dose/sampling time point.

c. GMFRs and the corresponding 2-sided 95% CIs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

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Table 64. Number (%) of Subjects Achieving a ≥ 4 -Fold Rise From Before Vaccination to Each Subsequent Time Point - Phase 1, 2 Doses, 21 Days Apart - BNT162b2 (30 μ g)/Placebo - Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Vaccine Group (as Randomized) | | | | | | | |
|------------------------------------------------|----------------------------------------------|-------------------------------|----------------------------------------------|----------------|----------------------------------------------|-----------------------|----------------------------------------------|---------|------------------------|
| | | 18-55 Years of Age | | | | 65-85 Years of Age | | | |
| | | BNT162b2 (30 μ g) | | Placebo | | BNT162b2 (30 μ g) | | Placebo | |
| N ^b | n ^c (%) (95% CI ^d) | N ^b | n ^c (%) (95% CI ^d) | N ^b | n ^c (%) (95% CI ^d) | N ^b | n ^c (%) (95% CI ^d) | | |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 1/Day 21 | 12 | 6 (50.0) (21.1, 78.9) | 2 | 0 (0.0) (0.0, 84.2) | 11 | 1 (9.1) (0.2, 41.3) | 3 | 0 (0.0) (0.0, 70.8) |
| | 2/1 Month | 11 | 11 (100.0) (71.5, 100.0) | 2 | 0 (0.0) (0.0, 84.2) | 11 | 9 (81.8) (48.2, 97.7) | 2 | 0 (0.0) (0.0, 84.2) |
| | 2/6 Months | 10 | 6 (60.0) (26.2, 87.8) | 0 | 0 (NE) (NE, NE) | 11 | 3 (27.3) (6.0, 61.0) | 0 | 0 (NE) (NE, NE) |
| S1-binding IgG level assay (U/mL) | 1/Day 21 | 12 | 12 (100.0) (73.5, 100.0) | 2 | 0 (0.0) (0.0, 84.2) | 11 | 11 (100.0) (71.5, 100.0) | 3 | 0 (0.0) (0.0, 70.8) |
| | 2/1 Month | 11 | 11 (100.0) (71.5, 100.0) | 2 | 0 (0.0) (0.0, 84.2) | 11 | 11 (100.0) (71.5, 100.0) | 2 | 0 (0.0) (0.0, 84.2) |
| | 2/6 Months | 10 | 10 (100.0) (69.2, 100.0) | 0 | 0 (NE) (NE, NE) | 11 | 11 (100.0) (71.5, 100.0) | 0 | 0 (NE) (NE, NE) |

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Table 64. Number (%) of Subjects Achieving a ≥ 4 -Fold Rise From Before Vaccination to Each Subsequent Time Point - Phase 1, 2 Doses, 21 Days Apart - BNT162b2 (30 μ g)/Placebo - Evaluable Immunogenicity Population

| | | Vaccine Group (as Randomized) | | | | | | | |
|-------|----------------------------------------------|-------------------------------|----------------------------------------------|----------------|----------------------------------------------|-----------------------|----------------------------------------------|----------------|----------------------------------------------|
| | | 18-55 Years of Age | | | | 65-85 Years of Age | | | |
| | | BNT162b2 (30 μ g) | | Placebo | | BNT162b2 (30 μ g) | | Placebo | |
| Assay | Dose/ Sampling Time Point ^a | N ^b | n ^c (%) (95% CI ^d) | N ^b | n ^c (%) (95% CI ^d) | N ^b | n ^c (%) (95% CI ^d) | N ^b | n ^c (%) (95% CI ^d) |

Abbreviations: IgG = immunoglobulin G; LLOQ = lower limit of quantitation; NE = not estimable; NT50 = 50% neutralizing titer; S1 = spike protein S1 subunit; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Assay results below the LLOQ were set to $0.5 \times$ LLOQ in the analysis.

Note: The Dose 1 evaluable population was used for time points after Dose 1 and before Dose 2 and the Dose 2 evaluable population was used for time points after Dose 2.

Note: Blood samples from the Day 7 and Day 14 post-Dose 2 visits are not included since these samples were not retested with the 6-month post-Dose 2 samples.

a. Protocol-specified timing for blood sample collection.

b. N = number of subjects with valid and determinate assay results for the specified assay both before vaccination and at the given dose/sampling time point. These values are the denominators for the percentage calculations.

c. n = Number of subjects with ≥ 4 -fold rise from before vaccination for the given assay at the given dose/sampling time point.

d. Exact 2-sided CI based on the Clopper and Pearson method.

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Study C4591001 – Phase 2 Immunogenicity

Table 65. Immunogenicity Populations – Phase 2

| | Vaccine Group (as Randomized) | | | | |
|----------------------------------------------------------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------|
| | BNT162b2 (30 µg) | | | Placebo | Total n ^a (%) |
| | 18-55 Years n ^a (%) | 56-85 Years n ^a (%) | 18-85 Years n ^a (%) | 18-85 Years n ^a (%) | |
| Randomized ^b | 88 (100.0) | 92 (100.0) | 180 (100.0) | 180 (100.0) | 360 (100.0) |
| Dose 2 all-available immunogenicity population | 85 (96.6) | 91 (98.9) | 176 (97.8) | 176 (97.8) | 352 (97.8) |
| Subjects excluded from Dose 2 all-available immunogenicity population | 3 (3.4) | 1 (1.1) | 4 (2.2) | 4 (2.2) | 8 (2.2) |
| Reason for exclusion | | | | | |
| Did not receive Dose 2 | 1 (1.1) | 0 | 1 (0.6) | 0 | 1 (0.3) |
| Did not have at least 1 valid and determinate immunogenicity result after Dose 2 | 2 (2.3) | 1 (1.1) | 3 (1.7) | 4 (2.2) | 7 (1.9) |
| Dose 2 evaluable immunogenicity population | 80 (90.9) | 89 (96.7) | 169 (93.9) | 167 (92.8) | 336 (93.3) |
| Subjects excluded from Dose 2 evaluable immunogenicity population | 8 (9.1) | 3 (3.3) | 11 (6.1) | 13 (7.2) | 24 (6.7) |
| Reason for exclusion ^c | | | | | |
| Did not receive 2 doses of the vaccine to which they are randomly assigned | 1 (1.1) | 0 | 1 (0.6) | 0 | 1 (0.3) |
| Did not receive Dose 2 within 19-42 days after Dose 1 | 0 | 1 (1.1) | 1 (0.6) | 4 (2.2) | 5 (1.4) |
| Did not have at least 1 valid and determinate immunogenicity result after Dose 2 | 2 (2.3) | 1 (1.1) | 3 (1.7) | 4 (2.2) | 7 (1.9) |
| Did not have blood collection within 28-42 days after Dose 2 | 5 (5.7) | 2 (2.2) | 7 (3.9) | 7 (3.9) | 14 (3.9) |
| Had important protocol deviation(s) as determined by the clinician | 0 | 0 | 0 | 1 (0.6) | 1 (0.3) |

a. n = Number of subjects with the specified characteristic, or the total sample.

b. These values are the denominators for the percentage calculations.

c. Subjects may have been excluded for more than 1 reason.

PFIZER CONFIDENTIAL SDTM Creation: 02NOV2020 (19:23) Source Data: adsl Table Generation: 12NOV2020 (02:19)

(Cutoff Date: 12OCT2020, Snapshot Date: 02NOV2020) Output File: ./nda2_unblinded/C4591001_IA_P2_Serology/adva_s008_imm_pop_p2

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| | Vaccine Group (as Randomized) | | | | |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------|-----------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------------|------------------------------------------------------|
| | BNT162b2 (30 µg) | | | Placebo | Total (N ^a =336) n ^b (%) |
| | 18-55 Years (N ^a =80) n ^b (%) | 56-85 Years (N ^a =89) n ^b (%) | 18-85 Years (N ^a =169) n ^b (%) | 18-85 Years (N ^a =167) n ^b (%) | |
| Sex | | | | | |
| Male | 41 (51.3) | 49 (55.1) | 90 (53.3) | 85 (50.9) | 175 (52.1) |
| Female | 39 (48.8) | 40 (44.9) | 79 (46.7) | 82 (49.1) | 161 (47.9) |
| Race | | | | | |
| White | 64 (80.0) | 83 (93.3) | 147 (87.0) | 138 (82.6) | 285 (84.8) |
| Black or African American | 9 (11.3) | 3 (3.4) | 12 (7.1) | 22 (13.2) | 34 (10.1) |
| American Indian or Alaska native | 0 | 1 (1.1) | 1 (0.6) | 1 (0.6) | 2 (0.6) |
| Asian | 5 (6.3) | 0 | 5 (3.0) | 4 (2.4) | 9 (2.7) |
| Multiracial | 1 (1.3) | 1 (1.1) | 2 (1.2) | 1 (0.6) | 3 (0.9) |
| Not reported | 1 (1.3) | 1 (1.1) | 2 (1.2) | 1 (0.6) | 3 (0.9) |
| Ethnicity | | | | | |
| Hispanic/Latino | 13 (16.3) | 3 (3.4) | 16 (9.5) | 20 (12.0) | 36 (10.7) |
| Non-Hispanic/non-Latino | 66 (82.5) | 85 (95.5) | 151 (89.3) | 145 (86.8) | 296 (88.1) |
| Not reported | 1 (1.3) | 1 (1.1) | 2 (1.2) | 2 (1.2) | 4 (1.2) |
| Age at vaccination (years) | | | | | |
| Mean (SD) | 41.0 (10.47) | 65.9 (6.64) | 54.1 (15.18) | 51.6 (15.92) | 52.8 (15.58) |
| Median | 43.5 | 65.0 | 56.0 | 56.0 | 56.0 |
| Min, max | (18, 55) | (56, 85) | (18, 85) | (20, 83) | (18, 85) |
| <p>a. N = number of subjects in the specified group, or the total sample. This value is the denominator for the percentage calculations.</p> <p>b. n = Number of subjects with the specified characteristic.</p> <p>PFIZER CONFIDENTIAL SDTM Creation: 02NOV2020 (19:23) Source Data: adsl Table Generation: 12NOV2020 (00:12) (Cutoff Date: 12OCT2020, Snapshot Date: 02NOV2020) Output File: ./nda2_unblinded/C4591001_IA_P2_Serology/adsl_s005_demo_p2_d2_eval</p> | | | | | |

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Table 67. Summary of Geometric Mean Titers/Concentrations – Phase 2 – Dose 2 Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Vaccine Group (as Randomized) | | | | | | | |
|------------------------------------------------|----------------------------------------------|-------------------------------|---------------------------------------------------------------|----------------|---------------------------------------------------------------|----------------|---------------------------------------------------------------|----------------|---------------------------------------------------------------|
| | | BNT162b2 (30 µg) | | | | | | Placebo | |
| | | n ^b | 18-55 Years GMT/GMC ^c (95% CI ^c) | n ^b | 56-85 Years GMT/GMC ^c (95% CI ^c) | n ^b | 18-85 Years GMT/GMC ^c (95% CI ^c) | n ^b | 18-85 Years GMT/GMC ^c (95% CI ^c) |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 1/Prevax | 80 | 10.1 (9.9, 10.4) | 88 | 10.3 (9.9, 10.7) | 168 | 10.2 (10.0, 10.5) | 167 | 10.4 (10.0, 10.9) |
| | 2/1 Month | 80 | 399.4 (342.1, 466.2) | 87 | 255.0 (205.7, 316.0) | 167 | 316.1 (275.6, 362.6) | 167 | 10.6 (10.0, 11.3) |
| S1-binding IgG level assay (U/mL) | 1/Prevax | 80 | 0.8 (0.6, 0.9) | 88 | 0.8 (0.7, 1.1) | 168 | 0.8 (0.7, 0.9) | 167 | 0.8 (0.7, 0.9) |
| | 2/1 Month | 80 | 7122.8 (6217.4, 8160.2) | 87 | 3960.7 (3007.2, 5216.6) | 167 | 5246.5 (4460.3, 6171.4) | 167 | 1.0 (0.8, 1.2) |

Abbreviations: GMC = geometric mean concentration; GMT = geometric mean titer; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; NT50 = 50% neutralizing titer; S1 = spike protein S1 subunit; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

- a. Protocol-specified timing for blood sample collection.
- b. n = Number of subjects with valid and determinate assay results for the specified assay at the given dose/sampling time point.
- c. GMTs, GMCs, and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers or concentrations and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

PFIZER CONFIDENTIAL SDTM Creation: 02NOV2020 (19:23) Source Data: adva Table Generation: 12NOV2020 (00:12)

(Cutoff Date: 12OCT2020, Snapshot Date: 02NOV2020) Output File: ./nda2_unblinded/C4591001_IA_P2_Serology/adva_s001_gm_p2_eval

Table 68. Summary of Geometric Mean Fold Rises From Before Vaccination to Each Subsequent Time Point – Phase 2 – Dose 2 Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Vaccine Group (as Randomized) | | | | | | | |
|------------------------------------------------|----------------------------------------------|-------------------------------|------------------------------------------------------------|----------------|------------------------------------------------------------|----------------|------------------------------------------------------------|----------------|------------------------------------------------------------|
| | | BNT162b2 (30 µg) | | | | | | Placebo | |
| | | n ^b | 18-55 Years GMFR ^c (95% CI ^c) | n ^b | 56-85 Years GMFR ^c (95% CI ^c) | n ^b | 18-85 Years GMFR ^c (95% CI ^c) | n ^b | 18-85 Years GMFR ^c (95% CI ^c) |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 2/1 Month | 80 | 39.4 (34.0, 45.6) | 86 | 24.9 (20.2, 30.9) | 166 | 31.1 (27.2, 35.5) | 167 | 1.0 (1.0, 1.1) |
| S1-binding IgG level assay (U/mL) | 2/1 Month | 80 | 9167.2 (7452.8, 11276.0) | 86 | 4975.5 (3655.9, 6771.4) | 166 | 6679.4 (5511.6, 8094.7) | 167 | 1.2 (1.0, 1.4) |

Abbreviations: GMFR = geometric mean fold rise; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; NT50 = 50% neutralizing titer; S1 = spike protein S1 subunit; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

a. Protocol-specified timing for blood sample collection.

b. n = Number of subjects with valid and determinate assay results for the specified assay at both prevaccination and the given dose/sampling time point.

c. GMFRs and the corresponding 2-sided 95% CIs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

PFIZER CONFIDENTIAL SDTM Creation: 02NOV2020 (19:23) Source Data: adva Table Generation: 12NOV2020 (00:12)

(Cutoff Date: 12OCT2020, Snapshot Date: 02NOV2020) Output File: ./nda2_unblinded/C4591001_IA_P2_Serology/adva_s001_gmfr_p2_eval

**Table 69. Summary of Geometric Mean Titers/Concentrations by Baseline SARS-CoV-2 Status – Phase 2 – Dose 2
Evaluable Immunogenicity Population**

| Assay | Dose/ Sampling Time Point ^a | Baseline SARS-CoV-2 Status ^b | Vaccine Group (as Randomized) | | | | | | | |
|---------------------------------------------------|----------------------------------------------|-----------------------------------------------|-------------------------------|---------------------------------------------------------------|----------------|---------------------------------------------------------------|----------------|---------------------------------------------------------------|----------------|---------------------------------------------------------------|
| | | | BNT162b2 (30 µg) | | | | | | Placebo | |
| | | | n ^c | 18-55 Years GMT/GMC ^d (95% CI ^d) | n ^c | 56-85 Years GMT/GMC ^d (95% CI ^d) | n ^c | 18-85 Years GMT/GMC ^d (95% CI ^d) | n ^c | 18-85 Years GMT/GMC ^d (95% CI ^d) |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 1/Prevax | POS | 1 | 31.0 (NE, NE) | 4 | 18.1 (5.6, 58.2) | 5 | 20.2 (8.7, 46.9) | 4 | 38.4 (5.2, 282.5) |
| | | NEG | 79 | 10.0 (10.0, 10.0) | 83 | 10.0 (10.0, 10.0) | 162 | 10.0 (10.0, 10.0) | 162 | 10.1 (9.9, 10.2) |
| | 2/1 Month | POS | 1 | 4233.0 (NE, NE) | 2 | 3469.9 (0.1, 9.247E7) | 3 | 3707.6 (495.5, 27743.3) | 4 | 53.2 (5.5, 515.3) |
| | | NEG | 79 | 387.6 (335.4, 448.0) | 84 | 237.7 (194.4, 290.7) | 163 | 301.3 (264.7, 342.9) | 162 | 10.2 (9.8, 10.7) |
| S1-binding IgG level assay (U/mL) | 1/Prevax | POS | 1 | 246.1 (NE, NE) | 4 | 36.9 (0.5, 2848.7) | 5 | 53.9 (2.4, 1222.0) | 4 | 153.0 (12.7, 1844.4) |
| | | NEG | 79 | 0.7 (0.6, 0.8) | 83 | 0.7 (0.6, 0.8) | 162 | 0.7 (0.7, 0.8) | 162 | 0.7 (0.7, 0.8) |
| | 2/1 Month | POS | 1 | 45474.1 (NE, NE) | 2 | 23255.3 (106.2, 5.092E6) | 3 | 29080.6 (6983.3, 121100.2) | 4 | 144.4 (9.5, 2189.7) |
| | | NEG | 79 | 6957.6 (6113.5, 7918.3) | 84 | 3759.2 (2847.3, 4963.2) | 163 | 5066.1 (4308.9, 5956.5) | 162 | 0.8 (0.7, 1.0) |

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**Table 69. Summary of Geometric Mean Titers/Concentrations by Baseline SARS-CoV-2 Status – Phase 2 – Dose 2
Evaluable Immunogenicity Population**

| Assay | Dose/ Sampling Time Point ^a | Baseline SARS-CoV-2 Status ^b | Vaccine Group (as Randomized) | | | | | | | |
|-------|----------------------------------------------|-----------------------------------------------|-------------------------------|---------------------------------------------------------------|----------------|---------------------------------------------------------------|----------------|---------------------------------------------------------------|----------------|---------------------------------------------------------------|
| | | | BNT162b2 (30 µg) | | | | | | Placebo | |
| | | | n ^c | 18-55 Years GMT/GMC ^d (95% CI ^d) | n ^c | 56-85 Years GMT/GMC ^d (95% CI ^d) | n ^c | 18-85 Years GMT/GMC ^d (95% CI ^d) | n ^c | 18-85 Years GMT/GMC ^d (95% CI ^d) |

Abbreviations: GMC = geometric mean concentration; GMT = geometric mean titer; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; NAAT = nucleic acid amplification test; NE = not estimable; NEG = negative; NT50 = 50% neutralizing titer; POS = positive;

S1 = spike protein S1 subunit; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Subjects whose baseline SARS-CoV-2 status cannot be determined due to missing N-binding antibody or NAAT at Visit 1 were not included in the analysis.

- a. Protocol-specified timing for blood sample collection.
- b. Positive = Positive N-binding antibody at Visit 1, or positive NAAT at Visit 1, or had medical history of COVID-19. Negative = Negative N-binding antibody at Visit 1 and negative NAAT at Visit 1.
- c. n = Number of subjects with valid and determinate assay results for the specified assay at the given dose/sampling time point.
- d. GMTs, GMCs, and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of the titers or concentration and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ.

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(Cutoff Date: 12OCT2020, Snapshot Date: 02NOV2020) Output File: ./nda2_unblinded/C4591001_IA_P2_Serology/adva_s001_gm_lt_p2_eval

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Table 70. Summary of Geometric Mean Fold Rises From Before Vaccination to Each Subsequent Time Point by Baseline SARS-CoV-2 Status – Phase 2 – Dose 2 Evaluable Immunogenicity Population

| Assay | Dose/ Sampling Time Point ^a | Baseline SARS-CoV-2 Status ^b | Vaccine Group (as Randomized) | | | | | | | |
|---------------------------------------------------|----------------------------------------------|-----------------------------------------------|---------------------------------------------|-----------------------------|---------------------------------------------|----------------------------|---------------------------------------------|----------------------------|-------------|-------------------|
| | | | BNT162b2 (30 µg) | | | | | | Placebo | |
| | | | 18-55 Years | | 56-85 Years | | 18-85 Years | | 18-85 Years | |
| n ^c | GMFR ^d (95% CI ^d) | n ^c | GMFR ^d (95% CI ^d) | n ^c | GMFR ^d (95% CI ^d) | n ^c | GMFR ^d (95% CI ^d) | | | |
| SARS-CoV-2 neutralization assay - NT50 (titer) | 2/1 Month | POS | 1 | 136.5 (NE, NE) | 2 | 163.6 (0.0, 6.156E10) | 3 | 154.0 (3.2, 7377.7) | 4 | 1.4 (0.9, 2.0) |
| | | NEG | 79 | 38.8 (33.5, 44.8) | 83 | 23.6 (19.3, 29.0) | 162 | 30.1 (26.4, 34.3) | 162 | 1.0 (1.0, 1.1) |
| S1-binding IgG level assay (U/mL) | 2/1 Month | POS | 1 | 184.7 (NE, NE) | 2 | 191.8 (0.0, 1.993E6) | 3 | 189.4 (31.0, 1156.2) | 4 | 0.9 (0.6, 1.5) |
| | | NEG | 79 | 9631.6 (8008.6, 11583.6) | 83 | 5312.3 (3946.8, 7150.4) | 162 | 7100.7 (5925.1, 8509.7) | 162 | 1.2 (1.0, 1.4) |

Abbreviations: GMFR = geometric mean fold rise; IgG = immunoglobulin G; LLOQ = lower limit of quantitation; NAAT = nucleic acid amplification test; NE = not estimable; NEG = negative; NT50 = 50% neutralizing titer; POS = positive; S1 = spike protein S1 subunit; SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.

Note: Subjects whose baseline SARS-CoV-2 status cannot be determined due to missing N-binding antibody or NAAT at Visit 1 were not included in the analysis.

- a. Protocol-specified timing for blood sample collection.
- b. Positive = Positive N-binding antibody at Visit 1, or positive NAAT at Visit 1, or had medical history of COVID-19. Negative = Negative N-binding antibody at Visit 1 and negative NAAT at Visit 1.
- c. n = Number of subjects with valid and determinate assay results for the specified assay at both prevaccination and the given dose/sampling time point.
- d. GMFRs and 2-sided 95% CIs were calculated by exponentiating the mean logarithm of fold rises and the corresponding CIs (based on the Student t distribution). Assay results below the LLOQ were set to 0.5 × LLOQ in the analysis.

PFIZER CONFIDENTIAL SDTM Creation: 02NOV2020 (19:23) Source Data: adva Table Generation: 12NOV2020 (00:12)

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