2.5 CLINICAL OVERVIEW

TABLE OF CONTENTS

LIST OF IN-TEXT TABLES

LIST OF IN-TEXT FIGURES

ABBREVIATIONS

Abbreviation	Definition
ACE-2	angiotensin-converting enzyme 2
ADR	adverse reaction
AE	adverse event
AESI	adverse event of special interest
BMI	body mass index
C4591001 Efficacy Final Analysis Interim CSR	Study C4591001 interim clinical study report including prespecified final analysis of efficacy and available immunogenicity and safety data up to data cutoff date of 14 November 2020
C4591001 6-Month Update Interim CSR	Study C4591001 interim clinical study report including updated efficacy, immunogenicity, and safety up to 6 months after Dose 2 up to data cutoff date of 13 March 2021
CBER	(US FDA) Center for Biologics Evaluation and Research
CDC	(US) Centers for Disease Control and Prevention
CDS	Core Data Sheet
CFR	case fatality rate
CHMP	Committee for Human Products for Medicinal Use
CMC	chemistry, manufacturing, and controls
CoV	Coronavirus
COVID-19	Coronavirus Disease 2019
CTA	Clinical Trial Application
DART	developmental and reproductive toxicity
DMC	(US Study C4591001) Data Monitoring Committee
ELISPOT	enzyme-linked immuno-spot
EMA	European Medicines Agency
EU	European Union
EUA	Emergency Use Application
FACS	fluorescence-activated cell sorting
FDA	(US) Food and Drug Administration
FIH	first-in-human
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GMFR	geometric mean-fold rise
GMT/GMC	geometric mean titer/concentration
HIV	human immunodeficiency virus
ICH	International Council on Harmonisation
ICU	intensive care unit
ID	intradermal(ly)
IFNγ	interferon-gamma
IL-2	interleukin-2
IL-4	interleukin-4
IM	intramuscular(ly)
IND	Investigational New Drug application
iPSP	initial Pediatric Study Plan
IRC	(US Study C4591001) Internal Review Committee

Abbreviation	Definition
IRR	illness rate ratio
LLN	lower limit of normal
LNP	lipid nanoparticle
LPX	lipoplex
MedDRA	Medical Dictionary for Regulatory Activities
MERS	Middle East respiratory syndrome
modRNA	nucleoside-modified messenger RNA
mRNA	messenger RNA
NAAT	nucleic acid amplification testing
NHP	non-human primate
NI	Non-inferiority
P2 S	SARS-CoV-2 full-length, P2 mutant, “heads up,” prefusion spike glycoprotein
PDCO	Paediatric Committee
PCR	polymerase chain reaction
PIP	Paediatric Investigational Plan
PSP	Pediatric Study Plan
PT	Preferred Term
RBD	receptor binding domain
RNA-LNP	RNA lipid nanoparticle
saRNA	self-amplifying messenger RNA
SRC	(German Study BNT162-01) Safety Review Committee
ssRNA	single-stranded RNA
SAE	serious adverse event
SARS	severe acute respiratory syndrome
SARS-CoV-2	SARS Coronavirus-2; virus causing the disease COVID-19
S glycoprotein, S	spike glycoprotein
SmPC	Summary of Product Characteristics
SMQ	Standard MedDRA query
SOC	System Organ Class
Th1/Th2	helper T cell type 1/type 2
UK	United Kingdom
uRNA	non-modified uridine containing mRNA
US	United States
USP	United States Pharmacopeia
VAE(R)D	vaccine-associated enhanced (respiratory) disease
VE	vaccine efficacy
WHO	World Health Organization

2.5. CLINICAL OVERVIEW

This Clinical Overview (CO) describes the clinical data for a prophylactic, RNA-based SARS-CoV-2 vaccine developed by BioNTech and Pfizer. Evidence is presented in this CO for the efficacy, immunogenicity, and safety and tolerability of the vaccine compared with placebo administered to healthy participants ≥12 years of age.

The pivotal data are derived from a single registrational study, Phase 1/2/3 Study C4591001, conducted under a United States (US) Investigational New Drug (IND) Application. Supporting data are presented from the first-in-human (FIH) dose-finding study, Phase 1/2 Study BNT162-01, conducted in Germany under a Clinical Trial Application (CTA). The clinical experience reflected in this CO represents approximately 44,000 study participants ≥16 years of age, including individuals with stable infections and common comorbidities that represent real-world population characteristics.

The proposed indication and dosing administration for BNT162b2 (30 μg) are:

- **Proposed indication**: Active immunization to prevent COVID-19 disease caused by SARS-CoV-2 virus, in individuals ≥16 years of age

- **Dosing administration**: single 0.3-mL intramuscular (IM) dose followed by a second 0.3-mL dose 3 weeks later

Efficacy analyses are event-driven in Study C4591001 Phase 2/3 participants ≥12 years of age. Prespecified analyses were conducted on 94 confirmed COVID-19 cases (interim analysis data cutoff date: 04 November 2020) and 170 confirmed cases (final analysis data cutoff date: 14 November 2020) reported in participants without evidence of past SARS-CoV-2 infection before or during the vaccination regimen. Updated analyses of 1165 confirmed cases in blinded placebo-controlled follow-up from Dose 1 to a data cutoff date of 13 March 2021 evaluated duration of protection.

Immunogenicity analyses of adults (18 to 85 years of age) in Study C4591001 include data up to 1 month after Dose 2 in Phase 2, and up to 6 months after Dose 2 in Phase 1.

Safety data are collected cumulatively in Study C4591001. Some participants ≥16 years of age have been unblinded to treatment assignment, therefore safety data are presented separately for blinded placebo-controlled and open-label periods. Key safety data in the CO include:

- **Blinded placebo-controlled period**: Dose 1 to 1 month after Dose 2 and to unblinding date:
  - Phase 1 participants randomized to BNT162b2 30 μg (to ~6 months after Dose 2)
  - Phase 2/3 participants ≥16 years of age including HIV+ subset (to ~5 months after Dose 2)

- **Open-label observational period**: from unblinding data to data cutoff date:
  - Phase 2/3 participants ≥16 years of age originally randomized to BNT162b2
  - Phase 2/3 participants ≥16 years of age originally randomized to placebo who then received BNT162b2 after being unblinded

- **Cumulative follow-up from Dose 1 to 6 months after Dose 2**: Phase 2/3 participants originally randomized to BNT162b2 (inclusive of blinded data and open-label data), comprised of at least 3000 in each adult age group (16 to 55 years of age, >55 years of age)

Supportive analyses from Study BNT162-01 are presented for immunogenicity data including T cell responses, and safety data including reactogenicity and adverse events (AEs), for adult participants in the Phase 1 portion of the study.

2.5.1. Product Development Rationale

2.5.1.1. Therapeutic Context

2.5.1.1.1. Disease or Condition

COVID-19 is caused by SARS-CoV-2, a zoonotic virus that first emerged as a human pathogen in China and has rapidly spread around the world by human to human transmission.

In December 2019, a pneumonia outbreak of unknown cause occurred in Wuhan, China. In January 2020, it became clear that a novel Coronavirus (2019-nCoV) was the underlying cause. In early January 2020, the genetic sequence of the 2019-nCoV became available to the World Health Organization (WHO) and public (MN908947.3), and the virus was categorized in the Betacoronavirus subfamily. By sequence analysis, the phylogenetic tree revealed a closer relationship to severe acute respiratory syndrome (SARS) virus isolates than to other coronaviruses that infect humans, including the Middle East respiratory syndrome (MERS) coronavirus.[1,2]

SARS-CoV-2 infections and the resulting disease COVID-19 have spread globally, and on 11 March 2020 the WHO characterized the COVID-19 outbreak as a pandemic. As of April 2021, there have been >145 million globally confirmed COVID-19 cases and >3 million deaths, with 192 countries/regions affected; among these, the US leads with the highest number of reported cases at >31 million confirmed cases and >570,000 deaths.[3]

At the time of this submission, the ongoing pandemic remains a significant challenge to public health and economic stability worldwide, for which for a licensed prophylactic vaccine is a necessary and critical mitigation.

2.5.1.1.2. Clinical Features and Epidemiology of COVID-19

COVID-19 presentation is generally with cough and fever, with chest radiography showing ground-glass opacities or patchy shadowing.[4] However, many patients present without fever or radiographic changes, and infections may be asymptomatic which is relevant to controlling transmission. For symptomatic patients, disease progression may lead to acute respiratory distress syndrome requiring ventilation, subsequent multi-organ failure, and death.[4]

Common symptoms in hospitalized patients (in order of highest to lowest frequency) include fever, dry cough, shortness of breath, fatigue, myalgias, nausea/vomiting or diarrhea, headache, weakness, and rhinorrhea.[4] Anosmia (loss of smell) or ageusia (loss of taste) may be the sole presenting symptom in approximately 3% of individuals who have COVID-19.[4]

The US Centers for Disease Control and Prevention (CDC) defined COVID-19 symptoms as including 1 or more of the following:[5]

- 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
- Fatigue
- Headache
- Nasal congestion or runny nose
- Nausea

All ages may present with the disease, but notably, case fatality rates (CFR) are elevated in persons >60 years of age.[6] Comorbidities are also associated with increased CFR, including cardiovascular disease, diabetes, hypertension, and chronic respiratory disease.[7] Healthcare workers are over-represented among COVID-19 patients due to occupational exposure to infected patients.[7]

2.5.1.2. Vaccine Clinical Development Program

2.5.1.2.1. Rationale for Development

2.5.1.2.1.1. Current Therapies

Clinical management of COVID-19 includes a variety of therapies, which are primarily recommended for use in a hospitalized or clinical trial setting, such as:[8]

- Severe disease or critical care hospital setting
  - dexamethasone (corticosteroid)
  - tocilizumab (targeted immunotherapy agent)
  - remdesivir (antiviral agent)
  - baricitinib (JAK inhibitor) in combination with remdesivir
- Ambulatory care setting
  - casirivimab and imdevimab (monoclonal antibodies)
  - bamlanivimab (monoclonal antibody)
- Clinical trial setting
  - convalescent plasma
  - famatodine (H2 blocker)
  - ivermectin (anti-parasitic).

Currently available therapies have different benefit-risk considerations depending on the stage of illness and disease manifestations.[4,8] While care for individuals who have COVID-19 has improved with clinical experience, there remains an urgent and unmet need for a licensed prophylactic vaccine during the ongoing pandemic.

2.5.1.2.1.2. BNT162b2 Development

Pfizer and BioNTech developed an investigational vaccine that targets SARS-CoV-2, intended to prevent COVID-19, for which BioNTech initiated a FIH study in April 2020 in Germany (BNT162-01) and Pfizer initiated a Phase 1/2/3 study (C4591001) shortly afterwards in the US which expanded to include global sites upon initiation of the Phase 2/3 part of the study. Additional information on Study BNT162-01 is provided in Section 2.5.1.2.3.2.1, and on Study C4591001 is provided in Section 2.5.1.2.3.2.2.

The vaccine is based on SARS-CoV-2 spike glycoprotein (S) antigens encoded in RNA formulated in lipid nanoparticles (LNPs) and is referred to as BNT162b2 (BioNTech code number BNT162, Pfizer code number PF-07302048). The structural elements of the vector backbones of BNT162 vaccines are optimized for prolonged and strong translation of the antigen-encoding RNA. The potency of RNA vaccines is further optimized by encapsulation of the RNA into LNPs, which protect the RNA from degradation by RNAses and enable transfection of host cells after IM delivery.

Development of RNA-based vaccines encoding viral antigens provides significant advantages over more traditional vaccine approaches:

- RNA-based vaccines do not carry risks associated with infection.
- RNA-based vaccines can mimic antigen expression during natural infection by directing expression of a pathogen antigen with high precision and flexibility of antigen design.
- RNA occurs naturally in the body, is metabolized and eliminated by the body's natural mechanisms, does not integrate into the genome, and is transiently expressed.
- RNA-based vaccines are manufactured by a cell-free in vitro transcription process, which allows easy and rapid production and the prospect of producing high numbers of vaccine doses within a shorter time period than could be traditionally achieved with conventional vaccine approaches. This capability is pivotal to enable the most effective response in outbreak scenarios and makes RNA-based vaccines an attractive platform to achieve a timely and effective response to emerging infectious disease threats.

BioNTech is a pioneer in the field of RNA technology. The core innovation 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.[9,10,11]

2.5.1.2.2. Vaccine Product Information

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. Each modRNA candidate encodes either a P2 mutant S (P2 S) or the trimerized receptor binding domain (RBD) of S. Each candidate is given a V number to indicate the specific version of the optimized insert genomic sequence. BNT162 vaccine candidates tested in German Study BNT162-01 and pivotal Study C4591001 are:

- **BNT162b1** (RBP020.3) modRNA encoding RBD (V5)
- **BNT162b2** (RBP020.2) modRNA encoding P2 S (V9)

Vaccine candidates based on other RNA platforms that were tested in Study BNT162-01 but were not tested in pivotal Study C4591001 are not discussed further herein.

2.5.1.2.2.1. Characterization of the Vaccine Product

Coronavirus Spike Glycoprotein as Vaccine Target

Coronaviruses are a family of (+) ssRNA enveloped viruses that encode four structural proteins. Among these four structural proteins, S is the key target antigen for vaccine development. The vaccine candidates used for clinical testing featured the following vaccine antigens:

- Secreted, trimerized variant RBD of SARS-CoV-2 S (V5)[12]

- Membrane-anchored, full-length S with 2 point mutations within central helix domain (V9). Mutation of these 2 amino acids to proline locks S in an antigenically preferred prefusion conformation.[13,14]

Lipid Nanoparticle Formulation

Vaccine candidates are encapsulated into LNPs, which enable transfection of the RNA into host cells after IM injection. The same LNP formulation is used for all vaccine candidates.

The LNPs are composed of four different lipids in a defined ratio. During mixing of the RNA and the dissolved lipids, the lipids form the nanoparticles encapsulating the RNA. After injection, the LNPs are taken up by the cells, and the RNA is released into the cytosol. In the cytosol, the RNA is translated into the encoded viral protein. The encoded antigen induces an adaptive immune response. The antigen may be incorporated into cellular membranes (P2 S) or secreted into the extracellular environment (RBD) and induces an adaptive immune response. As S is the antigen that recognizes the host cell receptor and enables infection of the host cells, it is a key target of virus neutralizing antibodies. Further, as RNA-expressed S is being degraded intracellularly, the resulting peptides can be presented at the cell surface, triggering a specific T cell-mediated immune response with activity against the virus.

Additional details on the product formulation are provided in Section 2.5.2.1.

2.5.1.2.3. Vaccine Development Program

2.5.1.2.3.1. Nonclinical Studies

Key nonclinical evaluations of BNT162b2 included pharmacology (mouse immunogenicity studies, non-human primate [NHP] immunogenicity and challenge studies) and toxicity (two Good Laboratory Practice [GLP] rat repeat-dose toxicity studies) in vitro and in vivo. A developmental and reproductive toxicity (DART) study was completed in rats.

Nonclinical studies in mice and NHP demonstrate that BNT162b2 elicits a rapid antibody response with measurable SARS-CoV-2 neutralizing titers after a single dose and substantial increases in titers after a second dose that exceed titers in sera from SARS-CoV- 2/ COVID-19-recovered individuals. A Th1-dominant T cell response was evident in both mice and NHPs. S-specific CD8+ T cell responses were also detectable in BNT162b2-immunized animals. The strongly Th1-biased CD4+ T cell response and interferon-γ (IFNγ)+ CD8+ T cell response after immunization with BNT162b2 is a pattern favored for vaccine safety and efficacy and provided added reassurance for clinical safety.[15] In A SARS-CoV-2 rhesus challenge model, BNT162b2 provided complete protection from the presence of detectable viral RNA in the lungs compared to the saline control with no clinical, radiological, or histopathological evidence of vaccine-elicited disease enhancement.[16]

Administration of BNT162b2 by IM injection to male and female Wistar Han rats once every week, for a total of 3 weekly cycles of dosing, was tolerated without evidence of systemic toxicity in GLP-compliant repeat-dose toxicity studies.

In a DART study, 0.06 mL of a vaccine formulation containing the same quantity of nucleoside-modified mRNA (30 µg) and other ingredients included in a single human dose of BNT162b2 was administered to female rats by the IM route on four occasions: 21 and 14 days prior to mating, and on gestation days 9 and 20. No vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported in the study.

In summary, the nonclinical package summarized above supports BNT162b2 administered twice by IM injection at a dose of 30 µg RNA. Additional details of nonclinical studies are provided in Module 2.4.

2.5.1.2.3.2. Clinical Studies

2.5.1.2.3.2.1. Phase 1/2 Study BNT162-01

Study BNT162-01 is the ongoing, FIH, Phase 1 dose level-finding study, in which healthy younger adults (18 to 55 years of age) and older adults (56 to 85 years of age) all receive active vaccine. This study is evaluating the safety and immunogenicity of several different candidate vaccines at various dose levels. The available Phase 1 safety and immunogenicity data for younger and older adults are reported in this submission.

Multiple vaccine candidates are being evaluated in this study. For each vaccine candidate, participants received escalating dose levels (N=12 per dose level) with progression to subsequent dose levels based on recommendation from a Sponsor Safety Review Committee (SRC).

The study design is detailed in the Module 5.3.5.1 BNT162-01 Protocol.

Study Eligibility Criteria

The BNT162-01 study population includes male and female adult participants deemed healthy and without COVID-19 symptoms or evidence of SARS-CoV-2 infection within 30 days prior to entering the study. Inclusion criteria allowed for preexisting stable disease defined as disease not requiring significant change in therapy or hospitalization for worsening disease during the 6 weeks prior to enrollment. Individuals with medical conditions considered to possibly confound evaluation of vaccine safety or immunogenicity were excluded.

Phase 1

In Study BNT162-01, vaccine candidates from the modRNA platform, administered IM in the upper arm in a two-dose regimen separated by approximately 21 days, were:

- **BNT162b1** (dose levels: 1, 3, 10, 20, 30, 50, 60 µg)
- **BNT162b2** (dose levels: 1, 3, 10, 20, 30, 50, 60 µg)

For each vaccine candidate, participants received escalating dose levels (N=12 per dose level) with progression to subsequent dose levels based on recommendation from a Sponsor Safety Review Committee (SRC). Note: the SRC recommended that a second dose of BNT162b1 at 60 µg not be administered due to reactogenicity after the first dose. Note that at the time of BNT162-01 Interim CSR preparation, data for BNT162b2 dose levels of 50 µg and 60 µg were not available.

Dosing with other candidates on different platforms, BNT162a1 (uRNA) and BNT162c2 (saRNA), is not discussed as it is not relevant to progression with modRNA candidates.

Safety and immunogenicity data (including T cell immune response data) from the Phase 1 part of Study BNT162-01 are summarized in this submission in support of the larger dataset from the Phase 1/2/3 registration Study C4591001.

2.5.1.2.3.2.2. Phase 1/2/3 Study C4591001

Study C4591001 is the ongoing, randomized, placebo-controlled, Phase 1/2/3 registration study. It was started as a Phase 1/2 study in adults in the US, was then amended to expand the study to a global Phase 2/3 study planning to enroll enough participants to accrue sufficient COVID-19 cases to conduct a timely efficacy assessment; amended to include older adolescents 16 to 17 years of age, then later amended to include younger adolescents 12 to 15 years of age.

The study design is detailed in Module 5.3.5.1 C4591001 Protocol.

Study Eligibility Criteria

In Phase 1, two age groups were studied separately, younger participants (18 to 55 years of age) and older participants (65 to 85 years of age). The study population includes male and

female participants deemed healthy as determined by medical history, physical examination (if required), and clinical judgment of the investigator to be eligible for inclusion in the study. Exclusions included screened individuals with high risk of exposure to SARS-CoV-2 infection due to exposure in the workplace and/or medical conditions that represent risk factors, clinically important prior illness or laboratory abnormalities, serological evidence of prior SARS-CoV-2 infection or current SARS-CoV-2 infection as measured by polymerase chain reaction (PCR).

In Phase 2/3, participants were enrolled with stratification of younger adults (18 to 55 years of age) and older adults (>55 years of age) to achieve approximately 40% enrollment in the older adult group. Additional adolescents were added later by a protocol amendment: older adolescents 16 to 17 years of age are included in the younger adult stratum (ie, 16 to 55 years of age), and younger adolescents 12 to 15 years of age were analyzed as a separate age stratum. Eligibility in Phase 2/3 included higher risk for acquiring COVID-19 in the investigator's judgment, due to medical conditions or exposure, such as:

- Chronic condition (eg, hypertension; diabetes; asthma; pulmonary, liver, or kidney disease)
- Autoimmune disease requiring therapeutic intervention (or history of)
- Chronic HIV, HCV, or HBV infection that is stable and controlled
- Vaping or smoking (or history of smoking within the prior year)
- Resident in a long-term facility
- Occupation with high risk of SARS-CoV-2 exposure (eg, healthcare, emergency response)

Phase 1

The Phase 1 part of the study, randomized participants 4:1 to receive active vaccine or placebo. The vaccines candidates, administered IM in the upper arm in a two-dose regimen separated by approximately 21 days, were:

- **BNT162b1** (dose levels: 10, 20, 30, 100 µg)
- **BNT162b2** (dose levels: 10, 20, 30 µg)

Phase 1 of Study C4591001 was conducted in the US. For each of the two vaccine candidates evaluated, younger participants received escalating dose levels (N=15 per dose level, 4:1 randomization ratio between vaccine and placebo) with progression to subsequent dose levels and the older age group (N=15 per dose level, 4:1 randomization ratio between vaccine and placebo) based on recommendation from an Internal Review Committee (IRC). Note: the IRC recommended that a second dose of BNT162b1 at 100 µg not be administered and discontinued due to reactogenicity after the first dose in the younger age group. Participants in this group of younger adults instead received a second dose of BNT162b1 at the 10 µg dose level approximately 3 months after Dose 1, and the 100 µg dose level was discontinued (ie, not administered to older adults receiving BNT162b1).

The Sponsor/agent study team was not blinded in this part of the study. Participants who enrolled in Phase 1 are followed for cases of COVID-19 but do not contribute to the efficacy assessment. Safety follow-up will continue for at least 2 years and/or end of study. Based upon review of safety and immunogenicity from the Phase 1 part of the study, the final

candidate and dose level was selected as BNT162b2 at 30 µg given twice 21 days apart. Details are provided in Section 2.5.1.2.5.

Booster Evaluation

Phase 1 participants who were randomized to either BNT162b1 or BNT162b2 at dose levels of 10, 20, or 30 µg are being offered booster vaccination with BNT162b2 at 30 µg, approximately 6 to 12 months after their second dose of BNT162b1 or BNT162b2. This provides an early assessment of the safety and immunogenicity associated with a third vaccine dose. Data from Phase 1 participants who receive a booster are not included in this submission and will be reported at a later time.

Phase 2

Phase 2/3 of Study C4591001 commenced with the selected vaccine candidate and dose level administered to participants who were randomized 1:1 to receive vaccine or placebo.

Phase 2 was conducted in the US. The Phase 2 portion of the study evaluated reactogenicity and immunogenicity for 360 participants 18 to 85 years of age enrolled into the study when the Phase 2/3 part commenced, balancing younger (≤55 years of age) and older (>55 years of age) strata within each group. Phase 2 participants in this blinded part of the study also contribute to the overall efficacy and safety assessments in the Phase 3 portion of the study.

Phase 3

Phase 3 (which is ongoing) included planned interim analyses of the first primary efficacy endpoint, ongoing efficacy and safety evaluations including reactogenicity assessment in a subset of participants, and exploratory vaccine immunogenicity evaluation in a subset of participants. Phase 3 is being conducted at sites in the US, Brazil, Argentina, Turkey, South Africa, and Germany. Participants were stratified by age group as previously described. The final efficacy analysis was conducted when at least the prespecified total number of 164 efficacy events accrued. Safety and long-term persistence of efficacy follow-up will continue for at least 2 years and/or end of study. Safety and efficacy analyses included the 360 participants who were analyzed for Phase 2.

Booster and Variant Strain Evaluation

For further evaluation of booster effects and protection against emerging SARS-CoV-2 variants of concern, a subset of existing Phase 3 participants 18 to 55 years of age will be randomized 1:1 to receive either receive a third dose of BNT162b2 or a third dose of prototype based upon the South African variant, BNT162b2$_{SA}$, approximately 5 to 7 months after their second dose of BNT162b2. An additional subset of existing Phase 3 participants 18 to 55 years of age will be enrolled to receive a third and fourth dose of BNT162b2$_{SA}$. A new cohort will be recruited who are COVID-19 vaccine-naïve (ie, have not received BNT162b2) and have not experienced COVID-19 to receive BNT162b2$_{SA}$ as a two-dose series 21 days apart. Data from Phase 3 participants who receive a booster and/or BNT162b2$_{SA}$ are not included in this submission and will be reported at a later time.

Unblinding Considerations

Unblinding to randomized treatment assignment has begun for participants ≥16 years of age in the study, with respect to the participants, Sponsor, and site personnel. This is subsequent to authorizations/approvals granted in the US and other regions starting in December 2020 (refer to Section 2.5.1.3).

Individuals 16 years of age or older have been unblinded at such time that they become locally eligible and wish to know their treatment assignment to confirm prior vaccination with BNT162b2 (if randomized to this group), or to receive BNT162b2 (if randomized to placebo). Unblinded recipients originally randomized to BNT162b2 continue to be followed in an open-label (ie, observational) manner. Unblinded recipients originally randomized to placebo are offered BNT162b2 vaccination and thereafter followed in an open-label manner.

Participants randomized to placebo who became eligible for vaccination with BNT162b2 (or another COVID-19 vaccine) had the opportunity to receive BNT162b2 in a phased manner as part of the study (no later than at the approximate time participants in Phase 2/3 reach Visit 4). The investigator ensured the participant met at least one of the recommendation criteria. Any participant who originally received placebo and subsequently received BNT162b2 was moved to a new visit schedule to receive both doses of BNT162b2 at each of two additional vaccination visits (Visits 101 and 102).

Sponsor and site personnel who are responsible for the ongoing conduct of the study remain blinded to the data from participants whose treatment assignment has not been disclosed in the ongoing study (ie, not unblinded), with regard to individual participants' randomization. Safety evaluation for these participants by the study team remains blinded until a decision is made to unblind the entire study. A separate (from study conduct) unblinded submissions team is responsible for regulatory submissions.

All participants continue to be expected to remain in study follow-up for a maximum of approximately 2 years after Dose 2 of randomized study intervention.

2.5.1.2.3.2.3. Planned Studies

The following studies (or additional analyses from ongoing studies) are planned in 2021:

- Pediatric studies in children <12 years of age: C4591007
- Maternal immunization during pregnancy: C4591015
- Immunocompromised adults, children <18 years of age: BNT162-01, C4591024
- Lot consistency: C4591017
- Lyophilized product bridging: C4591020
- Process 1 and Process 2 comparison: C4591001
- Booster vaccination(s) with BNT162b2: C4591001
- SARS-CoV-2 variant strain change ($BNT162b2_{SA}$): C4591001

2.5.1.2.4. Proposed Indication

The proposed indication for BNT162b2 (30 µg) is:

- Active immunization to prevent COVID-19 disease caused by SARS-CoV-2 virus, in individuals ≥16 years of age.

Supplemental applications are planned for (b) (4) (b) (4), pending conclusion of the appropriate studies/analyses and Agency feedback.

2.5.1.2.5. Rationale for Candidate and Dose Selection

BioNTech has evaluated multiple RNA-LNP platforms, including nucleoside-modified RNA (modRNA) which has blunted innate immune sensor activating capacity and thus augmented antigen expression. Two modRNA candidates were evaluated in the Phase 1 portions of Studies BNT162-01 and C4591001. The final candidate and dose level (BNT162b2 at 30 µg) was selected following review of immunogenicity and safety data from the Phase 1 part of Study C4591001 and available nonclinical data.

The final vaccine candidate selection for clinical development in Phase 2/3 was based on:

- NHP challenge data; BNT162b2 led to earlier virus clearance, no evidence of virus in lung
- Favorable reactogenicity for BNT162b2 in both younger and older Phase 1 participants
- Robust immunogenicity in both younger and older Phase 1 participants at 30 µg dose level.

BNT162b2 at 30 µg proceeded into the Phase 2/3 portion of Study C4591001 because this dose and construct provided the optimum combination of a favorable reactogenicity profile and a robust immune response, likely to afford protection against COVID-19 in younger and older age groups.

2.5.1.3. Regulatory Status

BNT162b2 has received temporary authorizations for emergency supply in 28 countries and conditional marketing authorizations in 39 countries globally. The name of the product supplied under emergency/temporary use authorization for all applicable regions is Pfizer-BioNTech COVID-19 Vaccine. The name of the product supplied under conditional marketing authorization for all applicable regions is COMIRNATY [COVID-19 mRNA Vaccine (nucleoside modified)].

United States

In the US, the vaccine is in clinical development under an Investigative New Drug (IND) application, BB-IND 19,736. Fast Track Designation was granted on 07 July 2020 for individuals ≥18 years of age. An EUA application was filed to the US Food and Drug Administration (FDA) on 20 November 2020 and the product was authorized for emergency use in the US on 11 December 2020 for individuals ≥16 years of age (EUA 27034). An amendment to the EUA was submitted 09 April 2021 to support emergency use in participants 12 to 15 years of age.

The agreed Pediatric Study Plan (PSP) was submitted to the FDA on 02 April 2021 and was agreed by the FDA on 23 April 2021.

European Union

A rolling Marketing Authorization Application (MAA) was initiated on 05 October 2020 with nonclinical data, followed by Module 3 documents submitted on 05 November 2020, and completed with submission of clinical modules on 07 December 2020. Conditional marketing approval was granted by the European Medicines Agency (EMA) on 21 December 2020 for individuals ≥16 years of age. A Type II Variation to support use individuals ≥12 years of age is planned to be submitted to EMA in second quarter 2021.

A Paediatric Investigational Plan (PIP) was submitted to the Paediatric Committee (PDCO) on 21 September 2020. An agreed PIP decision was received 27 November 2020. A PIP modification request was submitted to PDCO on 24 March 2021 and was agreed by PDCO on 21 April 2021.

Rest of World

Marketing Authorization Applications were initiated beginning in October 2020 and have been approved in many countries globally including Switzerland, Japan, Australia, New Zealand and Brazil. Requests for temporary authorization for emergency supply have been filed and approved in many countries globally under emergency or temporary use authorization procedures or special import procedures beginning in November 2020 (including the UK and Canada). The World Health Organization (WHO) issued a positive opinion on the Emergency Use Listing of COMIRNATY on 31 December 2021.

2.5.1.4. Ethical Considerations

All studies in the clinical development program were conducted in compliance with the ethical principles originating in or derived from the Declaration of Helsinki and in compliance with all International Council on Harmonisation (ICH) Good Clinical Practice (GCP) Guidelines. They were designed, performed, and analyzed in accordance with all applicable regulations, laws, and guidelines in effect at the time they were conducted from the US FDA, EU Directive 2001/20/EC, and local regulatory agencies in countries where the study was conducted. The study design reflects recommendations from local review boards/committees, and other local regulatory authorities.

The pivotal Phase 1/2/3 Study C4591001 was conducted at sites in the US, Brazil, Argentina, Turkey, South Africa, and Germany; the majority of participants were enrolled at sites in the US (refer to Section 2.5.5.5.1). The supporting Phase 1/2 Study BNT162-01 was conducted at sites in Germany.

2.5.2. Overview of Biopharmaceutics

2.5.2.1. Formulation Development

The BNT162b2 vaccine is provided in a multi-dose vial that contains a frozen concentrated solution that is preservative-free and must be thawed and diluted prior to administration. The

BNT162b2 concentrate must be diluted in its original vial using 0.9% Sodium Chloride Injection, USP, resulting in an off-white suspension. The 0.9% Sodium Chloride Injection, USP is not packaged with the vaccine and must be sourced separately.

The vaccine is administered IM as a series of two 30-µg doses of the diluted vaccine solution (0.3 mL each) according to the following schedule: a single 0.3-mL dose followed by a second 0.3-mL dose 21 days later.

Details of formulation development and storage conditions are provided in Module 3.

Manufacturing Process

The scale of BNT162b2 manufacturing has been increased to support future supply. The safety and immunogenicity of prophylactic BNT162b2 in Study C4591001 participants vaccinated with material generated using the existing manufacturing process (Process 1) and with material from lots generated using the manufacturing process supporting increased supply (Process 2) is planned to be evaluated (as noted in in Section 2.5.1.2.3.2.3).

2.5.2.2. Biopharmaceutical Studies

Bioavailability and bioequivalence assessments are not relevant to vaccine antigenicity and have not been measured.

The major pharmacodynamic effect of a vaccine, unlike a drug, is to elicit an immune response to the antigens included in the vaccine. Vaccine induced activation of antigen-presenting cells takes place at the site of injection (ie, muscle) which is rapidly followed by antigen-presenting cell migration via lymphatic vessels towards the draining lymph node where vaccine antigens activate specific B and T cells. There is no specific vaccine antigen blood level required to elicit the immune response.

2.5.2.3. Bioanalytical and Analytical Methods Used in Human Studies

Information on assays used to assess SARS-CoV-2 infection and immune response is in Module 2.7.1. Only validated (PCR and neutralization immunoassay) or qualified (Luminex immunoassay) methods were used.

2.5.3. Overview of Clinical Pharmacology

Pharmacokinetic studies are not usually required for vaccines. Measurement of the plasma concentration of the vaccine over time is not feasible.

2.5.4. Overview of Efficacy (Including Immunogenicity)

Efficacy was evaluated in Phase 2/3 of pivotal study C4591001; the methods for evaluation of efficacy are provided in Section 2.5.4.1 and results are in Section 2.5.4.3.

Immunogenicity was evaluated in Phase 1 of Study BNT162-01 and in all phases of Study C4591001. The methods for evaluation of immunogenicity are provided in Section 2.5.4.2, and results are provided in Section 2.5.4.4. Phase 3 immunogenicity analyses are planned to be completed at a later time and are not included in this submission.

Details of efficacy and immunogenicity analysis methods in Study C4591001 are provided in the Module 5.3.5.1 C4591001 Protocol and SAP, and for Study BNT162-01 are provided in the Module 5.3.5.1 BNT162-01 Protocol and SAP.

2.5.4.1. Efficacy Endpoints and Analysis Methods

Methods and validation of the PCR test for efficacy analyses are provided in Module 2.7.1. Details of efficacy evaluations are provided in Module 2.7.3 and summarized below. Statistical analysis methods are summarized in Section 2.5.4.1.2.

2.5.4.1.1. Efficacy Endpoints in Study C4591001

Efficacy was assessed based on confirmed cases of COVID-19, where the case onset date was the date that symptoms were first experienced by the participant and the cases met evaluable criteria as summarized below.

2.5.4.1.1.1. Primary Efficacy Endpoints

Study C4591001 is the pivotal (and only) efficacy study. The primary efficacy endpoints in the Phase 3 part of the study were:

- **First primary endpoint**: COVID-19 incidence per 1000 person-years of follow-up in participants without serological or virological evidence of past SARS-CoV-2 infection before and during the vaccination regimen – cases confirmed ≥7 days after Dose 2

- **Second primary endpoint**: COVID-19 incidence per 1000 person-years of follow-up in participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen – cases confirmed ≥7 days after Dose 2.

2.5.4.1.1.2. Secondary Efficacy Endpoints

Study C4591001 has secondary endpoints based on different approaches to COVID-19 case evaluation criteria as follows:

- **COVID-19 confirmed at least 14 days after Dose 2**: COVID-19 incidence per 1000 person-years of follow-up in participants either (1) without or (2) with or without serological or virological evidence of past SARS-CoV-2 infection before and during the vaccination regimen – cases confirmed ≥14 days after Dose 2

- **Severe COVID-19**: incidence per 1000 person-years of follow-up in participants either (1) without or (2) with or without evidence of past SARS-CoV-2 infection before and during the vaccination regimen – cases confirmed either (1) ≥7 days after Dose 2 or (2) ≥14 days after Dose 2

- **CDC-defined COVID-19**: incidence per 1000 person-years of follow-up in participants either (1) without or (2) with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen – cases confirmed either (1) ≥7 days after Dose 2 or (2) ≥14 days after Dose 2.

2.5.4.1.1.3. COVID-19 Case Determination

Participants who developed any potential COVID-19 symptoms listed in the protocol were to contact the site immediately and if confirmed to participate in an in-person or telehealth visit as soon as possible (optimally within 3 days of symptom onset, and at the latest 4 days after symptom resolution). At the visit (or prior to the visit, if a participant utilized a self-swab as permitted per protocol), investigators were to collect clinical information and results from local standard-of-care tests sufficient to confirm a COVID-19 diagnosis.

Investigators were to obtain a nasal swab (mid-turbinate) for testing at a central laboratory using a validated reverse transcription–polymerase chain reaction (RT-PCR) test (Cepheid; EUA200047/A001) 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. A local nucleic acid amplification test (NAAT) result was only acceptable if it met protocol-specified criteria and if a central laboratory result was not available, in which case a local NAAT result could be used if 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)
- Abbott Molecular/RealTime SARS-CoV-2 assay (EUA200023/A001).

Evidence of prior SARS-CoV-2 infection were determined by virological testing via NAAT on mid-turbinate swab and serological testing for SARS-CoV-2 N-binding antibodies.

Case Definitions

COVID-19 cases (defined per FDA guidance)[17] were based on SARS-CoV-2 positive test result per central laboratory or local testing facility (using an acceptable test per protocol and if no central laboratory result was available) and presence of <u>at least 1 of the following</u>:

- 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

CDC criteria-defined COVID-19 cases could include the following <u>additional</u> symptoms:

- Fatigue
- Headache
- Nasal congestion or runny nose
- Nausea

Severe COVID-19 cases (defined per FDA guidance)[17] included presence of at least 1 of the following:

- Clinical signs at rest indicative of severe systemic illness:
  - Respiratory rate ≥30 breaths per minute
  - Heart rate ≥125 beats per minute
  - SpO_2 ≤93% on room air at sea level or PaO_2/FiO_2 <300 mm Hg
- Respiratory failure:
  - needing high-flow oxygen
  - noninvasive ventilation
  - mechanical ventilation
  - ECMO
- Evidence of shock:
  - Systolic blood pressure <90 mm Hg
  - Diastolic blood pressure <60 mm Hg
  - Requiring vasopressors
- Significant acute renal, hepatic, or neurologic dysfunction
- Admission to an intensive care unit (ICU)
- Death

Efficacy analysis for severe COVID-19 cases was also conducted using the CDC definition of severe COVID-19 (hospitalization, admission to the ICU, intubation or mechanical ventilation, or death).[18]

2.5.4.1.2. Efficacy Analysis Methods in Study C4591001

The statistical analyses of efficacy data presented in this CO are from Study C4591001 and were based on the evaluable efficacy and all-available populations.

2.5.4.1.2.1. Sample Size Determination

For Phase 1: the study sample size was not based on any statistical hypothesis testing. Efficacy was not evaluated in Phase 1.

For Phase 2/3: the sample size assumed a true VE of 60% after the second dose of study intervention, for which a total of approximately 164 first confirmed COVID-19 illness cases would provide approximately 90% power. This would be achieved with 17,600 evaluable participants per group (or 21,999 vaccine recipients randomized in a 1:1 ratio with placebo) for a total sample size of 43,998. This assumed a 1.3% illness rate per year in the placebo group, accrual of 164 primary endpoint cases within 6 months, and 20% of the participants being non-evaluable or having serological evidence of prior infection with SARS-CoV-2 (potentially making them immune to further infection).

2.5.4.1.2.2. Efficacy Analysis Methods

The statistical analyses of efficacy data from Study C4591001 were based on the evaluable efficacy populations and all-available efficacy populations (described in Module 2.7.3).

Interim Analysis

During Phase 2/3, interim analyses were pre-specified in the protocol to be conducted after accrual of at least 62, 92, and 120 evaluable COVID-19 cases, where overwhelming efficacy could be declared if the primary endpoint was met with a posterior probability that the true VE is >30% (ie, Pr[VE >30%|data] >99.5% at an interim analysis or >98.6% at the final analysis). The success threshold for each interim analysis was calibrated to protect overall type I error at 2.5%. Futility was also assessed, and the study could be stopped for lack of benefit if the predicted probability of demonstrating vaccine efficacy at the final analysis was <5% at any of the first 2 planned interim analyses. Efficacy and futility boundaries were applied in a nonbinding way. The calculation of posterior probability and the credible interval were adjusted for surveillance time. For subgroup analyses of the primary efficacy endpoint, a 2-sided 95% confidence interval (CI) was calculated.

VE is defined as 100% × (1 – IRR), where illness rate ratio (IRR) is calculated as the ratio of first confirmed COVID-19 illness rate in the vaccine group to the corresponding illness rate in the placebo group. VE is demonstrated if there is convincing evidence (ie, posterior probability greater than 99.5% at an interim analysis or greater than 98.6% at the final analysis) that the true VE of BNT162b2 is >30% using a beta-binomial model, where VE represents efficacy for prophylactic BNT162b2 against confirmed COVID-19 in participants without evidence of past SARS-CoV-2 infection before and during the vaccination regimen. 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 VE. Cases were counted from 7 days after Dose 2.

Interim analysis was performed for the first primary efficacy endpoint only. Other efficacy data analyzed for the interim analysis were summarized with descriptive summary statistics, including COVID-19 case counts in the BNT162b2 and placebo groups on the basis of:

- evidence of prior SARS-CoV-2 infection at baseline per NAAT or N-antigen binding assay
- demographic subgroup (ie, age, sex, race, ethnicity, country)
- COVID-19 cases meeting protocol criteria as severe after the first and second doses.

Overwhelming efficacy success criteria on the first primary efficacy endpoint were met at the first planned interim analysis of 94 accrued COVID-19 cases as of 04 November 2020, after which additional formal interim analyses were not conducted.

Final Analysis

The final analysis of primary and secondary efficacy endpoints was pre-specified in the protocol to be conducted after accrual of the final number of COVID-19 cases (at least 164 cases). Subgroup analyses of VE based on baseline SARS-CoV-2 status and demographics were performed for the primary endpoints and secondary endpoint of severe COVID-19 cases. Additional post hoc analyses of subgroups defined by comorbidity risk assessment were

performed. Secondary efficacy was analyzed in the same manner as primary efficacy (Section 2.5.4.1.2.2), using the case definitions for severe COVID-19 and CDC criteria for COVID-19 (Section 2.5.4.1.1.2).

Final analysis of efficacy was based on 170 COVID-19 cases accrued in the evaluable efficacy population of participants without evidence of past SARS-CoV-2 infection before and during the vaccination regimen as of 14 November 2020. The prespecified final analyses of efficacy included primary and secondary endpoints in the evaluable and all-available efficacy populations. No additional formal hypothesis testing for analyses of clinically confirmed COVID-19 cases is planned.

Updated Analysis

Following the protocol specified interim analysis of efficacy and final analysis of efficacy, updated descriptive efficacy analyses were conducted for the two primary efficacy endpoints, including subgroup analyses, and for the secondary efficacy endpoint of severe disease, using statistical methods described in the study statistical analysis plan.

The point estimate of VE and associated 2-sided 95% CI derived using the Clopper-Pearson method adjusted for surveillance time were provided as descriptive summary. Updated analyses in the EUA amendment include COVID-19 cases accrued in blinded follow-up to the data cutoff date (13 March 2021).

2.5.4.2. Immunogenicity Endpoints and Analysis Methods

Assay methods and qualification/validation reports for immunoassays are provided in Module 2.7.1. Details of immunogenicity analyses are provided in Module 2.7.3 and summarized below. Statistical analysis methods are provided in Section 2.5.4.2.3.

2.5.4.2.1. Immunogenicity Endpoints in Study BNT162-01

In Study BNT162-01, immunogenicity was evaluated in Phase 1 using a SARS-CoV-2 serum neutralization assay to determine neutralizing titers and the fold rise in SARS-CoV-2 serum neutralizing titers. Only validated neutralization assays were used. Immunogenicity was assessed at Day 1 (before Dose 1) and at 7 days after Dose 1 (Day 8); and at Day 22 (before Dose 2) and at 7 days after Dose 2 (Day 29), 21 days after Dose 2 (Day 43), 28 days (approximately 1 month) after Dose 2 (Day 50), and 63 days (9 weeks or approximately 2 months) after Dose 2 (Day 85).

T cells isolated from peripheral blood mononuclear cells (PBMCs) obtained from whole blood samples of vaccinated Phase 1 participants were evaluated by enzyme-linked immuno-spot (ELISPOT) and intracellular cytokine staining visualized with fluorescence-activated cell sorting (FACS). Blood samples were collected prior to Dose 1 and on Day 29 (7 days after Dose 2). In a subset of study participants who received 10, 20, and 30 µg BNT162b2, blood samples were also collected on Day 85 (63 days, or approximately 2 months, after Dose 2) and Day 184 (162 days, or approximately 6 months, after Dose 2) and analyzed. Assessments included cytokines associated with Th1 responses such as IFNγ and IL-2 and those associated with Th2 responses such as IL-4, to analyze the induction of balanced versus Th1-dominant or Th2-dominant immune responses.

2.5.4.2.2. Immunogenicity Endpoints in Study C4591001

In Study C4591001, immunogenicity was evaluated in Phase 1 and Phase 2 using a SARS-CoV-2 serum neutralization assay to determine titers and a SARS-CoV-2 RBD- or S1-binding IgG direct Luminex immunoassay to determine antibody binding levels. Only validated neutralization and qualified Luminex assays were used.

In Phase 1, immunogenicity was assessed at Day 1 (before Dose 1) and 7 days after Dose 1; and at Day 21 (before Dose 2) and 7 days, 14 days, 1 month, and 6 months after Dose 2. Data were summarized for each dose level and age group.

In Phase 2, immunogenicity was assessed at Day 1 (before Dose 1) and 1 month after Dose 2. Data were summarized by age group and by evidence of prior SARS-CoV-2 infection at baseline per NAAT (PCR) or N-binding IgG assay. Data from the 6-month post Dose 2 time point were not available at the time of the submission data cutoff date (13 March 2021).

In Phase 2/3, exploratory immunogenicity assessments are planned at time points up to 24 months, to be reported at a later time.

2.5.4.2.3. Immunogenicity Analysis Methods

2.5.4.2.3.1. Immunogenicity Analysis Methods in Study BNT162-01

The statistical analyses of immunogenicity data from Study BNT162-01 were based on the immunogenicity set (described in Module 2.7.3).

Immunogenicity data from the SARS-CoV-2 neutralization assay were analyzed for Study BNT162-01 participants similarly to data in Study C4591001 (refer to Section 2.5.4.2.3.2).

T cells were isolated from CD4- and CD8- depleted PBMCs obtained from whole blood samples of vaccinated Phase 1 participants. PBMCs were tested for antigen induced cytokine production, evaluated by ELISPOT and intracellular cytokine staining with FACS analysis.

ELISPOT

Sample controls included anti-CD3 antibody-mediated stimulation (positive), medium (negative), and an optional mix of viral antigens for T cell response benchmarking:

- **CEF:** HLA class I restricted peptides originating from cytomegalovirus (CMV), Epstein-Barr Virus (EBV), and influenza virus, which are expected to stimulate IFNγ production from CD8+ T cells in the majority of donors.

- **CEFT:** HLA class II restricted peptides originating from CMV, EBV, influenza virus, and tetanus toxin, which are expected to stimulate IFNγ production from CD4+ T cells in the majority of donors.

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 were

placed in ELISPOT plates pre-coated with antibodies specific for IFNγ and incubated overnight (≥18 hours) with peptides originating from the vaccine antigens (ie, from RBD or full-length S protein). IFNγ secreted by CD4+ or CD8+ cells in response to stimulation by the peptides was bound to the plate by the coating antibody. After incubation, the plates were developed by addition of alkaline phosphatase conjugated secondary anti-IFNγ antibody followed by enzyme substrate; each spot corresponds to the IFNγ secreted by a single cell. Developed plates were read by an AID ELISPOT Reader.

Intracellular Cytokine Staining with FACS Analysis

Intracellular cytokine staining is a flow cytometry-based assay to detect production and accumulation of cytokines intracellularly upon cell stimulation. Antigen stimulation was performed using synthetic peptides covering the encoded antigens (eg, 15-mer overlapping peptides covering the whole length of the vaccine antigen with 11 amino acid overlap). These peptide pools represent the vaccine-encoded SARS-CoV-2 RBD, and SARS-CoV-2 S1 subpool 1 and subpool 2 pepmixes as well as a combination of subpool 1 and subpool 2.

Briefly, vaccine antigen-stimulated PBMCs were treated with protein transport inhibitors to retain intracellular cytokines and labelled on the extracellular surface with fluor-conjugated antibodies for CD4, CD8, and CD3. PBMCs were fixed and permeabilized for intracellular cytokine staining of cytokines with fluor-conjugated antibodies, and samples 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.

Comparisons between pre- and post-vaccination samples for each subject were used as a surrogate for induction or expansion of cellular immune responses, and to characterize the balance of generated Th1 and Th2 responses upon vaccination. For benchmarking, PBMCs from recovered COVID-19 patients were used.

2.5.4.2.3.2. Immunogenicity Analysis Methods in Study C4591001

The statistical analyses of immunogenicity data from Study C4591001 were based on the evaluable immunogenicity populations and all-available immunogenicity populations (described in Module 2.7.3).

Data were reported for SARS-CoV-2 serum neutralizing titers and SARS-CoV-2 S1-binding and RBD-binding IgG concentrations, including:

- geometric mean titers/concentrations (GMTs/GMCs)
- geometric mean-fold rise (GMFR)

For immunogenicity results of SARS-CoV-2 serum neutralizing titers and S1- or RBD-binding IgG concentrations, GMTs or GMCs were computed with associated 95% CIs. The GMTs and GMCs were calculated as the mean of assay results after 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 titers, calculating the 95% CI with reference to Student's t-distribution, and then exponentiating the confidence limits.

GMFRs were limited to participants with non-missing values prior to first dose and the post-dose time point. The GMFR was calculated by exponentiating the mean of the difference of logarithm transformed assay results: (later time point) – (earlier time point). Two-sided CIs were obtained by calculating CIs using Student's t-distribution for the mean difference of the logarithm transformed assay results and exponentiating the confidence limits.

Exact 95% CIs for binary endpoints were computed using F distribution (Clopper-Pearson).

2.5.4.2.3.3. Human Convalescent Sera Panel for Serology Comparisons

To facilitate interpretation of immunogenicity data generated in Studies BNT162-01 and C4591001, 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).[19,20] 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 (35/38) including 1 who had been hospitalized.

2.5.4.3. Efficacy Results

Details of efficacy analysis results from the first planned (and successful) interim analysis and the planned final analysis of efficacy are provided in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 10 and Section 11. Updated efficacy results are provided in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Section 10 and Section 11.

All efficacy data are also presented in Module 2.7.3 and summarized below.

2.5.4.3.1. Interim Analysis of Efficacy in Study C4591001

A prespecified interim analysis of efficacy was conducted after accrual of 94 COVID-19 cases. 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 an interim analysis cutoff date of 04 November 2020. Data are summarized for the efficacy populations. Additional analyses were conducted by subgroups (age, sex, race, ethnicity, country, and baseline SARS-CoV-2 status).

COVID-19 case evaluation is discussed in Section 2.5.4.1. For the first primary efficacy endpoint, VE for BNT162b2 against confirmed COVID-19 was evaluated in participants without evidence of past SARS-CoV-2 infection before and during the vaccination regimen. Participants with positive or unknown NAAT results at any illness visit prior to 7 days after Dose 2 were not included in VE evaluation. Cases were counted from 7 days after Dose 2.

Efficacy population characteristics in the interim analysis are presented in Section 2.5.4.3.1.1, and results of the interim analysis are presented in Section 2.5.4.3.1.2 (first primary endpoint) and Section 2.5.4.3.1.3 (additional descriptive results).

2.5.4.3.1.1. Efficacy Populations – Interim Analysis

The proportions of participants included in the interim analysis efficacy populations was similar in the BNT162b2 and placebo groups (Table 1). 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 on or prior to 7 days after Dose 2.

Table 1. 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)

Table 1. 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.
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 eff pop

Demographics of participants in the interim analysis evaluable efficacy population for participants without evidence of infection before and during the vaccination regimen were similar in the BNT162b2 and placebo groups (Table 2). This analysis population had generally similar demographics compared to the safety population (refer to Section 2.5.5.5.1).

Demographic characteristics for the interim analysis Dose 2 all-available efficacy population were similar to the evaluable efficacy population.

Table 2. 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)

Table 2. 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] (%)
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)			
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

2.5.4.3.1.2. Primary Efficacy – 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 2).

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 3). 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 past SARS-CoV-2 infection before and during the 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 3. 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

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

Efficacy in Subgroups – 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 4).

Results for the Dose 2 all-available population were similar, with no clinically meaningful differences in VE on the basis of subgroup.

Table 4. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=16061)		Placebo (N[a]=16218)			
Efficacy Endpoint Subgroup	**n1[b]**	**Surveillance Time[c] (n2[d])**	**n1[b]**	**Surveillance Time[c] (n2[d])**	**VE (%)**	**(95% CI[e])**
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)

Table 4. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=16061)		Placebo (N[a]=16218)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])

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 eval

2.5.4.3.1.3. Additional Descriptive Efficacy Results – Interim Analysis

2.5.4.3.1.3.1. 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.

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.

2.5.4.3.1.3.2. Efficacy for Severe COVID-19 Cases – Interim Analysis

Severe cases of COVID-19 were evaluated from after Dose 1 onwards, reported for the Dose 1 all-available efficacy population (see efficacy analysis populations in Section 2.5.4.3.1.1).

As of the time of the interim analysis of efficacy, a total of 7 severe cases of COVID-19 were reported as occurring from Dose 1 onwards (Table 5). 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.

Severe COVID-19 cases are also discussed in Section 2.5.5.7.1 with regard to safety and the hypothetical risk of vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD).

Table 5. Severe COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population – Interim Analysis 1

	Vaccine Group (as Randomized)	
	BNT162b2 (30 µg) (N[a]=21617)	Placebo (N[a]=21633)
Efficacy Endpoint	**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.
PFIZER CONFIDENTIAL SDTM Creation: 05NOV2020 (20:48) Source Data: adc19ef Table Generation: 06NOV2020 (18:47)
(Cutoff Date: 04Nov2020, Snapshot Date: 04Nov2020) Output File: ./nda2_unblinded_ia/C4591001_IA_62/adc19ef_sev_cov_d1_aai

2.5.4.3.1.4. Efficacy Conclusions – Interim Analysis

Interim Analysis of Efficacy Against Confirmed COVID-19

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 the vaccination regimen, and a >99.99% posterior probability for the true VE being >30%, conditioning on available data.

Interim Analysis of Efficacy in Subgroups

There was no clinically meaningful difference 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 and 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.

Interim Analysis of Efficacy Against Severe Disease

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.

Overall Conclusions from Interim Analysis of Efficacy

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.

2.5.4.3.2. 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, in the prespecified final analysis of primary and secondary endpoints after accrual of 170 confirmed COVID-18 cases, with a final analysis cutoff date of 14 November 2020. Data were analyzed for the efficacy populations.

COVID-19 case evaluation for primary and secondary efficacy endpoints is discussed in Section 2.5.4.1. 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 the vaccination regimen. Participants with positive or unknown NAAT results at any illness visit prior to either 7 days after Dose 2 or 14 days after Dose 2 (depending on the primary or secondary endpoint definition) were not included in the evaluation for VE. Cases were counted from either 7 days or 14 days (depending on the endpoint definition) after Dose 2.

Efficacy population characteristics in the final analysis are presented in Section 2.5.4.3.2.1.1, and results of the final analysis are presented in Section 2.5.4.3.2.1.2 (primary endpoints) and Section 2.5.4.3.2.1.3 (secondary endpoints).

2.5.4.3.2.1.1. Efficacy Populations – Final Analysis

The proportions of participants included in the final analysis efficacy populations was similar in the BNT162b2 and placebo groups (Table 6). 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 (1.4%) in the BNT162b2 group and 60 participants (0.3%) in the placebo group excluded for having important protocol deviations on or prior to 7 days after Dose 2. A post hoc evaluation was performed to assess the imbalance of these important protocol deviations in the BNT162b2 and placebo groups for the final analysis of efficacy. This showed that the majority of exclusions from the evaluable efficacy (7 days) population in the BNT162b2 group were due to dosing/administration errors or administration of study intervention that was deemed not suitable for use. This is detailed in the C4591001 Final Analysis Interim CSR and in Module 2.7.3.

Table 6. Efficacy Populations

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) n[a] (%)	Placebo n[a] (%)	Total 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)

Table 6. Efficacy Populations

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) n[a] (%)	Placebo n[a] (%)	Total n[a] (%)
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)
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

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 in the BNT162b2 and placebo groups (Table 7). This analysis population had generally similar demographics compared to the safety population (refer to Section 2.5.5.5.1).

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 the Dose 2 evaluable efficacy (7 days) population.

Table 7. 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)
>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)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adsl_demo_7d_eval_eff

2.5.4.3.2.1.2. Primary Efficacy – Final Analysis

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

Signs and symptoms of COVID-19 cases contributing to efficacy analyses are presented in the C4591001 Final Analysis Interim CSR.

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

As noted above, overwhelming efficacy was declared at the first (and only) interim analysis for the first primary efficacy endpoint. A descriptive update based on 170 evaluable cases accrued at the time of the final analysis (of the other efficacy endpoints) is summarized below.

Among participants without evidence of SARS-CoV-2 infection before and during the 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 8). 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 (Table 9).

Table 8. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=18198)		Placebo (N[a]=18325)				
Efficacy Endpoint	**n1[b]**	**Surveillance Time[c] (n2[d])**	**n1[b]**	**Surveillance Time[c] (n2[d])**	**VE (%)**	**(95% CI[e])**	**Pr (VE >30% | data)[f]**
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.
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_eval

Table 9. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=18650)		Placebo (N[a]=18570)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]
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

2.5.4.3.2.1.2.2. 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 the 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 10). 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 11).

Table 10. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=19965)		Placebo (N[a]=20172)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]
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.
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 eval

Table 11. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=20488)		Placebo (N[a]=20459)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]
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

All Confirmed Cases of COVID-19 After Dose 1 – All-Available Efficacy 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 12, 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 (Table 12). 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 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.

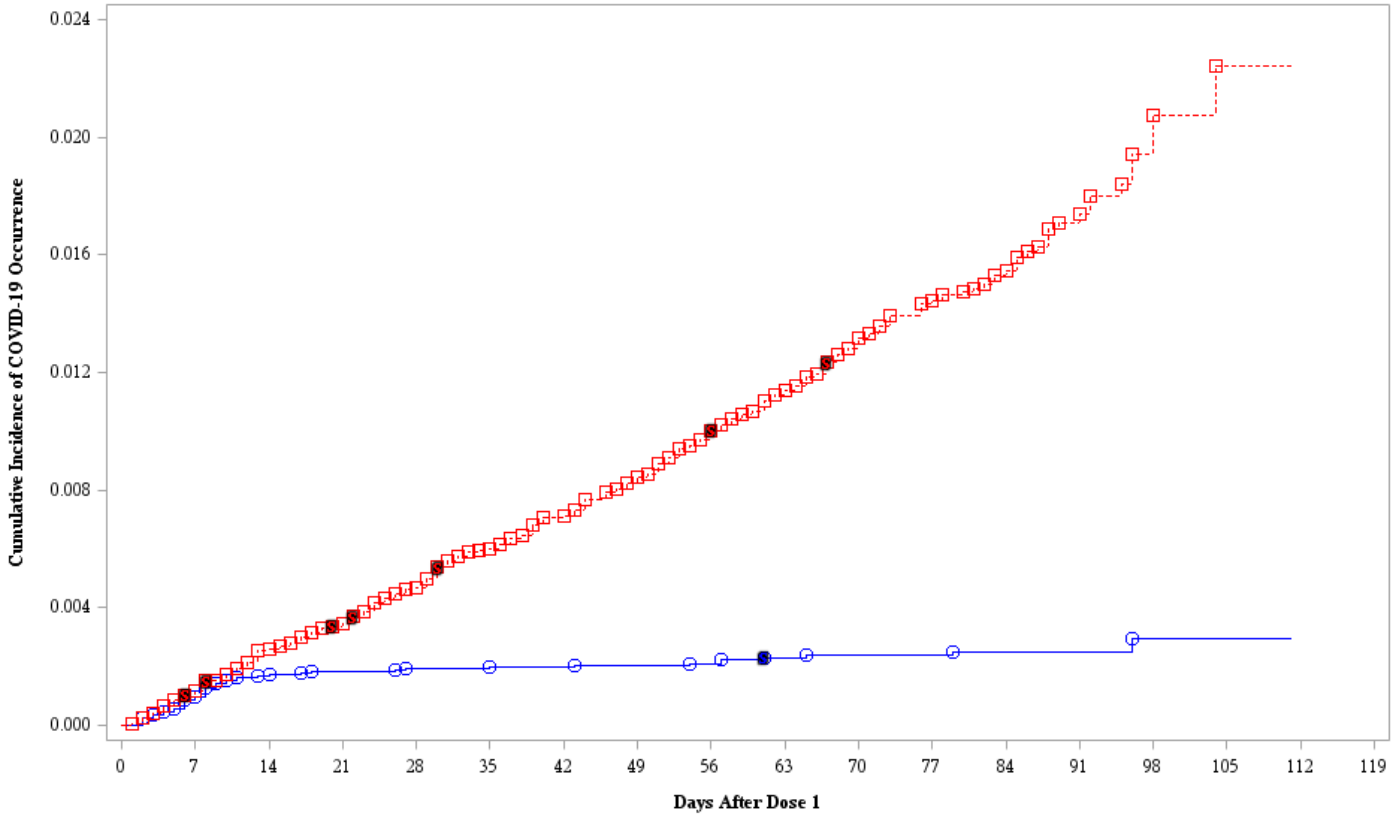
Table 12. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21669)		Placebo (N[a]=21686)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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; note that there are instances in which 2 cases in the placebo group are "overlapping" relative to the placebo curve. Severe COVID-19 cases reported in the final analysis are discussed further in Section 2.5.4.3.2.1.3.2.

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



No. with events/No. at risk

A:	0/21314	21/21230	37/21054	39/20481	41/19314	42/18377	42/17702	43/17186	44/15464	47/14038	48/12169	48/9591	49/6403	49/3374	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.
PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (10:49) Source Data: adc19ef Table Generation: 17NOV2020 (21:40)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adc19ef_f001_km_d1_aai

2.5.4.3.2.1.2.3. Vaccine Efficacy by Subgroup – Final Analysis

Subgroup Analyses by Age, Sex, Race, Ethnicity, and Country

For both primary endpoints, VE was also evaluated for subgroups of participants by age, sex race, ethnicity, and country (Table 13) (without evidence of prior infection) and Table 14 (with or without evidence of prior infection).

Among participants without prior evidence of SARS-CoV-2 infection, VE was >93% in all subgroups, with the exception of "all others" race group (89.3% VE) and Brazil (87.7% VE) (Table 13). Notably, VE was 94.7% (2-sided 95% CI: 66.7%, 99.9%) in participants ≥65 years of age (1 case in BNT162b2 group vs 19 cases in placebo group).

An additional analysis of age subgroups showed observed 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 15).

Among participants with or without prior evidence of SARS-CoV-2 infection, 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 14).

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 based on risk status were performed. Risk assessment included select comorbidities. At-risk participants were those meeting at least one Charlson Comorbidity Index condition (see Section 2.5.5.5.1 for Charlson comorbidities) or who were obese (defined as body mass index ≥30 kg/m^2).

Among participants without prior evidence of SARS-CoV-2 infection before and during the vaccination regimen, VE for at-risk participants was 95.3%, as compared with 94.7% for those not at-risk (Table 16). 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 comorbidity is provided in Table 17.

Table 13. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=18198)		Placebo (N[a]=18325)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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 13. 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

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

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

Table 14. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=19965)		Placebo (N[a]=20172)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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)

Table 14. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=19965)		Placebo (N[a]=20172)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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

Table 15. 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

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

Table 15. 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

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

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

Table 16. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=18198)		Placebo (N[a]=18325)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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 16. 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

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

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/m^2).
g. Obese is defined as BMI ≥30 kg/m^2.
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

Table 17. 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

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

Table 17. 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

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

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/m^2.
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

2.5.4.3.2.1.3. Secondary Efficacy – Final Analysis

2.5.4.3.2.1.3.1. Vaccine Efficacy For COVID-19 Occurring at Least 14 Days After Dose 2 – Final Analysis

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 the 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 18). 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 18. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=18175)		Placebo (N[a]=18261)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]
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)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File:
./nda2 unblinded/C4591001 Efficacy FA 164/adc19ef ve cov 14pd2 wo eval

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 the 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 19). 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 19. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=19965)		Placebo (N[a]=20171)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]
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.
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 14pd2 eval

2.5.4.3.2.1.3.2. 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.

Among participants without evidence of SARS-CoV-2 infection before and during the 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 20). 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 20. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=18198)		Placebo (N[a]=18325)				
Efficacy Endpoint	**n1[b]**	**Surveillance Time[c] (n2[d])**	**n1[b]**	**Surveillance Time[c] (n2[d])**	**VE (%)**	**(95% CI[e])**	**Pr (VE >30% | data)[f]**
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

Table 20. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=18198)		Placebo (N[a]=18325)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]

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)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File:
./nda2 unblinded/C4591001 Efficacy FA 164/adc19ef ve sev cov 7pd2 wo eval

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 the vaccination regimen, VE against severe COVID-19 occurring at least 7 days after Dose 2 was 66.3%, with 1 and 3 cases in the BNT162b2 and placebo groups respectively (Table 21). The posterior probability for the true vaccine efficacy greater than 30% is 74.19%.

Table 21. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=19965)		Placebo (N[a]=20172)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]
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 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 22). 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% (1 case in BNT162b2 and 4 cases in placebo groups) against severe COVID-19 occurring at least 7 days after Dose 2.

In addition to the C4591001 protocol specified definition of severe COVID-19 (provided in Section 2.5.4.1.1.3), a post hoc efficacy analysis for severe COVID-19 cases was conducted using the CDC definition of severe COVID-19 (hospitalization, admission to the ICU, intubation or mechanical ventilation, or death).[18] In this analysis, 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 23). The estimated VE against severe COVID-19 occurring after Dose 1 was 92.9% (2-sided 95% CI: 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 22. Vaccine Efficacy – First Severe COVID-19 Occurrence After Dose 1 – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21669)		Placebo (N[a]=21686)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adc19ef_ve_sev_cov_pd1_aai

Table 23. Vaccine Efficacy – First Severe COVID-19 Occurrence Based on CDC-Definition After Dose 1 – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=21669)		Placebo (N[a]=21686)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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_VRBPAC/adc19ef_ve_sev_cdc_pd1_aai

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

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 the 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 24). The posterior probability for the true vaccine efficacy greater than 30% is 74.32%.

Table 24. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=18175)		Placebo (N[a]=18261)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]
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.
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_14pd2_wo_eval

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

Among participants with or without evidence of SARS-CoV-2 infection before and during vaccination phase, 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 25). The posterior probability for the true vaccine efficacy greater than 30% is 74.18%.

Table 25. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=19965)		Placebo (N[a]=20171)				
Efficacy Endpoint	**n1[b]**	**Surveillance Time[c] (n2[d])**	**n1[b]**	**Surveillance Time[c] (n2[d])**	**VE (%)**	**(95% CI[e])**	**Pr (VE >30% | data)[f]**
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.
PFIZER CONFIDENTIAL SDTM Creation: 17NOV2020 (09:48) Source Data: adc19ef Table Generation: 17NOV2020 (16:47)
(Cutoff Date: 14NOV2020, Snapshot Date: 16NOV2020) Output File: ./nda2_unblinded/C4591001_Efficacy_FA_164/adc19ef_ve_sev_cov_14pd2_eval

2.5.4.3.2.1.3.3. Efficacy for COVID-19 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 the 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 26).

Table 26. 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

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

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

Among participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen, VE against CDC-defined COVID-19 occurring at least 7 days after 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 27).

Table 27. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=19965)		Placebo (N[a]=20172)			
Efficacy Endpoint	**n1[b]**	**Surveillance Time[c] (n2[d])**	**n1[b]**	**Surveillance Time[c] (n2[d])**	**VE (%)**	**(95% CI[e])**
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

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 the 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.

2.5.4.3.2.2. Efficacy Conclusions – Final Analysis

Final Analysis of Efficacy in the Evaluable Efficacy Population

In the final efficacy analysis, among participants without evidence of SARS-CoV-2 infection before and during the 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 the 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 endpoint analyses, 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 the 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 >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 the 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 >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 the 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 after Dose 2 in the study.

The efficacy analyses using CDC defined symptoms to identify a COVID-19 case gave similar efficacy results as the primary endpoints.

Final Analysis of Efficacy in the 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. Similar results were observed when using the CDC definition of severe disease.

Overall Conclusions from Final Analysis of Efficacy

Final efficacy results show that BNT162b2 at 30 µg provided protection against COVID-19 in participants with or without evidence of prior infection with SARS-CoV-2, including across demographic subgroups, with severe cases observed predominantly in the placebo group.

2.5.4.3.3. Updated Analysis of Efficacy in Study C4591001

Updated analyses of 1165 confirmed cases in blinded placebo-controlled follow-up from Dose 1 to the data cutoff date (13 March 2021) evaluated duration of protection. Updated 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. Data are summarized for the efficacy populations.

COVID-19 case evaluation for primary and secondary efficacy endpoints is discussed in Section 2.5.4.1. Efficacy endpoints evaluated confirmed COVID-19 cases in participants either without or with or without evidence of past SARS-CoV-2 infection before and during the vaccination regimen. Participants with positive or unknown NAAT results at any illness visit prior to either 7 days after Dose 2 were not included in the evaluation for VE. Cases were counted from 7 days after Dose 2.

Efficacy population characteristics in the updated analysis are presented in Section 2.5.4.3.3.1, and results of the updated analysis are presented in Section 2.5.4.3.3.2 and Section 2.5.4.3.3.3 (VE for participants either without or with or without prior evidence of SARS-CoV-2 infection, respectively), Section 2.5.4.3.3.4 (VE in demographic, risk, and comorbidity subgroups), and Section 2.5.4.3.3.5 (VE for severe disease as defined by the FDA and by the CDC).

2.5.4.3.3.1. Efficacy Populations – Updated Analysis

Disposition and Data Sets Analyzed

The proportions of participants included in the updated efficacy populations were similar in the BNT162b2 and placebo groups (Table 28).

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). Specifically, in the BNT162b2 group most PDs were due to dosing/administration errors (errors in dilution of the vaccine, 76 participants) or administration of investigational product that was deemed not suitable for use (temperature excursions in shipment or storage at the distributor, 110 participants) that would have not applied to placebo.

Table 28. 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]			

Table 28. Efficacy Populations – Blinded Placebo-Controlled Follow-up Period

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) n[a] (%)	Placebo n[a] (%)	Total n[a] (%)
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)
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

Demographics

Demographics of participants in the updated 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 29). This analysis population had generally similar demographics compared to the safety population (refer to Section 2.5.5.5.1).

Demographic characteristics for the Dose 1 all-available efficacy population and for participants with or without evidence of infection prior to 7 days after Dose 2 (evaluable efficacy [7 days] population) were similar to the evaluable efficacy (7 days) population.

Table 29. 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)
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)

Table 29. 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] (%)
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)

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/m^2 (≥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)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA/adsl demo 7d eval eff

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

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 30). The 2-sided 95% CI for vaccine efficacy was 89.0% to 93.2%. The posterior probability for the true VE being >30%, given the available data, was >99.99%.

The vaccine efficacy 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 30. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=20998)		Placebo (N[a]=21096)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]
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

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

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 31). The 2-sided 95% CI for vaccine efficacy was 88.8% to 93.0%. The posterior probability for the true VE being >30%, given the available data, was >99.99%.

The vaccine efficacy of BNT162b2 for the same efficacy 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 31. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=22166)		Placebo (N[a]=22320)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]
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)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adc19ef_ve_cov_7pd2_eval

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

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 <7 days after Dose 2.

All reports of COVID-19 with onset at any time after Dose 1 are accounted for in Table 32, which provides a summary of confirmed cases for all participants in the Dose 1 all-available efficacy (modified intention-to-treat) population adjusted for exposure, 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 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% 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.

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 32), at which point the curves diverge with cases steadily accumulating in the placebo group and remaining virtually flat in the BNT162b2 group.

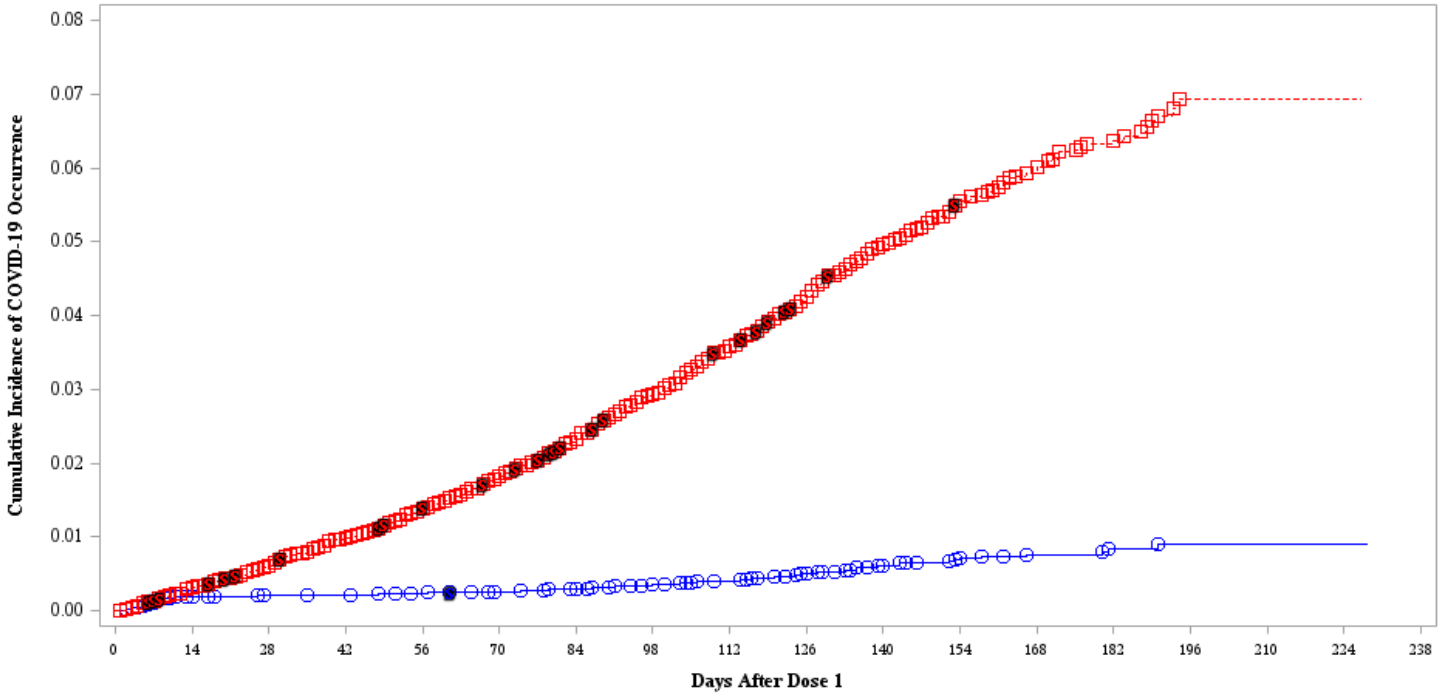
The darker-appearing symbols for both BNT162b2 (blue circles) and placebo (red squares) curves in Figure 2 have an "S" written inside the open symbol, which denotes severe cases. Severe COVID-19 cases reported in the updated analysis are discussed further in Section 2.5.4.3.3.5.

Table 32. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=23040)		Placebo (N[a]=23037)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2 unblinded/C4591001 BLA/adc19ef ve cov pd1 aai

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 – Updated Analysis



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

Note: "S" indicates subjects with severe COVID-19.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adc19ef Table Generation: 27MAR2021 (11:38)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adc19ef_f001_km_d1_aai

2.5.4.3.3.4. Vaccine Efficacy by Subgroup – Updated Analysis

Subgroup Analyses by Demographics and by Country

For both primary endpoints, VE was also evaluated for subgroups of participants by age, sex, race, ethnicity, country, and baseline SARS-CoV-2 status. Overall, the results show high VE across the subgroups. In the evaluable efficacy population among participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE was ≥90% in most subgroups, similar to the estimated 91.3% overall VE (Table 33).

High estimated VE was observed across age ranges/groups:

- 100.0% in participants 12 to 15 years of age
- 90.6% in participants 16 to 64 years of age
- 94.5% in participants ≥65 years of age
- 96.2% in those ≥75 years of age.

Estimated VE was 90.1% and 92.4% in male and female participants, respectively.

Estimated VE among race/ethnicity groups was:

- 91.3% among White participants
- 87.6% among Asian participants
- 88.5% among Hispanic/Latino participants.

Estimated VE by country was:

- 92.6% in the US
- 86.5% in Argentina
- 86.2% in Brazil
- 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 34). 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 35).

Subgroup Analyses by Baseline SARS-CoV-2 Status

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 34), and in the Dose 1 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 35).

It is important to note that the subgroup defined above includes participants with both past infections (positive for 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 34), 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 35). 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-2 infection.

Subgroup Analyses by Risk Status

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 BMI ≥30 kg/m^2).

Among participants without evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE was similar for participants at risk (91.6%) and for participants not at risk (91.0%) (Table 36). 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. The estimated VE was similar in obese (91.6%) and non-obese (91.1%) participants.

Results were similar among participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen (Table 37).

Subgroup Analyses by Comorbidity

Among participants without prior evidence of SARS-CoV-2 infection before and during the vaccination regimen, the estimated VE was similar for participants with any comorbidity (91.6% with 2-sided 95% CI of 88.2% to 94.3%) and for those with no comorbidity (91.0% with 2-sided 95% CI of 87.6% to 93.6%) (Table 38). When evaluated by type of comorbidity, the estimated VE was >85% for participants with each comorbidity evaluated, including any malignancy, cardiovascular disease, chronic pulmonary disease, diabetes, obesity, and hypertension.

Results were similar for participants with or without evidence of SARS-CoV-2 infection before and during the vaccination regimen (Table 39).

Table 33. 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

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

Table 33. 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

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

Table 33. 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

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

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: 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 wo sg eval

Table 34. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=22166)		Placebo (N[a]=22320)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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)

Table 34. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=22166)		Placebo (N[a]=22320)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Female	37	3.133 (10539)	462	3.093 (10769)	92.1	(88.9, 94.5)
Race						
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)

Table 34. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=22166)		Placebo (N[a]=22320)			
Efficacy Endpoint Subgroup	**n1[b]**	**Surveillance Time[c] (n2[d])**	**n1[b]**	**Surveillance Time[c] (n2[d])**	**VE (%)**	**(95% CI[e])**
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)
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)

Table 34. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=22166)		Placebo (N[a]=22320)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])

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

Table 35. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=23040)		Placebo (N[a]=23037)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[c])
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)

Table 35. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=23040)		Placebo (N[a]=23037)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
Race						
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						

Table 35. Vaccine Efficacy – First COVID-19 Occurrence After Dose 1, by Subgroup – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=23040)		Placebo (N[a]=23037)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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)
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

Table 36. 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

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

Table 36. 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

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

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/m^2 [≥16 Years of age] or BMI ≥95th percentile [12-15 Years of age]).
g. Subjects (≥16 Years of age) who had BMI ≥30 kg/m^2. 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

Table 37. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=22166)		Placebo (N[a]=22320)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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)
At risk[f]						
Yes	36	2.925 (9601)	410	2.807 (9570)	91.6	(88.1, 94.2)
No	45	3.584 (12041)	463	3.466 (12119)	90.6	(87.2, 93.2)
Age group (years) and at risk						
12-15 and not at risk	0	0.132 (867)	11	0.129 (864)	100.0	(61.1, 100.0)
12-15 and at risk	0	0.038 (242)	7	0.035 (230)	100.0	(36.2, 100.0)
16-64 and not at risk	44	2.887 (9254)	397	2.779 (9289)	89.3	(85.4, 92.4)
16-64 and at risk	30	2.186 (6964)	330	2.100 (6980)	91.3	(87.3, 94.2)
≥65 and not at risk	1	0.566 (1920)	55	0.559 (1966)	98.2	(89.6, 100.0)
≥65 and at risk	6	0.701 (2395)	73	0.672 (2360)	92.1	(82.0, 97.2)
Obese[g]						
Yes	28	2.207 (7139)	319	2.158 (7235)	91.4	(87.4, 94.4)
No	53	4.301 (14497)	554	4.114 (14448)	90.8	(87.9, 93.2)
Age group (years) and obese						
12-15 and not obese	0	0.148 (969)	14	0.145 (970)	100.0	(70.5, 100.0)
12-15 and obese	0	0.022 (140)	4	0.019 (124)	100.0	(-31.1, 100.0)
16-64 and not obese	49	3.303 (10629)	458	3.158 (10614)	89.8	(86.2, 92.5)
16-64 and obese	25	1.768 (5584)	269	1.719 (5649)	91.0	(86.4, 94.3)
≥65 and not obese	4	0.850 (2899)	82	0.811 (2864)	95.3	(87.6, 98.8)
≥65 and obese	3	0.417 (1415)	46	0.420 (1462)	93.4	(79.5, 98.7)

Table 37. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Risk Status – 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=22166)		Placebo (N[a]=22320)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])

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. Includes subjects who had at least one of the Charlson Comorbidity Index (CMI) category or obesity (BMI ≥30 kg/m^2 [≥16 Years of age] or BMI ≥95th percentile [12-15 Years of age]).
g. Subjects (≥16 Years of age) who had BMI ≥30 kg/m^2. 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 rg eval

Table 38. 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

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

Table 38. 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

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

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/m^2 (≥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

Table 39. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Comorbidity Status – 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=22166)		Placebo (N[a]=22320)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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)
Comorbidity						
No comorbidity	45	3.584 (12041)	463	3.466 (12119)	90.6	(87.2, 93.2)
Any comorbidity[f]	36	2.925 (9601)	410	2.807 (9570)	91.6	(88.1, 94.2)
Any malignancy	3	0.234 (792)	27	0.217 (762)	89.7	(66.5, 98.0)
Cardiovascular	3	0.180 (607)	23	0.163 (569)	88.2	(60.9, 97.7)
Chronic pulmonary disease	8	0.512 (1764)	72	0.480 (1750)	89.6	(78.4, 95.7)
Diabetes	9	0.485 (1597)	62	0.463 (1582)	86.1	(71.9, 93.9)
Obese (≥30.0 kg/m^2 [≥16 Years of age])	28	2.185 (6999)	315	2.139 (7111)	91.3	(87.2, 94.3)
Obese (≥95th percentile [12-15 Years of age])	0	0.022 (140)	4	0.019 (124)	100.0	(-31.1, 100.0)
Hypertension	15	1.535 (5078)	193	1.479 (5077)	92.5	(87.3, 95.9)
Diabetes (including gestational diabetes)	9	0.488 (1606)	64	0.466 (1596)	86.5	(72.8, 94.1)

Table 39. Vaccine Efficacy – First COVID-19 Occurrence From 7 Days After Dose 2, by Comorbidity Status – 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=22166)		Placebo (N[a]=22320)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])

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. 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/m^2 (≥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_cg_eval

2.5.4.3.3.5. Vaccine Efficacy for Severe COVID-19 Cases – Updated Analysis

Efficacy Against Severe COVID-19 (≥7 Days After Dose 2)

Participants Without Evidence of Infection Before and During Vaccination Regimen

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 40). The posterior probability for the true vaccine efficacy being >30%, given the available data, was >99.99%.

Table 40. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=20998)		Placebo (N[a]=21096)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]
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

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).[18] Among 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 41).

Table 41. 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

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

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 the vaccination regimen, 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: 70.9%, 99.9%), with 1 and 21 cases in the BNT162b2 and placebo groups, respectively (Table 42). The posterior probability for the true vaccine efficacy being >30%, given the available data, was >99.99%.

Table 42. 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

	Vaccine Group (as Randomized)						
	BNT162b2 (30 µg) (N[a]=22166)		Placebo (N[a]=22320)				
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])	Pr (VE >30% | data)[f]
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

In a supportive analysis conducted for efficacy against severe cases of COVID-19 using the CDC definition of severe COVID-19, among participants with or 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: 88.0%, 100.0%), with 0 and 32 cases in the BNT162b2 and placebo groups, respectively (Table 43).

Table 43. 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

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=22166)		Placebo (N[a]=22320)			
Efficacy Endpoint	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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.
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 eval

All Confirmed Cases of Severe COVID-19 After Dose 1 – Dose 1 All-Available 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 44). The estimated VE against severe COVID-19 occurring after Dose 1 was 96.7% (2-sided 95% CI: 80.3%, 99.9%).

In a supportive analysis conducted for efficacy against severe cases of COVID-19 using the CDC definition of severe COVID-19, among participants in the Dose 1 all-available efficacy population, 1 case of CDC-defined severe COVID-19 occurred after Dose 1 in the BNT162b2 group (but before Dose 2) compared to 45 cases in the placebo group. The estimated VE against severe CDC-defined COVID-19 occurring after Dose 1 was 97.8% (2-sided 95% CI: 87.2%, 99.9%).

Table 44. Vaccine Efficacy – First Severe COVID-19 Occurrence After Dose 1 – Blinded Placebo-Controlled Follow-up Period – Dose 1 All-Available Efficacy Population

	Vaccine Group (as Randomized)					
	BNT162b2 (30 µg) (N[a]=23040)		Placebo (N[a]=23037)			
Efficacy Endpoint Subgroup	n1[b]	Surveillance Time[c] (n2[d])	n1[b]	Surveillance Time[c] (n2[d])	VE (%)	(95% CI[e])
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.
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 cov pd1 aai

2.5.4.3.3.6. Efficacy Conclusions – Updated Analysis

Updated Analysis of Efficacy Against Confirmed COVID-19

In the updated descriptive efficacy analysis (data 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% (2-sided 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% (2-sided 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 Dose 1 all-available (modified intention-to-treat) population, regardless of evidence of infection before or during the vaccination regimen. In this analysis, the 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 this same Dose 1 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% 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.

Updated Analysis of Efficacy in 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 for demographic and risk subgroups, as follows:

- Estimated VE was ≥90% in most demographic subgroups, similar to the estimated 91.3% overall VE.

- High estimated VE was observed across age subgroups:
  - 100.0% in participants 12 to 15 years of age
  - 90.6% in participants 16 to 64 years of age
  - 94.5% in participants ≥65 years of age
  - 96.2% in participants ≥75 years of age.

- Estimated VE by country was 86.5% in Argentina; 86.2% in Brazil; 92.6% in the US; and 100.0% in South Africa, Germany, and Turkey.

The estimated VE was similar for participants at risk (91.6%) and those not at risk (91.0%). The estimated VE for participants ≥65 years of age who were at risk was 91.8%, as compared with 98.1% for those ≥65 years of age and not at risk. The estimated VE was similar in obese (91.6%) and non-obese (91.1%) participants. When evaluated by type of comorbidity, the estimated VE was >85% for participants with each comorbidity evaluated, including any malignancy, cardiovascular disease, chronic pulmonary disease, diabetes, obesity, and hypertension.

Updated Analysis of Efficacy Against Severe Disease

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 before and during the

vaccination regimen, also with 0 and 32 cases in the BNT162b2 and placebo groups, respectively.

Among participants in the Dose 1 all-available (modified intention-to-treat) population, regardless of evidence of infection before or during the vaccination regimen, the estimated VE against FDA-defined severe cases of COVID-19 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.

Overall Conclusions from Updated Analysis of Efficacy

Updated efficacy results show that BNT162b2 at 30 µg provided protection against COVID-19 in participants regardless of evidence of past infection with SARS-CoV-2, including across demographic and risk subgroups, with severe cases observed predominantly in the placebo group.

2.5.4.4. Immunogenicity Results

Details of immunogenicity results, including for additional endpoints, are presented as follows:

Study BNT162-01: Module 5.3.5.1 BNT162-01 Interim CSR.

Study C4591001:

Phase 1: immunogenicity results for all candidates and dose levels up to 1 month after Dose 2 are presented in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR; immunogenicity results for Phase 1 participants in the BNT162b2 30 µg up to 6 months after Dose 2 are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR.

Phase 2: immunogenicity results up to 1 month after Dose 2 are presented in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR.

Immunogenicity data are also presented in Module 2.7.3 and summarized below.

2.5.4.4.1. Phase 1 Immunogenicity in Study BNT162-01

Details of immunogenicity results from the Phase 1 portion of Study BNT162-01 are presented in Module 5.3.5.1 BNT162-01 Interim CSR Section 10 and Section 11 and summarized below.

This section focuses primarily on Study BNT162-01 immune response data for BNT162b2, which was the candidate selected for further development in Phase 2/3 of pivotal Study C4591001. Summary serology data for the BNT162b1 groups are also presented.

In Study BNT162-01, T cell data are presented for BNT162b2 groups up to 7 days after Dose 2; a subset of participants had blood samples collected on Day 85 (9 weeks, or approximately 2 months, after Dose 2) and Day 184 (approximately 6 months after Dose 2) and analyzed. Immunogenicity data (neutralizing titers) are summarized for both BNT162b1 and BNT162b2 groups up to approximately 2 months after Dose 2. Evaluable ELISPOT data (data cutoff date: 02 March 2021) were available from 76 participants across dose levels of

BNT162b2: 47 younger participants 18 to 55 years of age (dose range: 1 to 30 µg), and 29 older participants 56 to 85 years of age (dose range: 10 to 30 µg).

Evaluable intracellular cytokine staining and FACS data (data cutoff date: 02 March 2021) were available for 76 participants across dose levels of BNT162b2: 47 younger participants (dose range: 1 to 30 µg) and 29 older participants (dose range: 10 to 30 µg).

Serum neutralizing titers (data cutoff date: 23 October 2020) were available for younger participants who received BNT162b1 across dose levels (dose range: 1 to 60 µg; n=12 per group), with no data available for older participants at this time; and for younger participants who received BNT162b2 (dose range: 1 to 30 µg; n=12 per group) and older participants who received BNT162b2 (dose level: 20 µg; n=12 per group).

The immunogenicity set was generally similar to the safety set (refer to Section 2.5.5.2.1).

2.5.4.4.1.1. T Cell Response Data

T cell mediated immune responses were evaluated using ELISPOT and intracellular cytokine staining visualized with FACS, for data available up to a cutoff date of 02 March 2021. BNT162b2 induced poly-functional and pro-inflammatory CD4+ and CD8+ T cell responses in most participants in both the younger and older age groups. Re-stimulation of PBMCs with peptide pools representing the encoded antigen (full-length S protein) demonstrated a helper response characterized by a robust IFNγ and IL-2 response and only minor IL-4 production. This cytokine profile indicates presence of a favorable Th1 response and absence of a potentially deleterious Th2 immune response.

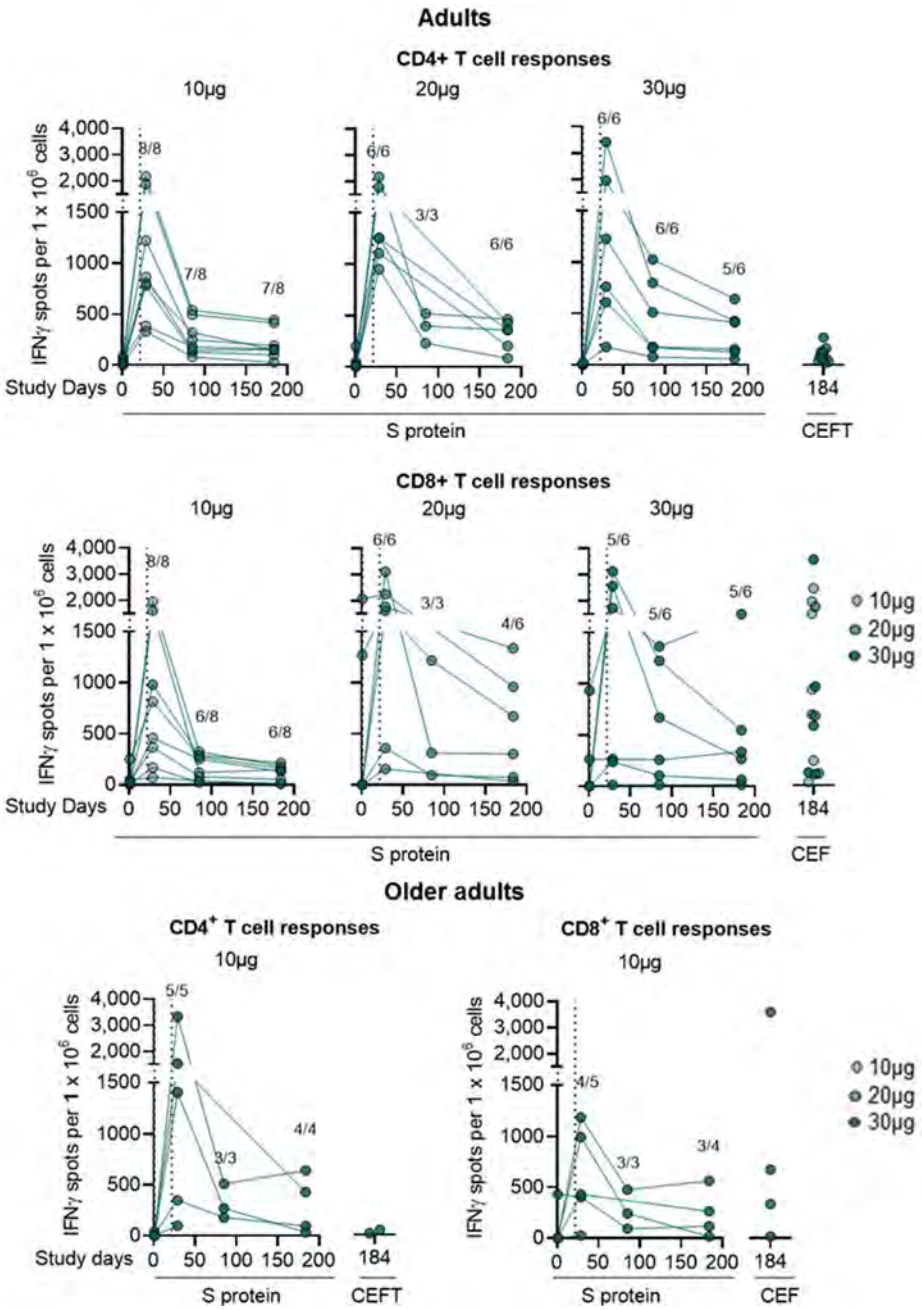
2.5.4.4.1.1.1. ELISPOT Results

BNT162b2 induced strong SARS-CoV-2 S protein-specific CD4+ T cell responses in all participants in all of the dosed younger and older participants (76/76). CD8+ T cell responses were induced in 45/47 younger participants (95.7%) of in 24/29 older participants (82.8%). Overall, the magnitude of the BNT162b2 induced responses was comparable in younger and older participants receiving 30 µg of BNT162b2 (Figure 3). 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.

Dosing twice with BNT162b2 led to a substantial increase in incidence and magnitude of T cell responses in both age groups. While the magnitude of responses was similar across BNT162b2 dose levels, the magnitude of CD8+ T cell responses was highest in the 30 µg group. Participants with the strongest CD4+ T cell responses had >10-fold of the memory responses observed in the same individuals against immunodominant peptides from the benchmarking epitope pool, CEFT (Figure 3). CD8+ T cell responses in these same individuals were comparable with memory responses against the epitope benchmarking pool, CEF. BNT162b2 induced CD4+ and CD8+ T cell responses were decreased on Day 85 (approximately 2 months after Dose 2) but remained detectable on Day 184 (approximately 6 months after Dose 2) in almost all participants vaccinated with dose levels >10 µg, at levels higher than or within range of recall antigen memory responses (Figure 3).

BNT162b2 induced de novo RBD and S protein specific T cell responses were observed for CD4+ T cells in 100% of participants and for CD8+ T cells in 96.6% of participants.

Figure 3. Durability of BNT162b2 Induced CD4+ and CD8+ T Cell Responses Against Full-Length S Protein



ELISPOT data are plotted for BNT162b2 groups from Day 1 (before Dose 1), Day 29, Day 85, and Day 184. Vertical dotted lines indicate the time of administration of Dose 2 (on Day 22). Common pathogen epitope pools (CEF, CEFT) assessed T cell reactivity; cell culture medium was a negative control. Each dot represents the sum of normalized mean spot count from duplicate wells stimulated with 2 peptide pools corresponding to full-length wild-type S protein for 1 study participant after subtracting medium-only control. Ratios above the data points represent the number of participants with detectable CD4+ or CD8+ T cell responses within the total number of participants with available data at that timepoint and within that group.

2.5.4.4.1.1.2. Intracellular Cytokine Production

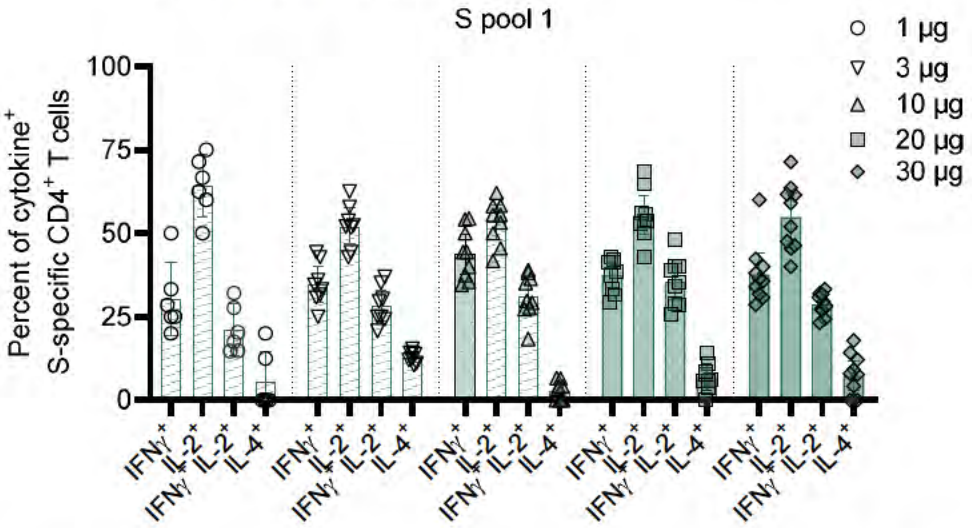
Functionality and polarization of S-specific BNT162b2 induced SARS-CoV-2 T cells were assessed by intracellular accumulation of cytokines IFNγ, IL-2, and IL-4 measured after stimulation with overlapping peptide pools representing the full-length sequence of the whole SARS-CoV-2 S protein. For benchmarking, PBMC fractions from convalescent patients with virologically confirmed COVID-19 were used.

BNT162b2 induced T cell responses, especially for CD8+ T cells, were not limited to the RBD, as pronounced and strong T cell recognition of non-RBD regions of the S protein were observed. BNT162b2 induced poly-functional and pro-inflammatory CD4+ and CD8+ T cell responses in most participants. The Th1 polarization of the T helper response was characterized by robust IFNγ and IL-2, and only minor IL-4, production upon antigen-specific re-stimulation (SARS-CoV-2 S protein peptide pools). No clear BNT162b2 dose dependency was observed, and cytokine responses in older participants were mostly identical in response pattern and intensity with that in younger participants.

Two doses of BNT162b2 induced CD4+ and CD8+ S-specific T cell responses in both age groups. Testing for SARS-CoV-2 S protein specific T cell responses was performed with two different peptide pools: sub-pool 1 comprising overlapping peptides from the N-terminal region (which is not equivalent to structural domains) and sub-pool 2 comprising C-terminal regions of the S protein.

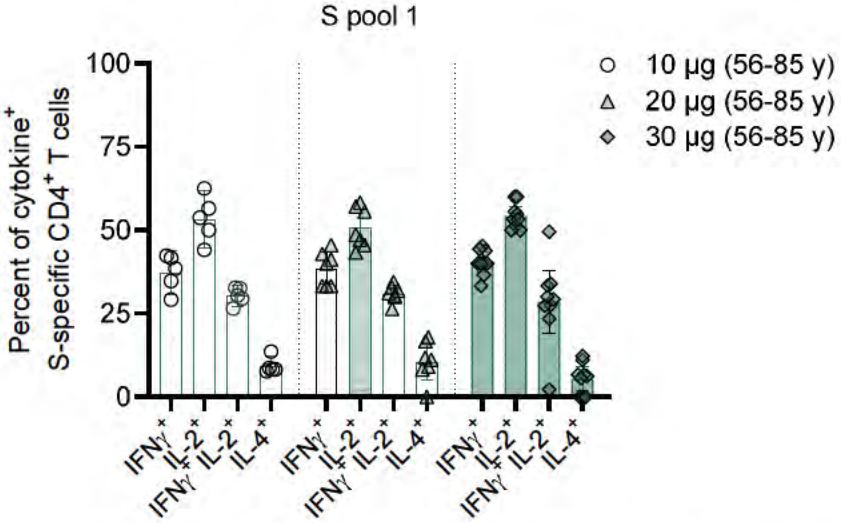
S-specific CD4+ T cells had a Th1-skewed cytokine profile with secretion of IFNγ or IL-2, or both (Figure 4 and Figure 5 for younger and older age groups in response to sub-pool 1 stimulation). Almost no Th2 cytokine IL-4 secreting T cells were detectable in response to S peptide sub-pool stimulations. BNT162b2 induced T cell cytokine production therefore suggested a Th1 profile characterized secreting IFNγ, or IL-2, or both at Day 29 (7 days after Dose 2).

Figure 4. S-Specific CD4+ T Cell Cytokine Production in Response to BNT162b2 – 18 to 55 Years of Age



Bars represent the arithmetic means with 95% CIs. Cytokine production was calculated by summing fractions of all CD4+ T cells positive for IFNγ, IL-2, IFNγ and IL-2, or IL-4 following stimulation with S peptide sub-pool 1, setting this sum to 100%, and calculating the fraction of each cytokine producing subset. CD4+ non-responders (ie, participants with frequency of total cytokine producing CD4+ T cells <0.03%) were excluded from analysis: 1 µg, n=2; 3 µg, n=1; and 10 µg, n=1.

Figure 5. S-Specific CD4+ T Cell Cytokine Production in Response to BNT162b2 – 56 to 85 Years of Age



Bars represent the arithmetic means with 95% CIs. Cytokine production was calculated by summing fractions of all CD4+ T cells positive for IFNγ, IL-2, IFNγ and IL-2, or IL-4 following stimulation with S peptide sub-pool 1, setting this sum to 100%, and calculating the fraction of each cytokine producing subset. CD4+ non-responders (ie, participants with frequency of total cytokine producing CD4+ T cells <0.03%) were excluded from analysis: 10 µg, n=4 and 20 µg, n=1.

S-specific IFNγ secretion was detected in CD8+ T cells at Day 29 in 65/79 participants (43/50 younger participants and 22/29 older participants); IL-2 secreting CD8+ T cells were also detected. Fractions of S-specific IFNγ+ CD8+ T cells targeting the N-terminal domain of the S protein reached up to 1.24% of total peripheral blood CD8+ T cells for the younger participants who received 20 or 30 µg dose levels, and up to 1.57% for older participants who received 30 µg. Preexisting CD8+ T cell responses against the C-terminal region of the S protein were detected in 17/79 dosed participants (range: 0.07 to 5.59% IFNγ-producing CD8+ T cells). In 5/17 participants, these preexisting responses were slightly amplified upon BNT162b2 dosing.

The mean fractions of S-specific CD4+ and CD8+ T cells from BNT162b2 vaccinated participants were substantially higher at Day 29 than that observed in 18 patients who recovered from COVID-19; the S protein sub-pool 1 IFNγ CD8+ response of 30 µg dosed participants was 12.5-fold higher. Importantly, for the clinically targeted 30 µg dose level, cytokine production elicited by BNT162b2 vaccination was mostly identical for older and younger participants with regard to cytokine response patterns and intensity.

For the majority of participants, the strong S-specific IFNγ+ and IL-2+ CD8+ T cell responses and Th1 CD4+ T cell responses contracted by Day 43 (3 weeks after Dose 2), and plateaued at a lower level towards Day 85 (approximately 2 months after Dose 2). This observation held true for all dose groups analyzed, with varying response magnitudes between individuals. For younger participants, the cell mediated immune responses were detectable until Day 184 (approximately 6 months after Dose 2). Note that Day 184 PBMC samples from older participants were not yet available at the time of this submission.

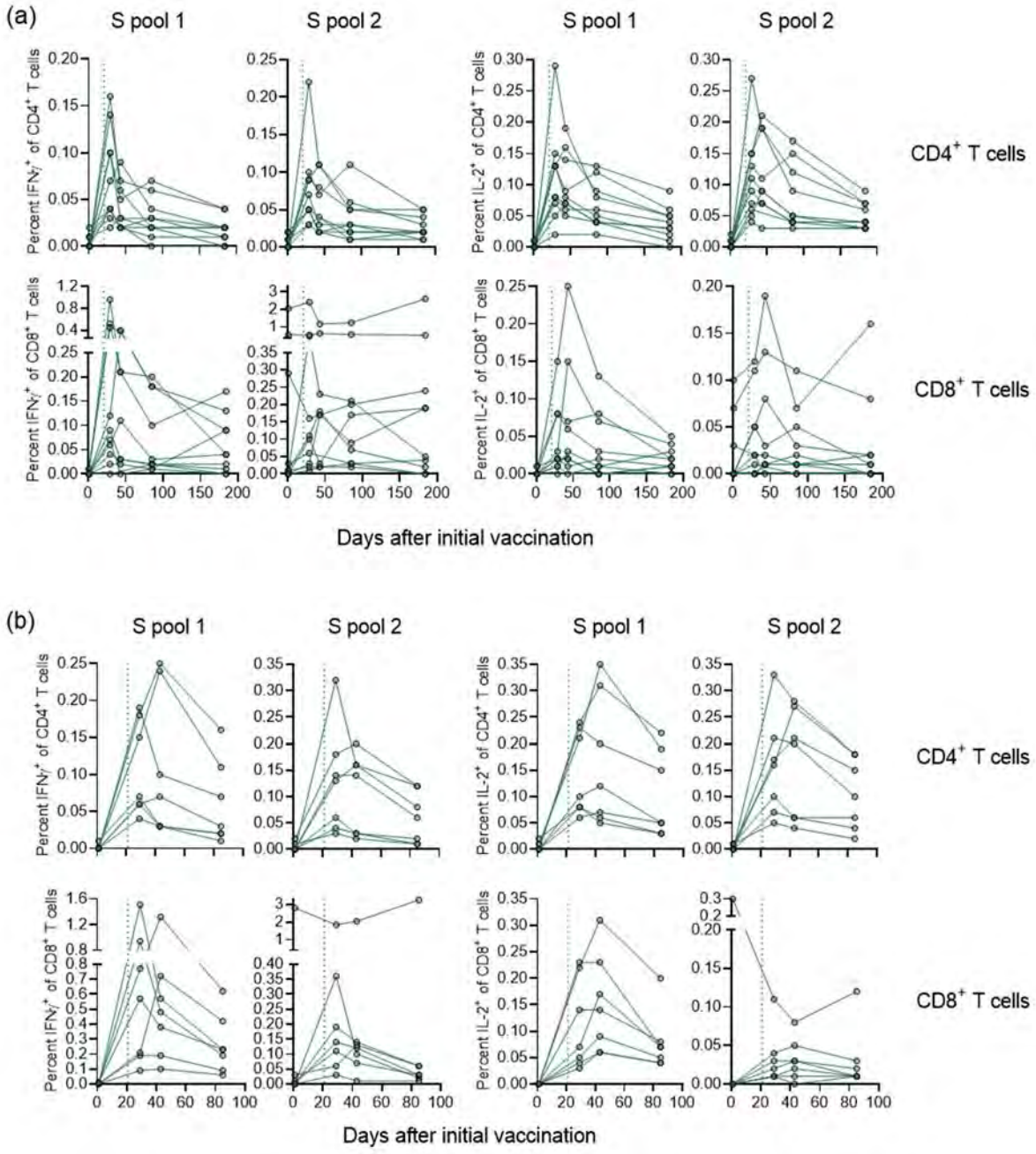
The impact of SARS-CoV-2 infection on persistence of vaccine induced immune response could not be evaluated since participants were not routinely monitored for infection in Study BNT162-01.

Persistence of S-specific CD4+ and CD8+ T cells producing the indicated cytokines (IFNγ and IL-2) as a fraction of the total circulating CD4+ and CD8+ T cells are shown in Figure 6, which includes data for the 30 µg BNT162b2 dose group in younger and older participants and is considered representative of observations for other dose groups.

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 indicating a polyvalent immune recognition of multiple independent CD4+ and CD8+ restricted epitopes across the entire S protein.

BNT162b2 induced poly-functional and pro-inflammatory CD4+ and CD8+ T cell responses in nearly all participants and persisted in the majority of participants for up to approximately 6 months. The Th1 polarization of the Th1 T cell response was characterized by robust production of IFNγ and IL-2. Only minor IL-4 production was observed upon antigen-specific (ie, wild-type SARS-CoV-2 S protein peptide pools) re-stimulation, which was reduced in magnitude, at later time points.

Figure 6. Persistence of S-Specific CD4+ T Cell Cytokine Production in Response to BNT162b2



Cytokine release data are plotted for the BNT162b2 30 µg dose level group from Day 1 (before Dose 1), Day 29, Day 43, Day 85, and Day 184. Vertical dotted lines indicate the time of administration of Dose 2 (on Day 22).
(a) Percentage of IFNγ+ CD4+ and CD8+ T cells for younger (n=10) participants who received BNT162b2 30 µg.
(b) Percentage of IFNγ+ CD4+ and CD8+ T cells for older (n=7) participants who received BNT162b2 30 µg.

2.5.4.4.1.2. SARS-CoV-2 Neutralization Titers

Results for serum neutralizing titers available for the immunogenicity set up to the immunogenicity data cutoff date (23 October 2020) as follows:

- **BNT162b1**: younger participants: N=60, n=12 each in 1, 10, 30, 50, and 60 µg groups with data available up to Day 43 for all doses; no data available for older participants.

- **BNT162b2**: younger participants: N=60, n=12 each in 1, 3, 10, 20, and 30 µg groups with data available up to Day 50 for 1 and 3 µg and up to Day 85 for 10, 20, and 30 µg; older participants: N=36, n=12 each in 10, 20, and 30 µg groups; up to Day 29 for 20 µg.

In Study BNT162-01, at 21 days after administration of Dose 1 and prior to administration of Dose 2 (Day 22), both BNT162b1 and BNT162b2 showed modest, dose-dependent increases in SARS-CoV-2 50% neutralizing GMTs over baseline for both age groups.

For BNT162b1, by 7 days after Dose 2 (Day 29) there was a clear dose-level booster response from 10 µg to 50 µg of BNT162b1 for younger participants. Note: the group receiving BNT162b1 at the 60 µg dose level did not receive a second dose per SRC decision based on reactogenicity of the initial 60 µg dose; for this dose group, neutralizing GMTs remained at a lower level, indicating a booster dose is necessary to increase functional antibody titers. No data for the older group are available at this time.

For BNT162b2, by 7 days after Dose 2 (Day 29) GMTs had increased substantially in younger participants who received doses of ≥3 µg and in older participants who received 20 µg. On Day 29 (1 week after Dose 2 of BNT162b2), neutralizing GMTs were comparable in the younger and older age groups at the 20 µg dose level. On Day 43 (3 weeks after Dose 2 of BNT162b2), neutralizing GMTs in the younger groups decreased at the 3, 20, and 30 µg dose levels. Thereafter, neutralizing GMTs remained stable up to Day 85 (approximately 2 months after Dose 2) for younger dose groups of 10, 20, and 30 µg.

Overall, both vaccine candidates elicited a boost effect after receiving Dose 2 that was most pronounced at the 30 µg dose level.

HCS Comparison

For benchmarking, neutralizing GMTs across 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.[19,20]

For younger BNT162b1 recipients, Day 43 (3 weeks after Dose 2) neutralizing GMTs ranged from 0.7- to 3.6-fold that of the HCS panel. Data for the older group are unavailable at this time.

For younger BNT162b2 recipients at 10 to 30 µg dose levels, Day 85 (approximately 2 months after Dose 2) neutralizing GMTs ranged from 1.3- to 1.9-fold that of the HCS panel. Preliminary data for older BNT162b2 recipients were available through Day 29 (1 week after Dose 2) for the 20 µg dose level, which showed neutralizing GMTs exceeding that of the HCS panel.

2.5.4.4.2. Phase 1 Immunogenicity in Study C4591001

Details of immunogenicity results from the Phase 1 portion of Study C4591001 up to 1 month after Dose 2 are presented in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 10 and Section 11.2.

Details of immunogenicity results for Phase 1 participants in the BNT162b2 30 µg up to 6 months after Dose 2 are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Section 10 and Section 11.2.

This section focuses on immunogenicity for dose level groups for both vaccine candidates that were administered as 2 doses at the same dose level. Note that the group receiving BNT162b1 at the 100 µg dose level received a second dose of 10 µg, per IRC decision based on reactogenicity of the initial 100 µg dose. This dose level was described in detail in the C4591001 Final Analysis Interim CSR but is not discussed further in this section.

The data cutoff date for immunogenicity analyses of Phase 1 participants was 24 August 2020 for up to 1 month after Dose 2 of both vaccine candidates (BNT162b1 and BNT162b2). Data up to 6 months after Dose 2 are available for participants who received BNT162b2 30 µg have a data cutoff of 13 March 2021.

The Phase 1 immunogenicity populations were generally similar to the Phase 1 safety population (refer to Section 2.5.5.3.1).

Results for the all-available immunogenicity population in the younger and older age groups were similar to those observed for the evaluable immunogenicity population.

2.5.4.4.2.1. SARS-CoV-2 Neutralizing Titers and Antigen-Binding IgG Concentrations

Geometric Mean Titers/Concentrations (GMTs/GMCs)

Overall, for both the BNT162b1 and the BNT162b2 recipients in both age groups, SARS-CoV-2 50% neutralizing GMTs modestly increased by at 3 weeks after Dose 1 and prior to receiving Dose 2 (Day 21) and were substantially increased by 7 days after Dose 2 (Day 28).

In the younger age groups, SARS-CoV-2 50% neutralizing GMTs modestly increased by 3 weeks after Dose 1 and prior to Dose 2 (Day 21) and were substantially increased by 7 days after Dose 2 of BNT162b1 (Day 28), with the highest neutralizing GMTs across vaccine candidates observed in the 30 µg dose groups.

Similar trends were observed in the older age groups for both vaccine candidates. Generally, neutralizing GMTs in the older age group tended to be somewhat lower than the GMTs in the younger age group at most time points for both BNT162b1 and BNT162b2 recipients.

Overall, for both the BNT162b1 and the BNT162b2 recipients, and in both age groups, RBD- and S1-binding GMCs increased substantially by 3 weeks after Dose 1 and prior to receiving Dose 2 (Day 21) and were further increased 7 days after Dose 2 (Day 28). Responses were maintained through 1 month after Dose 2 (Day 52).

In the younger age groups, RBD- or S1-binding GMCs increased substantially by Day 21 after Dose 1 of BNT162b1 and further increased 7 days after Dose 2 (Day 28) of BNT162b1, with higher GMCs observed in the 30 µg dose group.

Similar trends were observed in the older age groups, with higher S1-binding GMCs observed in the 20 µg and/or 30 µg dose groups for both vaccine candidates. GMCs in the older age group were generally lower than the GMCs in the younger age group.

HCS Comparison

BNT162b1 and BNT162b2 GMTs were compared with neutralizing antibody levels with an HCS panel, composed of 38 human SARS-CoV-2 infection/COVID-19 convalescent sera, drawn from participants 18 to 83 years of age at least 14 days after PCR-confirmed diagnosis, and at a time when participants were asymptomatic.[19,20] In Phase 1 of Study C4591001, GMTs measured 7 days after Dose 2 (Day 28) of BNT162b1 or BNT162b2 at the 30 µg dose level were 267.1 and 100.8 for younger and older participants who received BNT162b1, and 360.9 and 155.7 for younger and older participants who received BNT162b2. These GMTs were approximately 2.8- to 3.8-times that of the HCS panel GMT for younger participants, and 1.1- to 1.7-times that of the panel for older participants. By 1 month after Dose 2 (Day 52), GMTs were generally stable and were approximately 1.5- to 1.9-times that of the convalescent serum panel GMT for younger participants, and 1.5- to 1.6-times that of the panel for older participants. These comparisons to HCS further support the benefit of both candidates at the 30 µg dose level. The comparison of SARS-CoV-2 neutralizing titers to both study candidates to the HCS panel also showed the benefit of the second dose, with a dose response up to 30 µg.

Persistence of Immune Response Up to 6 Months After Dose 2 of BNT162b2 30 µg

Neutralizing GMTs and S1-binding GMCs were evaluated at 6 months after Dose 2 for the Phase 1 groups of participants who received BNT162b2 at 30 µg and corresponding placebo recipients. Samples from some earlier time points (ie, from Day 1 through Day 52) were re-analyzed with the 6-month post Dose 2 (Day 202) data for consistency in reporting.

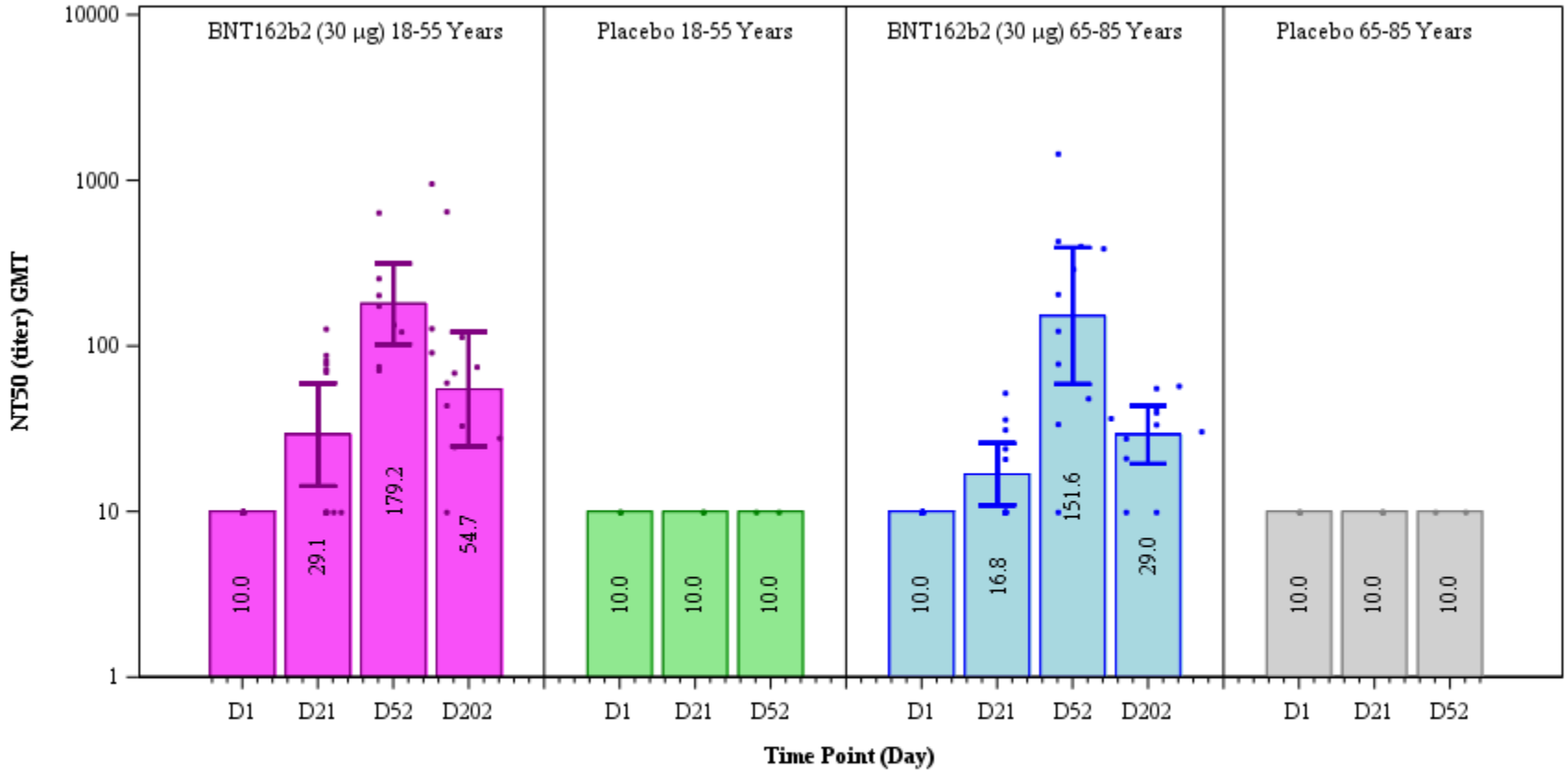
Geometric Mean Titers (GMTs) and Geometric Mean Concentrations (GMCs)

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. Observed S1-binding IgG GMCs at 6 months after Dose 2 also declined.

At 6 months after Dose 2, both GMTs and GMCs remained higher than pre-vaccination and placebo control levels.

For Phase 1 data available up to 6 months after Dose 2, GMTs are shown in Figure 7 and GMCs are shown in Figure 8.

Figure 7. 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.

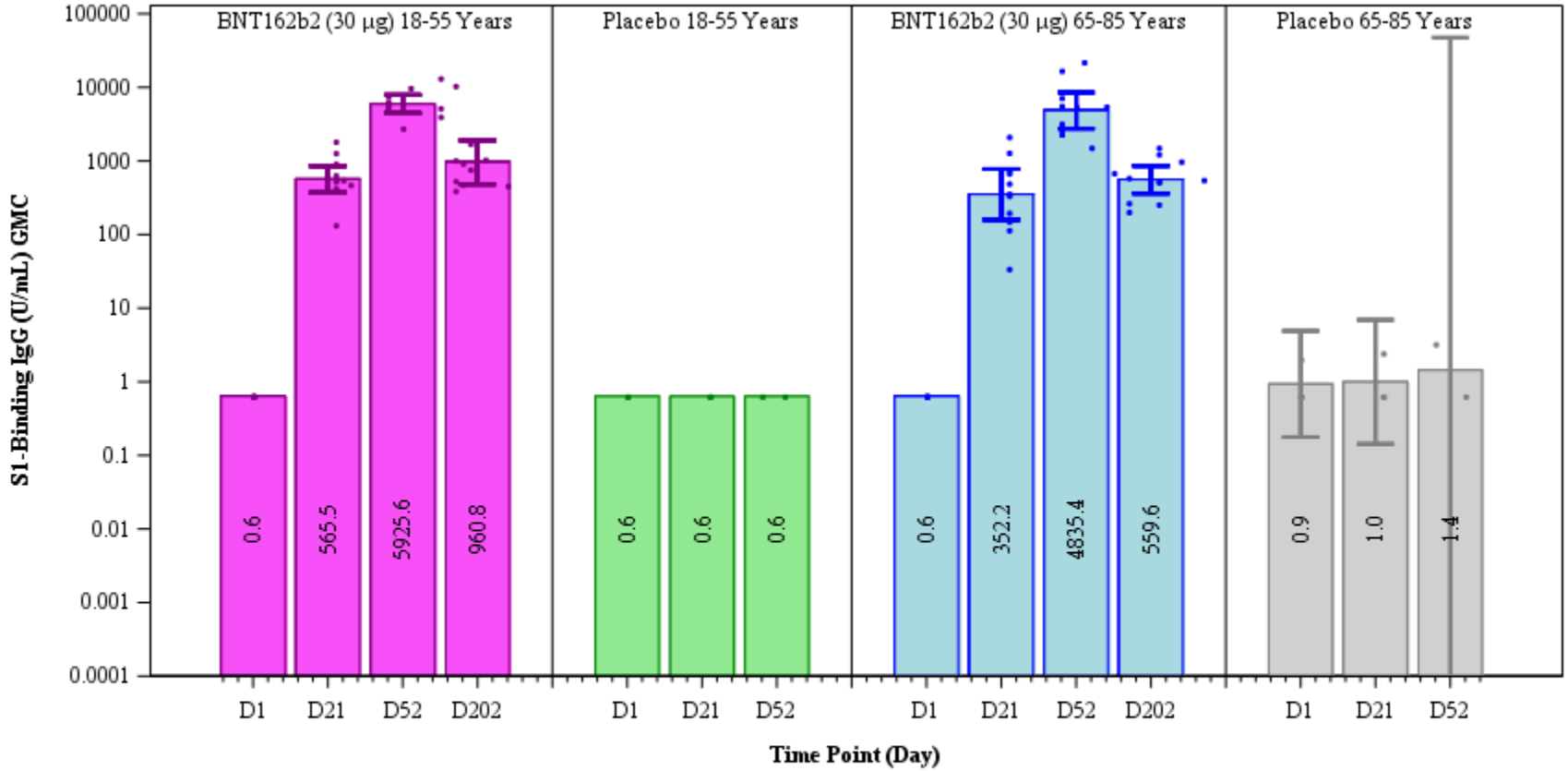
Note: Blood samples from the Day 7 and Day 14 post–Dose 2 visits are not included since these samples were not retested with the 6-month post–Dose 2 samples.

Note: Dots represent individual antibody levels.

Note: Number within each bar denotes geometric mean titer.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:25) Source Data: adva Table Generation: 01APR2021 (02:17) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA1/adva_f002_sars_50_b2_p1

Figure 8. 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.

PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:25) Source Data: adva Table Generation: 01APR2021 (02:19) (Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA1/adva_f002_s1_b2_p1

Geometric Mean Fold Rises (GMFRs)

In the younger and older age groups, respectively, GMFRs of SARS-CoV-2 serum 50% neutralizing titers from before vaccination with BNT162b2 30 µg to each subsequent time point were 2.9 and 1.7 at Day 21 (before Dose 2); 17.9 and 15.2 at 1 month after Dose 2; 5.5 and 2.9 at 6 months after Dose 2. Results for GMFRs of S1-binding IgG concentrations reflected similar trends.

Geometric Mean Ratios (GMRs)

At 6 months after Dose 2 of BNT162b2 30 µg, GMRs of SARS-CoV-2 50% neutralizing titers to S1-binding IgG levels were 0.057 in the younger age group and 0.052 in the older age group. These values are similar to those observed at Day 21.

Number (%) of Participants Achieving a ≥4-Fold Rise from Baseline

In the younger age group, the proportions of participants achieving a ≥4-fold rise 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 of BNT162b2 30 µg. In the older age group, 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 of BNT162b2 30 µg.

With respect to S1-binding IgG concentrations, 100% of participants in both age groups had a ≥4-fold increase from baseline at each of these time points.

2.5.4.4.3. Phase 2 Immunogenicity in Study C4591001

Details of immunogenicity results from the Phase 2 portion of Study C4591001 are presented in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 10 and Section 11 and summarized below.

The data cutoff date for immunogenicity analyses of Phase 2 participants was 12 October 2020 and included data up to 1 month after Dose 2. Data from the 6-month time point were not available at the time of the submission data cutoff date.

2.5.4.4.3.1. Immunogenicity Populations

Disposition and Data Sets Analyzed

The 360 participants enrolled in Phase 2 were randomized 1:1 to the BNT162b2 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 45).

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.

Immunogenicity results are currently available for the pre-vaccination 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 45. 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, according to 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 46).

Table 45. Immunogenicity Populations – Phase 2

	Vaccine Group (as Randomized)				
	BNT162b2 (30 µg)			Placebo	
	18-55 Years n[a] (%)	56-85 Years n[a] (%)	18-85 Years n[a] (%)	18-85 Years n[a] (%)	Total 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

Table 46. Demographic Characteristics – Phase 2 – Dose 2 Evaluable Immunogenicity Population

	Vaccine Group (as Randomized)				
	BNT162b2 (30 µg)			Placebo	
	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] (%)	Total (N[a]=336) 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)

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: 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

2.5.4.4.3.2. SARS-CoV-2 Neutralizing Titers and S1-Binding IgG Concentrations

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 defined by both SARS-CoV-2 50% neutralizing titers (GMTs) (Figure 9) and S1-binding IgG concentrations (GMCs) (Figure 10). GMTs/GMCs were higher in younger participants (18 to 55 years of age) than in older participants (56 to 85 years of age) (Table 47).

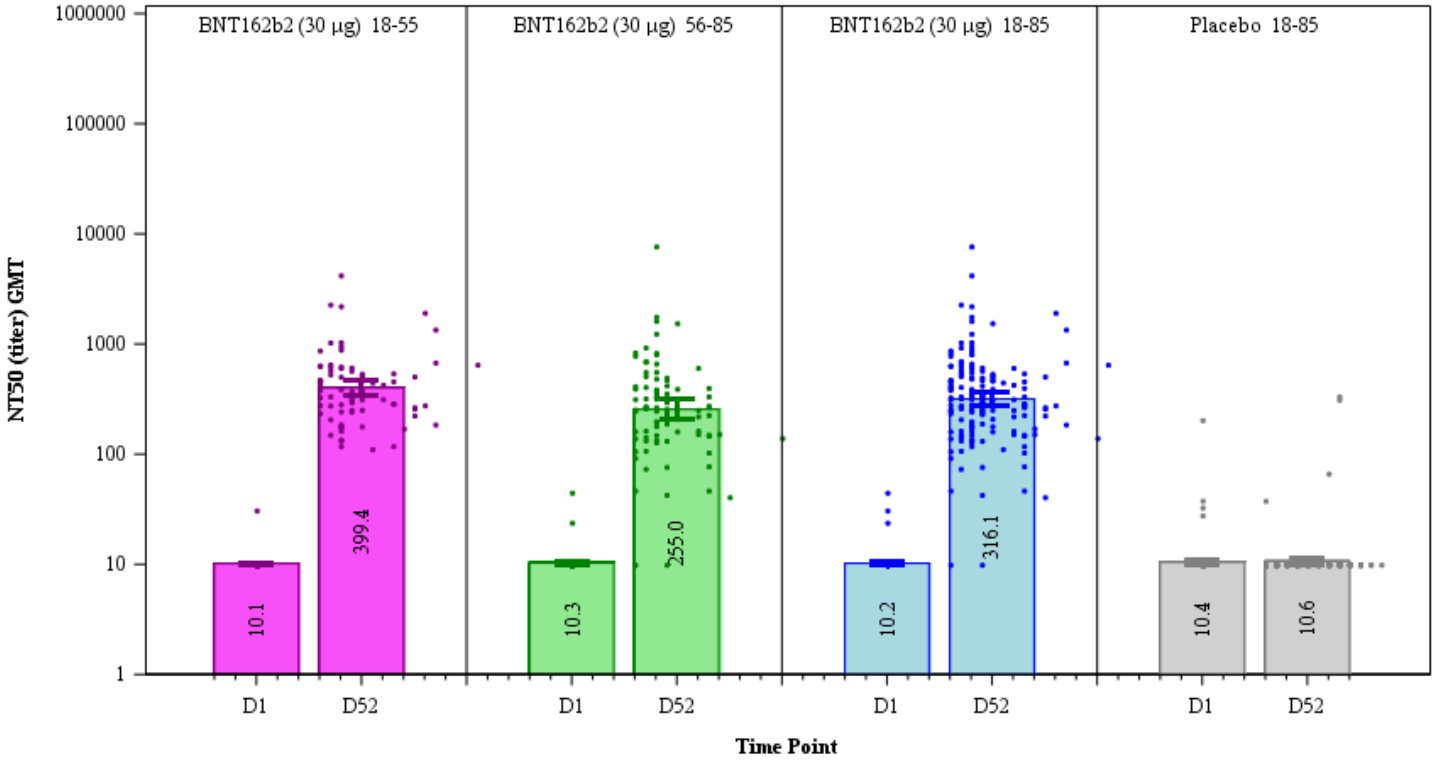
HCS Comparison

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).[19] The HCS is the same panel described in Section 2.5.4.2.3.3, except 5 sera from the N=38 serum panel had been depleted.

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

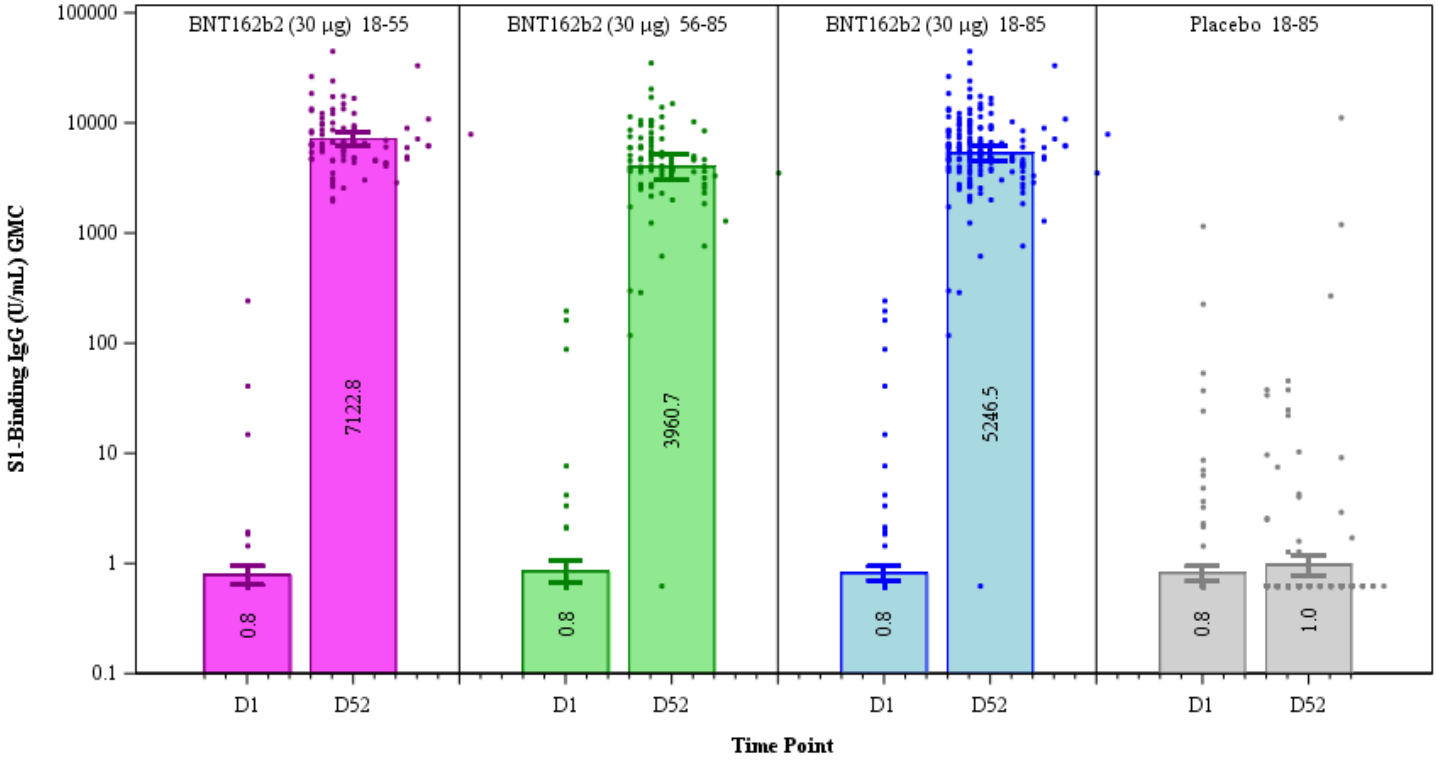
Results for GMFRs in SARS-CoV-2 50% neutralizing titers and S1-binding IgG concentrations were robust at 1 month after Dose 2 of BNT162b2, with higher GMFRs observed in younger participants than in older participants (Table 48).

Figure 9. Geometric Mean Titers: SARS-CoV-2 Neutralization Assay – NT50 – Evaluable Immunogenicity Population – 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.
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_f002_sars_50_p2

Figure 10. Geometric Mean Concentrations: SARS-CoV-2 S1-Binding IgG Level Assay – Evaluable Immunogenicity Population – 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.
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_f002_s1_p2

Table 47. 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	
		18-55 Years		56-85 Years		18-85 Years		18-85 Years	
		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	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 48. Summary of Geometric Mean Fold Rises From Before Vaccination to Each Subsequent Time Point – Phase 2 – Dose 2 Evaluable Immunogenicity Population

		Vaccine Group (as Randomized)							
		BNT162b2 (30 µg)						Placebo	
		18-55 Years		56-85 Years		18-85 Years		18-85 Years	
Assay	Dose/ Sampling Time Point[a]	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])
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

2.5.4.4.3.3. SARS-CoV-2 Neutralizing Titers and S1-Binding IgG Concentrations by Baseline SARS-CoV-2 Status

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 (Table 49). In general, at 1 month post Dose 2 among BNT162b2 recipients, SARS-CoV-2 50% neutralizing GMTs in participants with a positive baseline SARS-CoV-2 status (n=3) and S1-binding IgG GMCs in participants with a positive baseline SARS-CoV-2 status were numerically higher than those observed in participants with a negative baseline SARS-CoV-2 status (n=163) (Table 49). Participants with baseline negative SARS-CoV-2 status had SARS-CoV-2 50% neutralizing GMTs and S1-binding IgG GMCs similar to those in the combined baseline positive and negative participant group (Figure 9, Figure 10, and Table 47).

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 50), 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 47).

Table 49. Summary of Geometric Mean Titers/Concentrations by Baseline SARS-CoV-2 Status – Phase 2 – Dose 2 Evaluable Immunogenicity Population

			Vaccine Group (as Randomized)							
			BNT162b2 (30 µg)						Placebo	
			18-55 Years		56-85 Years		18-85 Years		18-85 Years	
Assay	Dose/ Sampling Time Point[a]	Baseline SARS-CoV-2 Status[b]	n[c]	GMT/GMC[d] (95% CI[d])	n[c]	GMT/GMC[d] (95% CI[d])	n[c]	GMT/GMC[d] (95% CI[d])	n[c]	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)

Table 49. Summary of Geometric Mean Titers/Concentrations by Baseline SARS-CoV-2 Status – Phase 2 – Dose 2 Evaluable Immunogenicity Population

			Vaccine Group (as Randomized)							
			BNT162b2 (30 µg)						Placebo	
			18-55 Years		56-85 Years		18-85 Years		18-85 Years	
Assay	Dose/ Sampling Time Point[a]	Baseline SARS-CoV-2 Status[b]	n[c]	GMT/GMC[d] (95% CI[d])	n[c]	GMT/GMC[d] (95% CI[d])	n[c]	GMT/GMC[d] (95% CI[d])	n[c]	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.
PFIZER CONFIDENTIAL SDTM Creation: 02NOV2020 (19:23) Source Data: adva Table Generation: 12NOV2020 (04:18)
(Cutoff Date: 12OCT2020, Snapshot Date: 02NOV2020) Output File: ./nda2_unblinded/C4591001_IA_P2_Serology/adva_s001_gm_lt_p2_eval

Table 50. 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

			Vaccine Group (as Randomized)							
			BNT162b2 (30 µg)						Placebo	
			18-55 Years		56-85 Years		18-85 Years		18-85 Years	
Assay	Dose/ Sampling Time Point[a]	Baseline SARS-CoV-2 Status[b]	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)
(Cutoff Date: 12OCT2020, Snapshot Date: 02NOV2020) Output File: ./nda2 unblinded/C4591001 IA P2 Serology/adva s002 gmfr lt p2 eval

2.5.4.4.4. Immunogenicity Conclusions

Phase 1

Study BNT162-01 provides evidence for robust T cell-mediated immunity, with antigen induced IFNγ expression demonstrating a Th1 CD4+ and CD8+ phenotype following the second dose of either BNT162b1 or BNT162b2. Immunogenicity data from Study BNT162-01 were generally concordant with results in pivotal Study C4591001, showing robust SARS CoV-2 neutralization following the second dose and complimentary T cell immune response data for both younger and older adults. The durability of T cell responses to BNT162b2 vaccination was evident from maintenance of the Th1 phenotype and persistent IFNγ and IL-2 production by CD4+ and CD8+ T cells up to approximately 6 months.

In Study C4591001, both BNT162b1 and BNT162b2 elicited robust SARS-CoV-2 neutralizing antibody response starting from 7 days after Dose 2 in younger and older adults. Responses were generally stronger in younger adults than in older adults. Neutralizing antibody response was maintained through Day 52 and was similar for the candidates within the corresponding age and dose groups. Comparisons of SARS-CoV-2 neutralizing titers for both vaccine candidates with a panel of HCS support the benefit of a two-dose vaccination regimen with a dose response up to 30 µg.

For the groups that received BNT162b2 at 30 µg, persistence of the immune response was observed through 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 above pre-vaccination and placebo levels.

The Phase 1 immunogenicity data from both the pivotal and supportive study collectively showed robust immunogenicity elicited by BNT162b2 in both younger and older adults at the 30 µg dose level, which was ultimately selected to proceed to Phase 2/3 development.

Phase 2

Based on immunogenicity results from 360 participants in Phase 2 of Study C4591001, 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 adult compared to the older adult cohort. Of note, GMTs for younger and older participants at 1 month after Dose 2 were comparable to the GMTs of a comparative panel of HCS. S1-binding GMCs were generally higher in the younger age cohort compared to the older age cohort, again concordant with observations in the Phase 1 portion of the study.

2.5.5. Overview of Safety

Safety was evaluated in Study BNT162-01 (Phase 1) and in all 3 phases of Study C4591001. The methods for evaluation of safety are provided in Section 2.5.5.1 and results are presented for BNT162-01 Phase 1 (Section 2.5.5.2 and Section 2.5.5.6.1); and all phases of Study C4591001 (Section 2.5.5.3 through Section 2.5.5.5).

Details of safety analysis methods in Study C4591001 are provided in the Module 5.3.5.1 C4591001 Protocol and SAP, and for Study BNT162-01 in the Module 5.3.5.1 BNT162-01 Protocol and SAP.

Details of safety results, including for additional endpoints, are presented as follows:

Study BNT162-01: Module 5.3.5.1 BNT162-01 Interim CSR.

Study C4591001:

Phase 1: safety results for all candidates and dose levels up to 1 month after Dose 2 are presented in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR; safety results for Phase 1 participants in the BNT162b2 30 µg up to 6 months after Dose 2 are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR.

Phase 2: safety results up to 1 month after Dose 2 are presented in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR.

Phase 2/3: safety results to 1 month after Dose 2 are presented in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR; safety results to 6 months after Dose 2 and to data cutoff date (blinded and open-label follow-up) are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR.

Note that data from Phase 2 participants were included in Phase 3 safety analyses. Safety data are also presented in Module 2.7.4 and summarized below.

2.5.5.1. Safety Endpoints and Analysis Methods

Details of safety methods and analyses are provided in Module 2.7.4 and summarized below. Statistical analyses are provided in Section 2.5.5.1.3.

2.5.5.1.1. Safety Endpoints in Study BNT162-01

In Study BNT162-01, all participants in Phase 1 recorded local reactions, systemic events, and antipyretic/pain medication usage for 7 days, each evening following administration of study intervention using a paper diary. Participants were asked to assess local reactions and systemic events from Day 1 through Day 7 after each dose.

Treatment-emergent AEs were recorded for up to 1 month after Dose 2 and categorized by frequency, maximum severity, seriousness, and relationship to study intervention using System Organ Class (SOC) and Preferred Term (PT) according to the Medical Dictionary for Regulatory Activities (MedDRA). AEs of special interest (AESIs) included enhanced

respiratory disease or flu-like symptomatology that did not resolve after 7 days or with symptom kinetics that were inconsistent with a relationship to RNA immunization.

Clinical laboratory tests were performed and classified as normal or abnormal (lower or higher than reference range) and abnormal results were graded as mild, moderate, severe, or life-threatening. Physical examinations, vital signs, and electrocardiograms (ECGs) were conducted prior to vaccine dose administration.

2.5.5.1.2. Safety Endpoints in Study C4591001

2.5.5.1.2.1. Phase 1 Safety Endpoints

In Phase 1 of Study C4591001, all participants were asked to record reactogenicity:[21] local reactions (pain, redness and swelling at the injection site), systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain), and antipyretic/pain medication usage for 7 days, each evening following administration of study intervention using prompts from an electronic diary (e-diary). This allowed recording of these assessments only within a fixed time window and provided an accurate representation of the participant's experience at that time. Participants were asked to assess local reactions and systemic events from Day 1 through Day 7 after each dose.

In Phase 1, AEs were recorded for up to 1 month after Dose 2 and categorized by frequency, maximum severity, seriousness, and relationship to study intervention using SOC and PT according to MedDRA. SAEs are being recorded for up to 6 months after Dose 2. For longer-term follow-up, AEs and SAEs continue to be reported until end of the study.

In Phase 1 only, abnormal hematology and chemistry laboratory values including grading shifts through Day 7 after Dose 2 were reported; abnormal clinical laboratory data were graded as mild, moderate, severe, or life-threatening. Physical examinations, vital signs, and ECGs were conducted prior to vaccine dose administration.

Stopping rules were in place for all Phase 1 participants, based on review of AE data and e-diary reactogenicity data, until the start of Phase 2/3 or 30 days after the last dose of study intervention in Phase 1, whichever was later. These data were monitored on an ongoing basis by the investigator (or medically qualified designee), Pfizer, and BioNTech in order to promptly identify and flag any event that potentially contributes to a stopping rule.

2.5.5.1.2.2. Phase 2/3 Safety Endpoints

Phase 2

In Phase 2, N~360 participants recorded local reactions, systemic events, and antipyretic/pain medication usage for 7 days, each evening following administration of study intervention using an e-diary from Day 1 through Day 7 after each dose.

In Phase 2, AEs and SAEs were recorded through 7 days after Dose 2 as a prespecified study endpoint and then further (to at least 1 month after Dose 2) for longer-term follow-up. AEs were categorized by frequency, maximum severity, seriousness, and relationship to

study intervention using SOC and PT according to MedDRA. For longer-term follow-up, AEs and SAEs continue to be reported until end of the study.

Note that Phase 2 participants are a subset of those in the Phase 2/3 portion of the study and are therefore included in Phase 3 safety analyses.

Phase 2/3

A subset of participants ≥16 years of age first enrolled in Phase 2/3 recorded local reactions, systemic events, and antipyretic/pain medication usage for 7 days, each evening following administration of study intervention using an e-diary from Day 1 through Day 7 after each dose. For participants who were not in the reactogenicity subset, local reactions and systemic events consistent with reactogenicity were detected and reported as AEs.

For Phase 2/3 safety analyses (which included the N~360 participants analyzed in Phase 2), AEs were reported for up to 1 month after Dose 2 and categorized by frequency, maximum severity, seriousness, and relationship to study intervention using SOC and PT according to MedDRA. SAEs were recorded for up to 6 months after Dose 2. For longer-term follow-up, AEs and SAEs continue to be reported until end of the study.

Phase 2/3 AE data were analyzed for safety population ≥16 years of age subgroups defined by:

- evidence of prior SARS-CoV-2 infection at baseline per NAAT or N-antigen binding assay
- demographics (ie, age, sex, race, and ethnicity).

Subgroups of the safety population for Phase 2/3 participants ≥16 years of age were analyzed and reported for the blinded placebo-controlled follow-up period up to the date of unblinding.

Additional subgroups were analyzed to evaluate safety for participants ≥16 years of age who were originally randomized to placebo, had prior evidence of SARS-CoV-2 infection at study baseline or had COVID-19 illness during the study, and were subsequently unblinded to receive BNT162b2 during open-label follow-up.

The subset of Phase 2/3 participants ≥16 years of age with stable HIV were analyzed separately per protocol as of the most recent cutoff date (13 March 2021).

AEs of special interest (AESIs) were not prespecified in the protocol; instead, Pfizer utilizes a safety review as part of the signal detection processes that highlights specified targeted medical events (TMEs) of clinical interest. These are a dynamic list of specific AE terms reviewed on an ongoing basis by routine safety data review procedures throughout the clinical study. The TME terms are chosen based on review of known pharmacology, toxicology findings, possible class effects, published literature, and potential signals arising from safety data assessments. For this study, the list of TMEs includes events of interest due to their association with COVID-19 and terms of interest for vaccines in general; during safety review, consideration was also given to the CDC defined list of AESIs associated with COVID-19 vaccination.

Data for adolescents 12 to 15 years of age are not included in this submission and will be reported at a later time.

2.5.5.1.2.3. Safety Assessments in All Phases

In Phase 2/3 of Study C4591001, prior infection with SARS-CoV-2 was assessed at baseline (NAAT, serology) and at Dose 2 (NAAT) and is being evaluated for up to 24 months to assess persistence of efficacy, explore efficacy against asymptomatic SARS-CoV-2 infections, and ensure safety in baseline SARS-COV-2 negative and positive participants. Prior infection was determined by virological testing via NAAT on mid-turbinate swab and serological testing for IgG to the SARS-CoV-2 N-antigen.

Participants in all phases were surveilled for potential COVID-19 illness from Visit 1 onwards. In Phase 1, Pfizer and BioNTech conducted unblinded reviews of the data, including for the purpose of safety assessment. Any NAAT-confirmed cases in Phase 1 were reviewed contemporaneously by the IRC and Data Monitoring Committee (DMC). In Phase 2/3, the unblinded team supporting the DMC (including an unblinded medical monitor) reviewed severe COVID-19 cases as they were received, and reviewed AEs at least weekly for additional potential cases of severe COVID-19. At any point, the unblinded team could discuss with the DMC chair whether the DMC should review cases for an adverse imbalance of COVID-19 and/or severe COVID-19 cases in the BNT162b2 and placebo groups.

Pregnancies were reported for participants in any phase of the study.

Narratives

Narratives are located in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 14 Subject Narratives (for data available as of the 14 November 2020 cutoff date) or Module 5.3.5.1 C4591001 6-Month Update Interim CSR Section 14 Subject Narratives (for data available as of the 13 March 2021 cutoff date). Narratives were prepared for participants ≥16 years of age if they were determined to meet these criteria:

- Deaths, vaccine-related SAEs, all other SAEs, safety-related withdrawals
- AEs of interest requested by FDA: anaphylaxis, Bell's palsy, lymphadenopathy, appendicitis, and pregnancy exposures and outcomes
- AESIs with a numerical imbalance with a higher frequency (or incidence rate) in the vaccine group vs placebo group that led to withdrawal, were related, or had biological plausibility
- COVID-19 cases (participants with severe and/or multiple episodes).

Note that imbalances in PTs in the BNT162b2 and placebo groups that corresponded to reactogenicity terms reported within 7 days after each dose, such as pain at injection site and headache and that were captured in participants' e-diaries for reactogenicity analysis, were generally excluded as criteria for narratives.

Study Groups and Follow-up Periods Contributing Safety Data

Safety evaluations from Study C4591001 presented in this CO include the following data from a total of approximately 44,000 enrolled participants ≥16 years of age, through a data cutoff date of 13 March 2021:

- Randomized BNT162b2 and placebo groups for period of available blinded follow-up to:
  - at least 6 months after Dose 2 for Phase 1 participants randomized to BNT162b2 30 µg, comparing younger (18 to 55 years of age) and older (65 to 85 years of age) groups
  - 1 month after Dose 2 and until unblinding for Phase 2/3 participants, comparing younger adult (16 to 55 years of age) and older adult (>55 years of age) groups
  - 1 month after Dose 1 and until unblinding for Phase 2/3 participants in HIV+ subset
- Open-label data for Phase 2/3 participants originally randomized to BNT162b2 from the time of unblinding through the data cutoff date
- Cumulative data for Phase 2/3 participants originally randomized to BNT162b2, including at least 3000 per age group (16 to 55, >55 years of age) with follow-up to at least 6 months after Dose 2 (inclusive of blinded and open-label data)
- Open-label data for Phase 2/3 participants originally randomized to placebo from the time of unblinding and vaccination with BNT162b2 (Dose 3) through the data cutoff date

2.5.5.1.3. Safety Analysis Methods

2.5.5.1.3.1. Study BNT162-01

Safety data were analyzed and reported using descriptive summary statistics for the safety set (described in Module 2.7.4). Analyses were performed for endpoints described in Section 2.5.5.1.1, separately by protocol defined age group (younger and older adults).

Reactogenicity: Summary statistics including counts and percentages provided by study group.

Adverse Events: Summary statistics including counts and percentages provided by study group.

Clinical Laboratory Evaluations: Values at each timepoint and change from baseline to post-baseline time points summarized using descriptive summary statistics by study group. Values were flagged as abnormal and/or clinically significant.

2.5.5.1.3.2. Study C4591001

Safety data were analyzed and reported using descriptive summary statistics for the safety population for each study phase (described in Module 2.7.4). Analyses were performed for endpoints described in Section 2.5.5.1.2, separately by protocol defined age groups (adolescents, younger adults, older adults) and for the HIV+ subset and reactogenicity subset. Analyses of subgroups were performed for those described in Section 2.5.5.1.2.2.

Reactogenicity

Descriptive statistics were provided for each reactogenicity endpoint for each dose and vaccine group. Local reactions and systemic events from Day 1 through Day 7 after each vaccination will be presented by severity cumulatively across severity levels. Descriptive summary statistics included counts and percentages of participants with the indicated endpoint and the associated Clopper-Pearson 2-sided 95% confidence intervals (CIs). Missing reactogenicity e-diary data were not imputed.

Adverse Events

Descriptive summary statistics including counts, percentages, and associated Clopper-Pearson 2-sided 95% CIs were provided for AEs for by study group.

AE analyses of participants who had different durations of follow-up time due to unblinding in the study (per protocol) were summarized as incidence rates (IR) adjusted for exposure time. This was calculated as: (number of participants reporting event) / (total exposure time across all participants in the specified group). This accounts for variable exposure since unblinding began for individual participants (as described in Section 2.5.1.2.3.2.2). Two-sided 95% CIs for the IRs were provided based on Poisson distribution.

Clinical Laboratory Evaluations

Descriptive statistics were provided for abnormal hematology and chemistry laboratory values after each vaccine dose (in Phase 1 only). This includes grading shifts in hematology and chemistry laboratory values from baseline to 1 and 7 days after Dose 1, and to before Dose 2 and 7 days after Dose 2. Descriptive summary statistics include counts and percentages of participants with the indicated endpoint and the associated Clopper-Pearson 2-sided 95% CIs.

2.5.5.2. Safety Results – Phase 1 Safety in Study BNT162-01

Details of study population and safety analysis results in Study BNT162-01 are provided in Module 5.3.5.1 BNT162-01 Interim CSR Section 10 and Section 12, in Module 2.7.4, and summarized below.

Safety data (reactogenicity and AE analyses) up to 1 month after Dose 2 are available up through the safety data cutoff date (23 October 2020) and summarized below as follows:

- **BNT162b1**: younger participants: N=84, n=12 each in 1, 3, 10, 20, 30, 50, 60 µg groups (note: 60 µg group received only Dose 1 per SRC decision due to Dose 1 reactogenicity); older participants: N=36, n=12 each in 10, 20, 30 µg groups (note: 10 µg group had data to 1 month after Dose 2; 20 and 30 µg groups had available data to 7 days after Dose 2).

- **BNT162b2**: younger participants: N=60, n=12 each in 1, 3, 10, 20, and 30 µg groups; older participants: N=36, n=12 each in 10, 20, and 30 µg groups.

2.5.5.2.1. Safety Populations – Phase 1

The safety set for Study BNT162-01 is described below; the immunogenicity set was generally similar.

BNT162b1

In the younger group (18 to 55 years of age), BNT162b1 was administered to 84 participants among whom 52% were male and 48% were female, 96% were White and 2% were Hispanic/Latino, with a median 36 years of age.

In the older group (56 to 85 years of age), BNT162b1 was administered to 36 participants among whom 36% were male and 64% were female, all were White and none were Hispanic/Latino, with a median 67 years of age.

Among the BNT162b1 groups in the Phase 1 portion of Study BNT162-01, 80/84 younger and 11/36 older participants completed the study (ie, through the end of treatment visit). Four premature discontinuations have occurred. One younger participant in the 10 µg group discontinued prematurely from the study due to an AE after Dose 1; this AE was assessed as not related to study treatment. Three younger participants discontinued prematurely for other reasons: in the 20 µg group due to withdrawal by participant (n=1) after Dose 1 and due to other/private reason (n=1) after Dose 2; and in the 50 µg group due to other/private reason (n=1) after Dose 1. Another younger participant in the 20 µg group discontinued prematurely after 1 month of follow-up post Dose 2, but did not complete the end of treatment visit. No older participants have prematurely discontinued the study; some have completed the study and the others remain in follow-up.

BNT162b2

In the younger group (18 to 55 years of age), BNT162b2 was administered to 60 participants among whom 43% were male and 57% were female, 100% were White, none were Hispanic/Latino, with a median 42 years of age.

In the older group (56 to 85 years of age), BNT162b2 was administered to 36 participants among whom 50% were male and 50% were female, 100% were White, none were Hispanic/Latino, with a median 65 years of age.

Among the BNT162b2 groups in the Phase 1 portion of Study BNT162-01, 53/60 younger and 30/36 older participants completed the study (ie, through end of treatment visit). Two premature discontinuations have occurred. One younger participant in the 10 µg group discontinued prematurely due to AEs after Dose 1; these AEs were assessed as not related to study treatment. One younger participant in the 1 µg group discontinued prematurely due to withdrawal by the participant after Dose 1. No older participants have prematurely discontinued the study; most have completed the study the others remain in follow-up.

2.5.5.2.2. Reactogenicity – Phase 1

This section summarizes reactogenicity collected in paper diaries from participants in the Phase 1 part of Study BNT162-01 for candidates BNT162b1 and BNT162b2.

Based on all available data from the Phase 1 part of Study BNT162-01, the reactogenicity profile observed for BNT162b2 is more favorable than that of BNT162b1. For BNT162b1, reactogenicity (particularly systemic events) increased after Dose 2 compared to Dose 1. For BNT162b2, dose level- and dose number-dependent increases in reactogenicity were minimal to modest. In general, older participants had milder reactogenicity compared to the younger groups for both vaccine candidates.

2.5.5.2.2.1. Local Reactions

Overall, solicited local reactions following administration across doses of BNT162b2 were milder and less frequent for participants compared with BNT162b1. Local reactions generally increased in frequency and/or severity with increasing dose level and number of doses of BNT162b1 and BNT162b2. Most local reactions were mild or moderate in severity and resolved within several days of onset.

For BNT162b1, the incidence of any local reactions after each dose was similar in younger and older age groups, but local reactions were generally milder in the older group. For BNT162b2, both incidence and severity of local reactions was general decreased after each dose in the older group compared with the younger group.

2.5.5.2.2.2. Systemic Events

Overall, solicited systemic events following administration across doses of BNT162b2 were milder and less frequent for participants compared with BNT162b1. Systemic events generally increased in frequency and/or severity with increasing dose level and number of doses of BNT162b1 and BNT162b2. Most systemic events were mild or moderate, arose within the first 1 to 2 days after dosing, and were short-lived.

For BNT162b1, the incidence of any systemic events after each dose was similar in the younger and older age groups, but systemic events were generally milder in the older group. For BNT162b2, the incidence of systemic events after each dose was similar in the older group compared with the younger group. Reports of severe systemic events were similar in the younger and older BNT162b2 groups and were substantially less frequent than the severe events reported for younger and older BNT162b1 groups.

2.5.5.2.3. Adverse Events – Phase 1

In the Phase 1 part of Study BNT162-01, 40% to 45% of participants who received BNT162b1 and BNT162b2 across age groups and across dose levels reported one or more AEs from Dose 1 through 28 days (ie, 1 month) after Dose 2. There was no overall pattern between vaccine candidates with regard to AE incidence or severity; however, AEs considered by the investigator as related to study intervention (after omitting events captured in paper diaries for reactogenicity) were less frequently reported for BNT162b2 groups compared with BNT162b1. Most AEs were considered by the investigator as not related to study intervention and mild to moderate in severity, and all AEs were reported as resolved.

Among BNT162b1 recipients, 1 younger participant in the 10 µg group discontinued the study due to a moderate AE of malaise (considered as not related to study intervention) after Dose 1 and 1 younger participant in the 60 µg group discontinued due to a dose-limiting toxicity of pyrexia after Dose 1. One older participant in the 20 µg group had an SAE of severe syncope (considered as not related to study intervention) after Dose 1 and study treatment was withdrawn.

Among BNT162b2 recipients, 1 younger participant in the 10 µg group discontinued the study due to a moderate AE of nasopharyngitis (considered as not related to study intervention) after Dose 1. One older participant in the 20 µg group had an SAE of ankle fracture (considered as not related to study intervention) after receiving both doses, was listed as recovering, and remains in follow-up.

No deaths occurred in the Phase 1 part of Study BNT162-01.

2.5.5.3. Safety Results – Phase 1 Safety in Study C4591001

Details of study population and safety analysis results in Phase 1 are provided in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 10 and Section 12.1 (up to 1 month after Dose 2), and Module 5.3.5.1 C4591001 6-Month Update Interim CSR Section 10 and Section 12 (up to 6 months after Dose 2).

C4591001 Phase 1 safety data are also presented in Module 2.7.4 and summarized below.

Safety results for Phase 1 vaccine candidates BNT162b1 and BNT162b2 for both adult age groups are presented up to 1 month after Dose 2 (data cutoff date: 24 August 2020) at the 10 µg, 20 µg, and 30 µg dose levels. Note that the younger group of participants 18 to 55 years of age who received 100 µg BNT162b1 did not receive a second dose of 100 µg BNT162b2 per IRC decision, and instead were given 10 µg for Dose 2. These participants were described in the C4591001 Final Analysis Interim CSR and are not detailed here as the dose level was discontinued.

Safety follow-up is also presented up to at least 6 months after Dose 2 (data cutoff date: 13 March 2021) for Phase 1 participants who received BNT162b2 30 µg.

2.5.5.3.1. Safety Populations – Phase 1

In the Phase 1 part of Study C4591001, participants in each dose level and age group were randomized 4:1 to receive vaccine or placebo. The safety population for Study C4591001 is described below; the immunogenicity population was generally similar.

All Phase 1 participants in Study C4591001 received both vaccine doses except for the younger group who received BNT162b1 at the 100 µg dose level which was discontinued after the first dose per IRC decision. Participants in this group were instead able to receive a second dose at the 10 µg dose level, and 11/12 were administered this second dose. No participants discontinued the Phase 1 part of the study as of 1 month after Dose 2.

BNT162b1

BNT162b1 was administered to 45 participants who received up to 30 µg in the younger (18 to 55 years of age) group among whom 62% were male and 38% were female, 82% were White, 4% were Hispanic/Latino, with a median 35 years of age.

BNT162b1 was administered to 45 participants in the older (65 to 85 years of age) group among whom 29% were male and 71% were female, 93% were White, 2% were Hispanic/Latino, with a median 69 years of age.

Further follow-up data on the BNT162b1 groups was not available as of the most recent data cutoff date (13 March 2021).

BNT162b2

In the Phase 1 portion of Study C4591001, BNT162b2 was administered to 45 younger participants among whom 42% were male and 58% were female, 87% were White, 4% were Hispanic/Latino, with a median 37 years of age.

BNT162b2 was administered to 45 older participants among whom 38% were male and 62% were female, 100% were White, none were Hispanic/Latino, with a median 68 years of age.

Safety Follow-Up to at Least 6 Months After Dose 2 in BNT162b2 30 µg Groups

All participants in each age group randomized to receive BNT162b2 completed the visit at 6 months after Dose 2, with most of these 6-month visits occurring during the open-label follow-up period. All participants in each age group randomized to the placebo group received both doses of BNT162b2 (Dose 3 and Dose 4 in the study) during the open-label period and completed the visit at 1 month after Dose 4, as of the data cutoff date of 13 March 2021. No participants were withdrawn from the study up to the data cutoff date.

2.5.5.3.2. Reactogenicity – Phase 1

Based on all available data in the Phase 1 portion of Study C4591001, the reactogenicity profile observed for BNT162b2 is more favorable than that of BNT162b1. For BNT162b1, reactogenicity (particularly systemic events) increased after Dose 2 compared to Dose 1. For BNT162b2, dose level- and dose number-dependent increases in reactogenicity were minimal to modest in younger (18 to 55 years of age) and older (65 to 85 years of age) participants.

2.5.5.3.2.1. Local Reactions

Overall, prompted local reactions following administration of both doses of BNT162b2 in the Phase 1 portion of Study C4591001 were milder and less frequent for participants in both age groups compared with BNT162b1. For both BNT162b1 and BNT162b2, the frequency of local reactions was lower for the older group compared to the younger group. Local reactions were generally infrequent in placebo recipients.

The majority of local reactions in the vaccine groups were mild or moderate in severity and resolved within several days of onset. No grade 4 (potentially life-threatening) reactions were reported.

Pain at the injection site was the most frequent prompted local reaction, increasing in frequency and/or severity with increasing dose level, for both BNT162b1 and BNT162b2.

2.5.5.3.2.2. Systemic Events

Overall, systemic events following administration of both doses of BNT162b2 in the Phase 1 portion of Study C4591001 were milder and less frequent for participants in both age groups compared with BNT162b1. Systemic events were generally infrequent in placebo recipients.

The frequency of systemic events was lower for the older group (65 to 85 years of age) compared to the younger group (18 to 55 years of age). Notably, for older adults who received BNT162b2, frequencies of systemic events after the first dose were similar in BNT162b2 and placebo recipients.

Prompted systemic events generally increased in frequency and/or severity with increasing dose level and number of doses of BNT162b1 and BNT162b2. Use of antipyretic/pain medication also increased in frequency with increasing dose level and number of doses.

Most systemic events were mild or moderate, arose within the first 1-2 days after dosing, and resolved within several days of onset. For participants who received the 30 µg dose level, fever had a median duration of 1 day across vaccine candidates and across age groups, and chills had a median duration of 1 to 2 days across vaccine candidates and age groups.
No grade 4 (potentially life-threatening) events were reported.

2.5.5.3.3. Adverse Events – Phase 1

In the Phase 1 portion of Study C4591001, the majority of participants who received both BNT162b1 and BNT162b2 across age groups and dose levels reported one or more AEs after vaccine dosing (from Dose 1 onwards). AEs were reported at higher frequencies in BNT162b1 and BNT162b2 vaccine groups compared with placebo, across age groups and dose levels. AE incidences were generally lower in the older age groups compared with the younger age groups. Across BNT162b1 dose levels, 42% to 50% of younger participants and 25% to 58% of older participants reported AEs. Across BNT162b2 dose levels, 33% to 42% of younger participants and 8% to 25% of older participants reported AEs. Placebo younger and older groups reported AEs in 22% to 44% of participants.

Overall, most AEs reported were considered by the investigator as not related to study intervention. Most AEs were mild to moderate in severity. No SAEs, deaths, or discontinuations due to AEs were reported in the Phase 1 part of the study up to 1 month after Dose 2.

Safety Follow-Up to at Least 6 Months After Dose 2 in BNT162b2 30 µg Groups

From Dose 1 of BNT162b2 30 µg to the unblinding date, 6 (50.0%) participants in the younger age group and 3 (25.0%) participants in the older age group reported at least 1 AE.

Two (16.7%) participants in the BNT162b2 30 µg younger age group and 1 (8.3%) participant in the BNT162b2 30 µg older age group reported at least 1 severe AE. In the BNT162b2 30 µg younger age group, 3 (25.0%) participants reported at least 1 related AE and 1 (8.3%) participant reported 1 severe SAE.

No AEs were reported in either the younger or older participants in the placebo group. No SAEs or related AEs were reported in the BNT162b2 30 µg older age group. No AEs leading to withdrawal, life-threatening AEs, or deaths were reported in either the younger or older participants in the BNT162b2 30 µg group.

From Dose 1 of BNT162b2 30 µg to the unblinding date, AEs were most commonly reported in the system organ class (SOC) of nervous system disorders (3 [25.0%] participants in the younger age group and 1 [8.3%] participant in the older age group), followed by musculoskeletal and connective tissue disorders (1 [8.3%] participant in each age group). All AEs by preferred term (PT) were reported by no more than 1 participant.

There were no Phase 1 participants randomized to BNT162b2 30 µg or corresponding placebo who died through the data cutoff date of 13 March 2021. From Dose 1 to the unblinding date, 1 participant in the BNT162b2 30 µg younger age group reported a severe SAE (neuritis) that was assessed by the investigator as not related to study intervention. No Phase 1 participants randomized to BNT162b2 30 µg or corresponding placebo reported any AEs leading to withdrawal from the study from Dose 1 to the unblinding date. AEs of special interest were not defined for Phase 1 of this study. Pregnancy was not reported in any Phase 1 participants through the data cutoff date of 13 March 2021.

2.5.5.4. Safety Results – Phase 2 Safety in Study C4591001

Details of study population and safety analysis results in Phase 2 are provided in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 10 and Section 12.2, in Module 2.7.4, and summarized below.

Note that the Phase 2 portion of Study C4591001 included 360 participants randomized 1:1 to receive BNT162b2 (30 µg) or placebo when the Phase 2/3 study commenced.

Safety data (reactogenicity and AE analyses) for the 360 participants in the Phase 2 portion of the study are presented up to Day 7 after Dose 2 (per protocol objective), with a data cutoff date of 02 September 2020. AE data from participants in Phase 2 after this time point are otherwise included with Phase 3 analyses in Section 2.5.5.5.3.

2.5.5.4.1. Safety Populations – Phase 2

Disposition of 360 participants randomized 1:1 in Phase 2 was similar in the BNT162b2 and placebo groups. A total of 2 participants received Dose 1 but did not receive Dose 2: 1 participant each in the BNT162b2 and placebo groups.

Overall, most participants were White (85.8%), followed by Black or African American (9.2%). The proportions of Hispanic/Latino participants were similar in the BNT162b2 (8.9%) and placebo (11.1%) groups. Within the BNT162b2 group, the younger age group had 14.8% of Hispanic/Latino participants and the older age group had 3.3%.

The median age was 56 years overall. Median age was 44 years for the BNT162b2 younger age group and 65 years for the BNT162b2 older age group. The male/female split was approximately 50/50 for both groups and for younger and older participants within the BNT162b2 group.

The participants evaluated in Phase 2 after receiving BNT162b2 included 88 participants in the younger group and 92 participants in the older group.

2.5.5.4.2. Reactogenicity – Phase 2

In Phase 2, reactogenicity (particularly systemic events) increased after Dose 2 compared to Dose 1. Dose number-dependent increases in incidence of local reactions were minimal to modest in the younger and older groups of participants who received BNT162b2.

Most local reactions were mild or moderate in severity, had a median onset between 1 to 3 days after dosing (Day 1 was the day of vaccination), and resolved after a median duration of 1 to 3 days after onset. No grade 4 (potentially life-threatening) reactions were reported.

Most systemic events were mild or moderate in severity, had a median onset of 2 to 3 days after dosing, and resolved after a median duration of 1 day after onset. Fever and chills each had a median duration of 1 day after either dose for both age groups.

2.5.5.4.2.1. Local Reactions

Pain at the injection site was the most frequent prompted local reaction in Phase 2 across doses and age groups (71% to 85%), with higher frequency in the BNT162b2 group compared to placebo (9% to 10%). Local reactions generally had similar incidence in the younger group (N=88 post Dose 1; N=86 post Dose 2) compared with the older group (N=92 post Dose 1; N=91 post Dose 2). Severe pain at injection site was reported by 2 participants, both in the BNT162b2 group: n=1 in the older group had severe injection site pain after Dose 1, and n=1 in the younger age group had severe injection site pain after Dose 2.

Across age groups and both doses, swelling (3% to 12%) and redness (3% to 8%) occurred at low frequencies after Doses 1 and 2. One BNT162b2 recipient in the older group reported severe redness after Dose 2.

Most local reactions were mild or moderate in severity, had a median onset between 1 to 3 days after dosing (Day 1 was the day of vaccination), and resolved after a median duration of 1 to 3 days after onset. No grade 4 (potentially life-threatening) reactions were reported.

2.5.5.4.2.2. Systemic Events

The most frequent prompted systemic events for any dose and age groups in Phase 2 were fatigue (36% to 59%), headache (27% to 51%), muscle pain (14% to 45%), chills (8% to 41%), diarrhea (9% to 20%), joint pain (4% to 17%), fever (0% to 17%), and vomiting (0% to 2%). Systemic events generally had increased frequency and/or severity after Dose 2 compared with after Dose 1. Systemic events were also generally increased in frequency in the younger group (N=88 post Dose 1; N=86 post Dose 2) compared with the older group

(N=92 post Dose 1; N=91 post Dose 2), with frequencies increasing with number of doses (Dose 1 vs Dose 2):

- fatigue: younger group (50.0% vs 59.3%) compared to older group (35.9% vs 52.7%)
- headache: younger group (31.8% vs 51.2%) compared to older group (27.2% vs 36.3%)
- muscle pain: younger group (23.9% vs 45.3%) compared to older group (14.1% vs 28.6%)
- chills: younger group (9.1% vs 40.7%) compared to older group (7.6% vs 20.9%)
- joint pain: younger group (9.1% vs 17.4%) compared to older group (4.3% vs 16.5%)
- fever: younger group (3.4% vs 17.4%) compared to older group (0.0% vs 11.0%)
- vomiting: similar in both age groups and after either dose
- diarrhea: reported less frequently in the older group and was similar after each dose.

Use of antipyretic/pain medication also increased in frequency with increasing number of doses and was used more frequently in the younger group compared with the older group.

Most systemic events were mild or moderate in severity, had a median onset of 2 to 3 days after dosing, and resolved after a median duration of 1 day after onset. Fever and chills each had a median duration of 1 day after either dose for both age groups.

Across age groups, severe systemic events were observed only after Dose 2 of BNT162b2 overall and were reported for fever (1.1%), fatigue (4.0%), headache (2.8%), chills (2.3%), and muscle pain (1.7%). No grade 4 (potentially life-threatening) events were reported.

Systemic events were infrequent in placebo recipients.

2.5.5.4.3. Adverse Events – Phase 2

AE analysis results for 360 participants of Study C4591001 evaluated for Phase 2 were included with the Phase 3 AE analyses, and summarized separately here for data corresponding to the protocol defined objective of 7 days after Dose 2. AE data from participants in Phase 2 after this time point are otherwise included with Phase 3 analyses in Section 2.5.5.5.3.

The proportions of participants who reported any AEs up to 7 days after Dose 2 were similar in the BNT162b2 and placebo groups overall. Incidences in the BNT162b2 and placebo were similar within the age groups for younger (9.1% vs 11.1%) and older (4.3% vs 8.9%) participants. Two severe events of myalgia and gastric adenocarcinoma (which was also an SAE) were reported for 2 participants in the BNT162b2 younger age group, both assessed by the investigator as not related to study intervention. No other SAEs or any deaths were reported up to 7 days after Dose 2. The only discontinuation due to an AE during this time was the participant in the BNT162b2 younger age group who reported an SAE of gastric adenocarcinoma (discontinued from the study on Day 23 after Dose 1 of BNT162b2). There were no immediate AEs after any dose of BNT162b2 30 µg or placebo.

2.5.5.5. Safety Results - Phase 2/3 Safety in Study C4591001

Details of study population and safety analysis results in Phase 2/3 are provided in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 10 and Section 12.3 (up to 1 month after Dose 2), and Module 5.3.5.1 C4591001 6-Month Update Interim CSR Section 10 and Section 12.2 (up to 6 months after Dose 2).

C4591001 Phase 2/3 safety data are also presented in Module 2.7.4 and summarized below. Note that Phase 2/3 analyses included the 360 participants who were analyzed in Phase 2.

Safety data (reactogenicity and AE analyses) for participants in the Phase 2/3 portion of Study C4591001 are included up to the most recent data cutoff date of 13 March 2021. Participants ≥16 years of age are included in safety analyses presented in this submission; safety data for adolescents 12 to 15 years of age will be reported at a later time.

2.5.5.5.1. Safety Populations – Phase 2/3

The safety population included a total of 44,050 participants: 22,026 participants in the BNT162b2 group and 22,021 participants in the placebo group (Table 51). Most of the total 115 (0.3%) participants excluded from the safety population were excluded because those participants did not receive study vaccine.

HIV+ participants are included in this summary and summarized separately (per protocol). Safety analysis results of HIV+ participants are presented for adult participants (≥16 years of age) for the reactogenicity set and for other safety endpoints during the blinded placebo-controlled follow-up period.

There were no clinically meaningful differences in the safety population by age group, baseline SARS-CoV-2 status, ethnicity, race, or sex.

Table 51. Safety Population – Phase 2/3 Subjects ≥16 Years of Age

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) n[a]	Placebo n[a]	Total n[a] (%)
Randomized[b]			44165
Vaccinated	22032	22025	44060 (99.8)
Safety population	22026	22021	44050 (99.7)
HIV-positive	100	100	200 (0.5)
Indeterminate vaccine[c]			3 (0.0)
Excluded from safety population			115 (0.3)
Reason for exclusion			
Subject did not receive study vaccine			105 (0.2)
Unreliable data due to lack of PI oversight			10 (0.0)

Table 51. Safety Population – Phase 2/3 Subjects ≥16 Years of Age

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) n[a]	Placebo n[a]	Total n[a] (%)

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately.
a. n = Number of subjects with the specified characteristic, or the total sample.
b. This value is the denominator for the percentage calculations.
c. "Indeterminate vaccine" refers to subjects whose vaccine group (as administered) could not be determined. These subjects were not included in the safety analysis but their safety data is listed separately.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (01:42)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adsl_s003_pop_all_p3

2.5.5.5.1.1. Duration of Follow-Up

During the blinded placebo-controlled follow-up period, 51.1% of participants in the BNT162b2 group and 51.4% of participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 (Table 52). Altogether, 25,651 participants (58.2%) ≥16 years of age were followed for ≥4 months after the second dose.

From Dose 2 to the cutoff date, 54.5% of participants in the BNT162b2 group had a total follow-up time of ≥6 months after the second dose.

In the younger age group, 48.5% of participants in the BNT162b2 group and 48.3% of participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 during the blinded placebo-controlled follow-up period. From Dose 2 to the cutoff date, 51.0% of participants in the BNT162b2 group had a total follow-up time of ≥6 months.

In the older age group, 54.8% of participants in the BNT162b2 group and 55.9% of participants in the placebo group had follow-up time between ≥4 months to <6 months after Dose 2 during the blinded placebo-controlled follow-up period. From Dose 2 to the cutoff date, 59.6% of participants in the BNT162b2 group had a total follow-up time of ≥6 months.

During the open-label follow-up period, 47.5% of original placebo participants had follow-up time between ≥1 month to <2 months after Dose 1 of BNT162b2.

Table 52. Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=22026) n[b] (%)	Placebo (N[a]=22021) n[b] (%)	Total (N[a]=44047) n[b] (%)
Subjects (%) with length of follow-up of:			
Original blinded placebo-controlled follow-up period			
<2 Months	1251 (5.7)	1331 (6.0)	2582 (5.9)
≥2 Months to <4 months	7744 (35.2)	8070 (36.6)	15814 (35.9)
≥4 Months to <6 months	11253 (51.1)	11316 (51.4)	22569 (51.2)
≥6 Months	1778 (8.1)	1304 (5.9)	3082 (7.0)
Total exposure from Dose 2 to cutoff date			
<2 Months	390 (1.8)		
≥2 Months to <4 months	679 (3.1)		
≥4 Months to <6 months	8951 (40.6)		
≥6 Months	12006 (54.5)		

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, 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: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (01:37)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adsl_fu_d2_p3_saf

Table 53. Follow-up Time After Dose 1 of BNT162b2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received Placebo) – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=19611) n[b] (%)
Subjects (%) with length of follow-up of:	
Open-label follow-up period	
<1 Month	4934 (25.2)
≥1 Month to <2 months	9323 (47.5)
≥2 Months to <3 months	4145 (21.1)
≥3 Months	1209 (6.2)

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, 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: 25MAR2021 (23:24) Source Data: adsl Table Generation: 27MAR2021 (01:37)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA/adsl fu d1 p3 saf

2.5.5.5.1.2. Disposition

The disposition of all Phase 2/3 participants randomized is presented for the blinded placebo-controlled and open-label follow-up periods in Table 54.

Disposition of all randomized participants ≥16 years of age was similar by age group. Disposition of HIV+ participants is included in this summary but summarized separately in safety analyses.

Note, several participants remain in the study but were erroneously reported as withdrawn because of AEs, which was subsequently queried and corrected as described in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Errata.

Blinded Placebo-Controlled Follow-Up Period

During the blinded placebo-controlled follow-up period, most participants randomized received Dose 1 (99.8%) and Dose 2 (98.1%). There were 352 (1.6%) participants in the BNT162b2 group and 528 (2.4%) participants in the placebo group who discontinued from the vaccination period (Dose 1 to 1 month after Dose 2) (Table 54). Most participants completed the visit at 1 month post-Dose 2 (≥96.4%). Few participants in the BNT162b2 and

placebo groups were withdrawn from the study (1.6% and 2.2%, respectively), and most were due to withdrawals by the participant, or they were lost to follow-up.

There were 7 participants with special data issues: 8 participant identification numbers from 4 participants who enrolled into the study more than once and 3 participants whose vaccine assignment was not confirmed in the IRT at the time of data cutoff.

- Three participants who were randomized and vaccinated, but actual vaccine assignment was not confirmed in IRT at the time of data cutoff. Participants were vaccinated as per CRF, but due to the inability to confirm consistency between the data in the CRF and IRT, these participants were not assigned to any actual dosing group. Safety data from these 3 participants were excluded from safety summary tables but their safety data are listed separately (Table 54).

- During the conduct of this study, 4 participants were each randomized twice with different participant identification numbers at 2 different sites. Because the significant misconduct of these participants compromised the integrity of the study data, results from these participants were excluded from all efficacy and safety analyses, including disposition and demographic tabulations. These participants who were discontinued from vaccination and/or from the study are listed separately.

Open-Label Follow-Up Period

Individuals ≥16 years of age have been unblinded as they became locally eligible and wished to know their vaccine assignment to confirm prior vaccination with BNT162b2 (if randomized to this group), or to receive BNT162b2 (if randomized to placebo). Unblinded participants originally randomized to BNT162b2 continue to be followed in an open-label manner. Unblinded participants originally randomized to placebo are offered BNT162b2 vaccination (Doses 3 and 4; first and second dose of BNT162b2 30 µg, respectively) and thereafter followed in an open-label manner.

Most Phase 2/3 participants in the originally randomized BNT162b2 (96.8%) and placebo (96.4%) groups completed the 1 month post-Dose 2 visit before unblinding (Table 54).

A total of 87 (0.4%) original BNT162b2 participants received Dose 1 of BNT162b2 during the blinded placebo-controlled follow-up period and then received Dose 2 of BNT162b2 30 µg during the open-label follow-up period (when they were unblinded). There were 105 (0.5%) participants withdrawn from the study, and most were due to withdrawals by the participant, or they had a protocol deviation.

During the open-label follow-up period, most participants originally randomized in the placebo group received Doses 3 and 4 (88.8% and 72.4%, respectively) of BNT162b2. There were few participants in this group (0.1%) who were withdrawn from the study, and most were due to withdrawals by the participant.

Table 54. Disposition of All Randomized Subjects – Phase 2/3 Subjects ≥16 Years of Age

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=22085) n[b] (%)	Placebo (N[a]=22080) n[b] (%)	Total (N[a]=44165) n[b] (%)
Randomized	22085 (100.0)	22080 (100.0)	44165 (100.0)
Not vaccinated	55 (0.2)	50 (0.2)	105 (0.2)
Original blinded placebo-controlled follow-up period			
Vaccinated	22030 (99.8)	22030 (99.8)	44060 (99.8)
Dose 1	22030 (99.8)	22030 (99.8)	44060 (99.8)
Dose 2	21675 (98.1)	21650 (98.1)	43325 (98.1)
Discontinued from original blinded placebo-controlled vaccination period[c]	352 (1.6)	528 (2.4)	880 (2.0)
Reason for discontinuation			
Lost to follow-up	151 (0.7)	153 (0.7)	304 (0.7)
Withdrawal by subject	109 (0.5)	181 (0.8)	290 (0.7)
No longer meets eligibility criteria	26 (0.1)	120 (0.5)	146 (0.3)
Adverse event	27 (0.1)	26 (0.1)	53 (0.1)
Physician decision	5 (0.0)	8 (0.0)	13 (0.0)
Pregnancy	6 (0.0)	6 (0.0)	12 (0.0)
Protocol deviation	3 (0.0)	8 (0.0)	11 (0.0)
Death	3 (0.0)	4 (0.0)	7 (0.0)
Medication error without associated adverse event	3 (0.0)	2 (0.0)	5 (0.0)
Withdrawal by parent/guardian	1 (0.0)	0	1 (0.0)
Other	18 (0.1)	20 (0.1)	38 (0.1)
Unblinded before 1-month post–Dose 2 visit	253 (1.1)	240 (1.1)	493 (1.1)
Completed 1-month post–Dose 2 visit	21382 (96.8)	21293 (96.4)	42675 (96.6)
Withdrawn from the study	343 (1.6)	484 (2.2)	827 (1.9)
Withdrawn after Dose 1 and before Dose 2	176 (0.8)	211 (1.0)	387 (0.9)
Withdrawn after Dose 2 and before 1-month post–Dose 2 visit	100 (0.5)	139 (0.6)	239 (0.5)
Withdrawn after 1-month post–Dose 2 visit	67 (0.3)	134 (0.6)	201 (0.5)
Reason for withdrawal from the study			
Lost to follow-up	174 (0.8)	191 (0.9)	365 (0.8)
Withdrawal by subject	122 (0.6)	226 (1.0)	348 (0.8)
Protocol deviation	11 (0.0)	24 (0.1)	35 (0.1)
Death	16 (0.1)	15 (0.1)	31 (0.1)
Adverse event	9 (0.0)	8 (0.0)	17 (0.0)
Physician decision	3 (0.0)	6 (0.0)	9 (0.0)
No longer meets eligibility criteria	1 (0.0)	4 (0.0)	5 (0.0)
Pregnancy	0	1 (0.0)	1 (0.0)
Medication error without associated adverse event	1 (0.0)	0	1 (0.0)
Withdrawal by parent/guardian	1 (0.0)	0	1 (0.0)
Other	5 (0.0)	9 (0.0)	14 (0.0)
Open-label follow-up period			

Table 54. Disposition of All Randomized Subjects – Phase 2/3 Subjects ≥16 Years of Age

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N[a]=22085) n[b] (%)	Placebo (N[a]=22080) n[b] (%)	Total (N[a]=44165) n[b] (%)
Originally randomized to BNT162b2	20404 (92.4)		
Received Dose 2/unplanned dose	87 (0.4)		
Completed 1-month post–Dose 2 visit	210 (1.0)		
Completed 6-month post–Dose 2 visit	6414 (29.0)		
Withdrawn from the study	105 (0.5)		
Withdrawn before 6-month post–Dose 2 visit	103 (0.5)		
Withdrawn after 6-month post–Dose 2 visit	2 (0.0)		
Reason for withdrawal from the study			
Withdrawal by subject	56 (0.3)		
Protocol deviation	35 (0.2)		
Lost to follow-up	4 (0.0)		
Death	3 (0.0)		
Physician decision	2 (0.0)		
Adverse event	1 (0.0)		
No longer meets eligibility criteria	1 (0.0)		
Other	3 (0.0)		
Originally randomized to placebo		20948 (94.9)	
Withdrawn from the study after unblinding and before Dose 3		497 (2.3)	
Received Dose 3 (first dose of BNT162b2 [30 µg])		19612 (88.8)	
Received Dose 4 (second dose of BNT162b2 [30 µg])		15986 (72.4)	
Discontinued from open-label vaccination period[d]		24 (0.1)	
Reason for discontinuation from open-label vaccination period			
Protocol deviation		6 (0.0)	
Adverse event		5 (0.0)	
Withdrawal by subject		5 (0.0)	
Pregnancy		4 (0.0)	
Death		2 (0.0)	
Lost to follow-up		2 (0.0)	
Completed 1-month post–Dose 4 visit		7209 (32.6)	
Withdrawn from the study		14 (0.1)	
Withdrawn after Dose 3 and before Dose 4		11 (0.0)	
Withdrawn after Dose 4 and before 1-month post–Dose 4 visit		2 (0.0)	
Withdrawn after 1-month post–Dose 4 visit		1 (0.0)	
Reason for withdrawal from the study			
Withdrawal by subject		7 (0.0)	
Protocol deviation		3 (0.0)	
Death		2 (0.0)	
Adverse event		1 (0.0)	

Table 54. Disposition of All Randomized Subjects – Phase 2/3 Subjects ≥16 Years of Age

	Vaccine Group (as Randomized)		
	BNT162b2 (30 µg) (N^a=22085) n^b (%)	Placebo (N^a=22080) n^b (%)	Total (N^a=44165) n^b (%)
Lost to follow-up		1 (0.0)	

Note: Human immunodeficiency virus (HIV)-positive subjects are included in this summary but analyzed and reported separately.
Note: Subjects randomized but did not sign informed consent or had a significant quality event due to lack of PI oversight are not included in any analysis population.
Note: Because of a dosing error, Subjects C4591001 1081 10811053, C4591001 1088 10881077, C4591001 1177 11771089 and C4591001 1231 12311057 received an additional dose of BNT162b2 (30 µg) at an unscheduled visit after receiving 1 dose of BNT162b2 (30 µg) and 1 dose of placebo.
a. N = number of randomized 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. Original blinded placebo-controlled vaccination period is defined as the time period from Dose 1 to 1 month post–Dose 2.
d. Open-label vaccination period is defined as the time period from Dose 3 (first dose of BNT162b2 [30 µg]) to 1 month post–Dose 4 (second dose of BNT162b2 [30 µg]).
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:20) Source Data: adds Table Generation: 27MAR2021 (16:34)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA/adds s002 all p3 rand

2.5.5.5.1.3. Demographics

2.5.5.5.1.3.1. Participants ≥16 Years of Age

Demographic characteristics for all Phase 2/3 participants ≥16 years of age were similar in the BNT162b2 and placebo groups (Table 55). Overall, most participants were White (82.0%), with 9.6% Black or African American participants and 4.3% Asian participants, and all other racial groups were ≤2.5%. There were 25.9% Hispanic/Latino participants. Median age was 51.0 years and 50.9% of participants were male. Obesity was reported in 34.4% of participants in this safety population.

Baseline SARS-CoV-2 status was positive (defined as a positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19) in 3.1% of participants in the BNT162b2 group and 3.3% of participants in the placebo group.

Demographic data for participants 12 to 15 years of age in this study are provided in the Module 5.3.5.1 C4591001 6-Month Update Interim CSR. These participants were included in the efficacy populations, as defined in the protocol, for updated analyses of efficacy; safety data for participants 12 to 15 years of age will be reported separately at a later time.

Table 55. Demographic Characteristics – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=22026) n[b] (%)	Placebo (N[a]=22021) n[b] (%)	Total (N[a]=44047) n[b] (%)
Sex			
Male	11322 (51.4)	11098 (50.4)	22420 (50.9)
Female	10704 (48.6)	10923 (49.6)	21627 (49.1)
Race			
White	18056 (82.0)	18064 (82.0)	36120 (82.0)
Black or African American	2098 (9.5)	2118 (9.6)	4216 (9.6)
American Indian or Alaska Native	221 (1.0)	217 (1.0)	438 (1.0)
Asian	952 (4.3)	942 (4.3)	1894 (4.3)
Native Hawaiian or other Pacific Islander	58 (0.3)	32 (0.1)	90 (0.2)
Multiracial	550 (2.5)	533 (2.4)	1083 (2.5)
Not reported	91 (0.4)	115 (0.5)	206 (0.5)
Racial designation			
Japanese	78 (0.4)	78 (0.4)	156 (0.4)
Ethnicity			
Hispanic/Latino	5704 (25.9)	5695 (25.9)	11399 (25.9)
Non-Hispanic/non-Latino	16211 (73.6)	16212 (73.6)	32423 (73.6)
Not reported	111 (0.5)	114 (0.5)	225 (0.5)
Country			
Argentina	2883 (13.1)	2881 (13.1)	5764 (13.1)
Brazil	1452 (6.6)	1448 (6.6)	2900 (6.6)
Germany	249 (1.1)	250 (1.1)	499 (1.1)
South Africa	401 (1.8)	399 (1.8)	800 (1.8)
Turkey	249 (1.1)	249 (1.1)	498 (1.1)
USA	16792 (76.2)	16794 (76.3)	33586 (76.3)
Age group (at vaccination)			
16-55 Years	13069 (59.3)	13095 (59.5)	26164 (59.4)
>55 Years	8957 (40.7)	8926 (40.5)	17883 (40.6)
Age at vaccination (years)			
Mean (SD)	49.7 (15.99)	49.6 (16.05)	49.7 (16.02)
Median	51.0	51.0	51.0
Min, max	(16, 89)	(16, 91)	(16, 91)
Baseline SARS-CoV-2 status			
Positive[c]	689 (3.1)	716 (3.3)	1405 (3.2)
Negative[d]	21185 (96.2)	21180 (96.2)	42365 (96.2)
Missing	152 (0.7)	125 (0.6)	277 (0.6)
Body mass index (BMI)			
Underweight (<18.5 kg/m^2)	271 (1.2)	304 (1.4)	575 (1.3)
Normal weight (≥18.5 kg/m^2 - 24.9 kg/m^2)	6535 (29.7)	6524 (29.6)	13059 (29.6)
Overweight (≥25.0 kg/m^2 - 29.9 kg/m^2)	7670 (34.8)	7558 (34.3)	15228 (34.6)

Table 55. Demographic Characteristics – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=22026) n[b] (%)	Placebo (N[a]=22021) n[b] (%)	Total (N[a]=44047) n[b] (%)
Obese (≥30.0 kg/m^2)	7543 (34.2)	7629 (34.6)	15172 (34.4)
Missing	7 (0.0)	6 (0.0)	13 (0.0)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
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, or the total sample. This value is the denominator for the percentage calculations.
b. n = Number of subjects with the specified characteristic.
c. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
d. 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 (23:24) Source Data: adsl Table Generation: 27MAR2021 (15:19)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adsl_s005_demo_all_p3_saf

Within each age group, most demographic characteristics were similar in the BNT162b2 group and the placebo group. Overall, 4.0% of participants in the younger age group were SARS-CoV-2 baseline positive, and 1.9% of participants in the older age group were SARS-CoV-2 baseline positive, and the proportions were similar in the BNT162b2 and placebo groups. There was a lower proportion of non-Hispanic/non-Latino participants in the younger BNT162b2 and placebo groups (68.6% and 68.8%, respectively) than in the older BNT162b2 and placebo groups (80.9% and 80.7%, respectively).

Within each baseline SARS-CoV-2 status group, demographic characteristics were similar in the BNT162b2 group and the placebo group. Most participants were White regardless of baseline status; however, there was a higher proportion of White participants among those with a negative baseline status (82.9%) than with a positive baseline status (57.7%). The median age was 43.0 years in participants with a positive baseline status and 51.0 years in participants with a negative baseline status. There were 41.4% and 34.2% of participants who were obese with positive and negative baseline status, respectively.

Participants ≥16 years of age had a diverse medical history profile consistent with that of individuals in the general population in the same age group. In the BNT162b2 group, conditions in the surgical and medical procedures (8430 [38.3%]), metabolism and nutrition disorders (6587[29.9%]), and immune system disorders (5987 [27.2%]; of which 3303 [15.0%] were seasonal allergy) SOCs were most frequently reported.

Overall, 20.7% of participants had any comorbidity (per the Charlson comorbidity index). The most frequently reported comorbidities were diabetes without chronic complications (7.7%), chronic pulmonary disease (8.1%), and any malignancy (3.6%), which were reported at similar frequencies in each vaccine group.

- In the younger age group, 13.3% of participants had any comorbidity. The most frequently reported comorbidities were diabetes without chronic complications (3.7%) and chronic pulmonary disease (7.4%), which were reported at similar frequencies in each vaccine group.

- In the older age group, 31.6% of participants had any comorbidity. The most frequently reported comorbidities were diabetes without chronic complications (13.6%) and chronic pulmonary disease (9.1%), which were reported at similar frequencies in each vaccine group.

HIV+ Participants

Demographic characteristics for participants with confirmed stable HIV disease were similar in the BNT162b2 and the placebo groups. Overall, 54.5% of participants were Black or African American, 40.5% of participants were White, and all other racial groups were ≤1.5%. There were 16.0% Hispanic/Latino participants. Median age was 49.5 years and 67.5% of participants were male. Obese participants made up 39.0% of this population.

2.5.5.5.1.3.2. Participants With at Least 6 Months Follow-Up Time – BNT162b2 Group

Demographic characteristics for all original BNT162b2 Phase 2/3 participants ≥16 years of age and had at least 6 months of follow-up time after Dose 2 are presented in Table 56. Overall, most participants were White (86.4%), with 7.1% Black or African American participants and 3.8% Asian participants, and other racial groups were ≤1.6%. There were 27.8% Hispanic/Latino participants. Median age was 53.0 years and 50.3% of participants were male. Obese participants made up 34.2% of this safety population.

Table 56. Demographic Characteristics – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=12006) n[b] (%)
Sex	
Male	6040 (50.3)
Female	5966 (49.7)
Race	
White	10370 (86.4)
Black or African American	851 (7.1)
American Indian or Alaska Native	55 (0.5)

Table 56. Demographic Characteristics – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=12006) n[b] (%)
Asian	452 (3.8)
Native Hawaiian or other Pacific Islander	31 (0.3)
Multiracial	195 (1.6)
Not reported	52 (0.4)
Racial designation	
Japanese	44 (0.4)
Ethnicity	
Hispanic/Latino	3339 (27.8)
Non-Hispanic/non-Latino	8604 (71.7)
Not reported	63 (0.5)
Country	
Argentina	2118 (17.6)
Brazil	596 (5.0)
USA	9292 (77.4)
Age group (at vaccination)	
16-55 Years	6666 (55.5)
>55 Years	5340 (44.5)
Age at vaccination (years)	
Mean (SD)	51.4 (15.44)
Median	53.0
Min, max	(18, 85)
Baseline SARS-CoV-2 status	
Positive[c]	250 (2.1)
Negative[d]	11678 (97.3)
Missing	78 (0.6)
Body mass index (BMI)	
Underweight (<18.5 kg/m^2)	136 (1.1)
Normal weight (≥18.5 kg/m^2 - 24.9 kg/m^2)	3527 (29.4)
Overweight (≥25.0 kg/m^2 - 29.9 kg/m^2)	4232 (35.2)
Obese (≥30.0 kg/m^2)	4107 (34.2)
Missing	4 (0.0)

Table 56. Demographic Characteristics – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=12006) n[b] (%)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
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.
c. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
d. 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 (23:24) Source Data: adsl Table Generation: 27MAR2021 (15:19)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA/adsl s005 demo 6m p3 saf

2.5.5.5.1.3.3. Placebo Group Who Received BNT162b2

Demographic characteristics for all original placebo Phase 2/3 participants who then received BNT162b2 later during the open-label follow-up period are presented in Table 57. Overall, most participants were White (83.1%), with 8.3% Black or African American participants and 4.3% Asian participants, and all other racial groups were ≤2.6%. There were 25.5% Hispanic/Latino participants. Median age was 51.0 years and 50.2% of participants were male. Obese participants made up 34.4% of this safety population.

Table 57. Demographic Characteristics – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=19611) n[b] (%)
Sex	
Male	9841 (50.2)
Female	9770 (49.8)
Race	
White	16299 (83.1)

Table 57. Demographic Characteristics – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=19611) n[b] (%)
Black or African American	1636 (8.3)
American Indian or Alaska Native	189 (1.0)
Asian	849 (4.3)
Native Hawaiian or other Pacific Islander	28 (0.1)
Multiracial	509 (2.6)
Not reported	101 (0.5)
Racial designation	
Japanese	77 (0.4)
Ethnicity	
Hispanic/Latino	5002 (25.5)
Non-Hispanic/non-Latino	14499 (73.9)
Not reported	110 (0.6)
Country	
Argentina	2612 (13.3)
Brazil	1428 (7.3)
Germany	241 (1.2)
South Africa	362 (1.8)
Turkey	242 (1.2)
USA	14726 (75.1)
Age group (at vaccination)	
16-55 Years	11404 (58.2)
>55 Years	8207 (41.8)
Age at vaccination (years)	
Mean (SD)	50.1 (15.91)
Median	51.0
Min, max	(16, 91)
Baseline SARS-CoV-2 status	
Positive[c]	590 (3.0)
Negative[d]	18909 (96.4)
Missing	112 (0.6)
Body mass index (BMI)	
Underweight (<18.5 kg/m^2)	258 (1.3)
Normal weight (≥18.5 kg/m^2 - 24.9 kg/m^2)	5805 (29.6)
Overweight (≥25.0 kg/m^2 - 29.9 kg/m^2)	6790 (34.6)
Obese (≥30.0 kg/m^2)	6753 (34.4)
Missing	5 (0.0)

Table 57. Demographic Characteristics – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=19611) n[b] (%)

Abbreviation: SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2.
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.
c. Positive N-binding antibody result at Visit 1, positive NAAT result at Visit 1, or medical history of COVID-19.
d. 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 (23:24) Source Data: adsl Table Generation: 27MAR2021 (15:20)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2 unblinded/C4591001 BLA/adsl s005 demo cr p3 saf

2.5.5.5.2. Reactogenicity – Phase 2/3

Reactogenicity (local reactions and systemic events) was assessed via e-diary in a subset of participants in up to 7 days after each dose in the blinded placebo-controlled follow-up period.

Local reactions are summarized in Section 2.5.5.4.2.1 and systemic events are summarized in Section 2.5.5.4.2.2 for the reactogenicity subset of the safety population, subgroups of participants defined by baseline SARS-CoV-2 status, and participants with stable HIV.

The reactogenicity subset of the safety population included e-diary data for participants in each group as follows:

- BNT162b2 group:
  - Younger adults 16 to 55 years of age: N=2899 post Dose 1 and N=2682 post Dose 2
  - Older adults >55 years of age: N=2008 post Dose 1 and N=1860 post Dose 2

- Placebo group:
  - Younger adults 16 to 55 years of age: N=2908 post Dose 1 and N=2684 post Dose 2
  - Older adults >55 years of age: N=1989 post Dose 1 and N=1833 post Dose 2

The baseline SARS-CoV-2 positive reactogenicity subset was comprised of adults ≥16 years of age and included e-diary data for the N=177 post Dose 1 and N=153 post Dose 2 in the BNT162b2 group, and N=187 post Dose 1 and N=165 post Dose 2 in the placebo group.

The baseline SARS-CoV-2 negative reactogenicity subset was comprised of adults ≥16 years of age and included e-diary data for the N=4701 post Dose 1 and N=4368 post Dose 2 in the BNT162b2 group, and N=4690 post Dose 1 and N=4334 post Dose 2 in the placebo group.

The HIV+ reactogenicity subset was comprised of adults ≥16 years of age and included e-diary data for the N=54 post Dose 1 and N=60 post Dose 2 in the BNT162b2 group, and N=56 post Dose 1 and N=62 post Dose 2 in the placebo group.

2.5.5.5.2.1. Local Reactions

In the BNT162b2 group, pain at the injection site was reported more frequently in the younger age group than in the older age group and frequency was similar after Dose 1 compared with Dose 2 of BNT162b2 in the younger age group (83.7% vs 78.3%) and in the older age group (70.1% vs 66.1%) (Figure 11 and Figure 12, respectively). In the placebo group, pain at the injection site after Doses 1 and 2 was reported at slightly higher frequencies in the younger age group (14.2% and 11.6%, respectively) than in the older age group (9.3% and 7.8%, respectively).

In the BNT162b2 group, frequencies of redness and swelling were similar in the younger and older age group after Doses 1 and 2. Frequencies of redness were similar after Dose 1 compared with Dose 2 of BNT162b2 in the younger age group (5.4% vs 5.6%) and in the older age group (5.3% vs 7.2%). Frequencies of swelling were similar after Dose 1 compared with Dose 2 of BNT162b2 in the younger age group (6.3% vs 6.8%, respectively) and in the older age group (7.0% vs 7.8%). In the placebo group, redness and swelling were reported infrequently in the younger (≤1.0%) and older (≤1.2%) groups after Doses 1 and 2.

Overall, across age groups, pain at the injection site did not increase after Dose 2, and redness and swelling were generally similar in frequency after Dose 1 and Dose 2. Severe redness and swelling were reported infrequently and were similar in the younger and older age groups (≤0.7%) after any dose. Severe pain at the injection site occurred more frequently in the younger age group compared to the older age group (2.5% vs 0.7%). After the first and second dose and in both age groups, the majority of local reactions were mild or moderate in severity, and no grade 4 local reactions were reported.

The median onset for local reactions after either dose of BNT162b2 was between Day 1.0 and Day 2.0 in the younger age group and between Day 1.0 and Day 3.0 in the older age group (Day 1 was the day of vaccination). Local reactions resolved with median durations between 1.0 and 2.0 days in both age groups.

Subgroup Analyses

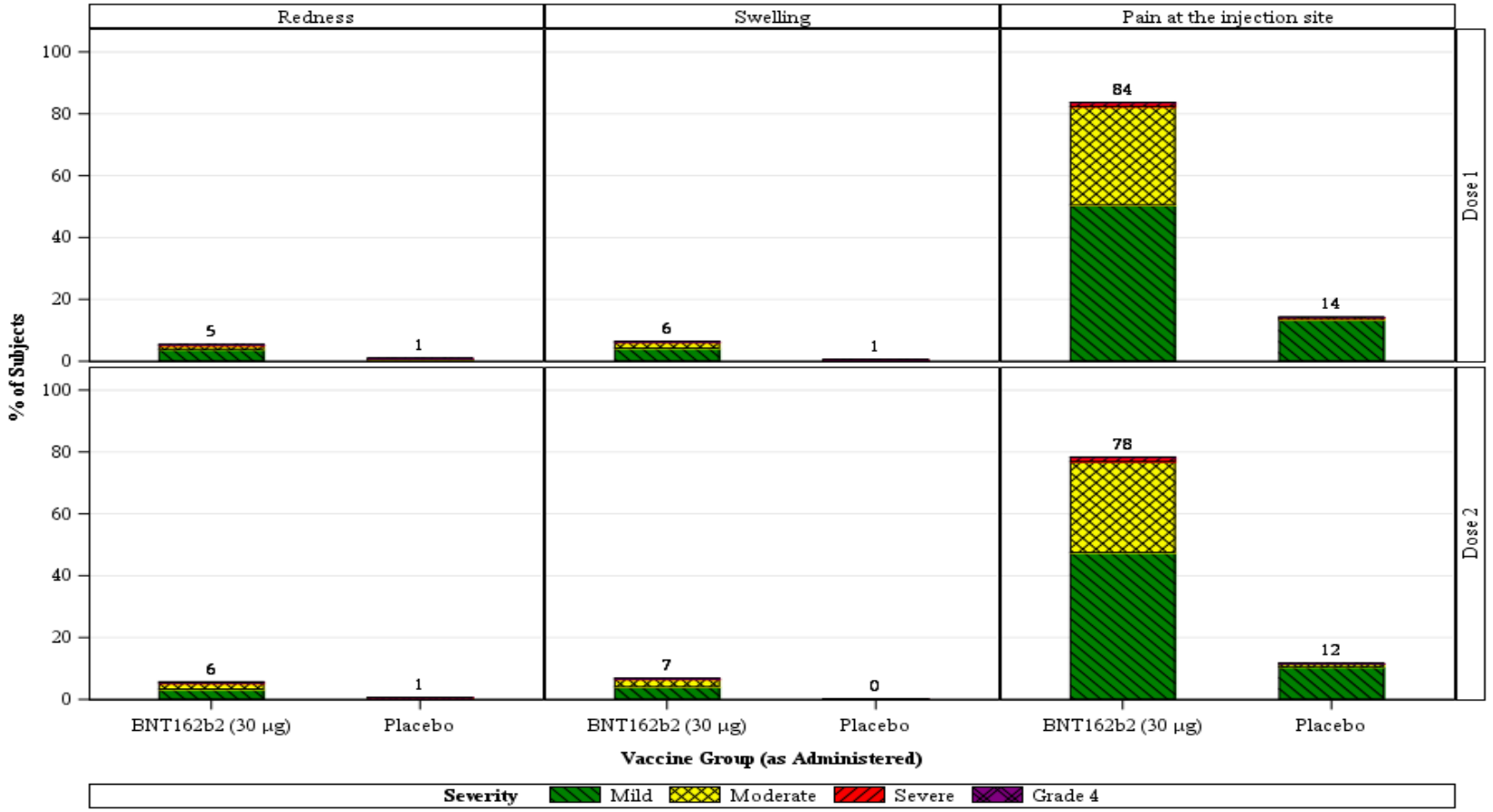
There were 177 BNT162b2 and 187 placebo participants with baseline positive SARS-CoV-2 status, and 4701 BNT162b2 and 4690 placebo participants with baseline negative SARS-CoV-2 status. For local reactions the frequency of redness, swelling, and pain at the injection site after any dose of BNT162b2 was 8.5%, 10.2%, and 80.2% compared with 9.9%, 11.1%, and 84.5% for those positive and negative at baseline, respectively.

While the frequency of local reactions was numerically higher in those negative at baseline, these differences are not clinically meaningful.

HIV+ Participants

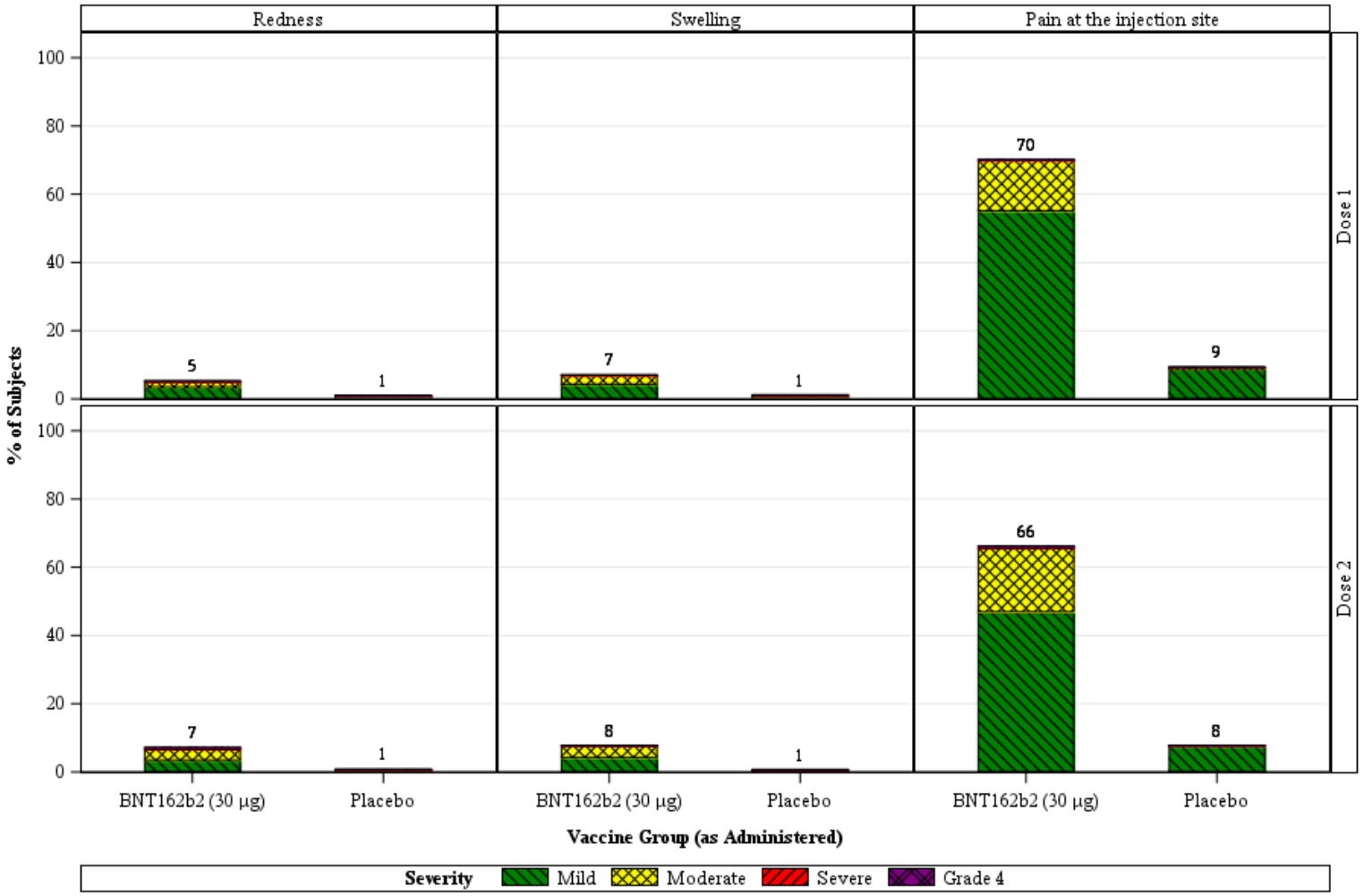
Local reactions in participants with confirmed stable HIV disease were similar to those observed for all participants ≥16 years of age by severity, onset day, and median duration. The frequency of pain at the injection site was similar after Dose 1 compared with Dose 2 of BNT162b2 (63.0% vs 53.3%). The frequency of redness and swelling was similar after Dose 1 compared with Dose 2 of BNT162b2 (redness: 3.7% vs 6.7%; swelling: 5.6% vs 8.3%, respectively). There was 1 (1.7%) severe reaction (pain at the injection site) reported after Dose 2 of BNT162b2 and no grade 4 reactions were reported.

Figure 11. Participants Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose, by Age Group – Reactogenicity Subset for Phase 2/3 Analysis – Safety Population Age Group: 16-55 Years



Note: Number above each bar denotes percentage of subjects reporting the reaction with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adfacevd Table Generation: 27MAR2021 (01:55)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adce_f001_lr_max_age_p3

Figure 12. Participants Reporting Local Reactions, by Maximum Severity, Within 7 Days After Each Dose, by Age Group – Reactogenicity Subset for Phase 2/3 Analysis – Safety Population Age Group: >55 Years



Note: Number above each bar denotes percentage of subjects reporting the reaction with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adfacevd Table Generation: 27MAR2021 (01:55)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adce_f001_lr_max_age_p3

2.5.5.5.2.2. Systemic Events

Systemic events were generally increased in frequency and severity in the younger group (Figure 13) compared with the older group (Figure 14), with frequencies and severity increasing with number of doses (Dose 1 vs Dose 2). Vomiting and diarrhea were exceptions, with vomiting reported similarly infrequently in both age groups and diarrhea reported at similar incidences after each dose.

Systemic events in the younger group compared with the older group, with frequencies increasing with number of doses (Dose 1 vs Dose 2), were:

- fatigue: younger group (49.4% vs 61.5%) compared to older group (33.7% vs 51.0%)
- headache: younger group (43.5% vs 54.0%) compared to older group (25.0% vs 39.4%)
- muscle pain: younger group (22.9% vs 39.3%) compared to older group (13.6% vs 28.9%)
- chills: younger group (16.5% vs 37.8%) compared to older group (6.5% vs 23.4%)
- joint pain: younger group (11.8% vs 23.8%) compared to older group (8.7% vs 19.0%)
- fever: younger group (4.1% vs 16.4%) compared to older group (1.3% vs 11.8%)
- vomiting: younger group (1.2% vs 2.2%) compared to older group (0.5% vs 0.7%)
- diarrhea: younger group (10.7% vs 10.0%) compared to older group (8.4% vs 8.2%).

Systemic events were generally reported less frequently in the placebo group than in the BNT162b2 group, for both age groups and doses, with some exceptions. In the younger age group, vomiting and diarrhea (after Dose 1 and Dose 2) were reported at similar frequencies in the placebo group and the BNT162b2 group (Figure 13). In the older age group, vomiting and diarrhea (after Dose 1 and Dose 2) were reported at similar frequencies in the placebo group and the BNT162b2 group (Figure 14).

Following both Dose 1 and Dose 2, use of antipyretic/pain medication was slightly less frequent in the older age group (19.0% vs 37.0%) than in the younger age group (27.8% vs 45.2%) after both doses, and medication use increased in both age groups after Dose 2 as compared with after Dose 1. Use of antipyretic/pain medication was less frequent in the placebo group than in the BNT162b2 group and was similar after Dose 1 and Dose 2 in the younger and older placebo groups (ranging from 9.3% to 13.7%).

Severe fever (>38.9 °C to 40.0 °C) increased in frequency with the number of doses (Dose 1 vs Dose 2) in younger (0.3% vs 1.5%) and older (0.0% vs 0.4%) participants who received BNT162b2 and was reported in 0.1% of participants who received placebo in both age group after both doses. One participant in the younger BNT162b2 group reported fever of 41.2 °C only on Day 2 after Dose 2 and was nonfebrile for all other days of the reporting period. Grade 4 fever was not reported in the older BNT162b2 group or in any placebo participants.

After the first and second dose and in both age groups, the majority of systemic events were mild or moderate in severity.

Systemic events in the younger and older age groups after either dose of BNT162b2 had a median onset day between Day 2.0 and Day 4.0 (Day 1.0 was the day of vaccination) and resolved with a median duration of 1 day in both age groups.

Subgroup Analyses

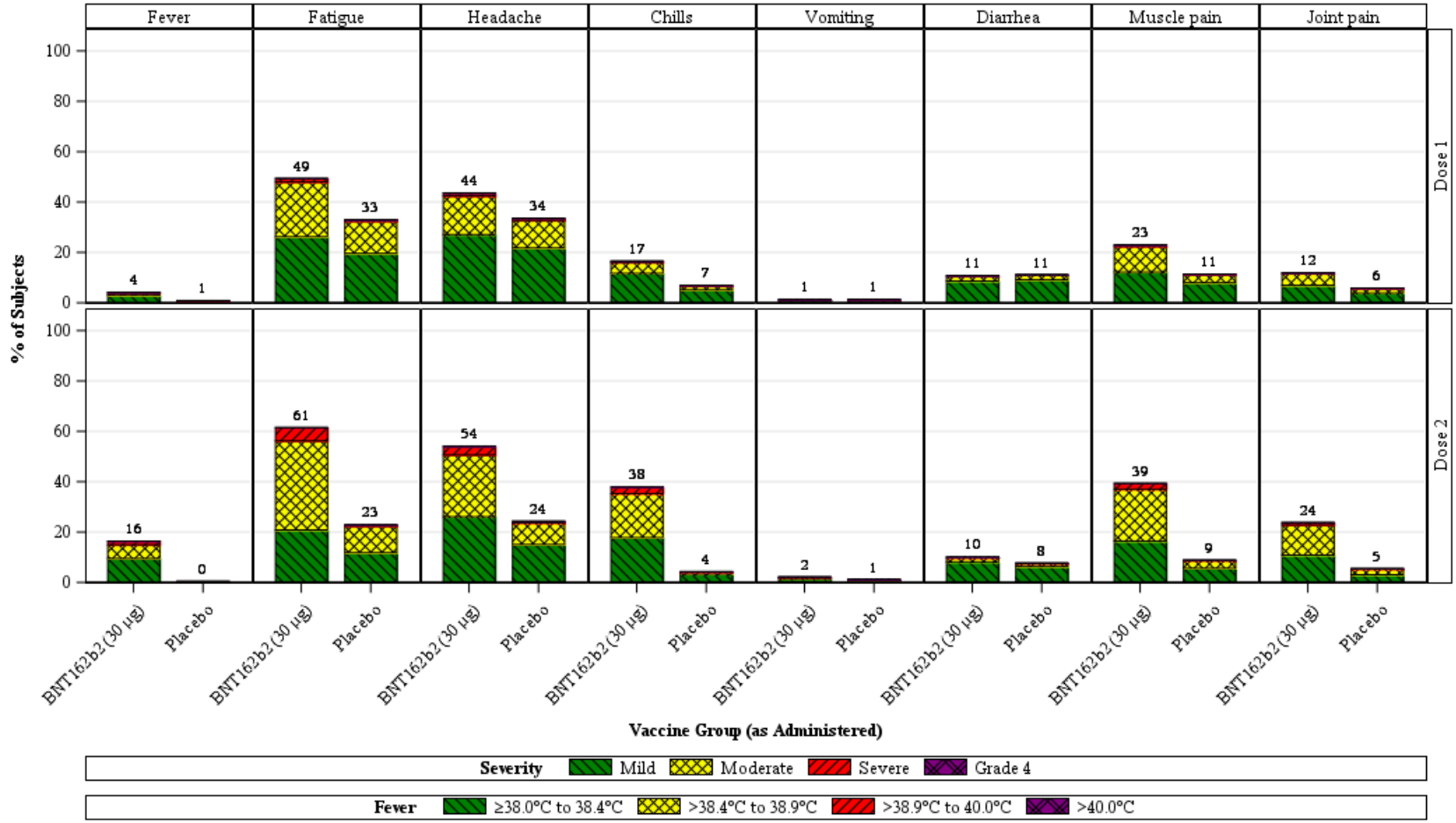
There were 177 BNT162b2 and 187 placebo participants with baseline positive SARS-CoV-2 status, and 4701 BNT162b2 and 4690 placebo participants with baseline negative SARS-CoV-2 status. For any fever after either dose of BNT162b2 there were 31 (17.5%) compared to 714 (15.1%) in those positive and negative for SARS-CoV-2 at baseline, respectively. Severe fever (>38.9 °C to 40.0 °C) was reported in 1 participant (0.6%) and 49 participants (1.0%) in those positive and negative for SARS-CoV-2 at baseline, respectively. The frequency for other systemic events after any dose was numerically lower for those positive at baseline: fatigue, headache and chills the frequency was 54.2%, 49.7% and 32.8% compared with 65%, 57.4%, 34.7% for those positive and negative for SARS-CoV-2 at baseline, respectively. Joint pain was another exception where 27.1% compared to 25.0% were reported in those positive and negative for SARS-CoV-2 at baseline.

Note that the baseline SARS-CoV-2 positive subgroup included far fewer participants the negative subgroup, so their results should be interpreted with caution.

HIV+ Participants

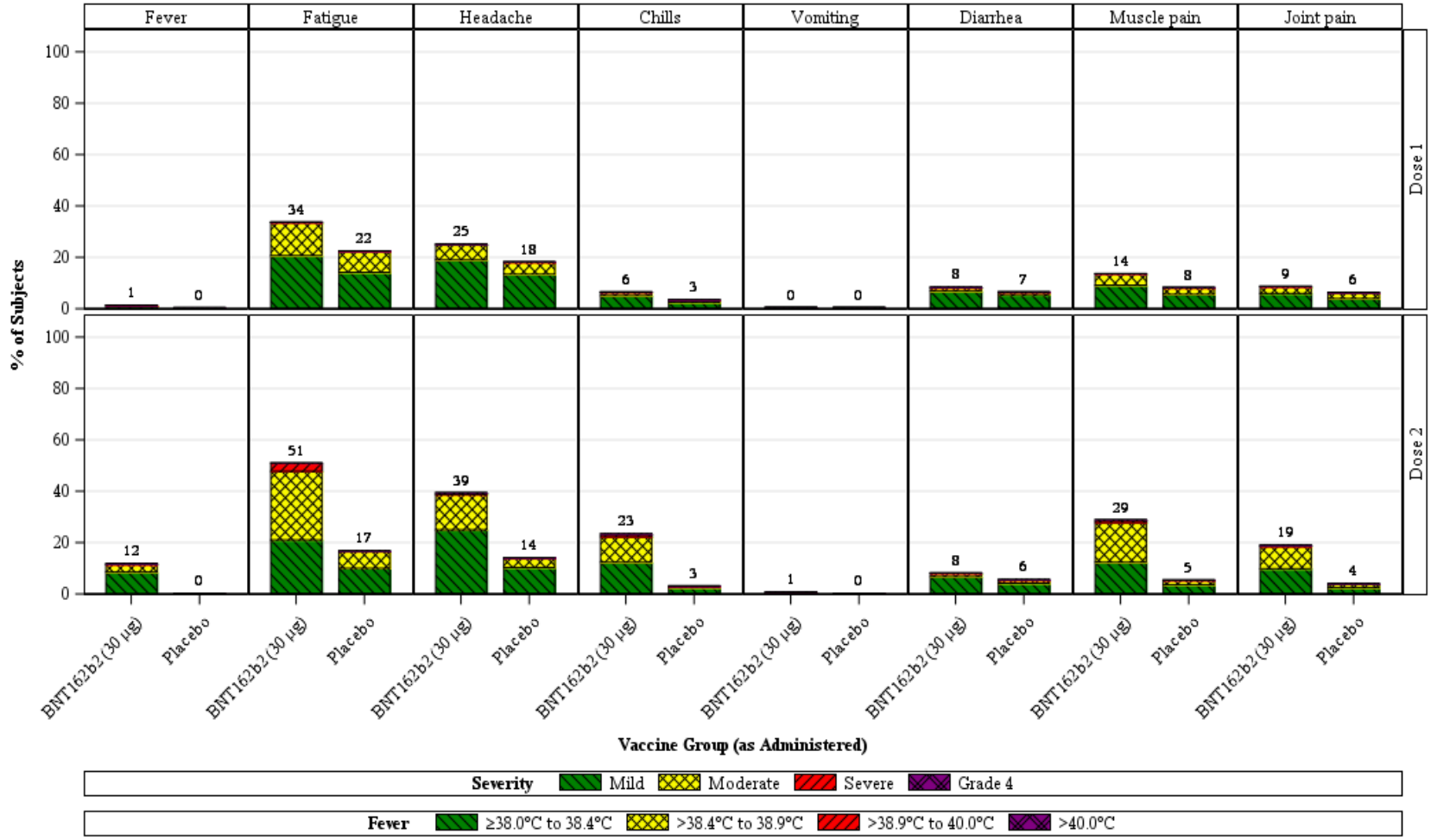
Systemic events from participants with confirmed stable HIV disease were similar to those observed for all participants ≥16 years of age by severity, onset day, and median duration. Fever, headache, chills, and joint pain increased in frequency from Dose 1 to Dose 2 while fatigue, vomiting, diarrhea, and muscle pain were similar after each dose. There were no severe systemic events after Dose 1 of BNT162b2, but after Dose 2, there was 1 (1.7%) severe fever (>38.9 °C to 40.0 °C), 3 participants (5.0%) with severe fatigue, 2 participants (3.3%) with severe headache, 1 participant (1.7%) with severe chills, and 1 participant (1.7%) with severe diarrhea. There were no grade 4 systemic events reported after either dose.

Figure 13. Participants Reporting Systemic Events, by Maximum Severity, Within 7 Days After Each Dose, by Age Group – Reactogenicity Subset for Phase 2/3 Analysis – Safety Population Age Group: 16-55 Years



Note: Number above each bar denotes percentage of subjects reporting the event with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adfacevd Table Generation: 27MAR2021 (01:55)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adce_f001_se_max_age_p3

Figure 14. Participants Reporting Systemic Events, by Maximum Severity, Within 7 Days After Each Dose, by Age Group – Reactogenicity Subset for Phase 2/3 Analysis – Safety Population Age Group: >55 Years



Note: Number above each bar denotes percentage of subjects reporting the event with any severity.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:22) Source Data: adfacevd Table Generation: 27MAR2021 (01:55)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adce_f001_se_max_age_p3

2.5.5.5.3. Adverse Events – Phase 2/3

AEs are presented separately for the blinded and open-label follow-up periods as follows.

Blinded follow-up: participants randomized to BNT162b2 and placebo:

- Younger (16 to 55 years of age) and older (>55 years of age) groups, including HIV+ subset
  - from Dose 1 up to 1 month after Dose 2
  - from Dose 1 up to end of blinded follow-up (date of unblinding)

Open-label follow-up for BNT162b2: participants originally randomized to BNT162b2, from date of unblinding through the data cutoff date.

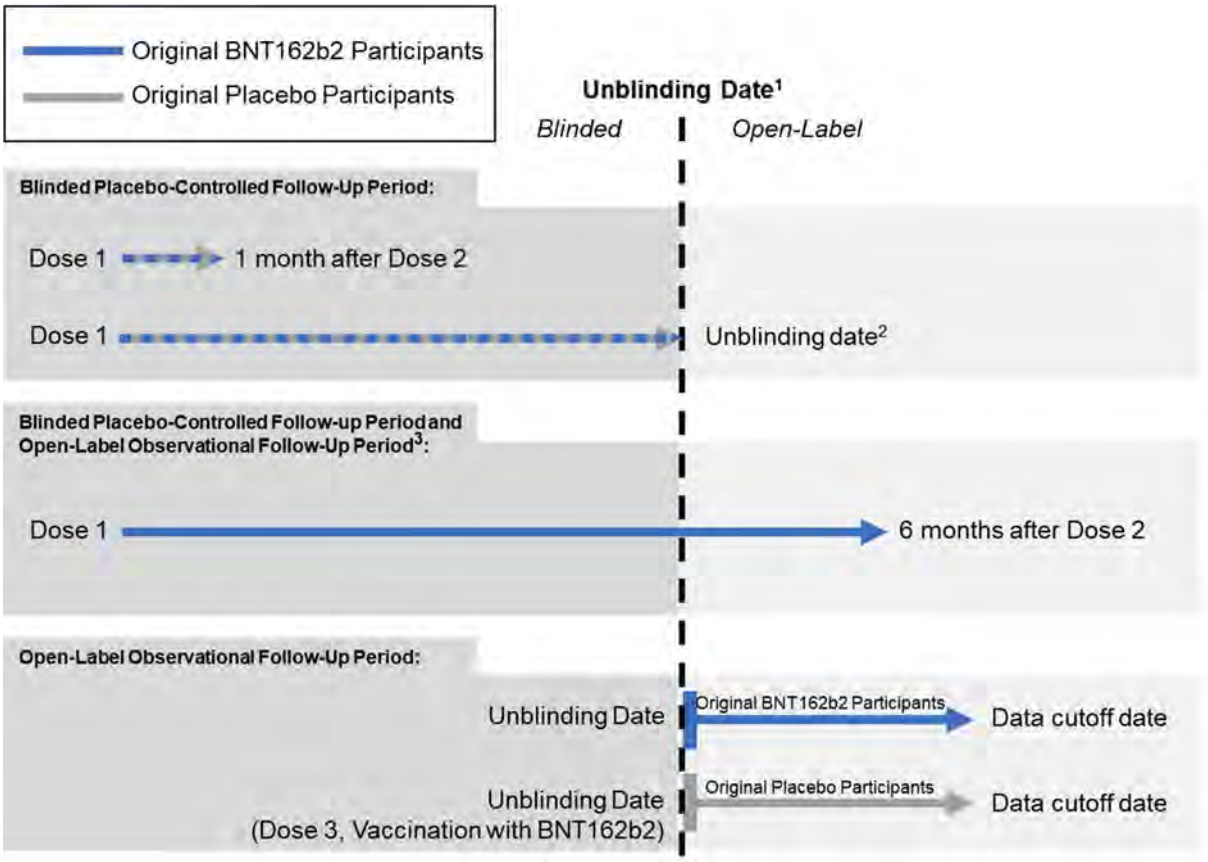
Cumulative blinded and open-label follow-up for BNT162b2: participants originally randomized to BNT162b2, inclusive of blinded and post-unblinding open-label periods, from Dose 1 up to at least 6 months after Dose 2 (at least 3000 participants per age group).

Open-label follow-up for placebo after receiving BNT162b2: participants originally randomized to placebo from time of unblinding/BNT162b2 vaccination (Dose 3) through the data cutoff date.

Note that due to individual study participant unblinding to treatment assignment (per protocol), safety data were calculated as IRs to adjust for variable exposure time in analyses of time intervals either up to, or starting from, the unblinding date.

A schematic of AE analyses by study group and time period is shown in Figure 15.

Figure 15. Study C4591001 Phase 2/3 Safety Analyses: Time Periods and Analysis Groups



[1] AE data analyzed from Dose 1 to unblinding date (on or after 14 December 2020) or from unblinding date to data cutoff date (13 March 2021) reported as IRs per 100 PY adjusted for exposure time; varies per participant.
[2] Blinded placebo-controlled follow-up period duration up to ~6 months after Dose 2.
[3] Cumulative BNT162b2 follow-up to ≥6 months after Dose 2, N≥3000/age group (16 -55, >55 years of age).

2.5.5.5.3.1. Blinded Follow-Up Period from Dose 1 Through 1 Month After Dose 2

2.5.5.5.3.1.1. Summary of Adverse Events

An overview of AEs from Dose 1 to 1 month after Dose 2 for participants during the blinded safety follow-up (including those analyzed in Phase 2) is presented in Table 58.

The numbers of overall participants who reported at least 1 AE and at least 1 related AE were higher in the BNT162b2 group (30.2% and 23.9%, respectively) as compared with the placebo group (13.9% and 6.0%, respectively). The higher frequencies in the BNT162b2 was due to terms consistent with reactogenicity reported at greater frequency in the BNT162b2 group versus the placebo group; this pattern is further analyzed in Section 2.5.5.5.3.1.2. Severe AEs were reported by 1.2% and 0.7% in in the BNT162b2 and placebo groups respectively, and life-threatening AEs were similar (0.1% in both groups).

SAEs and AEs leading to withdrawal were reported by ≤0.6% and ≤0.2%, respectively, in both groups. Discontinuations due to related AEs were reported in 13 participants in the BNT162b2 group and 11 participants in the placebo group (0.1% in both groups).

From Dose 1 to 1 month after Dose 2, there were 3 deaths in the BNT162b2 group and 5 deaths in the placebo group during the blinded follow-up period (Section 2.5.5.5.4.1).

In the younger age group, the number of participants who reported at least 1 AE from Dose 1 to 1 month after Dose 2 was 4233 (32.6%) and 1871 (14.4%) in the BNT162b2 and placebo groups, respectively. In the older age group, the number of participants who reported at least 1 AE from Dose 1 to 1 month after Dose 2 was 2384 (26.7%) and 1177 (13.2%) in the BNT162b2 and placebo groups, respectively.

Table 58. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2 – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)	
Adverse Event	**BNT162b2 (30 µg) (N[a]=21926) n[b] (%)**	**Placebo (N[a]=21921) n[b] (%)**
Any event	6617 (30.2)	3048 (13.9)
Related[c]	5241 (23.9)	1311 (6.0)
Severe	262 (1.2)	150 (0.7)
Life-threatening	21 (0.1)	26 (0.1)
Any serious adverse event	127 (0.6)	116 (0.5)
Related[c]	3 (0.0)	0
Severe	71 (0.3)	66 (0.3)
Life-threatening	21 (0.1)	26 (0.1)
Any adverse event leading to withdrawal	32 (0.1)	36 (0.2)
Related[c]	13 (0.1)	11 (0.1)
Severe	10 (0.0)	10 (0.0)
Life-threatening	3 (0.0)	7 (0.0)
Death	3 (0.0)	5 (0.0)

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
c. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:09)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA/adae s091 all pd2 p3 saf1

HIV+ Participants

From Dose 1 to 1 month after Dose 2, the subset of 200 HIV+ participants during the placebo-controlled follow-up showed generally similar trends as the overall population (likewise attributed to reactogenicity reported in the BNT162b2 group). The numbers of HIV+ participants who reported at least 1 AE and at least 1 related AE were higher in the BNT162b2 group (26.0% and 19.0%, respectively) as compared with the placebo group (13.0% and 3.0%, respectively). In this group, there was 1 severe AE and 1 AE leading to withdrawal (both in the BNT162b2 group), and there were no SAEs or deaths.

2.5.5.5.3.1.2. Analysis of Adverse Events

Adverse Events by System Organ Class and Preferred Term

Most AEs after Dose 1 up to 1 month after Dose 2 were reactogenicity events (Table 59). From Dose 1 to 1 month after Dose 2 during the blinded placebo-controlled follow-up period, 6617 (30.2%) BNT162b2 participants and 3048 (13.9%) placebo participants reported at least 1 AE. AE frequencies for all enrolled participants in these reactogenicity SOCs (BNT162b2 vs placebo) were:

- general disorders and administration site conditions: 4725 (21.5%) vs 993 (4.5%)
- musculoskeletal and connective tissue disorders: 1804 (8.2%) vs 527 (2.4%)
- nervous system disorders: 1565 (7.1%) vs 600 (2.7%)
- gastrointestinal disorders: 699 (3.2%) vs 464 (2.1%).

The number of BNT162b2 participants who reported at least 1 AE from Dose 1 to 1 month after Dose 2 was 4233 (32.6%) and 2384 (26.7%) in the younger and older groups. In the BNT162b2 age groups (younger vs older), AE frequencies in the SOCs were:

- general disorders and administration site conditions: 3161 (24.3%) vs 1564 (17.5%]
- musculoskeletal and connective tissue disorders: 1201 (9.2%) vs 603 (6.8%)
- nervous system disorders: 1067 (8.2%) vs 498 (5.6%)
- gastrointestinal disorders: 440 (3.4%) vs 259 (2.9%).

The most frequently reported AEs in the BNT162b2 group by PT overall were injection site pain (2915 [13.3%]), pyrexia (1517 [6.9%]), fatigue (1463 [6.7%]), chills (1365 [6.2%]), headache (1339 [6.1%]), and myalgia (1239 [5.7%]) (Table 59). During this time period from Dose 1 to 1 month after Dose 2, most of these AEs were reported during the e-diary 7-day reporting period (note, such events occurring in the reactogenicity reporting period are further analyzed below).

The frequency of AEs in the SOC of investigations was higher in the BNT162b2 group (0.8%) as compared with the placebo group (0.2%) mainly due to the higher frequency of the PT Body temperature increased (120 in the BNT162b2 group and 12 in the placebo group).

In the skin and subcutaneous tissue disorders SOC, there were 17 participants who reported night sweats in the BNT162b2 group (compared to 3 in the placebo group), and all but 1 of these participants reported the AE within the first 7 days after Dose 1 or 2, respectively, and

there were 31 participants who reported hyperhidrosis in the BNT162b2 group (compared to 9 in the placebo group), and all but 3 of these participants reported the AE within the first 7 days after Dose 1 or 2.

Nineteen study participants reported events in the hepatobiliary disorders SOC (14 BNT162b2 recipients and 5 placebo recipients) (Table 59). Of the 19 total participants, 3 participants had hepatic events:

- 1 participant in the placebo group reported hepatic cirrhosis
- 1 participant in the placebo group reported nonalcoholic fatty liver disease
- 1 participant in the BNT162b2 group reported alcoholic cirrhosis.

The remaining 16 participants reported biliary events (cholecystitis/cholecystitis acute, biliary colic, bile duct stone, and biliary dyskinesia): 13 participants in the BNT162b2 group and 3 participants in the placebo group.

- In the BNT162b2 group, 8 participants reported cholelithiasis (1 reported an event each of cholelithiasis and cholecystitis), 1 participant reported cholecystitis acute, 2 participants reported biliary colic, and 1 participant each reported bile duct stone/biliary dyskinesia.

- In the placebo group, 1 participant reported an event each of cholecystitis acute and cholelithiasis, 1 participant reported cholecystitis acute, and 1 participant reported cholelithiasis.

In the nervous systems disorder SOC, 3 participants who reported facial paralysis in the BNT162b2 group (compared to none in the placebo group). More details are presented in Section 2.5.5.5.7.

For lymphadenopathy the frequency in the BNT162b2 group was 0.4% compared to the frequency of 0.0% on the placebo group. Most AEs of lymphadenopathy in the BNT162b2 group were judged by the investigator as related to study intervention and are further discussed in Section 2.5.5.5.7.1.

Other events of clinical interest that were evaluated by the sponsor related to cardiac disorders, appendicitis, optic neuritis, and hypersensitivity/anaphylaxis are discussed in Section 2.5.5.5.7.3.

Analysis of Reactogenicity Terms Reported Within 7 Days After Each Dose

Beyond the 9839 participants included in the Phase 2/3 reactogenicity subset, events related to reactogenicity are no longer reported using an e-diary but are instead reported as AEs. An analysis was conducted to evaluate if the imbalance in AEs observed from Dose 1 to 1 month after Dose 2 was attributed to reactogenicity events. The analysis examined the AEs reported within 7 days after each dose, which represented the reactogenicity reporting period. The time period was chosen because many AEs were reported in the SOCs of general disorders and administration site conditions, musculoskeletal and connective tissue disorders, and nervous system disorders, which includes AEs consistent with reactogenicity events

(Section 2.5.5.5.2), and could only be attributed to reactogenicity if they occurred during this time period as opposed to occurring up to 1 month from each dose.

PTs reported from Dose 1 to 7 days after Dose 1 and from Dose 2 to 7 days after Dose 2 in the SOCs of general disorders and administration site conditions (injection site pain, chills, fatigue, and pyrexia), musculoskeletal and connective tissue disorders (myalgia), and nervous system disorders (headache) represented the majority of PTs reported in those SOCs. AEs reported from Dose 1 to 7 days after Dose 1 and from Dose 2 to 7 days after Dose 2 were largely attributable to reactogenicity events. This observation provides a reasonable explanation for the greater rates of AEs observed overall in the BNT162b2 group compared with the placebo group.

In addition to analysis of AEs corresponding to e-diary terms that were reported within 7 days after Dose 1 or Dose 2 that are attributable to reactogenicity, additional consideration was given to AE terms that are reported at higher frequency in the BNT162b2 group compared to placebo. The following additional AEs were identified: pain in extremity, decreased appetite, lethargy, asthenia, malaise, night sweats, and hyperhidrosis. Careful examination of these terms after either dose of BNT162b2 shows that these events are clustered within the 7-day period when reactogenicity events are known to occur. Since the majority of the participants did not have an e-diary and reported reactogenicity as AEs, there is considerable leeway in how symptoms are described by participants from multiple countries, interpreted by investigators, and reported as AEs. As these events are occurring when reactogenicity is being reported, these events are considered to be attributable to the experience of reactogenicity events and are plausibly associated with local reactions and systemic events.

Reactogenicity PTs were reported more frequently in the younger age group than in the older age group, which is consistent with the pattern of reactogenicity observed based on e-diary data (Section 2.5.5.5.2).

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	6617 (30.2)	(29.6, 30.8)	3048 (13.9)	(13.4, 14.4)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	105 (0.5)	(0.4, 0.6)	19 (0.1)	(0.1, 0.1)
Lymphadenopathy	83 (0.4)	(0.3, 0.5)	7 (0.0)	(0.0, 0.1)
Iron deficiency anaemia	8 (0.0)	(0.0, 0.1)	1 (0.0)	(0.0, 0.0)
Anaemia	4 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Lymph node pain	7 (0.0)	(0.0, 0.1)	1 (0.0)	(0.0, 0.0)
Blood loss anaemia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Leukocytosis	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Neutropenia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Thrombocytopenia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Thrombocytosis	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Hypochromic anaemia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Leukopenia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Lymphadenitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Lymphadenopathy mediastinal	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Lymphopenia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Splenomegaly	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
CARDIAC DISORDERS	56 (0.3)	(0.2, 0.3)	50 (0.2)	(0.2, 0.3)
Palpitations	6 (0.0)	(0.0, 0.1)	14 (0.1)	(0.0, 0.1)
Tachycardia	13 (0.1)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Atrial fibrillation	7 (0.0)	(0.0, 0.1)	9 (0.0)	(0.0, 0.1)
Coronary artery disease	3 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Acute myocardial infarction	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Acute coronary syndrome	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Cardiac failure congestive	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Myocardial infarction	0	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Angina unstable	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Bradycardia	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Left ventricular hypertrophy	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Mitral valve incompetence	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Angina pectoris	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Aortic valve incompetence	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Arrhythmia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Arteriospasm coronary	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Atrial flutter	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Cardiac arrest	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Mitral valve prolapse	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Myocardial ischaemia	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Sinus tachycardia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Supraventricular tachycardia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tricuspid valve incompetence	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Ventricular extrasystoles	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Acute left ventricular failure	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Arrhythmia supraventricular	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Atrioventricular block complete	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Atrioventricular block first degree	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Bundle branch block left	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Bundle branch block right	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cardiac disorder	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cardiac failure acute	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cardiovascular disorder	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Coronary artery dissection	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Coronary artery occlusion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Junctional ectopic tachycardia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Left atrial enlargement	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Left ventricular dysfunction	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Myocarditis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pericardial effusion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pericarditis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Tachyarrhythmia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Ventricular arrhythmia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Ventricular tachycardia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Congenital bladder neck obstruction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Congenital cystic kidney disease	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Heart disease congenital	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Type V hyperlipidaemia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
EAR AND LABYRINTH DISORDERS	65 (0.3)	(0.2, 0.4)	43 (0.2)	(0.1, 0.3)
Vertigo	25 (0.1)	(0.1, 0.2)	20 (0.1)	(0.1, 0.1)
Ear pain	11 (0.1)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Tinnitus	9 (0.0)	(0.0, 0.1)	8 (0.0)	(0.0, 0.1)
Vertigo positional	8 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Deafness unilateral	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Ear discomfort	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cerumen impaction	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Ear disorder	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Meniere's disease	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Allergic otitis media	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Deafness	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Deafness neurosensory	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Ear pruritus	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Eustachian tube dysfunction	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hyperacusis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypoacusis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Otorrhoea	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Sudden hearing loss	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Tympanic membrane perforation	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
ENDOCRINE DISORDERS	13 (0.1)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Hypothyroidism	6 (0.0)	(0.0, 0.1)	4 (0.0)	(0.0, 0.0)
Hypogonadism	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Thyroid mass	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Autoimmune thyroiditis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Goitre	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hyperprolactinaemia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Thyroid cyst	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
EYE DISORDERS	60 (0.3)	(0.2, 0.4)	50 (0.2)	(0.2, 0.3)
Cataract	6 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Eye pain	7 (0.0)	(0.0, 0.1)	4 (0.0)	(0.0, 0.0)
Eye irritation	6 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Vision blurred	7 (0.0)	(0.0, 0.1)	2 (0.0)	(0.0, 0.0)
Chalazion	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Vitreous detachment	4 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Blepharitis	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Conjunctival haemorrhage	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Conjunctivitis allergic	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dry eye	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Keratitis	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Ocular hyperaemia	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Glaucoma	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Lacrimation increased	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Photophobia	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Retinal detachment	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Vitreous floaters	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Asthenopia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Blepharospasm	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Diplopia	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Eye pruritus	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Amaurosis fugax	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Choroidal neovascularisation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Conjunctival hyperaemia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Conjunctival oedema	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Corneal irritation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Dacryostenosis acquired	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Diabetic retinopathy	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Episcleritis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Eye allergy	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Eye inflammation	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Eye swelling	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Eyelid haematoma	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Eyelid oedema	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Eyelid pain	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Eyelids pruritus	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Iritis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Ocular discomfort	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Retinal artery occlusion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Scleral discolouration	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Swelling of eyelid	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Ulcerative keratitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Visual acuity reduced	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Visual impairment	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
GASTROINTESTINAL DISORDERS	699 (3.2)	(3.0, 3.4)	464 (2.1)	(1.9, 2.3)
Diarrhoea	248 (1.1)	(1.0, 1.3)	188 (0.9)	(0.7, 1.0)
Nausea	274 (1.2)	(1.1, 1.4)	87 (0.4)	(0.3, 0.5)
Vomiting	66 (0.3)	(0.2, 0.4)	32 (0.1)	(0.1, 0.2)
Toothache	24 (0.1)	(0.1, 0.2)	27 (0.1)	(0.1, 0.2)
Abdominal pain upper	25 (0.1)	(0.1, 0.2)	15 (0.1)	(0.0, 0.1)
Abdominal pain	19 (0.1)	(0.1, 0.1)	19 (0.1)	(0.1, 0.1)
Gastrooesophageal reflux disease	12 (0.1)	(0.0, 0.1)	16 (0.1)	(0.0, 0.1)
Dyspepsia	12 (0.1)	(0.0, 0.1)	11 (0.1)	(0.0, 0.1)
Odynophagia	13 (0.1)	(0.0, 0.1)	8 (0.0)	(0.0, 0.1)
Constipation	7 (0.0)	(0.0, 0.1)	11 (0.1)	(0.0, 0.1)
Dental caries	8 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Gastritis	3 (0.0)	(0.0, 0.0)	10 (0.0)	(0.0, 0.1)
Haemorrhoids	3 (0.0)	(0.0, 0.0)	10 (0.0)	(0.0, 0.1)
Aphthous ulcer	8 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Abdominal discomfort	5 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Abdominal distension	6 (0.0)	(0.0, 0.1)	1 (0.0)	(0.0, 0.0)
Flatulence	4 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Irritable bowel syndrome	4 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Dry mouth	2 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Large intestine polyp	2 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Abdominal pain lower	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Dysphagia	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Inguinal hernia	1 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Stomatitis	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Diverticulum	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Gastrointestinal disorder	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hiatus hernia	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Paraesthesia oral	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Retching	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Small intestinal obstruction	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Cheilitis	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Faeces soft	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Food poisoning	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Gingival pain	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypoaesthesia oral	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Lip swelling	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Rectal haemorrhage	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Swollen tongue	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tooth impacted	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Umbilical hernia	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Colitis microscopic	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Diverticulum intestinal	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Eructation	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Gingival discomfort	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Glossodynia	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Haematochezia	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Mouth ulceration	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Noninfective gingivitis	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Oral pain	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pancreatitis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pancreatitis acute	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Parotid duct obstruction	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Salivary gland calculus	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Abdominal adhesions	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Abdominal hernia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Abdominal rigidity	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Abnormal faeces	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Acute abdomen	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Anal pruritus	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Angular cheilitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Appendix disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Chronic gastritis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Colitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Colitis ulcerative	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Diverticular perforation	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Diverticulum intestinal haemorrhagic	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Epiploic appendagitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Femoral hernia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Frequent bowel movements	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Gastric polyps	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Gastric ulcer	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Gastric ulcer haemorrhage	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Gastritis erosive	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Gastrointestinal haemorrhage	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Gastrointestinal mucosa hyperaemia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Gastrointestinal pain	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Gastrointestinal sounds abnormal	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Gingival bleeding	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Gingival swelling	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Glossitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Haemorrhoidal haemorrhage	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypoaesthesia teeth	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Impaired gastric emptying	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Incarcerated inguinal hernia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Intestinal obstruction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Lip oedema	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Loose tooth	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Obstructive pancreatitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Oesophageal food impaction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Oesophageal spasm	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Oesophageal ulcer	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Oesophageal varices haemorrhage	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Oesophagitis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Oral discomfort	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Oral lichenoid reaction	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Oral mucosa haematoma	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Palatal disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pancreatic failure	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Peptic ulcer	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Proctalgia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Salivary gland mucocoele	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Teething	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tongue discolouration	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tongue discomfort	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tongue oedema	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Tongue pruritus	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Tongue ulceration	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Tooth disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Varices oesophageal	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Volvulus	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	4725 (21.5)	(21.0, 22.1)	993 (4.5)	(4.3, 4.8)
Injection site pain	2915 (13.3)	(12.8, 13.8)	397 (1.8)	(1.6, 2.0)
Fatigue	1463 (6.7)	(6.3, 7.0)	379 (1.7)	(1.6, 1.9)
Pyrexia	1517 (6.9)	(6.6, 7.3)	77 (0.4)	(0.3, 0.4)
Chills	1365 (6.2)	(5.9, 6.6)	120 (0.5)	(0.5, 0.7)
Pain	628 (2.9)	(2.6, 3.1)	61 (0.3)	(0.2, 0.4)
Injection site erythema	185 (0.8)	(0.7, 1.0)	28 (0.1)	(0.1, 0.2)
Injection site swelling	140 (0.6)	(0.5, 0.8)	23 (0.1)	(0.1, 0.2)
Malaise	130 (0.6)	(0.5, 0.7)	22 (0.1)	(0.1, 0.2)
Asthenia	76 (0.3)	(0.3, 0.4)	25 (0.1)	(0.1, 0.2)
Injection site pruritus	38 (0.2)	(0.1, 0.2)	5 (0.0)	(0.0, 0.1)
Injection site bruising	13 (0.1)	(0.0, 0.1)	18 (0.1)	(0.0, 0.1)
Influenza like illness	23 (0.1)	(0.1, 0.2)	4 (0.0)	(0.0, 0.0)
Chest pain	12 (0.1)	(0.0, 0.1)	11 (0.1)	(0.0, 0.1)
Injection site warmth	14 (0.1)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Axillary pain	14 (0.1)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Injection site induration	10 (0.0)	(0.0, 0.1)	4 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Injection site oedema	12 (0.1)	(0.0, 0.1)	0	(0.0, 0.0)
Non-cardiac chest pain	5 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Oedema peripheral	5 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Peripheral swelling	5 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Chest discomfort	5 (0.0)	(0.0, 0.1)	4 (0.0)	(0.0, 0.0)
Feeling hot	8 (0.0)	(0.0, 0.1)	1 (0.0)	(0.0, 0.0)
Injection site discomfort	6 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Swelling face	2 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Injection site haematoma	2 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Injection site haemorrhage	3 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Injection site reaction	5 (0.0)	(0.0, 0.1)	1 (0.0)	(0.0, 0.0)
Injection site mass	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Injection site paraesthesia	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Swelling	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Adverse drug reaction	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cyst	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Feeling abnormal	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injection site discolouration	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Injection site nodule	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injection site papule	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injection site rash	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Sensation of foreign body	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Application site pain	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Face oedema	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Feeling cold	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injury associated with device	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Medical device pain	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Nodule	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Sluggishness	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Thirst	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Vessel puncture site bruise	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Vessel puncture site haematoma	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Application site erythema	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Application site pruritus	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Application site rash	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Application site reaction	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Capsular contracture associated with breast implant	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Death	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Discomfort	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Drug withdrawal syndrome	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Effusion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Exercise tolerance decreased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Facial pain	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Gait disturbance	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Illness	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Induration	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Inflammation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injection site dermatitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injection site hyperaesthesia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injection site injury	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Injection site irritation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injection site lymphadenopathy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injection site macule	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injection site plaque	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Injection site urticaria	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Mass	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Medical device site granuloma	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Mucosal disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Shoulder injury related to vaccine administration	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Temperature intolerance	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Therapeutic response unexpected	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Vaccination site induration	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Vaccination site pain	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Vaccination site swelling	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Vascular stent occlusion	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Vessel puncture site induration	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
HEPATOBILIARY DISORDERS	14 (0.1)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Cholelithiasis	8 (0.0)	(0.0, 0.1)	2 (0.0)	(0.0, 0.0)
Cholecystitis acute	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Biliary colic	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Bile duct stone	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Biliary dyskinesia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cholecystitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cirrhosis alcoholic	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hepatic cirrhosis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Nonalcoholic fatty liver disease	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
IMMUNE SYSTEM DISORDERS	22 (0.1)	(0.1, 0.2)	25 (0.1)	(0.1, 0.2)
Seasonal allergy	8 (0.0)	(0.0, 0.1)	13 (0.1)	(0.0, 0.1)
Drug hypersensitivity	7 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Food allergy	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Hypersensitivity	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Allergy to arthropod bite	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Allergy to arthropod sting	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Anaphylactic reaction	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Anaphylactic shock	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Milk allergy	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
INFECTIONS AND INFESTATIONS	337 (1.5)	(1.4, 1.7)	365 (1.7)	(1.5, 1.8)
Urinary tract infection	58 (0.3)	(0.2, 0.3)	52 (0.2)	(0.2, 0.3)
Tooth infection	24 (0.1)	(0.1, 0.2)	29 (0.1)	(0.1, 0.2)
Sinusitis	18 (0.1)	(0.0, 0.1)	27 (0.1)	(0.1, 0.2)
Cellulitis	12 (0.1)	(0.0, 0.1)	15 (0.1)	(0.0, 0.1)
Herpes zoster	12 (0.1)	(0.0, 0.1)	10 (0.0)	(0.0, 0.1)
Ear infection	9 (0.0)	(0.0, 0.1)	12 (0.1)	(0.0, 0.1)
Conjunctivitis	9 (0.0)	(0.0, 0.1)	11 (0.1)	(0.0, 0.1)
Hordeolum	8 (0.0)	(0.0, 0.1)	11 (0.1)	(0.0, 0.1)
Cystitis	6 (0.0)	(0.0, 0.1)	11 (0.1)	(0.0, 0.1)
Gastroenteritis	5 (0.0)	(0.0, 0.1)	10 (0.0)	(0.0, 0.1)
Rhinitis	5 (0.0)	(0.0, 0.1)	10 (0.0)	(0.0, 0.1)
Tooth abscess	9 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Upper respiratory tract infection	9 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Diverticulitis	8 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Otitis externa	6 (0.0)	(0.0, 0.1)	7 (0.0)	(0.0, 0.1)
Otitis media	7 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Vulvovaginal mycotic infection	5 (0.0)	(0.0, 0.1)	8 (0.0)	(0.0, 0.1)
Appendicitis	7 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Gingivitis	5 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Oral herpes	4 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Acute sinusitis	1 (0.0)	(0.0, 0.0)	7 (0.0)	(0.0, 0.1)
Pneumonia	2 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Skin infection	3 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Vaginal infection	0	(0.0, 0.0)	7 (0.0)	(0.0, 0.1)
Vulvovaginal candidiasis	4 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Fungal skin infection	1 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Onychomycosis	3 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Periodontitis	3 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Pharyngitis streptococcal	4 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Pyelonephritis	5 (0.0)	(0.0, 0.1)	1 (0.0)	(0.0, 0.0)
Folliculitis	5 (0.0)	(0.0, 0.1)	0	(0.0, 0.0)
Furuncle	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Localised infection	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Nasopharyngitis	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Otitis media acute	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Paronychia	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Tonsillitis	0	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Genital herpes	0	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Herpes simplex	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Influenza	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pharyngitis	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Postoperative wound infection	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Tinea versicolour	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Bacterial vulvovaginitis	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Bronchitis	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Chronic sinusitis	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Eye infection	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Gingival abscess	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Impetigo	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Infected bite	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Parotitis	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Pustule	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Subcutaneous abscess	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Tinea infection	0	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Abscess	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Abscess limb	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Acarodermatitis	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Anal abscess	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Appendicitis perforated	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Bacterial vaginosis	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
COVID-19	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Conjunctivitis bacterial	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Erysipelas	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Escherichia urinary tract infection	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Gastroenteritis viral	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Kidney infection	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Labyrinthitis	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Laryngitis	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Ophthalmic herpes zoster	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Oral candidiasis	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Papilloma viral infection	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Peritonsillar abscess	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pharyngotonsillitis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Rash pustular	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Sialoadenitis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Sinusitis bacterial	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Trichomoniasis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Vulvovaginitis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Abdominal abscess	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Abscess intestinal	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Abscess jaw	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Abscess neck	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Anal fistula infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Bacterial blepharitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Bacterial infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Bacterial sepsis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Balanitis candida	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Bartholin's abscess	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Bartholinitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Blister infected	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Bone abscess	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Brain abscess	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Campylobacter infection	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Carbuncle	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cellulitis orbital	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Clostridium difficile infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Complicated appendicitis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Coxsackie viral infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dental fistula	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dermatitis infected	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Device related infection	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Empyema	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Eye infection bacterial	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Genital herpes simplex	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Gonorrhoea	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Groin abscess	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Helicobacter gastritis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Helicobacter infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hepatitis A	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hepatitis C	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Injection site abscess	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Lyme disease	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Meningitis bacterial	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Nail infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Oral fungal infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Oral infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Orchitis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Osteomyelitis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Otitis media bacterial	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Parasitic gastroenteritis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pelvic inflammatory disease	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Peritoneal abscess	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Peritonitis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pharyngitis bacterial	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pilonidal cyst	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pulmonary tuberculosis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Puncture site infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pyelonephritis acute	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Respiratory tract infection viral	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Sepsis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Shigella sepsis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Skin bacterial infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Soft tissue infection	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Staphylococcal infection	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Subacute endocarditis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Suspected COVID-19	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Syphilis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tinea cruris	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tonsillitis bacterial	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Urosepsis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Varicella	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Viral infection	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Viral upper respiratory tract infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Wound infection	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	215 (1.0)	(0.9, 1.1)	269 (1.2)	(1.1, 1.4)
Fall	48 (0.2)	(0.2, 0.3)	51 (0.2)	(0.2, 0.3)
Ligament sprain	19 (0.1)	(0.1, 0.1)	22 (0.1)	(0.1, 0.2)
Skin laceration	14 (0.1)	(0.0, 0.1)	22 (0.1)	(0.1, 0.2)
Contusion	12 (0.1)	(0.0, 0.1)	19 (0.1)	(0.1, 0.1)
Exposure during pregnancy	10 (0.0)	(0.0, 0.1)	19 (0.1)	(0.1, 0.1)
Muscle strain	14 (0.1)	(0.0, 0.1)	15 (0.1)	(0.0, 0.1)
Road traffic accident	9 (0.0)	(0.0, 0.1)	15 (0.1)	(0.0, 0.1)
Skin abrasion	8 (0.0)	(0.0, 0.1)	13 (0.1)	(0.0, 0.1)
Arthropod bite	12 (0.1)	(0.0, 0.1)	7 (0.0)	(0.0, 0.1)
Limb injury	7 (0.0)	(0.0, 0.1)	11 (0.1)	(0.0, 0.1)
Foot fracture	5 (0.0)	(0.0, 0.1)	8 (0.0)	(0.0, 0.1)
Joint injury	5 (0.0)	(0.0, 0.1)	8 (0.0)	(0.0, 0.1)
Tooth fracture	7 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Procedural pain	8 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Meniscus injury	4 (0.0)	(0.0, 0.0)	6 (0.0)	(0.0, 0.1)
Animal bite	2 (0.0)	(0.0, 0.0)	6 (0.0)	(0.0, 0.1)
Arthropod sting	3 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Facial bones fracture	4 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Joint dislocation	7 (0.0)	(0.0, 0.1)	1 (0.0)	(0.0, 0.0)
Rib fracture	3 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Ankle fracture	2 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Concussion	3 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Muscle rupture	1 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Wound	2 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Chest injury	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Corneal abrasion	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Ligament rupture	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Thermal burn	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Vaccination complication	5 (0.0)	(0.0, 0.1)	0	(0.0, 0.0)
Epicondylitis	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Fibula fracture	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Hand fracture	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Head injury	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Humerus fracture	0	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Overdose	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Radius fracture	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Tendon rupture	0	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Wrist fracture	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Bone contusion	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Craniocerebral injury	0	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Maternal exposure during pregnancy	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Muscle injury	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Spinal compression fracture	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Ulna fracture	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Administration related reaction	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Burns second degree	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cervical vertebral fracture	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Ligament injury	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Lower limb fracture	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Procedural dizziness	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Skin injury	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Stress fracture	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Tendon injury	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Upper limb fracture	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Alcohol poisoning	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Anaemia postoperative	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Brain contusion	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Burn oral cavity	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Burns first degree	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Clavicle fracture	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Colon injury	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dental restoration failure	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Ear canal abrasion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Ear injury	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Exposure to communicable disease	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Eye contusion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Femur fracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Flail chest	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Forearm fracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Foreign body	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Foreign body aspiration	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Foreign body in eye	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hip fracture	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injury	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Limb fracture	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Limb traumatic amputation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Lip injury	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Lumbar vertebral fracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Maternal exposure during breast feeding	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Mouth injury	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Multiple injuries	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Muscle contusion	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Patella fracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pelvic fracture	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Penis injury	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pharyngeal perforation	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Post concussion syndrome	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Post procedural discomfort	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Post procedural haemorrhage	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Post procedural swelling	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Postoperative ileus	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Procedural haemorrhage	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Procedural hypotension	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Respiratory fume inhalation disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Scapula fracture	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Scar	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Soft tissue injury	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Spinal column injury	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Spinal cord injury cervical	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Spinal fracture	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Stab wound	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Stoma site rash	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Subdural haematoma	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Sunburn	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Tibia fracture	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Toxicity to various agents	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Traumatic haemothorax	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Traumatic intracranial haemorrhage	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Venom poisoning	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Vulvovaginal injury	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
INVESTIGATIONS	172 (0.8)	(0.7, 0.9)	37 (0.2)	(0.1, 0.2)
Body temperature increased	120 (0.5)	(0.5, 0.7)	12 (0.1)	(0.0, 0.1)
Blood pressure increased	6 (0.0)	(0.0, 0.1)	7 (0.0)	(0.0, 0.1)
Blood glucose increased	8 (0.0)	(0.0, 0.1)	1 (0.0)	(0.0, 0.0)
Heart rate increased	4 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Blood cholesterol increased	5 (0.0)	(0.0, 0.1)	0	(0.0, 0.0)
Low density lipoprotein increased	4 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Blood thyroid stimulating hormone increased	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Weight decreased	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Blood glucose abnormal	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hepatic enzyme increased	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
High density lipoprotein increased	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Mammogram abnormal	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Prostatic specific antigen increased	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Alanine aminotransferase increased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Blood chloride decreased	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Blood creatinine decreased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Blood creatinine increased	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Blood glucose fluctuation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Blood potassium decreased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Blood pressure diastolic increased	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Blood pressure systolic increased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Blood sodium decreased	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Blood testosterone decreased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Blood testosterone increased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Blood triglycerides increased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Body temperature	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Body temperature decreased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
C-reactive protein	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cardiac stress test abnormal	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Electrocardiogram QT prolonged	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Fractional exhaled nitric oxide increased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Glomerular filtration rate decreased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Heart rate irregular	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hepatitis C antibody positive	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Herpes simplex test positive	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Intraocular pressure increased	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Mean cell volume decreased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Monocyte count increased	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Platelet count increased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Respiratory rate increased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
SARS-CoV-2 antibody test positive	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Thyroid function test abnormal	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Troponin increased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Urine ketone body present	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Weight increased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
White blood cell count increased	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
White blood cells urine positive	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
METABOLISM AND NUTRITION DISORDERS	100 (0.5)	(0.4, 0.6)	73 (0.3)	(0.3, 0.4)
Decreased appetite	39 (0.2)	(0.1, 0.2)	9 (0.0)	(0.0, 0.1)
Type 2 diabetes mellitus	8 (0.0)	(0.0, 0.1)	8 (0.0)	(0.0, 0.1)
Vitamin D deficiency	9 (0.0)	(0.0, 0.1)	7 (0.0)	(0.0, 0.1)
Hypercholesterolaemia	4 (0.0)	(0.0, 0.0)	9 (0.0)	(0.0, 0.1)
Hyperlipidaemia	6 (0.0)	(0.0, 0.1)	4 (0.0)	(0.0, 0.0)
Hypokalaemia	5 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Dyslipidaemia	4 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Gout	5 (0.0)	(0.0, 0.1)	2 (0.0)	(0.0, 0.0)
Dehydration	2 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Hyperglycaemia	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Glucose tolerance impaired	0	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Vitamin B12 deficiency	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Diabetes mellitus inadequate control	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Hypoglycaemia	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Insulin resistance	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hypertriglyceridaemia	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypocalcaemia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hypocholesterolaemia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Obesity	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Polydipsia	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Diabetes mellitus	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Diabetic ketoacidosis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Fluid retention	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Folate deficiency	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Food intolerance	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Hyperkalaemia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypernatraemia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hyperuricaemia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypomagnesaemia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hyponatraemia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypovolaemia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Impaired fasting glucose	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Increased appetite	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Iron deficiency	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Lactic acidosis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1804 (8.2)	(7.9, 8.6)	527 (2.4)	(2.2, 2.6)
Myalgia	1239 (5.7)	(5.3, 6.0)	168 (0.8)	(0.7, 0.9)
Arthralgia	268 (1.2)	(1.1, 1.4)	102 (0.5)	(0.4, 0.6)
Pain in extremity	185 (0.8)	(0.7, 1.0)	44 (0.2)	(0.1, 0.3)
Back pain	97 (0.4)	(0.4, 0.5)	85 (0.4)	(0.3, 0.5)
Neck pain	29 (0.1)	(0.1, 0.2)	33 (0.2)	(0.1, 0.2)
Muscle spasms	27 (0.1)	(0.1, 0.2)	15 (0.1)	(0.0, 0.1)
Osteoarthritis	11 (0.1)	(0.0, 0.1)	16 (0.1)	(0.0, 0.1)
Musculoskeletal stiffness	12 (0.1)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Tendonitis	10 (0.0)	(0.0, 0.1)	7 (0.0)	(0.0, 0.1)
Intervertebral disc protrusion	8 (0.0)	(0.0, 0.1)	8 (0.0)	(0.0, 0.1)
Bursitis	10 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Muscular weakness	10 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Musculoskeletal chest pain	10 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Muscle contracture	4 (0.0)	(0.0, 0.0)	6 (0.0)	(0.0, 0.1)
Rotator cuff syndrome	3 (0.0)	(0.0, 0.0)	7 (0.0)	(0.0, 0.1)
Plantar fasciitis	4 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Arthritis	3 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Exostosis	5 (0.0)	(0.0, 0.1)	2 (0.0)	(0.0, 0.0)
Flank pain	3 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Joint swelling	2 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Joint stiffness	5 (0.0)	(0.0, 0.1)	1 (0.0)	(0.0, 0.0)
Musculoskeletal discomfort	4 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Osteoporosis	0	(0.0, 0.0)	6 (0.0)	(0.0, 0.1)
Costochondritis	5 (0.0)	(0.0, 0.1)	0	(0.0, 0.0)
Joint range of motion decreased	5 (0.0)	(0.0, 0.1)	0	(0.0, 0.0)
Muscle fatigue	4 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Muscle twitching	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Musculoskeletal pain	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Spinal osteoarthritis	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Intervertebral disc degeneration	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Limb discomfort	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pain in jaw	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Synovial cyst	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tenosynovitis stenosans	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Bone pain	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Temporomandibular joint syndrome	0	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Tendon disorder	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Torticollis	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Arthropathy	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Axillary mass	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Coccydynia	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Fibromyalgia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Groin pain	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Joint effusion	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Metatarsalgia	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Mobility decreased	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Osteitis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Periarthritis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Psoriatic arthropathy	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Spinal stenosis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Spondylitis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Synovitis	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Trigger finger	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Arthritis reactive	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Bone swelling	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dupuytren's contracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Intervertebral disc disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Joint instability	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Muscle discomfort	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Muscle tightness	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Osteochondritis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Osteochondrosis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Osteopenia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Rhabdomyolysis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Rheumatoid arthritis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Scoliosis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Spinal disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Systemic lupus erythematosus	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Tendon pain	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	32 (0.1)	(0.1, 0.2)	36 (0.2)	(0.1, 0.2)
Basal cell carcinoma	3 (0.0)	(0.0, 0.0)	8 (0.0)	(0.0, 0.1)
Lipoma	2 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Uterine leiomyoma	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Colon adenoma	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Malignant melanoma	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Breast cancer	0	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Prostate cancer	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Acrochordon	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Fibroadenoma of breast	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Squamous cell carcinoma of skin	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Adenocarcinoma gastric	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Adenocarcinoma pancreas	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Adenoma benign	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Adrenal gland cancer	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Benign breast neoplasm	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Benign pancreatic neoplasm	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Biliary cancer metastatic	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Chondroma	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Chronic myeloid leukaemia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Glomus tumour	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Infected naevus	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Intraductal proliferative breast lesion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Invasive ductal breast carcinoma	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Leydig cell tumour of the testis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Lymphoproliferative disorder	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Malignant melanoma of eyelid	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Meningioma	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Metastases to central nervous system	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Metastases to liver	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Oropharyngeal squamous cell carcinoma	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Ovarian germ cell teratoma benign	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Pancreatic carcinoma	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Penile neoplasm	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Penile squamous cell carcinoma	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Prostate cancer metastatic	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Seborrhoeic keratosis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Squamous cell carcinoma	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Thyroid cancer	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
NERVOUS SYSTEM DISORDERS	1565 (7.1)	(6.8, 7.5)	600 (2.7)	(2.5, 3.0)
Headache	1339 (6.1)	(5.8, 6.4)	424 (1.9)	(1.8, 2.1)
Dizziness	78 (0.4)	(0.3, 0.4)	60 (0.3)	(0.2, 0.4)
Paraesthesia	22 (0.1)	(0.1, 0.2)	23 (0.1)	(0.1, 0.2)
Migraine	24 (0.1)	(0.1, 0.2)	11 (0.1)	(0.0, 0.1)
Lethargy	25 (0.1)	(0.1, 0.2)	6 (0.0)	(0.0, 0.1)
Syncope	11 (0.1)	(0.0, 0.1)	11 (0.1)	(0.0, 0.1)
Sciatica	11 (0.1)	(0.0, 0.1)	10 (0.0)	(0.0, 0.1)
Dysgeusia	12 (0.1)	(0.0, 0.1)	8 (0.0)	(0.0, 0.1)
Somnolence	9 (0.0)	(0.0, 0.1)	11 (0.1)	(0.0, 0.1)
Tension headache	8 (0.0)	(0.0, 0.1)	9 (0.0)	(0.0, 0.1)
Presyncope	8 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Hypoaesthesia	5 (0.0)	(0.0, 0.1)	7 (0.0)	(0.0, 0.1)
Tremor	6 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Burning sensation	3 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Parosmia	5 (0.0)	(0.0, 0.1)	1 (0.0)	(0.0, 0.0)
Subarachnoid haemorrhage	4 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Carpal tunnel syndrome	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Cervical radiculopathy	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Disturbance in attention	4 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hyperaesthesia	4 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Neuropathy peripheral	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Sinus headache	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Aphasia	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cerebrovascular accident	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Dizziness postural	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Facial paralysis	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Migraine without aura	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Nerve compression	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Radiculopathy	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Amnesia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Head discomfort	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Ischaemic stroke	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Mental impairment	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Migraine with aura	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Post herpetic neuralgia	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Restless legs syndrome	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Taste disorder	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Transient ischaemic attack	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Trigeminal neuralgia	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Ageusia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Amyotrophic lateral sclerosis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Balance disorder	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cerebellar infarction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cerebral atrophy	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cerebral capillary telangiectasia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cerebral infarction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cervicogenic headache	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Depressed level of consciousness	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Diabetic neuropathy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Drug withdrawal headache	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Dyskinesia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Dystonia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Facial paresis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Generalised tonic-clonic seizure	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Haemorrhagic stroke	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hemiplegic migraine	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hypersomnia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypogeusia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hyposmia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Idiopathic intracranial hypertension	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Motor dysfunction	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Myoclonus	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Nystagmus	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Paraparesis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Parkinsonism	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Periodic limb movement disorder	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Peripheral sensory neuropathy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Piriformis syndrome	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Sciatic nerve neuropathy	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Seizure	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Spinal cord compression	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Transient global amnesia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Uraemic encephalopathy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
VIth nerve paralysis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
PREGNANCY, PUERPERIUM AND PERINATAL CONDITIONS	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Abortion spontaneous	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Abortion spontaneous incomplete	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
PRODUCT ISSUES	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Device breakage	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Device connection issue	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
PSYCHIATRIC DISORDERS	97 (0.4)	(0.4, 0.5)	75 (0.3)	(0.3, 0.4)
Anxiety	21 (0.1)	(0.1, 0.1)	24 (0.1)	(0.1, 0.2)
Insomnia	25 (0.1)	(0.1, 0.2)	8 (0.0)	(0.0, 0.1)
Depression	17 (0.1)	(0.0, 0.1)	15 (0.1)	(0.0, 0.1)
Attention deficit hyperactivity disorder	3 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Irritability	4 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Panic attack	2 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Anxiety disorder	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Disorientation	5 (0.0)	(0.0, 0.1)	0	(0.0, 0.0)
Sleep disorder	4 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Abnormal dreams	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Depressed mood	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Suicidal ideation	0	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Alcohol withdrawal syndrome	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Bipolar disorder	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Bruxism	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Mental disorder	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Mental status changes	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Nightmare	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Confusional state	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Depression suicidal	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dysphemia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Gastrointestinal somatic symptom disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Generalised anxiety disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Libido decreased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Libido increased	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Listless	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Mental fatigue	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Mood swings	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Panic disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Panic reaction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Paranoia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Post-traumatic stress disorder	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Psychotic disorder	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Restlessness	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Schizophrenia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Stress	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Substance abuse	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Suicide attempt	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
RENAL AND URINARY DISORDERS	34 (0.2)	(0.1, 0.2)	34 (0.2)	(0.1, 0.2)
Nephrolithiasis	6 (0.0)	(0.0, 0.1)	8 (0.0)	(0.0, 0.1)
Dysuria	7 (0.0)	(0.0, 0.1)	4 (0.0)	(0.0, 0.0)
Haematuria	4 (0.0)	(0.0, 0.0)	7 (0.0)	(0.0, 0.1)
Acute kidney injury	3 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Pollakiuria	5 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Renal colic	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Urinary retention	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Bladder spasm	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Chronic kidney disease	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Costovertebral angle tenderness	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hydronephrosis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Micturition urgency	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Nocturia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Obstructive nephropathy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Oedematous kidney	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Perinephric oedema	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Renal atrophy	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Renal cyst haemorrhage	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Subcapsular renal haematoma	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Urethral discharge	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Urinary bladder polyp	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Urinary tract obstruction	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Urine odour abnormal	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	45 (0.2)	(0.1, 0.3)	39 (0.2)	(0.1, 0.2)
Dysmenorrhoea	4 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Erectile dysfunction	1 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Ovarian cyst	4 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pelvic pain	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Amenorrhoea	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Benign prostatic hyperplasia	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Breast pain	4 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Breast mass	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Menorrhagia	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Prostatitis	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Vaginal haemorrhage	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Breast cyst	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Genital erythema	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Haemorrhagic ovarian cyst	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Menstruation delayed	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Menstruation irregular	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Metrorrhagia	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pruritus genital	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Testicular pain	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Uterine haemorrhage	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Adenomyosis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Breast calcifications	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Breast hyperplasia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cervical dysplasia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cervical polyp	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Dysfunctional uterine bleeding	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Endometriosis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Haematospermia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Mammary duct ectasia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Menometrorrhagia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Nipple pain	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Ovarian mass	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Penile vein thrombosis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Polycystic ovaries	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Postmenopausal haemorrhage	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Premenstrual syndrome	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Prostatomegaly	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Scrotal pain	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Uterine inflammation	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Uterine prolapse	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Vaginal discharge	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Vulvovaginal pruritus	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	194 (0.9)	(0.8, 1.0)	168 (0.8)	(0.7, 0.9)
Oropharyngeal pain	36 (0.2)	(0.1, 0.2)	31 (0.1)	(0.1, 0.2)
Nasal congestion	25 (0.1)	(0.1, 0.2)	32 (0.1)	(0.1, 0.2)
Cough	23 (0.1)	(0.1, 0.2)	15 (0.1)	(0.0, 0.1)
Rhinorrhoea	20 (0.1)	(0.1, 0.1)	13 (0.1)	(0.0, 0.1)
Rhinitis allergic	12 (0.1)	(0.0, 0.1)	11 (0.1)	(0.0, 0.1)
Asthma	12 (0.1)	(0.0, 0.1)	8 (0.0)	(0.0, 0.1)
Dyspnoea	6 (0.0)	(0.0, 0.1)	10 (0.0)	(0.0, 0.1)
Throat irritation	6 (0.0)	(0.0, 0.1)	9 (0.0)	(0.0, 0.1)
Epistaxis	5 (0.0)	(0.0, 0.1)	8 (0.0)	(0.0, 0.1)
Upper-airway cough syndrome	6 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Sinus congestion	6 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Paranasal sinus discomfort	4 (0.0)	(0.0, 0.0)	6 (0.0)	(0.0, 0.1)
Pulmonary embolism	3 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Sneezing	3 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Chronic obstructive pulmonary disease	4 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dysphonia	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Upper respiratory tract congestion	4 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Bronchospasm	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dyspnoea exertional	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Productive cough	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Respiratory tract congestion	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Sleep apnoea syndrome	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Wheezing	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Acute respiratory failure	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Asthma exercise induced	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Dry throat	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pharyngeal swelling	0	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Allergic sinusitis	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Asthmatic crisis	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Interstitial lung disease	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Oropharyngeal discomfort	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pneumonia aspiration	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Reflux laryngitis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Snoring	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Allergic respiratory disease	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Atelectasis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Emphysema	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Haemoptysis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hiccups	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypoxia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Lung infiltration	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Nasal discomfort	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Nasal obstruction	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Nasal polyps	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Nasal septum deviation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Nasal turbinate hypertrophy	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Paranasal sinus hypersecretion	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pleurisy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pleuritic pain	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pneumonitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pneumothorax	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pulmonary hypertension	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pulmonary mass	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pulmonary oedema	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pulmonary pain	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Respiratory arrest	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Rhinalgia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Rhinitis perennial	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Sinus disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tonsillar hypertrophy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	224 (1.0)	(0.9, 1.2)	158 (0.7)	(0.6, 0.8)
Rash	54 (0.2)	(0.2, 0.3)	41 (0.2)	(0.1, 0.3)
Pruritus	23 (0.1)	(0.1, 0.2)	18 (0.1)	(0.0, 0.1)
Hyperhidrosis	31 (0.1)	(0.1, 0.2)	9 (0.0)	(0.0, 0.1)
Dermatitis contact	14 (0.1)	(0.0, 0.1)	19 (0.1)	(0.1, 0.1)
Urticaria	15 (0.1)	(0.0, 0.1)	12 (0.1)	(0.0, 0.1)
Night sweats	17 (0.1)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Rash pruritic	7 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Erythema	9 (0.0)	(0.0, 0.1)	2 (0.0)	(0.0, 0.0)
Alopecia	5 (0.0)	(0.0, 0.1)	4 (0.0)	(0.0, 0.0)
Eczema	6 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Skin lesion	3 (0.0)	(0.0, 0.0)	6 (0.0)	(0.0, 0.1)
Rash maculo-papular	5 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Dermatitis	4 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Dermatitis allergic	3 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Angioedema	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Dermal cyst	4 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Rash erythematous	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Actinic keratosis	1 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Blister	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Ecchymosis	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Hand dermatitis	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Papule	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Psoriasis	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Rash papular	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Acne	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Alopecia areata	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cold sweat	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Diabetic foot	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Drug eruption	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Macule	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pain of skin	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pityriasis rosea	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pruritus allergic	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Rosacea	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Seborrhoeic dermatitis	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Skin mass	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dermatitis acneiform	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Dermatitis bullous	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dermatitis exfoliative	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Dyshidrotic eczema	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Fixed eruption	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hangnail	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hidradenitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Ingrowing nail	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Livedo reticularis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Mechanical urticaria	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Onychomadesis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pityriasis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pseudofolliculitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Skin discolouration	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Skin induration	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Skin irritation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Skin ulcer	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Stasis dermatitis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Urticaria contact	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Urticaria papular	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
SOCIAL CIRCUMSTANCES	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Menopause	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
High risk sexual behaviour	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
SURGICAL AND MEDICAL PROCEDURES	28 (0.1)	(0.1, 0.2)	19 (0.1)	(0.1, 0.1)
Tooth extraction	6 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Dental implantation	5 (0.0)	(0.0, 0.1)	2 (0.0)	(0.0, 0.0)
Wisdom teeth removal	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Dental care	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Endodontic procedure	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Abortion induced	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Apicectomy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Botulinum toxin injection	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cardiac pacemaker replacement	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Carpal tunnel decompression	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cataract operation	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Drug titration	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Facet joint block	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Gingival operation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Inguinal hernia repair	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Lacrimal duct procedure	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Lens extraction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Medical device implantation	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Open reduction of fracture	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Postoperative care	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Rhinoplasty	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Sclerotherapy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 59. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Skin neoplasm excision	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Toe operation	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Vasectomy	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Wound drainage	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
VASCULAR DISORDERS	83 (0.4)	(0.3, 0.5)	82 (0.4)	(0.3, 0.5)
Hypertension	42 (0.2)	(0.1, 0.3)	46 (0.2)	(0.2, 0.3)
Hot flush	7 (0.0)	(0.0, 0.1)	9 (0.0)	(0.0, 0.1)
Flushing	11 (0.1)	(0.0, 0.1)	2 (0.0)	(0.0, 0.0)
Deep vein thrombosis	5 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Haematoma	4 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Hypotension	4 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Orthostatic hypotension	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Varicose vein	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Aortic aneurysm	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Arteriosclerosis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hypertensive crisis	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hypertensive urgency	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Accelerated hypertension	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Aortic dilatation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Aortic stenosis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Diastolic hypertension	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Essential hypertension	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Intermittent claudication	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Lymphoedema	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Lymphorrhoea	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pallor	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Phlebolith	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Raynaud's phenomenon	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Subgaleal haematoma	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Note: MedDRA (v23.1) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
c. Exact 2-sided CI based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:09)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s130_all_pd2_p3_saf

Related Adverse Events – Blinded Follow-Up to 1 Month After Dose 2

From Dose 1 to 1 month after Dose 2, AEs assessed as related by the investigator during the blinded placebo-controlled follow-up period were reported by 23.9% of participants in the BNT162b2 group and 6.0% of participants in the placebo group (Table 58). Most related AEs were reactogenicity events and in the SOC of general disorders and administration site conditions, reported by 4650 (21.2%) BNT162b2 recipients and 883 (4.0%) placebo recipients. Among BNT162b2 participants who had AEs of lymphadenopathy, 62 of 83 participants had events assessed by the investigator as related to study intervention; the majority of lymphadenopathy events occurred in the arm and neck region and were reported within 2 to 4 days after vaccination (discussed further in Section 2.5.5.5.7).

Immediate Adverse Events – Blinded Follow-Up

After Dose 1, participants with immediate AEs were low in frequency (≤0.5%). Most immediate AEs after Dose 1 were in the SOC of general disorders and administration site conditions, primarily injection site reactions in the BNT162b2 versus placebo groups, with injection site pain (0.3% vs 0.2%) most frequently reported.

After Dose 2, participants with immediate AEs were low in frequency (0.3%). Most immediate AEs after Dose 2 were in the SOC of general disorders and administration site conditions, primarily injection site reactions in the BNT162b2 versus placebo groups, with injection site pain (0.2% vs 0.1%) most frequently reported.

No immediate anaphylactic reactions occurred after either dose.

Severe or Life-Threatening Adverse Events – Blinded Follow-Up to 1 Month After Dose 2

From Dose 1 to 1 month after Dose 2, severe AEs reported during the blinded follow-up period were low in frequency, reported in 1.2% of BNT162b2 recipients and 0.7% of placebo recipients. Severe events were concentrated in the SOCs of general disorders and administration site conditions, generally reflecting terms consistent with reactogenicity, in the BNT162b2 versus placebo groups (0.4% vs 0.0%).

There were 21 participants (0.1%) in the BNT162b2 group and 26 participants (0.1%) in the placebo group who had at least 1 life-threatening AE from Dose 1 to 1 month after Dose 2. None of these AEs were assessed by the investigator as related to study intervention.

No clinically meaningful differences were observed for severe or life-threatening AEs by age group.

HIV+ Participants

From Dose 1 to 1 month after Dose 2, and similar to the overall population, most AEs reported for the subset of 200 HIV+ participants from Dose 1 to 1 month after Dose 2 were in SOCs with reactogenicity events. There were few AEs reported: 26 (26%) in the BNT162b2 group and 13 (13%) in the placebo group, including in the following SOCs (BNT162b2 vs placebo):

- general disorders and administration site conditions: 19.0% vs 2.0%
- musculoskeletal and connective tissue disorders: 6.0% vs 3.0%
- nervous system disorders: 5.0% vs 0.0%
- gastrointestinal disorders: 3.0% vs 4.0%
- infections and infestations: 2.0% vs 2.0%.

2.5.5.5.3.2. Blinded Follow-Up Period from Dose 1 to the Unblinding Date

2.5.5.5.3.2.1. Summary of Adverse Events

An overview of AEs from Dose 1 to the unblinding date for participants during the blinded safety follow-up (including those analyzed in Phase 2) is presented in Table 60.

IRs per 100 PY for participants who reported at least 1 AE were 83.2 in the BNT162b2 group and 43.4 in the placebo group. IRs per 100 PY for related AEs were 62.9 in the BNT162b2 group and 16.0 in the placebo group. IRs of severe AEs, SAEs, and AEs leading to withdrawal were ≤4.3, ≤3.3, and ≤0.6 per 100 PY, respectively, in both groups. IRs for discontinuations because of related AEs were 0.2 per 100 PY in the BNT162b2 group and 0.1 per 100 PY in the placebo group.

From Dose 1 to the unblinding date, there were 15 deaths (0.2 per 100 PY) in the BNT162b2 group and 14 (0.2 per 100 PY) deaths in the placebo group (Section 2.5.5.5.4.1).

In the younger age group, the IRs for participants who reported at least 1 AE from Dose 1 to the unblinding date were 88.4 per 100 PY and 43.5 per 100 PY in the BNT162b2 and placebo groups, respectively. In the older age group, the IRs for participants who reported at least 1 AE from Dose 1 to the unblinding date were 75.7 per 100 PY and 43.3 per 100 PY in the BNT162b2 and placebo groups, respectively.

Table 60. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=21926, TE[b]=83.4)			Placebo (N[a]=21921, TE[b]=82.2)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])
Any event	6947	83.2	(81.3, 85.2)	3568	43.4	(42.0, 44.9)
Related[f]	5246	62.9	(61.2, 64.6)	1313	16.0	(15.1, 16.9)
Severe	356	4.3	(3.8, 4.7)	256	3.1	(2.7, 3.5)
Life-threatening	48	0.6	(0.4, 0.8)	54	0.7	(0.5, 0.9)
Any serious adverse event	268	3.2	(2.8, 3.6)	268	3.3	(2.9, 3.7)
Related[f]	4	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)
Severe	148	1.8	(1.5, 2.1)	156	1.9	(1.6, 2.2)
Life-threatening	48	0.6	(0.4, 0.8)	54	0.7	(0.5, 0.9)

Table 60. Incidence Rates of at Least 1 Adverse Event From Dose 1 to Unblinding Date – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=21926, TE[b]=83.4)			Placebo (N[a]=21921, TE[b]=82.2)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])
Any adverse event leading to withdrawal	45	0.5	(0.4, 0.7)	51	0.6	(0.5, 0.8)
Related[f]	13	0.2	(0.1, 0.3)	12	0.1	(0.1, 0.3)
Severe	10	0.1	(0.1, 0.2)	12	0.1	(0.1, 0.3)
Life-threatening	15	0.2	(0.1, 0.3)	16	0.2	(0.1, 0.3)
Death	15	0.2	(0.1, 0.3)	14	0.2	(0.1, 0.3)

a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 1 to the end of blinded follow-up. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
f. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:11)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s092_all_unb_p3_saf

Subgroup Analyses

Baseline SARS-CoV-2 Status

In the BNT162b2 group, there were 674 baseline SARS-CoV-2 positive and 21,102 baseline SARS-CoV-2 negative participants, and there were 705 baseline SARS-COV-2 positive and 21,092 SARS-CoV-2 negative participants in the placebo group.

Similar to what was observed in the overall AEs irrespective of baseline status (Table 60), IRs of at least 1 AE in the baseline SARS-CoV-2 positive subgroup were 70.7 per 100 PY in the BNT162b2 group and 31.9 per 100 PY in the placebo group, and IRs of at least 1 AE in the baseline SARS-CoV-2 negative subgroup were 83.6 per 100 PY in the BNT162b2 group and 43.8 per 100 PY in the placebo group. IRs of related AEs in the BNT162b2 group were 51.8 per 100 PY (baseline positive) and 63.2 per 100 PY (baseline negative). The IRs of SAEs, related SAEs, severe SAEs, and life threatening SAEs were similar in the BNT162b2 and placebo groups, which support these events are not increased in baseline positive participants. Given the differences in exposure (2.5 vs 80.4) by baseline SARS-CoV-2 positive and negative status, respectively, direct comparisons should be interpreted with caution. Section 2.5.5.5.3.2.2 includes an analysis of AEs for baseline status subgroups,

which shows that there is no evidence that individuals who are positive at baseline report AEs at a higher rate than those who are negative at baseline.

IRs of any AEs and related AEs were similar in those positive and negative at baseline, with the IR for any AE of 70.7 per 100 PY (95% CI: 60.7, 81.9) and 83.6 per 100 PY (95% CI: 81.7, 85.7) and for related AE of 51.8 per 100 PY (95% CI: 43.3, 61.4) and 63.2 per 100 PY (95% CI: 61.5, 65.0), respectively. IRs for SAEs were 4.0 per 100 PY (95% CI: 1.9, 7.3) (baseline positive) and 3.2 per 100 PY (95% CI: 2.8, 3.6) (baseline negative); however, none of the SAEs in the positive baseline group were assessed by the investigator as related to BNT162b2. The death rates were also similar: 0.8 per 100 PY (95% CI: 0.1, 2.9) (baseline positive) and 0.2 per 100 PY (95% CI: 0.1, 0.3) (baseline negative).

Race/Ethnicity

IRs of at least 1 AE in the BNT162b2 group were 78.4 per 100 PY (95% CI: 74.9, 82.0; n=5684) in Hispanic/Latino participants and 85.4 per 100 PY (95% CI: 83.1, 87.8; n=16131) in Non-Hispanic/Non-Latino participants. IRs of SAEs, AEs leading to withdrawal, and death were similar in the Hispanic/Latino and Non-Hispanic/Non-Latino groups. None of the SAEs were considered related to BNT162b2 in the Hispanic/Latino group.

IRs of at least 1 AE in the BNT162b2 group were lower in Black or African American participants (53.5 per 100 PY) compared with White (83.1 per 100 PY) or All Other (120.1 per 100 PY) participants. Other IRs were similar in the groups.

Sex

IRs of at least 1 AE in the BNT162b2 group were greater in female participants (91.0 per 100 PY [95% CI: 88.1, 94.0]) than male participants (76.0 per 100 PY [95% CI: 73.4, 78.6]); that cannot be accounted for by the rates in placebo for female participants (46.8 per 100 PY [95% CI: 44.7, 49.0]) and male participants (40.1 per 100 PY [95% CI: 38.2, 42.1]) IRs for related and severe AEs were also greater in female participants (68.6 per 100 PY [95% CI: 66.1, 71.2] and 4.9 per 100 PY [95% CI: 4.2, 5.6], respectively) than in male participants (57.5 per 100 PY [95% CI: 55.3, 59.8] and 3.7 per 100 PY [95% CI: 3.2, 4.3], respectively). However, life-threatening AEs, SAEs, related SAEs, severe SAEs, life threatening SAEs and death IR were similar in male and female participants.

HIV+ Participants

The subset of 200 HIV+ participants during the blinded placebo-controlled follow-up period showed generally similar trends as the overall population. IRs for HIV+ participants who reported at least 1 AE and at least 1 related AE were 95.8 per 100 PY and 62.8 per 100 PY, respectively, for the BNT162b2 group and 52.0 per 100 PY and 10.4 per 100 PY, respectively, for the placebo group. There were 2 SAEs in the BNT162b2 group (1 severe and 1 life-threatening) and 2 SAEs in the placebo group (1 life-threatening). There were 2 AEs leading to withdrawal in the BNT162b2 group (1 life-threatening) and 1 AE (life-threatening) leading to withdrawal in the placebo group. There were 2 deaths, 1 each in the BNT162b2 and placebo groups; neither were assessed by the investigator as related to study intervention (see Section 2.5.5.5.4.1).

2.5.5.5.3.2.2. Analysis of Adverse Events

Adverse Events by System Organ Class and Preferred Term

AEs reported from Dose 1 to the unblinding date during the blinded placebo-controlled follow-up period are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Supplemental Table 14.119. Results were similar to IRs reported in the Dose 1 to 1 month after Dose 2 follow-up period (Section 2.5.5.5.3.1.2).

From Dose 1 to the unblinding date, the most common AEs by IRs were reactogenicity events and were reported at higher IRs in the BNT162b2 group than in the placebo group. IRs in these SOCs (BNT162b2 vs placebo) were:

- general disorders and administration site conditions: 56.9 per 100 PY vs 12.3 per 100 PY
- musculoskeletal and connective tissue disorders: 22.3 per 100 PY vs 7.6 per 100 PY
- nervous system disorders: 19.2 per 100 PY vs 7.7 per 100 PY
- gastrointestinal disorder: 9.0 per 100 PY vs 6.2 per 100 PY.

In the BNT162b2 age groups (younger versus older), IRs in these SOCs were:

- general disorders and administration site conditions: 63.7 per 100 PY vs 46.9 per 100 PY
- musculoskeletal and connective tissue disorders: 24.6 per 100 PY vs 18.8 per 100 PY
- nervous system disorders: 21.8 per 100 PY vs 15.3 per 100 PY
- gastrointestinal disorders: 9.5 per 100 PY vs 8.2 per 100 PY.

The higher rates of AEs in these SOC is consistent with the reactogenicity analysis that shows greater reactogenicity in the younger age group than in the older age group. AEs with the highest IRs in the BNT162b2 group by PT overall were injection site pain (35.0 per 100 PY), pyrexia (18.2 per 100 PY), fatigue (17.6 per 100 PY), chills (16.4 per 100 PY), headache (16.2 per 100 PY), and myalgia (14.9 per 100 PY).

IRs of AEs in the SOC of investigations was higher in the BNT162b2 group (2.2 per 100 PY) than in the placebo group (0.6 per 100 PY), mainly due to body temperature increased in the BNT162b2 group (IR of 1.5 per 100 PY vs 0.2 per 100 PY for the placebo group).

Analysis of reported night sweats and hyperhidrosis is discussed in Section 2.5.5.5.3.1.2 (most events were reported within 7 days after Dose 1 or 2 and are therefore likely consistent with reactogenicity).

In the nervous systems disorder SOC, there were 4 participants who reported facial paralysis in the BNT162b2 group (compared to 1 in the placebo group). There was 1 case of facial paresis reported in the placebo group. Hence, there are a total of 4 cases of facial paralysis/paresis in the in the BNT162b2 group and 2 in the placebo group. Further details are discussed in Section 2.5.5.5.7.1.

There was 1 case of COVID-19 pneumonia (reported in the BNT162b2 group) which led to death (see Section 2.5.5.5.4.1). This participant had COVID-19 diagnosed based on a local test

that was not protocol-approved and was not subsequently confirmed by a test result from the central laboratory (therefore not included in efficacy analyses).

Among the AEs of lymphadenopathy in the BNT162b2 group, the majority (62 of 87 participants; [0.7 per 100 PY]) were assessed by the investigator as related to study intervention. Most cases occurred in the arm and neck region and were reported within 1 to 4 days after vaccination. See Section 2.5.5.5.7.1 for additional details.

IRs for hepatobiliary disorders was 0.3 per 100 PY and 0.2 per 100 PY in the BNT162b2 and placebo group, respectively. There were 24 participants in the BNT162b2 group who had AEs in the SOC of hepatobiliary disorders compared to 16 participants in the placebo group.

A total of 11 cases of reported PTs associated with deafness in the blinded placebo-controlled follow-up period through the unblinding date included: deafness, deafness unilateral, deafness neurosensory, hypoacusis, and sudden hearing loss. Six participants were randomized to the BNT162b2 group (age range: 43 to 65 years of age), and 5 participants were randomized to placebo (age range: 36 to 74 years of age). For 1 participant in each group, onset was 19 days after Dose 1. Onset ranged from 1 to 55 days after Dose 2 for 5 participants in the BNT162b2, and from 2 to 94 days after Dose 2 for 4 participants in the placebo group. The duration ranged from 9 to 155 days after AE onset with 4 events still ongoing at the time of data cutoff (13 March 2021). The toxicity grades were mostly mild (4 BNT162b2 and 2 placebo) or moderate (1 BNT162b2 group and 3 placebo), with 1 being severe (BNT162b2). In the BNT162b2 group, 2 events were deemed related to study vaccine by the investigator. None of the reported events were SAEs.

Other PTs and further details of events of clinical interest including FDA-requested terms and those that were identified by the sponsor and/or from the CDC list of AESIs are discussed in Section 2.5.5.5.7.

Related Adverse Events – Blinded Follow-Up to Unblinding Date

From Dose 1 to the unblinding date, IRs of AEs assessed as related by the investigator during the blinded follow-up period were 62.9 per 100 PY and 16.0 per 100 PY in the BNT162b2 and in placebo groups, respectively (Table 60). IRs of related AEs were highest for reactogenicity events; in the SOC of general disorders and administration site conditions, IRs were 55.7 per 100 PY and 10.8 per 100 PY for BNT162b2 and placebo recipients, respectively. Additional terms identified as either synonymous with or otherwise plausibly associated with reactogenicity events (ie, secondary to reactogenicity events) occurring within 7 days after each dose were also considered related (pain in extremity, decreased appetite, lethargy, asthenia, malaise, night sweats, and hyperhidrosis) (see discussion of these types of events in Section 2.5.5.5.3.1.2).

For lymphadenopathy cases, IRs of related AEs in the younger and older age groups were 70.0 per 100 PY and 52.3 per 100 PY, respectively for the BNT162b2 group and 18.0 per 100 PY and 13.0 per 100 PY, respectively, for the placebo group. The majority of lymphadenopathy events occurred in the arm and neck region and were reported within 1 to 4 days after vaccination (discussed further as events of clinical interest in Section 2.5.5.5.7.1).

Severe or Life-Threatening Adverse Events – Blinded Follow-Up to Unblinding Date

From Dose 1 to the unblinding date, severe AE IRs during the blinded follow-up period were 4.3 per 100 PY (95% CI: 3.8, 4.7) and 3.1 per 100 PY (95% CI: 2.7, 3.5) in BNT162b2 and placebo recipients, respectively. Severe events in the general disorders and administration site conditions were generally reflecting terms consistent with reactogenicity, in the BNT162b2 versus placebo groups (1.2 per 100 PY vs 0.1 per 100 PY) as well as the Musculoskeletal SOC (0.6 per 100 PY vs 0.3 per 100 PY). The IR in all other SOCs were similar in the BNT162b2 and placebo groups.

IRs for participants who had at least 1 life-threatening AE from Dose 1 to the unblinding date were similar: 0.6 per 100 PY (95% CI: 0.4, 0.8) in the BNT162b2 group and 0.7 per 100 PY (95% CI: 0.5, 0.9) in the placebo group. All of the IRs for the SOCs were similar in the BNT162b2 and placebo groups.

Subgroup Analyses

No clinically meaningful differences in AEs by category or by frequency were observed up from Dose 1 up to the unblinding date for subgroups categorized by race, ethnicity, or baseline SARS-CoV-2 status. Sex-appropriate differences were observed in AE IRs.

Baseline SARS-CoV-2 Status

In the baseline SARS-CoV-2 positive subgroup, differences in IRs in the BNT162b2 (70.7 per 100 PY) and placebo (31.9 per 100 PY) groups were due to reactogenicity events (chills, fatigue, injection site pain, pyrexia, myalgia, and headache). In the baseline SARS-CoV-2 negative subgroup, differences in IRs in the BNT162b2 (83.6 per 100 PY) and placebo (43.8 per 100 PY) groups were due to reactogenicity events (diarrhea, vomiting, chill, fatigue, injection site reactions [pain, erythema, swelling], pyrexia, arthralgia, myalgia, and headache) as well as other AEs (lymphadenopathy, nausea, asthenia, malaise, pain, body temperature increase, and pain in extremity).

Given the differences in exposure (2.5 vs 80.4) by baseline SARS-CoV-2 positive and negative status, respectively, direct comparisons should be interpreted with caution . The overall rate of AEs was 70.7 per 100 PY (95% CI: 60.7, 81.9) (baseline positive) compared with 83.6 per 100 PY (95% CI: 81.7, 85.7) (baseline negative). For other SOCs, the IR were either numerically lower or similar for the baseline positive group compared to the baseline negative group. Overall, there is no evidence that individuals who are positive at baseline report AEs at a higher frequency than those who are negative at baseline.

Race/Ethnicity

In the BNT162b2 group, overall IRs for participants reporting at least 1 AE were highest for participants of all other races (120.1 per 100 PY) compared to White participants (83.1 per 100 PY), with Black or African American participants having the lowest IR (53.5 per 100 PY). The IR for nausea in the BNT162b2 group was higher in participants of all other races (4.7 per 100 PY BNT162b2 vs 1.6 per 100 PY placebo) and White participants (3.4 per 100 PY BNT162b2 vs 1.0 per 100 PY placebo) than in Black or African American participants where the IR was similar in both vaccine groups (1.3 per 100 PY BNT162b2 vs 1.2 per 100 PY placebo).

In the BNT162b2 group, the IR for participants reporting at least 1 AE was higher in non-Hispanic/non-Latino participants (85.4 per 100 PY BNT162b2 and 41.6 per 100 PY placebo) and Hispanic/Latino participants (78.4 per 100 PY BNT162b2 and 47.9 per 100 PY placebo) and lowest in the group where ethnicity was not reported (49.4 per 100 PY BNT162b2 and 43.3 per 100 PY placebo). IRs were higher for mainly reactogenicity events (chills, fatigue, myalgia, diarrhea, injection site reactions [pain, erythema, and swelling], pain, pyrexia, and headache) as well as lymphadenopathy, nausea, influenza like illness, malaise, increased body temperature, and pain in extremity.

Sex

Overall, female participants reported a higher IR of AEs (91.0 per 100 PY BNT162b2, 46.8 per 100 PY placebo) than male participants (76.0 per 100 PY BNT162b2, 40.1 per 100 PY placebo), with a greater difference in BNT162b2 groups than in placebo groups. The higher IRs in female participants were due to reactogenicity AEs (vomiting, chills, fatigue, pyrexia, myalgia, and headache) as well as other AEs (lymphadenopathy, nausea, pain, increased body temperature, and pain in extremity). There were sex-appropriate differences as well, such as higher IRs in the SOC of cardiac disorders in male participants (1.2 per 100 PY) versus female participants (0.9 per 100 PY) and lower IRs in the SOC of reproductive system and breast disorders in male participants (0.3 per 100 PY) versus female participants (0.9 per 100 PY).

HIV+ Participants

From Dose 1 to the unblinding date, and similar to the overall population, most AEs reported for the subset of 200 HIV+ participants from Dose 1 to the unblinding date were in SOCs with reactogenicity events (BNT162b2 vs placebo):

- general disorders and administration site conditions: 66.1 per 100 PY vs 6.9 per 100 PY
- musculoskeletal and connective tissue disorders: 19.8 per 100 PY vs 10.4 per 100 PY
- nervous system disorders: 16.5 per 100 PY vs 0.0 per 100 PY
- gastrointestinal disorders: 9.9 per 100 PY vs 13.9 per 100 PY.

2.5.5.5.3.3. Open-Label Follow-Up Period – Original BNT162b2 Participants

2.5.5.5.3.3.1. Summary of Adverse Events

An overview of AEs from the unblinding date to the data cutoff date for participants originally randomized to BNT162b2 during the open-label follow-up is presented in Table 61.

Note: per protocol, AEs are reported through 1 month after the Dose 2 and within 48 hours after a blood draw and SAEs are reported to approximately 6 months after the last dose of study intervention.

IRs for any AE, at least 1 related AE, and severe AE were 8.8 per 100 PY, 0.7 per 100 PY, and 1.6 per 100 PY, respectively, which is markedly reduced relative to those from Dose 1 to the unblinding date (83.2, 62.9, 4.3 respectively). The IR of life-threatening AEs is 0.4 per 100 PY (95% CI: 0.2, 0.8), which is similar to the IR from Dose 1 to the unblinding date (0.6 per 100 PY [95% CI: 0.4, 0.8]; Table 60).

The IR of SAEs during the open-label follow-up period, 2.0 per 100 PY (95% CI: 1.5, 2.6; Table 61), was lower than the IR from Dose 1 to the unblinding date, 3.2 per 100 PY (95% CI: 2.8, 3.6; Table 60). There was a single related SAE (myocardial infarction) for a participant in the open-label follow-up period (see Section 2.5.5.5.3.3.2 and Section 2.5.5.5.5.3). The IR of AEs leading to withdrawal also decreased (0.1 per 100 PY [95% CI: 0.0, 0.4]) in the open-label follow-up period compared with the blinded placebo-controlled period (0.5 per 100 PY [95% CI: 0.4, 0.7]; Table 60) but the IR of deaths were similar (0.1 per 100 PY vs 0.2 per 100 PY in the open-label and blinded placebo-controlled follow-up periods, respectively).

Three participants originally randomized to BNT162b2 died during open-label follow-up (Section 2.5.5.5.4.2).

Table 61. Incidence Rates of at Least 1 Adverse Event From Unblinding Date to Data Cutoff Date (13MAR2021) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2 – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=20309, TE[b]=27.7)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])
Any event	243	8.8	(7.7, 9.9)
Related[f]	20	0.7	(0.4, 1.1)
Severe	43	1.6	(1.1, 2.1)
Life-threatening	12	0.4	(0.2, 0.8)
Any serious adverse event	55	2.0	(1.5, 2.6)
Related[f]	1	0.0	(0.0, 0.2)

Table 61. Incidence Rates of at Least 1 Adverse Event From Unblinding Date to Data Cutoff Date (13MAR2021) – Open-Label Follow-up Period – Subjects Who Originally Received BNT162b2 – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=20309, TE[b]=27.7)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])
Severe	30	1.1	(0.7, 1.5)
Life-threatening	12	0.4	(0.2, 0.8)
Any adverse event leading to withdrawal	4	0.1	(0.0, 0.4)
Related[f]	0	0.0	(0.0, 0.1)
Severe	0	0.0	(0.0, 0.1)
Life-threatening	4	0.1	(0.0, 0.4)
Death	3	0.1	(0.0, 0.3)

a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from the unblinding date to data cutoff date. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
f. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:16)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s092_unb_cut_p3_saf

2.5.5.5.3.3.2. Analysis of Adverse Events

Adverse Events by System Organ Class and Preferred Term

AEs reported from the unblinding date to the data cutoff date for participants originally randomized to BNT162b2 during the open-label follow-up period are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Supplemental Table 14.142.

From the unblinding date to the data cutoff date, for participants originally randomized to BNT162b2 during the open-label follow-up period, the IRs for participants who reported at least 1 AE was 8.8 per 100 PY, as compared to 83.2 per 100 PY from Dose 1 to the unblinding date (Table 60).

Overall, the rates in all SOCs after the unblinding date decreased or remained similar to those in the blinded placebo-controlled period.

The IR for the SOC of injury, poisoning and procedural complications was 1.4 per 100 PY, with the PT fall having the highest IR (0.4 per 100 PY). The IR for the SOC of vascular disorders was 0.8 per 100 PY, with the PT hypertension having the highest IR (0.6 per 100 PY).

Related Adverse Events – Open-Label Follow-Up for Original BNT162b2 Participants

From the unblinding date to the data cutoff date, for participants originally randomized to BNT162b2, the IR of AEs assessed as related by the investigator during the open-label follow-up period was 0.7 per 100 PY (Table 61). IRs of related AEs were highest for reactogenicity events and in the SOC of general disorders and administration site conditions (0.5 per 100 PY), reflecting AEs from their initial vaccinations.

One younger participant had a life-threatening SAE of myocardial infarction occurring 71 days after Dose 2 that was assessed by the investigator as related to study intervention, which lasted 1 day and resolved the same day (see Section 2.5.5.5.5.3).

2.5.5.5.3.4. Cumulative Blinded and Open-Label Follow-Up Periods from Dose 1 to 6 Months After Dose 2 – BNT162b2 Group

2.5.5.5.3.4.1. Summary of Adverse Events

An overview of AEs from Dose 1 to 6 months after Dose 2 for participants in the BNT162b2 group during the blinded and open-label follow-up is presented in Table 62.

There were 12,006 participants who had at least 6 months of follow-up. Among these, 3454 participants (28.8%) reported at least 1 AE and 2245 participants (18.7%) reported at least 1 related AE. Severe AEs and SAEs were reported by 2.1% and 1.6%, respectively. One participant was reported as discontinued because of an AE (not related); however, this participant remains in the study as the withdrawal was subsequently queried and corrected as described in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Errata. There were no deaths during the blinded and open-label follow-up periods in the group of original BNT162b2 participants with at least 6 months of follow-up after Dose 2.

When frequencies of AEs for participants with at least 6 months of follow-up time are examined by time since the second BNT162b2 dose, the frequency of AEs and related AEs is 25.8% and 18.6% through 1 month after Dose 2 compared with 4.8% and 0.1% from 1 month after Dose 2 to 6 months after Dose 2 (Table 63). In the first month after vaccination, 0.5% of participants reported SAEs (including 1 related) and from 1 month to 6 months after Dose 2 the frequency of SAEs increased to 1.1% (including 1 related SAE).

In the younger age group, the number of participants who reported at least 1 AE and 1 related AE from Dose 1 to 6 months after Dose 2 was 2013 (30.2%) and 1386 (20.8%), respectively. In the older age group, the number of participants who reported at least 1 AE and 1 related AE from Dose 1 to 6 months after Dose 2 was 1441 (27.0%) and 859 (16.1%), respectively.

Table 62. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2 – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)
	BNT162b2 (30 µg) (N[a]=12006)
Adverse Event	n[b] (%)
Any event	3454 (28.8)
Related[c]	2245 (18.7)
Severe	248 (2.1)
Life-threatening	23 (0.2)
Any serious adverse event	190 (1.6)
Related[c]	2 (0.0)
Severe	116 (1.0)
Life-threatening	23 (0.2)
Any adverse event leading to withdrawal	1 (0.0)
Related[c]	0
Severe	0
Life-threatening	0
Death	0

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
c. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (14:48)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA/adae s091 all pd2 p3 saf2

Table 63. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by Time Period – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	Dose 1 to 1 Month Post Dose 2 (N[a]=12006)	After 1 Month Post Dose 2 to 6 Months Post Dose 2 (N[a]=12006)
Adverse Event	n[b] (%)	n[b] (%)
Any event	3092 (25.8)	572 (4.8)
Related[c]	2239 (18.6)	12 (0.1)
Severe	143 (1.2)	110 (0.9)
Life-threatening	8 (0.1)	15 (0.1)
Any serious adverse event	58 (0.5)	133 (1.1)
Related[c]	1 (0.0)	1 (0.0)
Severe	34 (0.3)	82 (0.7)
Life-threatening	8 (0.1)	15 (0.1)
Any adverse event leading to withdrawal	0	1 (0.0)
Related[c]	0	0
Severe	0	0
Life-threatening	0	0
Death	0	0

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
c. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 14APR2021 (08:45)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA RR/adae s091 all pd2 p3 tp saf2

2.5.5.5.3.4.2. Analysis of Adverse Events

Adverse Events by System Organ Class and Preferred Term

AEs reported during the cumulative period from Dose 1 up to 6 months after Dose 2 (inclusive of blinded and open-label follow-up) in the BNT162b2 group are summarized in Table 64.

From Dose 1 to 6 months after Dose 2 during the blinded and open-label follow-up period, 3454 (28.8%) original BNT162b2 participants reported at least 1 AE (Table 64). The most frequently reported AEs were reactogenicity events:

- general disorders and administration site conditions: 2016 (16.8%)
- musculoskeletal and connective tissue disorders: 905 (7.5%)
- nervous system disorders: 726 (6.0%)
- gastrointestinal disorders: 407 [3.4%).

The number of original BNT162b2 participants who reported at least 1 AE from Dose 1 to 6 months after Dose 2 was 2013 (30.2%) and 1441 (27.0%) in the younger and older groups, respectively.

In the BNT162b2 age groups, AE frequencies in reactogenicity SOCs (younger vs older) were:

- general disorders and administration site conditions: 1246 (18.7%) vs 770 (14.4%)
- musculoskeletal and connective tissue disorders: 539 (8.1%) vs 366 (6.9%)
- nervous system disorders: 449 (6.7%) vs 277 (5.2%)
- gastrointestinal disorders: 231 (3.5%) vs 176 (3.3%).

As shown in Table 64, the most frequently reported AEs in the BNT162b2 group were injection site pain (1191 [9.9%]), pyrexia (633 [5.3%]), chills (606 [5.0%]), fatigue (598 [5.0%]), headache (572 [4.8%]), and myalgia (549 [4.6%]).

When AEs are compared from 1 month after Dose 2 and from 1 month after Dose 2 to 6 months after Dose 2, the frequencies of AEs by most SOCs decreased or remained the same with the additional follow-up time. The overall frequency of any AE for participants from 1 month after Dose 2 to 6 months after Dose 2 (4.8%) was decreased relative to the frequency observed within 1 month of follow-up after Dose 2 (25.8%) for this group.

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Any event	3454 (28.8)	(28.0, 29.6)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	70 (0.6)	(0.5, 0.7)
Lymphadenopathy	50 (0.4)	(0.3, 0.5)
Anaemia	7 (0.1)	(0.0, 0.1)
Iron deficiency anaemia	5 (0.0)	(0.0, 0.1)
Lymph node pain	3 (0.0)	(0.0, 0.1)
Leukopenia	2 (0.0)	(0.0, 0.1)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Blood loss anaemia	1 (0.0)	(0.0, 0.0)
Coagulopathy	1 (0.0)	(0.0, 0.0)
Lymphadenopathy mediastinal	1 (0.0)	(0.0, 0.0)
Lymphocytosis	1 (0.0)	(0.0, 0.0)
Lymphopenia	1 (0.0)	(0.0, 0.0)
Neutropenia	1 (0.0)	(0.0, 0.0)
Pancytopenia	1 (0.0)	(0.0, 0.0)
Splenic infarction	1 (0.0)	(0.0, 0.0)
Splenomegaly	1 (0.0)	(0.0, 0.0)
CARDIAC DISORDERS	59 (0.5)	(0.4, 0.6)
Atrial fibrillation	9 (0.1)	(0.0, 0.1)
Tachycardia	9 (0.1)	(0.0, 0.1)
Palpitations	7 (0.1)	(0.0, 0.1)
Coronary artery disease	6 (0.0)	(0.0, 0.1)
Acute myocardial infarction	4 (0.0)	(0.0, 0.1)
Angina pectoris	4 (0.0)	(0.0, 0.1)
Myocardial infarction	4 (0.0)	(0.0, 0.1)
Cardiac failure congestive	3 (0.0)	(0.0, 0.1)
Angina unstable	2 (0.0)	(0.0, 0.1)
Acute coronary syndrome	1 (0.0)	(0.0, 0.0)
Arrhythmia	1 (0.0)	(0.0, 0.0)
Arrhythmia supraventricular	1 (0.0)	(0.0, 0.0)
Atrial flutter	1 (0.0)	(0.0, 0.0)
Atrioventricular block first degree	1 (0.0)	(0.0, 0.0)
Bradycardia	1 (0.0)	(0.0, 0.0)
Bundle branch block right	1 (0.0)	(0.0, 0.0)
Cardiac arrest	1 (0.0)	(0.0, 0.0)
Cardiac disorder	1 (0.0)	(0.0, 0.0)
Cardiomegaly	1 (0.0)	(0.0, 0.0)
Coronary artery occlusion	1 (0.0)	(0.0, 0.0)
Left ventricular dysfunction	1 (0.0)	(0.0, 0.0)
Mitral valve prolapse	1 (0.0)	(0.0, 0.0)
Pericarditis	1 (0.0)	(0.0, 0.0)
Sinus tachycardia	1 (0.0)	(0.0, 0.0)
Supraventricular tachycardia	1 (0.0)	(0.0, 0.0)
Ventricular tachycardia	1 (0.0)	(0.0, 0.0)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	3 (0.0)	(0.0, 0.1)
Congenital cystic kidney disease	1 (0.0)	(0.0, 0.0)
Gastrointestinal arteriovenous malformation	1 (0.0)	(0.0, 0.0)
Protein S deficiency	1 (0.0)	(0.0, 0.0)
EAR AND LABYRINTH DISORDERS	49 (0.4)	(0.3, 0.5)
Vertigo	21 (0.2)	(0.1, 0.3)
Ear pain	8 (0.1)	(0.0, 0.1)
Tinnitus	6 (0.0)	(0.0, 0.1)
Vertigo positional	4 (0.0)	(0.0, 0.1)
Cerumen impaction	3 (0.0)	(0.0, 0.1)
Deafness neurosensory	2 (0.0)	(0.0, 0.1)
Ear discomfort	2 (0.0)	(0.0, 0.1)
Deafness unilateral	1 (0.0)	(0.0, 0.0)
Hyperacusis	1 (0.0)	(0.0, 0.0)
Sudden hearing loss	1 (0.0)	(0.0, 0.0)
ENDOCRINE DISORDERS	15 (0.1)	(0.1, 0.2)
Hypothyroidism	6 (0.0)	(0.0, 0.1)
Hyperthyroidism	2 (0.0)	(0.0, 0.1)
Hypogonadism	2 (0.0)	(0.0, 0.1)
Thyroid mass	2 (0.0)	(0.0, 0.1)
Goitre	1 (0.0)	(0.0, 0.0)
Hyperprolactinaemia	1 (0.0)	(0.0, 0.0)
Oestrogen deficiency	1 (0.0)	(0.0, 0.0)
Pituitary cyst	1 (0.0)	(0.0, 0.0)
EYE DISORDERS	47 (0.4)	(0.3, 0.5)
Cataract	5 (0.0)	(0.0, 0.1)
Vision blurred	5 (0.0)	(0.0, 0.1)
Chalazion	3 (0.0)	(0.0, 0.1)
Eye irritation	3 (0.0)	(0.0, 0.1)
Eye pain	3 (0.0)	(0.0, 0.1)
Macular oedema	3 (0.0)	(0.0, 0.1)
Vitreous detachment	3 (0.0)	(0.0, 0.1)
Blepharitis	2 (0.0)	(0.0, 0.1)
Diplopia	2 (0.0)	(0.0, 0.1)
Dry eye	2 (0.0)	(0.0, 0.1)
Glaucoma	2 (0.0)	(0.0, 0.1)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Retinal tear	2 (0.0)	(0.0, 0.1)
Asthenopia	1 (0.0)	(0.0, 0.0)
Choroidal neovascularisation	1 (0.0)	(0.0, 0.0)
Conjunctival haemorrhage	1 (0.0)	(0.0, 0.0)
Corneal irritation	1 (0.0)	(0.0, 0.0)
Episcleritis	1 (0.0)	(0.0, 0.0)
Eye pruritus	1 (0.0)	(0.0, 0.0)
Eyelid oedema	1 (0.0)	(0.0, 0.0)
Eyelid pain	1 (0.0)	(0.0, 0.0)
Eyelids pruritus	1 (0.0)	(0.0, 0.0)
Keratitis	1 (0.0)	(0.0, 0.0)
Ophthalmic vein thrombosis	1 (0.0)	(0.0, 0.0)
Photophobia	1 (0.0)	(0.0, 0.0)
Retinal artery occlusion	1 (0.0)	(0.0, 0.0)
Scleral discolouration	1 (0.0)	(0.0, 0.0)
Vitreous floaters	1 (0.0)	(0.0, 0.0)
GASTROINTESTINAL DISORDERS	407 (3.4)	(3.1, 3.7)
Nausea	140 (1.2)	(1.0, 1.4)
Diarrhoea	123 (1.0)	(0.9, 1.2)
Vomiting	35 (0.3)	(0.2, 0.4)
Toothache	18 (0.1)	(0.1, 0.2)
Abdominal pain	15 (0.1)	(0.1, 0.2)
Gastrooesophageal reflux disease	14 (0.1)	(0.1, 0.2)
Dyspepsia	13 (0.1)	(0.1, 0.2)
Abdominal pain upper	10 (0.1)	(0.0, 0.2)
Odynophagia	10 (0.1)	(0.0, 0.2)
Constipation	7 (0.1)	(0.0, 0.1)
Dental caries	6 (0.0)	(0.0, 0.1)
Irritable bowel syndrome	5 (0.0)	(0.0, 0.1)
Abdominal distension	4 (0.0)	(0.0, 0.1)
Flatulence	4 (0.0)	(0.0, 0.1)
Gastritis	4 (0.0)	(0.0, 0.1)
Hiatus hernia	4 (0.0)	(0.0, 0.1)
Large intestine polyp	4 (0.0)	(0.0, 0.1)
Aphthous ulcer	3 (0.0)	(0.0, 0.1)
Diverticulum	3 (0.0)	(0.0, 0.1)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Food poisoning	3 (0.0)	(0.0, 0.1)
Haemorrhoids	3 (0.0)	(0.0, 0.1)
Colitis	2 (0.0)	(0.0, 0.1)
Gastritis erosive	2 (0.0)	(0.0, 0.1)
Gastrointestinal disorder	2 (0.0)	(0.0, 0.1)
Glossodynia	2 (0.0)	(0.0, 0.1)
Haematochezia	2 (0.0)	(0.0, 0.1)
Impaired gastric emptying	2 (0.0)	(0.0, 0.1)
Oral pain	2 (0.0)	(0.0, 0.1)
Small intestinal obstruction	2 (0.0)	(0.0, 0.1)
Abdominal discomfort	1 (0.0)	(0.0, 0.0)
Abdominal pain lower	1 (0.0)	(0.0, 0.0)
Abdominal rigidity	1 (0.0)	(0.0, 0.0)
Angular cheilitis	1 (0.0)	(0.0, 0.0)
Cheilitis	1 (0.0)	(0.0, 0.0)
Coeliac disease	1 (0.0)	(0.0, 0.0)
Colitis microscopic	1 (0.0)	(0.0, 0.0)
Colitis ulcerative	1 (0.0)	(0.0, 0.0)
Crohn's disease	1 (0.0)	(0.0, 0.0)
Diverticulum intestinal	1 (0.0)	(0.0, 0.0)
Dry mouth	1 (0.0)	(0.0, 0.0)
Dysphagia	1 (0.0)	(0.0, 0.0)
Epiploic appendagitis	1 (0.0)	(0.0, 0.0)
Eructation	1 (0.0)	(0.0, 0.0)
Faeces soft	1 (0.0)	(0.0, 0.0)
Femoral hernia	1 (0.0)	(0.0, 0.0)
Gastric antral vascular ectasia	1 (0.0)	(0.0, 0.0)
Gastric ulcer	1 (0.0)	(0.0, 0.0)
Gastric ulcer haemorrhage	1 (0.0)	(0.0, 0.0)
Gastrointestinal haemorrhage	1 (0.0)	(0.0, 0.0)
Gastrointestinal pain	1 (0.0)	(0.0, 0.0)
Gingival pain	1 (0.0)	(0.0, 0.0)
Glossitis	1 (0.0)	(0.0, 0.0)
Haematemesis	1 (0.0)	(0.0, 0.0)
Haemorrhoidal haemorrhage	1 (0.0)	(0.0, 0.0)
Hypoaesthesia oral	1 (0.0)	(0.0, 0.0)
Hypoaesthesia teeth	1 (0.0)	(0.0, 0.0)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Inguinal hernia	1 (0.0)	(0.0, 0.0)
Internal hernia	1 (0.0)	(0.0, 0.0)
Intestinal obstruction	1 (0.0)	(0.0, 0.0)
Intestinal polyp	1 (0.0)	(0.0, 0.0)
Intra-abdominal fluid collection	1 (0.0)	(0.0, 0.0)
Lip oedema	1 (0.0)	(0.0, 0.0)
Noninfective gingivitis	1 (0.0)	(0.0, 0.0)
Obstructive pancreatitis	1 (0.0)	(0.0, 0.0)
Oesophageal spasm	1 (0.0)	(0.0, 0.0)
Oral discomfort	1 (0.0)	(0.0, 0.0)
Oral lichenoid reaction	1 (0.0)	(0.0, 0.0)
Pancreatic calcification	1 (0.0)	(0.0, 0.0)
Pancreatitis	1 (0.0)	(0.0, 0.0)
Parotid duct obstruction	1 (0.0)	(0.0, 0.0)
Rectal haemorrhage	1 (0.0)	(0.0, 0.0)
Rectal polyp	1 (0.0)	(0.0, 0.0)
Retching	1 (0.0)	(0.0, 0.0)
Stomatitis	1 (0.0)	(0.0, 0.0)
Swollen tongue	1 (0.0)	(0.0, 0.0)
Tongue oedema	1 (0.0)	(0.0, 0.0)
Tongue pruritus	1 (0.0)	(0.0, 0.0)
Tongue ulceration	1 (0.0)	(0.0, 0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	2016 (16.8)	(16.1, 17.5)
Injection site pain	1191 (9.9)	(9.4, 10.5)
Pyrexia	633 (5.3)	(4.9, 5.7)
Chills	606 (5.0)	(4.7, 5.5)
Fatigue	598 (5.0)	(4.6, 5.4)
Pain	277 (2.3)	(2.0, 2.6)
Injection site erythema	91 (0.8)	(0.6, 0.9)
Injection site swelling	60 (0.5)	(0.4, 0.6)
Malaise	46 (0.4)	(0.3, 0.5)
Asthenia	20 (0.2)	(0.1, 0.3)
Injection site pruritus	19 (0.2)	(0.1, 0.2)
Chest pain	14 (0.1)	(0.1, 0.2)
Influenza like illness	10 (0.1)	(0.0, 0.2)
Injection site bruising	8 (0.1)	(0.0, 0.1)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Axillary pain	6 (0.0)	(0.0, 0.1)
Injection site warmth	6 (0.0)	(0.0, 0.1)
Feeling hot	5 (0.0)	(0.0, 0.1)
Injection site induration	5 (0.0)	(0.0, 0.1)
Oedema peripheral	5 (0.0)	(0.0, 0.1)
Peripheral swelling	4 (0.0)	(0.0, 0.1)
Injection site oedema	3 (0.0)	(0.0, 0.1)
Non-cardiac chest pain	3 (0.0)	(0.0, 0.1)
Adverse drug reaction	2 (0.0)	(0.0, 0.1)
Cyst	2 (0.0)	(0.0, 0.1)
Face oedema	2 (0.0)	(0.0, 0.1)
Injection site discomfort	2 (0.0)	(0.0, 0.1)
Injection site haematoma	2 (0.0)	(0.0, 0.1)
Injection site nodule	2 (0.0)	(0.0, 0.1)
Injection site papule	2 (0.0)	(0.0, 0.1)
Swelling	2 (0.0)	(0.0, 0.1)
Application site erythema	1 (0.0)	(0.0, 0.0)
Application site pain	1 (0.0)	(0.0, 0.0)
Application site pruritus	1 (0.0)	(0.0, 0.0)
Application site reaction	1 (0.0)	(0.0, 0.0)
Chest discomfort	1 (0.0)	(0.0, 0.0)
Drug withdrawal syndrome	1 (0.0)	(0.0, 0.0)
Illness	1 (0.0)	(0.0, 0.0)
Induration	1 (0.0)	(0.0, 0.0)
Inflammation	1 (0.0)	(0.0, 0.0)
Injection site discolouration	1 (0.0)	(0.0, 0.0)
Injection site haemorrhage	1 (0.0)	(0.0, 0.0)
Injection site hyperaesthesia	1 (0.0)	(0.0, 0.0)
Injection site irritation	1 (0.0)	(0.0, 0.0)
Injection site lymphadenopathy	1 (0.0)	(0.0, 0.0)
Injection site mass	1 (0.0)	(0.0, 0.0)
Injection site paraesthesia	1 (0.0)	(0.0, 0.0)
Injection site rash	1 (0.0)	(0.0, 0.0)
Injection site reaction	1 (0.0)	(0.0, 0.0)
Medical device pain	1 (0.0)	(0.0, 0.0)
Sensation of foreign body	1 (0.0)	(0.0, 0.0)
Shoulder injury related to vaccine administration	1 (0.0)	(0.0, 0.0)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Sluggishness	1 (0.0)	(0.0, 0.0)
Temperature intolerance	1 (0.0)	(0.0, 0.0)
Thirst	1 (0.0)	(0.0, 0.0)
Vaccination site induration	1 (0.0)	(0.0, 0.0)
Vascular stent occlusion	1 (0.0)	(0.0, 0.0)
Vessel puncture site bruise	1 (0.0)	(0.0, 0.0)
Vessel puncture site haematoma	1 (0.0)	(0.0, 0.0)
HEPATOBILIARY DISORDERS	21 (0.2)	(0.1, 0.3)
Cholelithiasis	7 (0.1)	(0.0, 0.1)
Biliary colic	4 (0.0)	(0.0, 0.1)
Cholecystitis acute	3 (0.0)	(0.0, 0.1)
Bile duct stone	2 (0.0)	(0.0, 0.1)
Biliary dyskinesia	1 (0.0)	(0.0, 0.0)
Cholecystitis	1 (0.0)	(0.0, 0.0)
Cholelithiasis obstructive	1 (0.0)	(0.0, 0.0)
Gallbladder disorder	1 (0.0)	(0.0, 0.0)
Hepatic steatosis	1 (0.0)	(0.0, 0.0)
Jaundice	1 (0.0)	(0.0, 0.0)
Portosplenomesenteric venous thrombosis	1 (0.0)	(0.0, 0.0)
Steatohepatitis	1 (0.0)	(0.0, 0.0)
IMMUNE SYSTEM DISORDERS	15 (0.1)	(0.1, 0.2)
Seasonal allergy	6 (0.0)	(0.0, 0.1)
Drug hypersensitivity	2 (0.0)	(0.0, 0.1)
Hypersensitivity	2 (0.0)	(0.0, 0.1)
Allergy to arthropod bite	1 (0.0)	(0.0, 0.0)
Allergy to arthropod sting	1 (0.0)	(0.0, 0.0)
Anaphylactic reaction	1 (0.0)	(0.0, 0.0)
Food allergy	1 (0.0)	(0.0, 0.0)
Jarisch-Herxheimer reaction	1 (0.0)	(0.0, 0.0)
INFECTIONS AND INFESTATIONS	295 (2.5)	(2.2, 2.7)
Urinary tract infection	57 (0.5)	(0.4, 0.6)
Tooth infection	20 (0.2)	(0.1, 0.3)
Sinusitis	16 (0.1)	(0.1, 0.2)
Appendicitis	10 (0.1)	(0.0, 0.2)
Herpes zoster	10 (0.1)	(0.0, 0.2)
Cellulitis	9 (0.1)	(0.0, 0.1)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Conjunctivitis	8 (0.1)	(0.0, 0.1)
Cystitis	8 (0.1)	(0.0, 0.1)
Ear infection	8 (0.1)	(0.0, 0.1)
Diverticulitis	7 (0.1)	(0.0, 0.1)
Gastroenteritis	7 (0.1)	(0.0, 0.1)
Tooth abscess	7 (0.1)	(0.0, 0.1)
Hordeolum	6 (0.0)	(0.0, 0.1)
Upper respiratory tract infection	6 (0.0)	(0.0, 0.1)
Folliculitis	5 (0.0)	(0.0, 0.1)
Rhinitis	5 (0.0)	(0.0, 0.1)
Nasopharyngitis	4 (0.0)	(0.0, 0.1)
Oral herpes	4 (0.0)	(0.0, 0.1)
Otitis externa	4 (0.0)	(0.0, 0.1)
Vulvovaginal mycotic infection	4 (0.0)	(0.0, 0.1)
Fungal skin infection	3 (0.0)	(0.0, 0.1)
Gingivitis	3 (0.0)	(0.0, 0.1)
Onychomycosis	3 (0.0)	(0.0, 0.1)
Paronychia	3 (0.0)	(0.0, 0.1)
Pharyngitis streptococcal	3 (0.0)	(0.0, 0.1)
Pneumonia	3 (0.0)	(0.0, 0.1)
Pyelonephritis	3 (0.0)	(0.0, 0.1)
Vulvovaginal candidiasis	3 (0.0)	(0.0, 0.1)
Device related infection	2 (0.0)	(0.0, 0.1)
Herpes simplex	2 (0.0)	(0.0, 0.1)
Influenza	2 (0.0)	(0.0, 0.1)
Kidney infection	2 (0.0)	(0.0, 0.1)
Laryngitis	2 (0.0)	(0.0, 0.1)
Localised infection	2 (0.0)	(0.0, 0.1)
Oral candidiasis	2 (0.0)	(0.0, 0.1)
Otitis media	2 (0.0)	(0.0, 0.1)
Otitis media acute	2 (0.0)	(0.0, 0.1)
Periodontitis	2 (0.0)	(0.0, 0.1)
Pustule	2 (0.0)	(0.0, 0.1)
Rash pustular	2 (0.0)	(0.0, 0.1)
Sepsis	2 (0.0)	(0.0, 0.1)
Sinusitis bacterial	2 (0.0)	(0.0, 0.1)
Skin infection	2 (0.0)	(0.0, 0.1)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Viral infection	2 (0.0)	(0.0, 0.1)
Abscess	1 (0.0)	(0.0, 0.0)
Abscess neck	1 (0.0)	(0.0, 0.0)
Abscess oral	1 (0.0)	(0.0, 0.0)
Acute sinusitis	1 (0.0)	(0.0, 0.0)
Appendicitis perforated	1 (0.0)	(0.0, 0.0)
Arthritis bacterial	1 (0.0)	(0.0, 0.0)
Bacteraemia	1 (0.0)	(0.0, 0.0)
Bacterial blepharitis	1 (0.0)	(0.0, 0.0)
Bacterial sepsis	1 (0.0)	(0.0, 0.0)
Bacterial vaginosis	1 (0.0)	(0.0, 0.0)
Bacterial vulvovaginitis	1 (0.0)	(0.0, 0.0)
Bartholinitis	1 (0.0)	(0.0, 0.0)
Bone abscess	1 (0.0)	(0.0, 0.0)
Bronchitis	1 (0.0)	(0.0, 0.0)
Cellulitis orbital	1 (0.0)	(0.0, 0.0)
Chronic sinusitis	1 (0.0)	(0.0, 0.0)
Clostridium difficile colitis	1 (0.0)	(0.0, 0.0)
Empyema	1 (0.0)	(0.0, 0.0)
Endocarditis	1 (0.0)	(0.0, 0.0)
Escherichia urinary tract infection	1 (0.0)	(0.0, 0.0)
Eye infection	1 (0.0)	(0.0, 0.0)
Fungal infection	1 (0.0)	(0.0, 0.0)
Furuncle	1 (0.0)	(0.0, 0.0)
Gangrene	1 (0.0)	(0.0, 0.0)
Gastroenteritis viral	1 (0.0)	(0.0, 0.0)
Gastrointestinal infection	1 (0.0)	(0.0, 0.0)
Genital herpes simplex	1 (0.0)	(0.0, 0.0)
Helicobacter gastritis	1 (0.0)	(0.0, 0.0)
Helicobacter infection	1 (0.0)	(0.0, 0.0)
Herpes zoster oticus	1 (0.0)	(0.0, 0.0)
Impetigo	1 (0.0)	(0.0, 0.0)
Infected bite	1 (0.0)	(0.0, 0.0)
Injection site abscess	1 (0.0)	(0.0, 0.0)
Mastoiditis	1 (0.0)	(0.0, 0.0)
Meningitis bacterial	1 (0.0)	(0.0, 0.0)
Mumps	1 (0.0)	(0.0, 0.0)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Papilloma viral infection	1 (0.0)	(0.0, 0.0)
Parasitic gastroenteritis	1 (0.0)	(0.0, 0.0)
Penile infection	1 (0.0)	(0.0, 0.0)
Peritoneal abscess	1 (0.0)	(0.0, 0.0)
Peritonitis	1 (0.0)	(0.0, 0.0)
Peritonsillar abscess	1 (0.0)	(0.0, 0.0)
Pharyngitis	1 (0.0)	(0.0, 0.0)
Pharyngotonsillitis	1 (0.0)	(0.0, 0.0)
Pilonidal cyst	1 (0.0)	(0.0, 0.0)
Postoperative abscess	1 (0.0)	(0.0, 0.0)
Respiratory tract infection viral	1 (0.0)	(0.0, 0.0)
Sialoadenitis	1 (0.0)	(0.0, 0.0)
Staphylococcal infection	1 (0.0)	(0.0, 0.0)
Subcutaneous abscess	1 (0.0)	(0.0, 0.0)
Tinea versicolour	1 (0.0)	(0.0, 0.0)
Varicella	1 (0.0)	(0.0, 0.0)
Vulval abscess	1 (0.0)	(0.0, 0.0)
Vulvovaginitis	1 (0.0)	(0.0, 0.0)
Wound infection	1 (0.0)	(0.0, 0.0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	207 (1.7)	(1.5, 2.0)
Fall	47 (0.4)	(0.3, 0.5)
Exposure during pregnancy	22 (0.2)	(0.1, 0.3)
Muscle strain	15 (0.1)	(0.1, 0.2)
Ligament sprain	13 (0.1)	(0.1, 0.2)
Contusion	12 (0.1)	(0.1, 0.2)
Procedural pain	11 (0.1)	(0.0, 0.2)
Road traffic accident	11 (0.1)	(0.0, 0.2)
Skin laceration	11 (0.1)	(0.0, 0.2)
Arthropod bite	7 (0.1)	(0.0, 0.1)
Limb injury	7 (0.1)	(0.0, 0.1)
Tooth fracture	6 (0.0)	(0.0, 0.1)
Ankle fracture	5 (0.0)	(0.0, 0.1)
Chest injury	5 (0.0)	(0.0, 0.1)
Foot fracture	5 (0.0)	(0.0, 0.1)
Hand fracture	5 (0.0)	(0.0, 0.1)
Joint dislocation	5 (0.0)	(0.0, 0.1)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Skin abrasion	5 (0.0)	(0.0, 0.1)
Joint injury	4 (0.0)	(0.0, 0.1)
Meniscus injury	4 (0.0)	(0.0, 0.1)
Wrist fracture	4 (0.0)	(0.0, 0.1)
Animal bite	3 (0.0)	(0.0, 0.1)
Arthropod sting	3 (0.0)	(0.0, 0.1)
Burns second degree	3 (0.0)	(0.0, 0.1)
Cervical vertebral fracture	3 (0.0)	(0.0, 0.1)
Facial bones fracture	3 (0.0)	(0.0, 0.1)
Humerus fracture	3 (0.0)	(0.0, 0.1)
Patella fracture	3 (0.0)	(0.0, 0.1)
Tibia fracture	3 (0.0)	(0.0, 0.1)
Upper limb fracture	3 (0.0)	(0.0, 0.1)
Vaccination complication	3 (0.0)	(0.0, 0.1)
Concussion	2 (0.0)	(0.0, 0.1)
Craniocerebral injury	2 (0.0)	(0.0, 0.1)
Ligament rupture	2 (0.0)	(0.0, 0.1)
Radius fracture	2 (0.0)	(0.0, 0.1)
Rib fracture	2 (0.0)	(0.0, 0.1)
Thermal burn	2 (0.0)	(0.0, 0.1)
Bone contusion	1 (0.0)	(0.0, 0.0)
Bone fissure	1 (0.0)	(0.0, 0.0)
Burn oral cavity	1 (0.0)	(0.0, 0.0)
Burns first degree	1 (0.0)	(0.0, 0.0)
Burns third degree	1 (0.0)	(0.0, 0.0)
Cartilage injury	1 (0.0)	(0.0, 0.0)
Chemical burns of eye	1 (0.0)	(0.0, 0.0)
Corneal abrasion	1 (0.0)	(0.0, 0.0)
Eyelid injury	1 (0.0)	(0.0, 0.0)
Fibula fracture	1 (0.0)	(0.0, 0.0)
Foreign body in eye	1 (0.0)	(0.0, 0.0)
Fractured sacrum	1 (0.0)	(0.0, 0.0)
Head injury	1 (0.0)	(0.0, 0.0)
Hip fracture	1 (0.0)	(0.0, 0.0)
Jaw fracture	1 (0.0)	(0.0, 0.0)
Limb fracture	1 (0.0)	(0.0, 0.0)
Limb traumatic amputation	1 (0.0)	(0.0, 0.0)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Maternal exposure before pregnancy	1 (0.0)	(0.0, 0.0)
Maternal exposure during pregnancy	1 (0.0)	(0.0, 0.0)
Muscle contusion	1 (0.0)	(0.0, 0.0)
Muscle rupture	1 (0.0)	(0.0, 0.0)
Overdose	1 (0.0)	(0.0, 0.0)
Pelvic fracture	1 (0.0)	(0.0, 0.0)
Penis injury	1 (0.0)	(0.0, 0.0)
Post concussion syndrome	1 (0.0)	(0.0, 0.0)
Post procedural discomfort	1 (0.0)	(0.0, 0.0)
Post procedural swelling	1 (0.0)	(0.0, 0.0)
Procedural dizziness	1 (0.0)	(0.0, 0.0)
Spinal compression fracture	1 (0.0)	(0.0, 0.0)
Spinal cord injury cervical	1 (0.0)	(0.0, 0.0)
Spinal fracture	1 (0.0)	(0.0, 0.0)
Stress fracture	1 (0.0)	(0.0, 0.0)
Subdural haematoma	1 (0.0)	(0.0, 0.0)
Sunburn	1 (0.0)	(0.0, 0.0)
Traumatic intracranial haemorrhage	1 (0.0)	(0.0, 0.0)
Ulna fracture	1 (0.0)	(0.0, 0.0)
INVESTIGATIONS	94 (0.8)	(0.6, 1.0)
Body temperature increased	50 (0.4)	(0.3, 0.5)
Blood glucose increased	8 (0.1)	(0.0, 0.1)
SARS-CoV-2 antibody test positive	5 (0.0)	(0.0, 0.1)
Blood pressure increased	4 (0.0)	(0.0, 0.1)
Blood cholesterol increased	3 (0.0)	(0.0, 0.1)
Alanine aminotransferase increased	2 (0.0)	(0.0, 0.1)
Blood thyroid stimulating hormone increased	2 (0.0)	(0.0, 0.1)
Weight increased	2 (0.0)	(0.0, 0.1)
Aspartate aminotransferase increased	1 (0.0)	(0.0, 0.0)
Blood creatinine decreased	1 (0.0)	(0.0, 0.0)
Blood glucose abnormal	1 (0.0)	(0.0, 0.0)
Blood immunoglobulin E increased	1 (0.0)	(0.0, 0.0)
Blood potassium decreased	1 (0.0)	(0.0, 0.0)
Blood triglycerides increased	1 (0.0)	(0.0, 0.0)
Body temperature decreased	1 (0.0)	(0.0, 0.0)
C-reactive protein	1 (0.0)	(0.0, 0.0)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Cardiac stress test abnormal	1 (0.0)	(0.0, 0.0)
Electrocardiogram QT prolonged	1 (0.0)	(0.0, 0.0)
Fractional exhaled nitric oxide increased	1 (0.0)	(0.0, 0.0)
Glomerular filtration rate decreased	1 (0.0)	(0.0, 0.0)
Haemoglobin decreased	1 (0.0)	(0.0, 0.0)
Heart rate increased	1 (0.0)	(0.0, 0.0)
Intraocular pressure increased	1 (0.0)	(0.0, 0.0)
Liver function test increased	1 (0.0)	(0.0, 0.0)
Lymphocyte count decreased	1 (0.0)	(0.0, 0.0)
Mean cell volume decreased	1 (0.0)	(0.0, 0.0)
Platelet count decreased	1 (0.0)	(0.0, 0.0)
Respiratory rate increased	1 (0.0)	(0.0, 0.0)
Troponin increased	1 (0.0)	(0.0, 0.0)
Weight decreased	1 (0.0)	(0.0, 0.0)
METABOLISM AND NUTRITION DISORDERS	81 (0.7)	(0.5, 0.8)
Decreased appetite	15 (0.1)	(0.1, 0.2)
Hyperlipidaemia	9 (0.1)	(0.0, 0.1)
Type 2 diabetes mellitus	9 (0.1)	(0.0, 0.1)
Vitamin D deficiency	8 (0.1)	(0.0, 0.1)
Hypercholesterolaemia	6 (0.0)	(0.0, 0.1)
Dyslipidaemia	5 (0.0)	(0.0, 0.1)
Glucose tolerance impaired	4 (0.0)	(0.0, 0.1)
Gout	3 (0.0)	(0.0, 0.1)
Hyperglycaemia	3 (0.0)	(0.0, 0.1)
Hypertriglyceridaemia	3 (0.0)	(0.0, 0.1)
Hypoglycaemia	3 (0.0)	(0.0, 0.1)
Hypokalaemia	3 (0.0)	(0.0, 0.1)
Dehydration	2 (0.0)	(0.0, 0.1)
Hyperkalaemia	2 (0.0)	(0.0, 0.1)
Hyperuricaemia	2 (0.0)	(0.0, 0.1)
Obesity	2 (0.0)	(0.0, 0.1)
Diabetes mellitus	1 (0.0)	(0.0, 0.0)
Diabetes mellitus inadequate control	1 (0.0)	(0.0, 0.0)
Diabetic ketoacidosis	1 (0.0)	(0.0, 0.0)
Hypocalcaemia	1 (0.0)	(0.0, 0.0)
Hypocholesterolaemia	1 (0.0)	(0.0, 0.0)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Insulin resistance	1 (0.0)	(0.0, 0.0)
Metabolic syndrome	1 (0.0)	(0.0, 0.0)
Polydipsia	1 (0.0)	(0.0, 0.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	905 (7.5)	(7.1, 8.0)
Myalgia	549 (4.6)	(4.2, 5.0)
Arthralgia	153 (1.3)	(1.1, 1.5)
Pain in extremity	93 (0.8)	(0.6, 0.9)
Back pain	62 (0.5)	(0.4, 0.7)
Neck pain	20 (0.2)	(0.1, 0.3)
Muscle spasms	19 (0.2)	(0.1, 0.2)
Osteoarthritis	14 (0.1)	(0.1, 0.2)
Tendonitis	9 (0.1)	(0.0, 0.1)
Musculoskeletal stiffness	8 (0.1)	(0.0, 0.1)
Intervertebral disc protrusion	6 (0.0)	(0.0, 0.1)
Arthritis	5 (0.0)	(0.0, 0.1)
Bursitis	5 (0.0)	(0.0, 0.1)
Muscular weakness	5 (0.0)	(0.0, 0.1)
Musculoskeletal chest pain	5 (0.0)	(0.0, 0.1)
Periarthritis	5 (0.0)	(0.0, 0.1)
Musculoskeletal discomfort	4 (0.0)	(0.0, 0.1)
Intervertebral disc degeneration	3 (0.0)	(0.0, 0.1)
Joint stiffness	3 (0.0)	(0.0, 0.1)
Muscle contracture	3 (0.0)	(0.0, 0.1)
Rotator cuff syndrome	3 (0.0)	(0.0, 0.1)
Arthropathy	2 (0.0)	(0.0, 0.1)
Coccydynia	2 (0.0)	(0.0, 0.1)
Costochondritis	2 (0.0)	(0.0, 0.1)
Flank pain	2 (0.0)	(0.0, 0.1)
Joint range of motion decreased	2 (0.0)	(0.0, 0.1)
Limb discomfort	2 (0.0)	(0.0, 0.1)
Muscle twitching	2 (0.0)	(0.0, 0.1)
Musculoskeletal pain	2 (0.0)	(0.0, 0.1)
Pain in jaw	2 (0.0)	(0.0, 0.1)
Plantar fasciitis	2 (0.0)	(0.0, 0.1)
Spinal osteoarthritis	2 (0.0)	(0.0, 0.1)
Tenosynovitis stenosans	2 (0.0)	(0.0, 0.1)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Bone disorder	1 (0.0)	(0.0, 0.0)
Bone pain	1 (0.0)	(0.0, 0.0)
Groin pain	1 (0.0)	(0.0, 0.0)
Intervertebral disc compression	1 (0.0)	(0.0, 0.0)
Joint effusion	1 (0.0)	(0.0, 0.0)
Joint instability	1 (0.0)	(0.0, 0.0)
Joint swelling	1 (0.0)	(0.0, 0.0)
Mobility decreased	1 (0.0)	(0.0, 0.0)
Muscle fatigue	1 (0.0)	(0.0, 0.0)
Muscle tightness	1 (0.0)	(0.0, 0.0)
Osteochondritis	1 (0.0)	(0.0, 0.0)
Osteopenia	1 (0.0)	(0.0, 0.0)
Psoriatic arthropathy	1 (0.0)	(0.0, 0.0)
Spinal stenosis	1 (0.0)	(0.0, 0.0)
Spondylitis	1 (0.0)	(0.0, 0.0)
Synovial cyst	1 (0.0)	(0.0, 0.0)
Temporomandibular joint syndrome	1 (0.0)	(0.0, 0.0)
Torticollis	1 (0.0)	(0.0, 0.0)
Trigger finger	1 (0.0)	(0.0, 0.0)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	53 (0.4)	(0.3, 0.6)
Prostate cancer	5 (0.0)	(0.0, 0.1)
Basal cell carcinoma	4 (0.0)	(0.0, 0.1)
Lipoma	4 (0.0)	(0.0, 0.1)
Malignant melanoma	4 (0.0)	(0.0, 0.1)
Breast cancer	3 (0.0)	(0.0, 0.1)
Invasive ductal breast carcinoma	2 (0.0)	(0.0, 0.1)
Skin papilloma	2 (0.0)	(0.0, 0.1)
Transitional cell carcinoma	2 (0.0)	(0.0, 0.1)
Acute myeloid leukaemia	1 (0.0)	(0.0, 0.0)
Adenocarcinoma pancreas	1 (0.0)	(0.0, 0.0)
Adenoma benign	1 (0.0)	(0.0, 0.0)
Adrenal gland cancer	1 (0.0)	(0.0, 0.0)
Benign breast neoplasm	1 (0.0)	(0.0, 0.0)
Benign hydatidiform mole	1 (0.0)	(0.0, 0.0)
Benign uterine neoplasm	1 (0.0)	(0.0, 0.0)
Bladder cancer	1 (0.0)	(0.0, 0.0)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Borderline serous tumour of ovary	1 (0.0)	(0.0, 0.0)
Brain cancer metastatic	1 (0.0)	(0.0, 0.0)
Breast cancer in situ	1 (0.0)	(0.0, 0.0)
Carcinoid tumour of the stomach	1 (0.0)	(0.0, 0.0)
Chondroma	1 (0.0)	(0.0, 0.0)
Colon adenoma	1 (0.0)	(0.0, 0.0)
Fibroma	1 (0.0)	(0.0, 0.0)
Gallbladder cancer stage II	1 (0.0)	(0.0, 0.0)
Gastric cancer	1 (0.0)	(0.0, 0.0)
Malignant melanoma of eyelid	1 (0.0)	(0.0, 0.0)
Meningioma benign	1 (0.0)	(0.0, 0.0)
Non-small cell lung cancer stage IV	1 (0.0)	(0.0, 0.0)
Seborrhoeic keratosis	1 (0.0)	(0.0, 0.0)
Skin cancer	1 (0.0)	(0.0, 0.0)
Squamous cell carcinoma	1 (0.0)	(0.0, 0.0)
Squamous cell carcinoma of skin	1 (0.0)	(0.0, 0.0)
Thyroid cancer	1 (0.0)	(0.0, 0.0)
Uterine cancer	1 (0.0)	(0.0, 0.0)
Uterine leiomyoma	1 (0.0)	(0.0, 0.0)
NERVOUS SYSTEM DISORDERS	726 (6.0)	(5.6, 6.5)
Headache	572 (4.8)	(4.4, 5.2)
Dizziness	43 (0.4)	(0.3, 0.5)
Paraesthesia	15 (0.1)	(0.1, 0.2)
Lethargy	14 (0.1)	(0.1, 0.2)
Migraine	14 (0.1)	(0.1, 0.2)
Sciatica	9 (0.1)	(0.0, 0.1)
Tension headache	9 (0.1)	(0.0, 0.1)
Syncope	8 (0.1)	(0.0, 0.1)
Presyncope	6 (0.0)	(0.0, 0.1)
Tremor	6 (0.0)	(0.0, 0.1)
Dysgeusia	5 (0.0)	(0.0, 0.1)
Somnolence	4 (0.0)	(0.0, 0.1)
Disturbance in attention	3 (0.0)	(0.0, 0.1)
Facial paralysis	3 (0.0)	(0.0, 0.1)
Hypoaesthesia	3 (0.0)	(0.0, 0.1)
Sinus headache	3 (0.0)	(0.0, 0.1)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Subarachnoid haemorrhage	3 (0.0)	(0.0, 0.1)
Burning sensation	2 (0.0)	(0.0, 0.1)
Cerebrovascular accident	2 (0.0)	(0.0, 0.1)
Cervical radiculopathy	2 (0.0)	(0.0, 0.1)
Dizziness postural	2 (0.0)	(0.0, 0.1)
Migraine without aura	2 (0.0)	(0.0, 0.1)
Nerve compression	2 (0.0)	(0.0, 0.1)
Optic neuritis	2 (0.0)	(0.0, 0.1)
Restless legs syndrome	2 (0.0)	(0.0, 0.1)
Seizure	2 (0.0)	(0.0, 0.1)
Transient ischaemic attack	2 (0.0)	(0.0, 0.1)
Aphasia	1 (0.0)	(0.0, 0.0)
Carpal tunnel syndrome	1 (0.0)	(0.0, 0.0)
Depressed level of consciousness	1 (0.0)	(0.0, 0.0)
Dyskinesia	1 (0.0)	(0.0, 0.0)
Hyperaesthesia	1 (0.0)	(0.0, 0.0)
Idiopathic intracranial hypertension	1 (0.0)	(0.0, 0.0)
Intracranial aneurysm	1 (0.0)	(0.0, 0.0)
Ischaemic stroke	1 (0.0)	(0.0, 0.0)
Neuralgia	1 (0.0)	(0.0, 0.0)
Parosmia	1 (0.0)	(0.0, 0.0)
Periodic limb movement disorder	1 (0.0)	(0.0, 0.0)
Peripheral nerve lesion	1 (0.0)	(0.0, 0.0)
Peripheral sensory neuropathy	1 (0.0)	(0.0, 0.0)
Post herpetic neuralgia	1 (0.0)	(0.0, 0.0)
Radiculopathy	1 (0.0)	(0.0, 0.0)
Seizure like phenomena	1 (0.0)	(0.0, 0.0)
Toxic encephalopathy	1 (0.0)	(0.0, 0.0)
Transient global amnesia	1 (0.0)	(0.0, 0.0)
Uraemic encephalopathy	1 (0.0)	(0.0, 0.0)
Vocal cord paralysis	1 (0.0)	(0.0, 0.0)
PREGNANCY, PUERPERIUM AND PERINATAL CONDITIONS	3 (0.0)	(0.0, 0.1)
Abortion spontaneous	2 (0.0)	(0.0, 0.1)
Exposure during pregnancy	1 (0.0)	(0.0, 0.0)
PRODUCT ISSUES	1 (0.0)	(0.0, 0.0)
Device connection issue	1 (0.0)	(0.0, 0.0)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
PSYCHIATRIC DISORDERS	65 (0.5)	(0.4, 0.7)
Insomnia	17 (0.1)	(0.1, 0.2)
Anxiety	16 (0.1)	(0.1, 0.2)
Depression	11 (0.1)	(0.0, 0.2)
Anxiety disorder	4 (0.0)	(0.0, 0.1)
Abnormal dreams	3 (0.0)	(0.0, 0.1)
Attention deficit hyperactivity disorder	3 (0.0)	(0.0, 0.1)
Irritability	3 (0.0)	(0.0, 0.1)
Sleep disorder	3 (0.0)	(0.0, 0.1)
Disorientation	2 (0.0)	(0.0, 0.1)
Nightmare	2 (0.0)	(0.0, 0.1)
Generalised anxiety disorder	1 (0.0)	(0.0, 0.0)
Libido increased	1 (0.0)	(0.0, 0.0)
Panic attack	1 (0.0)	(0.0, 0.0)
Restlessness	1 (0.0)	(0.0, 0.0)
Suicide attempt	1 (0.0)	(0.0, 0.0)
RENAL AND URINARY DISORDERS	42 (0.3)	(0.3, 0.5)
Nephrolithiasis	11 (0.1)	(0.0, 0.2)
Dysuria	6 (0.0)	(0.0, 0.1)
Pollakiuria	5 (0.0)	(0.0, 0.1)
Haematuria	3 (0.0)	(0.0, 0.1)
Acute kidney injury	2 (0.0)	(0.0, 0.1)
Bladder spasm	2 (0.0)	(0.0, 0.1)
Renal colic	2 (0.0)	(0.0, 0.1)
Urinary retention	2 (0.0)	(0.0, 0.1)
Bladder irritation	1 (0.0)	(0.0, 0.0)
Chronic kidney disease	1 (0.0)	(0.0, 0.0)
Hypertonic bladder	1 (0.0)	(0.0, 0.0)
Micturition urgency	1 (0.0)	(0.0, 0.0)
Obstructive nephropathy	1 (0.0)	(0.0, 0.0)
Renal cyst	1 (0.0)	(0.0, 0.0)
Renal haematoma	1 (0.0)	(0.0, 0.0)
Subcapsular renal haematoma	1 (0.0)	(0.0, 0.0)
Urethral stenosis	1 (0.0)	(0.0, 0.0)
Urinary tract obstruction	1 (0.0)	(0.0, 0.0)
Vesical fistula	1 (0.0)	(0.0, 0.0)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	36 (0.3)	(0.2, 0.4)
Dysmenorrhoea	4 (0.0)	(0.0, 0.1)
Ovarian cyst	3 (0.0)	(0.0, 0.1)
Benign prostatic hyperplasia	2 (0.0)	(0.0, 0.1)
Breast pain	2 (0.0)	(0.0, 0.1)
Endometriosis	2 (0.0)	(0.0, 0.1)
Genital erythema	2 (0.0)	(0.0, 0.1)
Menorrhagia	2 (0.0)	(0.0, 0.1)
Menstruation irregular	2 (0.0)	(0.0, 0.1)
Amenorrhoea	1 (0.0)	(0.0, 0.0)
Breast hyperplasia	1 (0.0)	(0.0, 0.0)
Cervical dysplasia	1 (0.0)	(0.0, 0.0)
Dysfunctional uterine bleeding	1 (0.0)	(0.0, 0.0)
Endometrial thickening	1 (0.0)	(0.0, 0.0)
Haematospermia	1 (0.0)	(0.0, 0.0)
Mammary duct ectasia	1 (0.0)	(0.0, 0.0)
Menometrorrhagia	1 (0.0)	(0.0, 0.0)
Metrorrhagia	1 (0.0)	(0.0, 0.0)
Pelvic pain	1 (0.0)	(0.0, 0.0)
Polycystic ovaries	1 (0.0)	(0.0, 0.0)
Postmenopausal haemorrhage	1 (0.0)	(0.0, 0.0)
Prostatitis	1 (0.0)	(0.0, 0.0)
Prostatomegaly	1 (0.0)	(0.0, 0.0)
Pruritus genital	1 (0.0)	(0.0, 0.0)
Scrotal pain	1 (0.0)	(0.0, 0.0)
Testicular pain	1 (0.0)	(0.0, 0.0)
Testicular torsion	1 (0.0)	(0.0, 0.0)
Uterine prolapse	1 (0.0)	(0.0, 0.0)
Vaginal haemorrhage	1 (0.0)	(0.0, 0.0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	145 (1.2)	(1.0, 1.4)
Oropharyngeal pain	24 (0.2)	(0.1, 0.3)
Nasal congestion	21 (0.2)	(0.1, 0.3)
Cough	17 (0.1)	(0.1, 0.2)
Rhinorrhoea	12 (0.1)	(0.1, 0.2)
Rhinitis allergic	9 (0.1)	(0.0, 0.1)
Asthma	8 (0.1)	(0.0, 0.1)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Dyspnoea	6 (0.0)	(0.0, 0.1)
Pulmonary embolism	6 (0.0)	(0.0, 0.1)
Sleep apnoea syndrome	5 (0.0)	(0.0, 0.1)
Throat irritation	5 (0.0)	(0.0, 0.1)
Upper-airway cough syndrome	5 (0.0)	(0.0, 0.1)
Paranasal sinus discomfort	4 (0.0)	(0.0, 0.1)
Chronic obstructive pulmonary disease	3 (0.0)	(0.0, 0.1)
Epistaxis	3 (0.0)	(0.0, 0.1)
Asthmatic crisis	2 (0.0)	(0.0, 0.1)
Bronchospasm	2 (0.0)	(0.0, 0.1)
Nasal polyps	2 (0.0)	(0.0, 0.1)
Productive cough	2 (0.0)	(0.0, 0.1)
Respiratory tract congestion	2 (0.0)	(0.0, 0.1)
Sinus congestion	2 (0.0)	(0.0, 0.1)
Upper respiratory tract congestion	2 (0.0)	(0.0, 0.1)
Wheezing	2 (0.0)	(0.0, 0.1)
Allergic sinusitis	1 (0.0)	(0.0, 0.0)
Atelectasis	1 (0.0)	(0.0, 0.0)
Dry throat	1 (0.0)	(0.0, 0.0)
Dyspnoea exertional	1 (0.0)	(0.0, 0.0)
Emphysema	1 (0.0)	(0.0, 0.0)
Haemoptysis	1 (0.0)	(0.0, 0.0)
Interstitial lung disease	1 (0.0)	(0.0, 0.0)
Nasal septum deviation	1 (0.0)	(0.0, 0.0)
Oropharyngeal discomfort	1 (0.0)	(0.0, 0.0)
Paranasal sinus hypersecretion	1 (0.0)	(0.0, 0.0)
Pleurisy	1 (0.0)	(0.0, 0.0)
Pneumonitis	1 (0.0)	(0.0, 0.0)
Pneumothorax	1 (0.0)	(0.0, 0.0)
Reflux laryngitis	1 (0.0)	(0.0, 0.0)
Respiratory failure	1 (0.0)	(0.0, 0.0)
Sneezing	1 (0.0)	(0.0, 0.0)
Snoring	1 (0.0)	(0.0, 0.0)
Tonsillar hypertrophy	1 (0.0)	(0.0, 0.0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	153 (1.3)	(1.1, 1.5)
Rash	35 (0.3)	(0.2, 0.4)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Hyperhidrosis	16 (0.1)	(0.1, 0.2)
Pruritus	15 (0.1)	(0.1, 0.2)
Dermatitis contact	11 (0.1)	(0.0, 0.2)
Urticaria	11 (0.1)	(0.0, 0.2)
Night sweats	8 (0.1)	(0.0, 0.1)
Rash pruritic	6 (0.0)	(0.0, 0.1)
Erythema	5 (0.0)	(0.0, 0.1)
Dermal cyst	4 (0.0)	(0.0, 0.1)
Dermatitis	4 (0.0)	(0.0, 0.1)
Eczema	4 (0.0)	(0.0, 0.1)
Acne	3 (0.0)	(0.0, 0.1)
Actinic keratosis	3 (0.0)	(0.0, 0.1)
Dermatitis allergic	3 (0.0)	(0.0, 0.1)
Rash maculo-papular	3 (0.0)	(0.0, 0.1)
Alopecia	2 (0.0)	(0.0, 0.1)
Acne cystic	1 (0.0)	(0.0, 0.0)
Angioedema	1 (0.0)	(0.0, 0.0)
Cold sweat	1 (0.0)	(0.0, 0.0)
Dermatitis exfoliative	1 (0.0)	(0.0, 0.0)
Diabetic foot	1 (0.0)	(0.0, 0.0)
Dry skin	1 (0.0)	(0.0, 0.0)
Ecchymosis	1 (0.0)	(0.0, 0.0)
Erythema nodosum	1 (0.0)	(0.0, 0.0)
Hand dermatitis	1 (0.0)	(0.0, 0.0)
Hangnail	1 (0.0)	(0.0, 0.0)
Intertrigo	1 (0.0)	(0.0, 0.0)
Macule	1 (0.0)	(0.0, 0.0)
Onycholysis	1 (0.0)	(0.0, 0.0)
Onychomadesis	1 (0.0)	(0.0, 0.0)
Pain of skin	1 (0.0)	(0.0, 0.0)
Papule	1 (0.0)	(0.0, 0.0)
Pityriasis	1 (0.0)	(0.0, 0.0)
Pseudofolliculitis	1 (0.0)	(0.0, 0.0)
Psoriasis	1 (0.0)	(0.0, 0.0)
Purpura	1 (0.0)	(0.0, 0.0)
Rash erythematous	1 (0.0)	(0.0, 0.0)
Rash papular	1 (0.0)	(0.0, 0.0)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Rosacea	1 (0.0)	(0.0, 0.0)
Skin discolouration	1 (0.0)	(0.0, 0.0)
Skin irritation	1 (0.0)	(0.0, 0.0)
Skin ulcer	1 (0.0)	(0.0, 0.0)
Transient acantholytic dermatosis	1 (0.0)	(0.0, 0.0)
SOCIAL CIRCUMSTANCES	2 (0.0)	(0.0, 0.1)
High risk sexual behaviour	1 (0.0)	(0.0, 0.0)
Miscarriage of partner	1 (0.0)	(0.0, 0.0)
SURGICAL AND MEDICAL PROCEDURES	29 (0.2)	(0.2, 0.3)
Dental implantation	5 (0.0)	(0.0, 0.1)
Tooth extraction	3 (0.0)	(0.0, 0.1)
Wisdom teeth removal	2 (0.0)	(0.0, 0.1)
Botulinum toxin injection	1 (0.0)	(0.0, 0.0)
Cardioversion	1 (0.0)	(0.0, 0.0)
Carpal tunnel decompression	1 (0.0)	(0.0, 0.0)
Drug titration	1 (0.0)	(0.0, 0.0)
Endodontic procedure	1 (0.0)	(0.0, 0.0)
Facet joint block	1 (0.0)	(0.0, 0.0)
Finger amputation	1 (0.0)	(0.0, 0.0)
Gingival operation	1 (0.0)	(0.0, 0.0)
Inguinal hernia repair	1 (0.0)	(0.0, 0.0)
Lacrimal duct procedure	1 (0.0)	(0.0, 0.0)
Mammoplasty	1 (0.0)	(0.0, 0.0)
Meniscus operation	1 (0.0)	(0.0, 0.0)
Metabolic surgery	1 (0.0)	(0.0, 0.0)
Open reduction of fracture	1 (0.0)	(0.0, 0.0)
Postoperative care	1 (0.0)	(0.0, 0.0)
Radioactive iodine therapy	1 (0.0)	(0.0, 0.0)
Retinal operation	1 (0.0)	(0.0, 0.0)
Rotator cuff repair	1 (0.0)	(0.0, 0.0)
Sclerotherapy	1 (0.0)	(0.0, 0.0)
VASCULAR DISORDERS	78 (0.6)	(0.5, 0.8)
Hypertension	48 (0.4)	(0.3, 0.5)
Deep vein thrombosis	6 (0.0)	(0.0, 0.1)
Hot flush	6 (0.0)	(0.0, 0.1)
Aortic aneurysm	3 (0.0)	(0.0, 0.1)

Table 64. Number (%) of Subjects Reporting at Least 1 Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Haematoma	3 (0.0)	(0.0, 0.1)
Flushing	2 (0.0)	(0.0, 0.1)
Hypotension	2 (0.0)	(0.0, 0.1)
Aortic dilatation	1 (0.0)	(0.0, 0.0)
Arterial occlusive disease	1 (0.0)	(0.0, 0.0)
Essential hypertension	1 (0.0)	(0.0, 0.0)
Intermittent claudication	1 (0.0)	(0.0, 0.0)
Lymphorrhoea	1 (0.0)	(0.0, 0.0)
Peripheral vascular disorder	1 (0.0)	(0.0, 0.0)
Systolic hypertension	1 (0.0)	(0.0, 0.0)
Thrombophlebitis superficial	1 (0.0)	(0.0, 0.0)
Varicose vein	1 (0.0)	(0.0, 0.0)

Note: MedDRA (v23.1) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
c. Exact 2-sided CI based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:16)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s130_all_bnt_pd2_p3_saf

Related Adverse Events – Cumulative Follow-Up to 6 Months After Dose 2 for BNT162b2 Group

From Dose 1 to 6 months after Dose 2, AEs assessed as related by the investigator during the cumulative blinded and open-label follow-up period were reported by 18.7% of participants in the BNT162b2 group (Table 62). Most related AEs were reactogenicity events and in the SOC of general disorders and administration site conditions (1944 [16.2%]).

The AE of lymphadenopathy in 29 (0.2%) participants was assessed by the investigator as related to study intervention.

Related AEs in the younger and older age groups were reported in 20.8% and 16.1% of original BNT162b2 participants.

2.5.5.5.3.5. Open-Label Follow-Up Period – Original Placebo Participants Who Received BNT162b2

2.5.5.5.3.5.1. Summary of Adverse Events

An overview of AEs for participants originally randomized to placebo from the time of vaccination with BNT162b2 (Dose 3) up to the data cutoff date during the open-label follow-up period is presented in Table 65.

Overall, there are 19,525 original placebo participants who then were unblinded and received open-label BNT162b2. IRs for any AE and at least 1 related AE were 205.4 per 100 PY and 189.5 per 100 PY, respectively. IRs of severe AEs, SAEs, and AEs leading to withdrawal were 6.0 per 100 PY, 2.7 per 100 PY, and 0.8 per 100 PY. The IR for discontinuations because of related AEs was 0.5 per 100 PY, and 2 participants died (Section 2.5.5.5.4.4).

IRs in Table 60 include all AEs reported for these participants including AEs reported while on placebo (in the blinded follow-up period). Additionally, all of these placebo participants received open-label BNT162b2, with shorter exposure time compared with participants who were originally randomized to BNT162b2 (23.8 per 100 PY vs 83.4 per 100 PY, respectively (Table 65 vs Table 60). As expected, in comparison to participants randomized to BNT162b2 from Dose 1 to the unblinding date, IRs for any AE and at least 1 related AE and severe AE for participants who originally received placebo and then received BNT162b2 are greater (205.4 per 100 PY, 189.5 per 100 PY, 6.0 per 100 PY) than IRs for participants who originally were randomized to BNT162b2, respectively (83.2 per 100 PY, 62.9 per 100 PY, 4.3 per 100 PY). However, IRs for life-threatening AEs, SAEs, AEs leading to withdrawal, and deaths were similar (0.5 per 100 PY, 2.7 per 100 PY, 0.8 per 100 PY, 0.1 per 100 PY vs 0.6 per 100 PY, 3.2 per 100 PY, 0.5 per 100 PY, 0.2 per 100 PY, respectively). There was 1 related SAE of anaphylactoid reaction for a placebo participant who was vaccinated with BNT162b2 (see details in Section 2.5.5.5.7.1).

Table 65. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
Adverse Event	n[c]	IR (/100 PY)[d]	(95% CI[e])
Any event	4885	205.4	(199.6, 211.2)
Related[f]	4508	189.5	(184.0, 195.1)
Severe	142	6.0	(5.0, 7.0)
Life-threatening	11	0.5	(0.2, 0.8)
Any serious adverse event	65	2.7	(2.1, 3.5)
Related[f]	1	0.0	(0.0, 0.2)

Table 65. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021) – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
Adverse Event	**n[c]**	**IR (/100 PY)[d]**	**(95% CI[e])**
Severe	37	1.6	(1.1, 2.1)
Life-threatening	11	0.5	(0.2, 0.8)
Any adverse event leading to withdrawal	19	0.8	(0.5, 1.2)
Related[f]	12	0.5	(0.3, 0.9)
Severe	2	0.1	(0.0, 0.3)
Life-threatening	4	0.2	(0.0, 0.4)
Death	2	0.1	(0.0, 0.3)

Note: Dose 3 = First dose of BNT162b2 (30 µg).
a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 3 to data cutoff date. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
f. Assessed by the investigator as related to investigational product.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:16)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s092_cr_cut_p3x_saf

Subgroup Analyses

IRs of AEs for original placebo participants who then received BNT162b2 were observed by baseline SARS CoV-2 positive and negative status subgroups. Overall, IRs for AEs were similar in the participants who were baseline positive (222.9 per 100 PY [95% CI: 186.5, 264.3]) compared to baseline negative (205 per 100 PY [95% CI 199.6, 211.3]). There were 2 SAEs (considered not related), 1 AE leading to withdrawal, and no deaths reported in the baseline positive group.

Open-Label Follow-Up Period – Original Placebo Participants who had COVID-19 Occurrence After Dose 1 and Then Received BNT162b2

The subset of participants originally randomized to placebo, who had a COVID-19 case after Dose 1 of placebo and were later unblinded to receive BNT162b2 (Dose 3), were evaluated for safety. Overall, a similar safety profile was observed for this participant group, compared to those originally randomized to BNT162b2.

There were 853 original placebo participants who developed COVID-19 and subsequently were vaccinated with BNT162b2. For original placebo participants who had COVID-19 occurrence after Dose 1 and then received BNT162b2, IRs for any AE and at least 1 related AE from Dose 3 (first dose of BNT162b2 30 µg) were 256.8 per 100 PY and 240.9 per 100 PY, respectively. IRs of severe AEs, SAEs, and AEs leading to withdrawal were 4.6 per 100 PY, 3.4 per 100 PY, and 3.4 per 100 PY. The IR for discontinuations because of related AEs was 3.4 per 100 PY.

IRs for SAEs were similar for the placebo participants who developed COVID-19 and subsequently were vaccinated with BNT162b2 (3.4 per 100 P [95% CI: 0.7, 10.0]) and participants originally randomized to BNT162b2 (3.2 per 100 PY [95% CI: 2.8, 3.6]), respectively. None of the SAEs in the placebo participants who developed COVID-19 and subsequently were vaccinated with BNT162b2 were considered related to BNT162b2. Three participants in this group had AEs leading to withdrawal that were assessed as related to BNT162b2: 1 participant with an AE of allergy to vaccine, 1 participant with an AE of pain, and 1 participant with 5 AEs (chills, injection site pain, myalgia, headache, and diarrhea). No deaths were reported in placebo participants who developed COVID-19 and subsequently were vaccinated with BNT162b2.

The exposure time for the group of placebo participants who developed COVID-19 and were subsequently vaccinated with BNT162b2 is small (0.9) compared to the exposure time in blinded placebo-controlled period (83.4; see Table 60), therefore direct comparisons must be interpreted with caution. In this context, rates of SAEs were similar in the groups (3.4 per 100 PY vs 3.2 per 100 PY, respectively).

2.5.5.5.3.5.2. Analysis of Adverse Events

Adverse Events by System Organ Class and Preferred Term

Among participants originally randomized to placebo from the time of vaccination with BNT162b2 (Dose 3) to the data cutoff date during open-label follow-up, the IR for participants who reported at least 1 AE was 205.4 per 100 PY (Table 66). Most AEs reported from Dose 3 (first dose of BNT162b2) to the data cutoff date were in SOCs with reactogenicity events:

- general disorders and administration site conditions: 175.3 per 100 PY
- musculoskeletal and connective tissue disorders: 52.3 per 100 PY
- nervous system disorders: 50.5 per 100 PY
- gastrointestinal disorders: 14.3 per 100 PY

As shown in Table 66, the most frequently reported AEs (IRs) overall were injection site pain (123.8 per 100 PY), fatigue (58.0 per 100 PY), headache (46.6 per 100 PY), chills (41.8 per 100 PY), myalgia (38.9 per 100 PY), and pyrexia (38.1 per 100 PY).

After participants who originally received placebo were unblinded and then received BNT162b2 after unblinding, events related to reactogenicity were not reported using an e diary but were instead reported as AEs. An analysis was conducted to evaluate if the imbalance in AEs observed from Dose 3 to the unblinding date was attributed to reactogenicity events. The analysis examined the AEs reported within 7 days after each dose (Dose 3 and Dose 4), which represented the reactogenicity reporting period.

PTs reported from Dose 3 to 7 days after Dose 3 and from Dose 4 to 7 days after Dose 4 in the SOCs of general disorders and administration site conditions (injection site pain, chills, fatigue, and pyrexia), musculoskeletal and connective tissue disorders (myalgia), and nervous system disorders (headache) represented the majority of PTs reported in those SOCs.

Allergy to vaccine, anaphylactoid reaction, and deep vein thrombosis were reported in 1 participant each from Dose 3 to 7 days after Dose 3:

- One participant reported an AE of grade 2 allergy to vaccine, which occurred on the day of Dose 3 vaccination, had a duration of 2 days, and resolved; this AE was assessed by the investigator as related to the study intervention.

- One participant with an ongoing medical history significant for drug hypersensitivity and food and seasonal allergies reported a life-threatening SAE of anaphylactoid reaction, which occurred 2 days after Dose 3 and was resolved that same day; this SAE was assessed by the investigator as related to the study intervention (detailed in Section 2.5.5.5.7.1).

- One participant with a past medical history significant for deep vein thrombosis, hypertension, pulmonary arterial hypertension, right ventricular enlargement, hypercholesteremia, atherosclerosis and bilateral peripheral neuropathy reported a grade 2 SAE of deep vein thrombosis (lower right extremity) and grade 1 SAE of pulmonary embolism, which both occurred 2 days after Dose 3, had both resolved with a duration of 3 days; both SAEs were assessed by the investigator as not related to the study intervention.

Analysis of Reactogenicity Terms Reported Within 7 Days After Each Dose

An analysis of AEs reported within 7 days after each dose of open-label BNT162b2, which represented the reactogenicity reporting period in the study, evaluated AEs consistent with reactogenicity events (Section 2.5.5.5.2). In addition to analysis of AEs corresponding to e-diary terms, consideration was given to additional AEs that were reported within 7 days after Dose 3 or Dose 4 such as pain in extremity, decreased appetite, lethargy, asthenia, malaise, night sweats, and hyperhidrosis. Similar to the analysis that examined these events 7 days within Dose 1 and Dose 2 of BNT162b2 in blinded follow-up (2.5.5.5.3.1.2), these events reported in open-label follow-up are interpreted as attributable to the experience of local

reactions and systemic events after vaccination with Dose 3 and Dose 4 (first and second dose of BNT162b2).

These results are consistent with the pattern seen during the blinded placebo-controlled follow-up period from Dose 1 to 1 month after Dose 2 (Section 2.5.5.5.3.1.2), which confirms that the greater rates of AEs observed overall in the BNT162b2 group compared with the placebo group were largely attributable to reactogenicity events for that time period.

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Any event	4885	205.4	(199.6, 211.2)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	88	3.7	(3.0, 4.6)
Anaemia	2	0.1	(0.0, 0.3)
Coagulopathy	1	0.0	(0.0, 0.2)
Iron deficiency anaemia	2	0.1	(0.0, 0.3)
Lymph node pain	6	0.3	(0.1, 0.5)
Lymphadenitis	2	0.1	(0.0, 0.3)
Lymphadenopathy	76	3.2	(2.5, 4.0)
CARDIAC DISORDERS	17	0.7	(0.4, 1.1)
Acute myocardial infarction	1	0.0	(0.0, 0.2)
Angina pectoris	1	0.0	(0.0, 0.2)
Arrhythmia	1	0.0	(0.0, 0.2)
Arteriospasm coronary	1	0.0	(0.0, 0.2)
Atrial fibrillation	5	0.2	(0.1, 0.5)
Atrial flutter	1	0.0	(0.0, 0.2)
Cardiac failure congestive	1	0.0	(0.0, 0.2)
Cardio-respiratory arrest	1	0.0	(0.0, 0.2)
Cardiovascular disorder	1	0.0	(0.0, 0.2)
Coronary artery disease	1	0.0	(0.0, 0.2)
Ischaemic cardiomyopathy	1	0.0	(0.0, 0.2)
Myocardial infarction	1	0.0	(0.0, 0.2)
Palpitations	1	0.0	(0.0, 0.2)
Supraventricular tachycardia	1	0.0	(0.0, 0.2)
Tachycardia	2	0.1	(0.0, 0.3)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	4	0.2	(0.0, 0.4)
Atrial septal defect	1	0.0	(0.0, 0.2)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
BRCA2 gene mutation	1	0.0	(0.0, 0.2)
Factor II mutation	1	0.0	(0.0, 0.2)
Hypertrophic cardiomyopathy	1	0.0	(0.0, 0.2)
EAR AND LABYRINTH DISORDERS	18	0.8	(0.4, 1.2)
Cerumen impaction	1	0.0	(0.0, 0.2)
Deafness neurosensory	1	0.0	(0.0, 0.2)
Deafness unilateral	1	0.0	(0.0, 0.2)
Ear discomfort	1	0.0	(0.0, 0.2)
Ear pain	4	0.2	(0.0, 0.4)
Eustachian tube dysfunction	2	0.1	(0.0, 0.3)
Hypoacusis	1	0.0	(0.0, 0.2)
Meniere's disease	1	0.0	(0.0, 0.2)
Sudden hearing loss	1	0.0	(0.0, 0.2)
Tinnitus	2	0.1	(0.0, 0.3)
Vertigo	6	0.3	(0.1, 0.5)
ENDOCRINE DISORDERS	4	0.2	(0.0, 0.4)
Hypothyroidism	2	0.1	(0.0, 0.3)
Thyroid disorder	1	0.0	(0.0, 0.2)
Thyroid mass	1	0.0	(0.0, 0.2)
EYE DISORDERS	26	1.1	(0.7, 1.6)
Blepharitis	1	0.0	(0.0, 0.2)
Cataract	4	0.2	(0.0, 0.4)
Conjunctival haemorrhage	1	0.0	(0.0, 0.2)
Dacryostenosis acquired	1	0.0	(0.0, 0.2)
Diplopia	1	0.0	(0.0, 0.2)
Dry eye	1	0.0	(0.0, 0.2)
Erythema of eyelid	1	0.0	(0.0, 0.2)
Eye irritation	1	0.0	(0.0, 0.2)
Eye pain	5	0.2	(0.1, 0.5)
Eye swelling	1	0.0	(0.0, 0.2)
Keratitis	2	0.1	(0.0, 0.3)
Lacrimation increased	3	0.1	(0.0, 0.4)
Meibomianitis	1	0.0	(0.0, 0.2)
Ocular discomfort	1	0.0	(0.0, 0.2)
Visual impairment	1	0.0	(0.0, 0.2)
Vitreous floaters	1	0.0	(0.0, 0.2)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
GASTROINTESTINAL DISORDERS	339	14.3	(12.8, 15.9)
Abdominal discomfort	4	0.2	(0.0, 0.4)
Abdominal distension	1	0.0	(0.0, 0.2)
Abdominal pain	12	0.5	(0.3, 0.9)
Abdominal pain lower	2	0.1	(0.0, 0.3)
Abdominal pain upper	13	0.5	(0.3, 0.9)
Anal fistula	2	0.1	(0.0, 0.3)
Anal prolapse	1	0.0	(0.0, 0.2)
Chronic gastritis	1	0.0	(0.0, 0.2)
Constipation	4	0.2	(0.0, 0.4)
Dental caries	1	0.0	(0.0, 0.2)
Diarrhoea	91	3.8	(3.1, 4.7)
Dry mouth	3	0.1	(0.0, 0.4)
Duodenitis	1	0.0	(0.0, 0.2)
Dyspepsia	5	0.2	(0.1, 0.5)
Gastric ulcer	1	0.0	(0.0, 0.2)
Gastritis	5	0.2	(0.1, 0.5)
Gastrointestinal haemorrhage	1	0.0	(0.0, 0.2)
Gastrointestinal necrosis	1	0.0	(0.0, 0.2)
Gastrointestinal sounds abnormal	1	0.0	(0.0, 0.2)
Gastrooesophageal reflux disease	7	0.3	(0.1, 0.6)
Gingival bleeding	1	0.0	(0.0, 0.2)
Haemorrhoids	1	0.0	(0.0, 0.2)
Hiatus hernia	2	0.1	(0.0, 0.3)
Hyperaesthesia teeth	1	0.0	(0.0, 0.2)
Hypoaesthesia oral	1	0.0	(0.0, 0.2)
Intestinal obstruction	1	0.0	(0.0, 0.2)
Intestinal ulcer perforation	1	0.0	(0.0, 0.2)
Irritable bowel syndrome	2	0.1	(0.0, 0.3)
Large intestine polyp	1	0.0	(0.0, 0.2)
Nausea	160	6.7	(5.7, 7.9)
Oedema mouth	1	0.0	(0.0, 0.2)
Oral mucosal blistering	1	0.0	(0.0, 0.2)
Oral pain	1	0.0	(0.0, 0.2)
Oral pruritus	1	0.0	(0.0, 0.2)
Pancreatitis acute	2	0.1	(0.0, 0.3)
Retching	1	0.0	(0.0, 0.2)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Small intestinal obstruction	1	0.0	(0.0, 0.2)
Stomatitis	2	0.1	(0.0, 0.3)
Submaxillary gland enlargement	1	0.0	(0.0, 0.2)
Tongue disorder	1	0.0	(0.0, 0.2)
Tongue oedema	1	0.0	(0.0, 0.2)
Toothache	1	0.0	(0.0, 0.2)
Umbilical hernia	1	0.0	(0.0, 0.2)
Vomiting	48	2.0	(1.5, 2.7)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	4169	175.3	(170.0, 180.7)
Application site pain	2	0.1	(0.0, 0.3)
Asthenia	36	1.5	(1.1, 2.1)
Axillary pain	3	0.1	(0.0, 0.4)
Chest discomfort	2	0.1	(0.0, 0.3)
Chest pain	4	0.2	(0.0, 0.4)
Chills	994	41.8	(39.2, 44.5)
Crying	1	0.0	(0.0, 0.2)
Discomfort	2	0.1	(0.0, 0.3)
Drug withdrawal syndrome	1	0.0	(0.0, 0.2)
Facial pain	1	0.0	(0.0, 0.2)
Fatigue	1379	58.0	(55.0, 61.1)
Feeling abnormal	6	0.3	(0.1, 0.5)
Feeling cold	2	0.1	(0.0, 0.3)
Feeling hot	6	0.3	(0.1, 0.5)
Gait disturbance	1	0.0	(0.0, 0.2)
Implant site pain	1	0.0	(0.0, 0.2)
Inflammation	1	0.0	(0.0, 0.2)
Influenza like illness	1	0.0	(0.0, 0.2)
Injection site bruising	16	0.7	(0.4, 1.1)
Injection site discomfort	3	0.1	(0.0, 0.4)
Injection site erythema	66	2.8	(2.1, 3.5)
Injection site haematoma	2	0.1	(0.0, 0.3)
Injection site haemorrhage	1	0.0	(0.0, 0.2)
Injection site hypersensitivity	1	0.0	(0.0, 0.2)
Injection site hypoaesthesia	2	0.1	(0.0, 0.3)
Injection site induration	1	0.0	(0.0, 0.2)
Injection site irritation	1	0.0	(0.0, 0.2)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Injection site lymphadenopathy	1	0.0	(0.0, 0.2)
Injection site mass	1	0.0	(0.0, 0.2)
Injection site nodule	2	0.1	(0.0, 0.3)
Injection site oedema	2	0.1	(0.0, 0.3)
Injection site pain	2944	123.8	(119.3, 128.3)
Injection site pruritus	18	0.8	(0.4, 1.2)
Injection site rash	4	0.2	(0.0, 0.4)
Injection site reaction	2	0.1	(0.0, 0.3)
Injection site swelling	65	2.7	(2.1, 3.5)
Injection site urticaria	1	0.0	(0.0, 0.2)
Injection site warmth	3	0.1	(0.0, 0.4)
Malaise	83	3.5	(2.8, 4.3)
Non-cardiac chest pain	1	0.0	(0.0, 0.2)
Oedema peripheral	2	0.1	(0.0, 0.3)
Pain	394	16.6	(15.0, 18.3)
Pelvic mass	1	0.0	(0.0, 0.2)
Peripheral swelling	7	0.3	(0.1, 0.6)
Pyrexia	906	38.1	(35.6, 40.6)
Swelling	3	0.1	(0.0, 0.4)
Swelling face	4	0.2	(0.0, 0.4)
Vaccination site pain	3	0.1	(0.0, 0.4)
Vaccination site reaction	1	0.0	(0.0, 0.2)
Vessel puncture site haematoma	1	0.0	(0.0, 0.2)
HEPATOBILIARY DISORDERS	3	0.1	(0.0, 0.4)
Cholecystitis	1	0.0	(0.0, 0.2)
Cholelithiasis	1	0.0	(0.0, 0.2)
Hepatitis acute	1	0.0	(0.0, 0.2)
IMMUNE SYSTEM DISORDERS	7	0.3	(0.1, 0.6)
Allergy to vaccine	1	0.0	(0.0, 0.2)
Anaphylactoid reaction	1	0.0	(0.0, 0.2)
Hypersensitivity	1	0.0	(0.0, 0.2)
Seasonal allergy	4	0.2	(0.0, 0.4)
INFECTIONS AND INFESTATIONS	136	5.7	(4.8, 6.8)
Abscess	1	0.0	(0.0, 0.2)
Appendicitis perforated	1	0.0	(0.0, 0.2)
Asymptomatic bacteriuria	1	0.0	(0.0, 0.2)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
COVID-19 pneumonia	1	0.0	(0.0, 0.2)
Candida infection	1	0.0	(0.0, 0.2)
Cellulitis	3	0.1	(0.0, 0.4)
Chlamydial infection	1	0.0	(0.0, 0.2)
Clostridium difficile infection	1	0.0	(0.0, 0.2)
Conjunctivitis	6	0.3	(0.1, 0.5)
Cystitis	1	0.0	(0.0, 0.2)
Demodicidosis	1	0.0	(0.0, 0.2)
Diverticulitis	2	0.1	(0.0, 0.3)
Ear infection	8	0.3	(0.1, 0.7)
Eye infection	1	0.0	(0.0, 0.2)
Focal peritonitis	1	0.0	(0.0, 0.2)
Folliculitis	1	0.0	(0.0, 0.2)
Fungal skin infection	3	0.1	(0.0, 0.4)
Genital herpes	1	0.0	(0.0, 0.2)
Genital herpes simplex	2	0.1	(0.0, 0.3)
Helicobacter gastritis	1	0.0	(0.0, 0.2)
Herpes simplex	2	0.1	(0.0, 0.3)
Herpes zoster	8	0.3	(0.1, 0.7)
Hordeolum	2	0.1	(0.0, 0.3)
Infected cyst	1	0.0	(0.0, 0.2)
Infection	1	0.0	(0.0, 0.2)
Labyrinthitis	1	0.0	(0.0, 0.2)
Localised infection	2	0.1	(0.0, 0.3)
Mastitis	1	0.0	(0.0, 0.2)
Onychomycosis	1	0.0	(0.0, 0.2)
Oral candidiasis	1	0.0	(0.0, 0.2)
Oral herpes	3	0.1	(0.0, 0.4)
Osteomyelitis	1	0.0	(0.0, 0.2)
Otitis externa	2	0.1	(0.0, 0.3)
Otitis media	2	0.1	(0.0, 0.3)
Pelvic abscess	1	0.0	(0.0, 0.2)
Pneumonia	2	0.1	(0.0, 0.3)
Postoperative wound infection	1	0.0	(0.0, 0.2)
Rhinitis	2	0.1	(0.0, 0.3)
Sinusitis	7	0.3	(0.1, 0.6)
Subcutaneous abscess	2	0.1	(0.0, 0.3)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Suspected COVID-19	1	0.0	(0.0, 0.2)
Taeniasis	1	0.0	(0.0, 0.2)
Tinea infection	1	0.0	(0.0, 0.2)
Tinea pedis	2	0.1	(0.0, 0.3)
Tonsillitis	2	0.1	(0.0, 0.3)
Tooth abscess	4	0.2	(0.0, 0.4)
Tooth infection	12	0.5	(0.3, 0.9)
Urinary tract infection	30	1.3	(0.9, 1.8)
Urosepsis	1	0.0	(0.0, 0.2)
Vulvitis	1	0.0	(0.0, 0.2)
Vulvovaginal candidiasis	3	0.1	(0.0, 0.4)
Vulvovaginal mycotic infection	1	0.0	(0.0, 0.2)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	90	3.8	(3.0, 4.7)
Animal bite	1	0.0	(0.0, 0.2)
Ankle fracture	2	0.1	(0.0, 0.3)
Arthropod bite	3	0.1	(0.0, 0.4)
Chest injury	1	0.0	(0.0, 0.2)
Contusion	9	0.4	(0.2, 0.7)
Corneal abrasion	1	0.0	(0.0, 0.2)
Exposure during pregnancy	5	0.2	(0.1, 0.5)
Eye contusion	1	0.0	(0.0, 0.2)
Facial bones fracture	1	0.0	(0.0, 0.2)
Fall	20	0.8	(0.5, 1.3)
Fibula fracture	2	0.1	(0.0, 0.3)
Foot fracture	4	0.2	(0.0, 0.4)
Frostbite	1	0.0	(0.0, 0.2)
Hand fracture	3	0.1	(0.0, 0.4)
Head injury	1	0.0	(0.0, 0.2)
Injection related reaction	1	0.0	(0.0, 0.2)
Joint dislocation	1	0.0	(0.0, 0.2)
Ligament injury	1	0.0	(0.0, 0.2)
Ligament sprain	6	0.3	(0.1, 0.5)
Limb injury	4	0.2	(0.0, 0.4)
Lip injury	1	0.0	(0.0, 0.2)
Lower limb fracture	1	0.0	(0.0, 0.2)
Maternal exposure during pregnancy	3	0.1	(0.0, 0.4)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Meniscus injury	1	0.0	(0.0, 0.2)
Muscle rupture	1	0.0	(0.0, 0.2)
Muscle strain	2	0.1	(0.0, 0.3)
Postoperative ileus	1	0.0	(0.0, 0.2)
Procedural pain	6	0.3	(0.1, 0.5)
Radius fracture	1	0.0	(0.0, 0.2)
Road traffic accident	2	0.1	(0.0, 0.3)
Scapula fracture	1	0.0	(0.0, 0.2)
Seroma	1	0.0	(0.0, 0.2)
Skin abrasion	2	0.1	(0.0, 0.3)
Skin laceration	10	0.4	(0.2, 0.8)
Spinal fracture	1	0.0	(0.0, 0.2)
Subdural haematoma	1	0.0	(0.0, 0.2)
Tendon injury	1	0.0	(0.0, 0.2)
Tendon rupture	1	0.0	(0.0, 0.2)
Thermal burn	2	0.1	(0.0, 0.3)
Tooth fracture	6	0.3	(0.1, 0.5)
Traumatic intracranial haemorrhage	1	0.0	(0.0, 0.2)
Upper limb fracture	2	0.1	(0.0, 0.3)
Wound	1	0.0	(0.0, 0.2)
Wrist fracture	1	0.0	(0.0, 0.2)
INVESTIGATIONS	107	4.5	(3.7, 5.4)
Alanine aminotransferase increased	2	0.1	(0.0, 0.3)
Antinuclear antibody positive	1	0.0	(0.0, 0.2)
Aspartate aminotransferase increased	2	0.1	(0.0, 0.3)
Blood cholesterol increased	3	0.1	(0.0, 0.4)
Blood pressure increased	6	0.3	(0.1, 0.5)
Blood testosterone decreased	2	0.1	(0.0, 0.3)
Body temperature increased	91	3.8	(3.1, 4.7)
C-reactive protein increased	1	0.0	(0.0, 0.2)
Heart rate increased	1	0.0	(0.0, 0.2)
SARS-CoV-2 antibody test positive	1	0.0	(0.0, 0.2)
Troponin increased	1	0.0	(0.0, 0.2)
METABOLISM AND NUTRITION DISORDERS	29	1.2	(0.8, 1.8)
Decreased appetite	14	0.6	(0.3, 1.0)
Diabetes mellitus	1	0.0	(0.0, 0.2)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Diabetes mellitus inadequate control	1	0.0	(0.0, 0.2)
Dyslipidaemia	2	0.1	(0.0, 0.3)
Glucose tolerance impaired	2	0.1	(0.0, 0.3)
Gout	1	0.0	(0.0, 0.2)
Hypercholesterolaemia	1	0.0	(0.0, 0.2)
Hyperglycaemia	2	0.1	(0.0, 0.3)
Insulin resistance	2	0.1	(0.0, 0.3)
Lactic acidosis	1	0.0	(0.0, 0.2)
Type 2 diabetes mellitus	2	0.1	(0.0, 0.3)
Vitamin D deficiency	1	0.0	(0.0, 0.2)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1245	52.3	(49.5, 55.3)
Arthralgia	149	6.3	(5.3, 7.4)
Arthritis	3	0.1	(0.0, 0.4)
Back pain	32	1.3	(0.9, 1.9)
Bursitis	1	0.0	(0.0, 0.2)
Flank pain	2	0.1	(0.0, 0.3)
Foot deformity	1	0.0	(0.0, 0.2)
Groin pain	1	0.0	(0.0, 0.2)
Intervertebral disc protrusion	2	0.1	(0.0, 0.3)
Joint range of motion decreased	2	0.1	(0.0, 0.3)
Joint swelling	1	0.0	(0.0, 0.2)
Limb discomfort	1	0.0	(0.0, 0.2)
Mobility decreased	1	0.0	(0.0, 0.2)
Muscle fatigue	2	0.1	(0.0, 0.3)
Muscle spasms	1	0.0	(0.0, 0.2)
Muscular weakness	4	0.2	(0.0, 0.4)
Musculoskeletal chest pain	1	0.0	(0.0, 0.2)
Musculoskeletal pain	1	0.0	(0.0, 0.2)
Musculoskeletal stiffness	12	0.5	(0.3, 0.9)
Myalgia	925	38.9	(36.4, 41.5)
Neck pain	11	0.5	(0.2, 0.8)
Osteoarthritis	9	0.4	(0.2, 0.7)
Osteoporosis	1	0.0	(0.0, 0.2)
Pain in extremity	154	6.5	(5.5, 7.6)
Periarthritis	1	0.0	(0.0, 0.2)
Plantar fasciitis	3	0.1	(0.0, 0.4)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Rheumatoid arthritis	1	0.0	(0.0, 0.2)
Rotator cuff syndrome	2	0.1	(0.0, 0.3)
Sacroiliitis	1	0.0	(0.0, 0.2)
Sjogren's syndrome	1	0.0	(0.0, 0.2)
Synovial cyst	1	0.0	(0.0, 0.2)
Temporomandibular joint syndrome	1	0.0	(0.0, 0.2)
Tendonitis	1	0.0	(0.0, 0.2)
Trigger finger	1	0.0	(0.0, 0.2)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	13	0.5	(0.3, 0.9)
Bladder neoplasm	1	0.0	(0.0, 0.2)
Bowen's disease	1	0.0	(0.0, 0.2)
Brain neoplasm	1	0.0	(0.0, 0.2)
Breast cancer	1	0.0	(0.0, 0.2)
Breast cancer stage II	1	0.0	(0.0, 0.2)
Hepatic cancer	1	0.0	(0.0, 0.2)
Lipoma	1	0.0	(0.0, 0.2)
Meningioma	1	0.0	(0.0, 0.2)
Neoplasm	1	0.0	(0.0, 0.2)
Non-small cell lung cancer stage III	1	0.0	(0.0, 0.2)
Rectal cancer	1	0.0	(0.0, 0.2)
Seborrhoeic keratosis	1	0.0	(0.0, 0.2)
Skin papilloma	1	0.0	(0.0, 0.2)
Squamous cell carcinoma	1	0.0	(0.0, 0.2)
NERVOUS SYSTEM DISORDERS	1201	50.5	(47.7, 53.4)
Amnesia	1	0.0	(0.0, 0.2)
Arachnoid cyst	1	0.0	(0.0, 0.2)
Balance disorder	2	0.1	(0.0, 0.3)
Brachial plexopathy	1	0.0	(0.0, 0.2)
Carpal tunnel syndrome	1	0.0	(0.0, 0.2)
Cerebrovascular accident	4	0.2	(0.0, 0.4)
Cervical radiculopathy	1	0.0	(0.0, 0.2)
Cognitive disorder	1	0.0	(0.0, 0.2)
Disturbance in attention	4	0.2	(0.0, 0.4)
Dizziness	47	2.0	(1.5, 2.6)
Dysgeusia	2	0.1	(0.0, 0.3)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Encephalopathy	1	0.0	(0.0, 0.2)
Facial paralysis	3	0.1	(0.0, 0.4)
Head discomfort	1	0.0	(0.0, 0.2)
Headache	1108	46.6	(43.9, 49.4)
Hemiplegia	1	0.0	(0.0, 0.2)
Hyperaesthesia	2	0.1	(0.0, 0.3)
Hypoaesthesia	2	0.1	(0.0, 0.3)
Hypogeusia	1	0.0	(0.0, 0.2)
Lethargy	9	0.4	(0.2, 0.7)
Loss of consciousness	1	0.0	(0.0, 0.2)
Mental impairment	2	0.1	(0.0, 0.3)
Migraine	6	0.3	(0.1, 0.5)
Migraine with aura	1	0.0	(0.0, 0.2)
Nerve compression	1	0.0	(0.0, 0.2)
Paraesthesia	14	0.6	(0.3, 1.0)
Parosmia	1	0.0	(0.0, 0.2)
Piriformis syndrome	1	0.0	(0.0, 0.2)
Presyncope	1	0.0	(0.0, 0.2)
Radiculopathy	1	0.0	(0.0, 0.2)
Sciatica	1	0.0	(0.0, 0.2)
Seizure	1	0.0	(0.0, 0.2)
Somnolence	13	0.5	(0.3, 0.9)
Speech disorder	1	0.0	(0.0, 0.2)
Syncope	4	0.2	(0.0, 0.4)
Transient ischaemic attack	2	0.1	(0.0, 0.3)
Tremor	2	0.1	(0.0, 0.3)
Visual field defect	1	0.0	(0.0, 0.2)
PSYCHIATRIC DISORDERS	43	1.8	(1.3, 2.4)
Abnormal dreams	1	0.0	(0.0, 0.2)
Alcohol withdrawal syndrome	1	0.0	(0.0, 0.2)
Anxiety	9	0.4	(0.2, 0.7)
Attention deficit hyperactivity disorder	3	0.1	(0.0, 0.4)
Bipolar disorder	1	0.0	(0.0, 0.2)
Completed suicide	1	0.0	(0.0, 0.2)
Confusional state	2	0.1	(0.0, 0.3)
Depression	3	0.1	(0.0, 0.4)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Generalised anxiety disorder	1	0.0	(0.0, 0.2)
Insomnia	12	0.5	(0.3, 0.9)
Irritability	2	0.1	(0.0, 0.3)
Major depression	1	0.0	(0.0, 0.2)
Mental fatigue	1	0.0	(0.0, 0.2)
Mental status changes	1	0.0	(0.0, 0.2)
Restlessness	2	0.1	(0.0, 0.3)
Sleep disorder	2	0.1	(0.0, 0.3)
Suicidal ideation	1	0.0	(0.0, 0.2)
Suicide attempt	1	0.0	(0.0, 0.2)
Thinking abnormal	1	0.0	(0.0, 0.2)
RENAL AND URINARY DISORDERS	21	0.9	(0.5, 1.3)
Acute kidney injury	1	0.0	(0.0, 0.2)
Bladder neck obstruction	1	0.0	(0.0, 0.2)
Chronic kidney disease	1	0.0	(0.0, 0.2)
Dysuria	6	0.3	(0.1, 0.5)
Haematuria	1	0.0	(0.0, 0.2)
Hypertonic bladder	2	0.1	(0.0, 0.3)
Nephrolithiasis	4	0.2	(0.0, 0.4)
Pollakiuria	1	0.0	(0.0, 0.2)
Urinary bladder polyp	1	0.0	(0.0, 0.2)
Urinary hesitation	1	0.0	(0.0, 0.2)
Urinary retention	1	0.0	(0.0, 0.2)
Urinary tract obstruction	1	0.0	(0.0, 0.2)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	12	0.5	(0.3, 0.9)
Benign prostatic hyperplasia	3	0.1	(0.0, 0.4)
Breast cyst	1	0.0	(0.0, 0.2)
Breast discharge	1	0.0	(0.0, 0.2)
Endometriosis	1	0.0	(0.0, 0.2)
Metrorrhagia	2	0.1	(0.0, 0.3)
Ovarian cyst	1	0.0	(0.0, 0.2)
Pelvic pain	1	0.0	(0.0, 0.2)
Sexual dysfunction	1	0.0	(0.0, 0.2)
Testicular pain	1	0.0	(0.0, 0.2)
Uterine haemorrhage	1	0.0	(0.0, 0.2)
Vaginal lesion	1	0.0	(0.0, 0.2)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	37	1.6	(1.1, 2.1)
Acute respiratory failure	2	0.1	(0.0, 0.3)
Asthma	1	0.0	(0.0, 0.2)
Chronic obstructive pulmonary disease	1	0.0	(0.0, 0.2)
Cough	3	0.1	(0.0, 0.4)
Dyspnoea	2	0.1	(0.0, 0.3)
Epistaxis	3	0.1	(0.0, 0.4)
Immune-mediated pneumonitis	1	0.0	(0.0, 0.2)
Nasal congestion	5	0.2	(0.1, 0.5)
Nasal septum deviation	1	0.0	(0.0, 0.2)
Oropharyngeal pain	1	0.0	(0.0, 0.2)
Paranasal sinus discomfort	1	0.0	(0.0, 0.2)
Pleuritic pain	1	0.0	(0.0, 0.2)
Pulmonary embolism	4	0.2	(0.0, 0.4)
Rhinitis allergic	4	0.2	(0.0, 0.4)
Rhinorrhoea	6	0.3	(0.1, 0.5)
Sinus congestion	1	0.0	(0.0, 0.2)
Upper respiratory tract congestion	1	0.0	(0.0, 0.2)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	85	3.6	(2.9, 4.4)
Acne	1	0.0	(0.0, 0.2)
Actinic keratosis	3	0.1	(0.0, 0.4)
Alopecia	2	0.1	(0.0, 0.3)
Angioedema	1	0.0	(0.0, 0.2)
Cold sweat	1	0.0	(0.0, 0.2)
Dermatitis	2	0.1	(0.0, 0.3)
Dermatitis contact	6	0.3	(0.1, 0.5)
Dry skin	1	0.0	(0.0, 0.2)
Ecchymosis	3	0.1	(0.0, 0.4)
Erythema	2	0.1	(0.0, 0.3)
Erythema nodosum	1	0.0	(0.0, 0.2)
Hyperhidrosis	15	0.6	(0.4, 1.0)
Ingrowing nail	3	0.1	(0.0, 0.4)
Lichen sclerosus	1	0.0	(0.0, 0.2)
Night sweats	7	0.3	(0.1, 0.6)
Petechiae	1	0.0	(0.0, 0.2)
Pruritus	6	0.3	(0.1, 0.5)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Rash	16	0.7	(0.4, 1.1)
Rash erythematous	2	0.1	(0.0, 0.3)
Rash pruritic	1	0.0	(0.0, 0.2)
Rash vesicular	1	0.0	(0.0, 0.2)
Skin lesion	4	0.2	(0.0, 0.4)
Skin ulcer	1	0.0	(0.0, 0.2)
Urticaria	7	0.3	(0.1, 0.6)
SURGICAL AND MEDICAL PROCEDURES	9	0.4	(0.2, 0.7)
Blepharoplasty	1	0.0	(0.0, 0.2)
Chondroplasty	1	0.0	(0.0, 0.2)
Finger repair operation	1	0.0	(0.0, 0.2)
Hysterectomy	2	0.1	(0.0, 0.3)
Injection	1	0.0	(0.0, 0.2)
Spinal fusion surgery	1	0.0	(0.0, 0.2)
Tooth extraction	2	0.1	(0.0, 0.3)
VASCULAR DISORDERS	45	1.9	(1.4, 2.5)
Aortic aneurysm	1	0.0	(0.0, 0.2)
Aortic arteriosclerosis	1	0.0	(0.0, 0.2)
Aortic stenosis	1	0.0	(0.0, 0.2)
Blood pressure fluctuation	1	0.0	(0.0, 0.2)
Deep vein thrombosis	3	0.1	(0.0, 0.4)
Flushing	5	0.2	(0.1, 0.5)
Haematoma	2	0.1	(0.0, 0.3)
Hot flush	2	0.1	(0.0, 0.3)
Hypertension	25	1.1	(0.7, 1.6)
Hypotension	1	0.0	(0.0, 0.2)
Peripheral coldness	1	0.0	(0.0, 0.2)
Thrombosis	1	0.0	(0.0, 0.2)
Venous thrombosis limb	1	0.0	(0.0, 0.2)

Table 66. Incidence Rates of at Least 1 Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])

Note: Dose 3 = First dose of BNT162b2 (30 µg).
Note: MedDRA (v23.1) coding dictionary applied.
a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 3 to data cutoff date. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (17:36)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s131_exp_age_p3x_saf

Related Adverse Events – Open-Label Follow-Up for Original Placebo Participants Who Received BNT162b2

From vaccination with BNT162b2 (Dose 3) to the data cutoff date for placebo participants, the IR of AEs assessed as related by the investigator during the open-label follow-up period was 189.5 per 100 PY (Table 65). IRs of related AEs were highest for reactogenicity events and in the SOC of general disorders and administration site conditions (4147 [174.3 per 100 PY]) for the following PTs:

- injection site pain: 2938 (123.5 per 100 PY)
- pyrexia: 905 (38.0 per 100 PY)
- fatigue: 1373 (57.7 per 100 PY)
- chills: 993 (41.7 per 100 PY).

Immediate Adverse Events – Open-Label Follow-Up for Original Placebo Participants Who Received BNT162b2

After vaccination with BNT162b2 (Dose 3/4), placebo participants who received BNT162b2 with immediate AEs were low in frequency (0.6%). Most immediate AEs after BNT162b2

doses were in the SOC of general disorders and administration site conditions, primarily injection site reactions, with injection site pain (0.4%) most frequently reported.

Other immediate AEs assessed by the investigator as related to study intervention included:

- 1 participant in the younger age group reported 2 immediate AEs of edema mouth and tongue edema (both mild in severity) after Dose 4. The AE of tongue edema resolved the same day and the AE of edema mouth resolved the following day.

- 1 participant in the younger age group reported an immediate AE of hypoesthesia oral (mild in severity) after Dose 3 and resolved the same day.

- 1 participant in the younger age group reported 3 immediate AEs of swelling face, allergy to vaccine, and flushing after Dose 3, which were all were moderate in severity. All 3 AEs resolved the following day. The participant also reported nausea and urticaria (hives abdomen) (both mild in severity) on the same day but were not immediate. The AE of nausea resolved the same day and the AE of urticaria resolved the following day. These 2 AEs were also assessed by the investigator as related to study intervention.

- 1 participant in the older age group reported an immediate AE of urticaria (hive on back of neck; moderate in severity) after Dose 4 and was ongoing at the time of the data cutoff date.

Severe or Life-Threatening Adverse Events – Open-Label Follow-Up for Original Placebo Participants Who Received BNT162b2

Severe Adverse Events

From Dose 3 (first Dose of BNT162b2) to the data cutoff date, the severe AE IR was 6.0 per 100 PY in original placebo participants. Those events reported as SAEs are discussed further in Section 2.5.5.5.5.5. Severe AEs included:

- 1 participant in the younger age group reported a severe AE of hypersensitivity 13 days after Dose 3, which resolved the following day and assessed by the investigator as not related to study intervention.

- 1 participant in the older age group reported a severe SAE of COVID-19 pneumonia 8 days after Dose 3, which resolved 4 days later and was assessed by the investigator as not related to study intervention.

- 1 participant in the older age group reported a severe SAE of cerebrovascular accident 16 days after Dose 4, which was assessed by the investigator as not related to study intervention and ongoing at the time of the data cutoff date.

- 1 participant in the younger age group reported a severe SAE of pulmonary embolism 5 days after Dose 4, which resolved the following day and was assessed by the investigator as not related to study intervention.

- 1 participant in the older age group reported severe SAEs of pulmonary embolism and thrombosis (occlusive thrombus in the right calf) 2 days after Dose 3. Both events resolved the following day, and both were assessed by the investigator as not related to study intervention.

- 1 participant in the younger age group reported 2 AEs of urticaria (moderate and severe) at 3 and 4 days after Dose 3, respectively. The moderate AE of urticaria (intermittent generalized) resolved the same day, and the severe AE of urticaria (left arm) resolved after 8 days. Both events were assessed by the investigator as related to study intervention.

Life-Threatening Adverse Events

The IR for original placebo participants who had at least 1 life-threatening AE from Dose 3 to the data cutoff date was 0.5 per 100 PY. The following life-threatening events were reported and were considered unrelated to vaccine as assessed by the investigator, with the exception of anaphylactoid reaction. Those reported as SAEs are discussed further in Section 2.5.5.5.5.5. Grade 4 life-threatening events included:

- 1 participant in the older age group had a grade 4 life-threatening SAE of cardio-respiratory arrest. The event occurred (b) (6) days after Dose 3 and the outcome was fatal.

- 1 participant in the younger age group had a grade 4 life-threatening SAE of gastrointestinal necrosis 29 days after Dose 4. The outcome was not recovered/not resolved at the time of this report.

- 1 participant in the younger age group had a grade 4 life-threatening SAE of pulmonary embolism and a grade 4 life-threatening SAE of deep vein thrombosis. Both events occurred 11 days after Dose 4 and the outcome for both events was recovering/resolving.

- 1 participant in the younger age group had a grade 4 life-threatening SAE of anaphylactoid reaction 2 days after Dose 3. The outcome was recovered/resolved and the event was considered related to vaccine. This participant is also discussed in Section 2.5.5.5.7.1.

Subgroup Analyses

No clinically meaningful differences in IRs of AEs for original placebo participants who then received BNT162b2 were observed by baseline SARS-CoV-2 positive (222.9 per 100 PY) and negative (205.4 per 100 PY) status subgroups. The IR for original baseline positive placebo participants who then received BNT162b2 (222.9 per 100 PY [95% CI: 186.5, 264.3]) was similar to baseline negative participants (205.4 per 100 PY [95% CI: 199.6, 211.3]). IRs in other SOCs were similar in the baseline positive and baseline negative groups, except for the musculoskeletal SOC which was higher in the baseline positive group. However, this was driven by a higher rate of myalgia (64.2 per 100 PY [95% CI: 45.4, 88.1]) in baseline positive participants compared to baseline negative participants (38.3 per 100 PY [95% CI: 35.8, 40.9])

Open-Label Follow-Up Period – Original Placebo Participants who had COVID-19 Occurrence After Dose 1 and Then Received BNT162b2

AEs reported from the unblinding date to the data cutoff date for original placebo participants who had COVID-19 occurrence after Dose 1 and then received BNT162b2 in the open-label follow-up period are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Supplemental Table 14.163.

For original placebo participants who had COVID-19 occurrence after Dose 1 and then received BNT162b2, the IR for at least 1 AE was 256.8 per 100 PY. Most AEs reported from Dose 3 (the first dose of BNT162b2) to the data cutoff date were in SOCs with reactogenicity events.

- general disorders and administration site conditions: 236.3 per 100 PY
- musculoskeletal and connective tissue disorders: 47.9 per 100 PY
- nervous system disorders: 66.2 per 100 PY
- gastrointestinal disorders: 17.1 per 100 PY.

2.5.5.5.4. Deaths – Phase 2/3

2.5.5.5.4.1. Blinded Follow-Up Period from Dose 1 to Unblinding Date

There were 15 deaths in the BNT162b2 group and 14 deaths in the placebo group from Dose 1 to the unblinding date during the blinded placebo-controlled follow-up period (Table 67). None of these deaths were assessed by the investigator as related to study intervention.

Table 67. Incidence Rates of Deaths From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=21926, TE[b]=83.4)			Placebo (N[a]=21921, TE[b]=82.2)		
	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])
Deaths	15	0.2	(0.1, 0.3)	14	0.2	(0.1, 0.3)
Cause of death[f]						
Acute respiratory failure	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)
Aortic rupture	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)
Arteriosclerosis	2	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)
Biliary cancer metastatic	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)
COVID-19	0	0.0	(0.0, 0.0)	2	0.0	(0.0, 0.1)
COVID-19 pneumonia	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)
Cardiac arrest	4	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)
Cardiac failure congestive	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)

Table 67. Incidence Rates of Deaths From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)					
	BNT162b2 (30 µg) (N[a]=21926, TE[b]=83.4)			Placebo (N[a]=21921, TE[b]=82.2)		
	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])
Cardio-respiratory arrest	1	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)
Chronic obstructive pulmonary disease	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)
Death	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)
Dementia	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)
Emphysematous cholecystitis	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)
Haemorrhagic stroke	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)
Hypertensive heart disease	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)
Lung cancer metastatic	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)
Metastases to liver	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)
Missing	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)
Multiple organ dysfunction syndrome	0	0.0	(0.0, 0.0)	2	0.0	(0.0, 0.1)
Myocardial infarction	0	0.0	(0.0, 0.0)	2	0.0	(0.0, 0.1)
Overdose	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)
Pneumonia	0	0.0	(0.0, 0.0)	2	0.0	(0.0, 0.1)
Sepsis	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)
Septic shock	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)
Shigella sepsis	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)
Unevaluable event	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)

a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 1 to the end of blinded follow-up. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified cause of death.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
f. Multiple causes of death can be reported for each subject.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (19:20) Source Data: dd Table Generation: 27MAR2021 (02:16)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/addd_s001_p3_saf

HIV+ Participants

Among participants with confirmed stable HIV disease, 2 deaths were reported as of the data cutoff date. Neither death was assessed by the investigator as related to study intervention.

- 1 female participant died due to COVID-19 pneumonia reported (b) (6) days after receiving Dose 2 of placebo. This participant was diagnosed based on a local COVID-19 test that could not be confirmed as protocol-approved and was not confirmed by a test result from

the central laboratory (case was not evaluable for efficacy analyses). This participant had unrelated SAEs that were diagnosed and reported prior to their death that are discussed further in Section 2.5.5.5.5.2.

- 1 female participant died due to a road traffic accident occurring (b) (6) days after receiving Dose 2.

2.5.5.5.4.2. Open-Label Follow-Up Period – Original BNT162b2 Participants

From the unblinding date to the data cutoff date of the open-label follow-up period, there were 3 deaths among original BNT162b2 participants, all in the older age group: 1 each due to road traffic accident, lung metastases, and myocardial infarction. None of these deaths were assessed by the investigator as related to study intervention.

2.5.5.5.4.3. Participants With at Least 6 Months Follow-Up Time – BNT162b2 Group

No deaths were reported among the participants originally randomized to BNT162b2 who had a cumulative ≥6 months (inclusive of blinded and open-label) follow-up.

2.5.5.5.4.4. Placebo Group Who Received BNT162b2

From the unblinding date to the data cutoff date of the open-label follow-up period, there were 2 deaths among original placebo participants who then received BNT162b2 , all in the older age group: 1 each due to cardiorespiratory arrest or completed suicide. Neither of these deaths were assessed by the investigator as related to study intervention

2.5.5.5.5. Serious Adverse Events – Phase 2/3

2.5.5.5.5.1. Blinded Follow-Up Period from Dose 1 Through 1 Month After Dose 2

From Dose 1 to 1 month after Dose 2 the proportions of participants who reported at least 1 SAE was similar in the BNT162b2 group (0.6%) and in the placebo group (0.5%) (Table 68).

The numbers of participants who reported at least 1 SAE were lower in the younger age group (52 [0.4%] and 49 [0.4%] for the BNT162b2 and placebo groups, respectively) than in the older age group (75 [0.8%] and 67 [0.8%] for the BNT162b2 and placebo groups, respectively).

Three of the SAEs in the BNT162b2 group and none in the placebo group were assessed by the investigator as related to study intervention (Table 58).

In the BNT162b2 group, 2 participants in the younger age group and 1 participant in the older age group had an SAE each assessed by the investigator as related to study intervention:

- 1 participant in the younger age group had an SAE of lymphadenopathy (right axilla) 13 days after Dose 1 which lasted 66 days and resolved. The participant was a 48-year-old woman with a relevant medical history of eczema and topical crisaborole use who was administered BNT162b2 vaccine in the left deltoid and had right axillary pain and lymphadenopathy. She had no injuries to the right arm, no fever, and no history of a similar incident. Her white blood cell count was normal with a normal lymphocyte count

and a right axilla ultrasound showed 4 enlarged lymph nodes (largest 2.5 × 1.1 × 2.4 cm). A biopsy was performed and was reported to be normal and without markers for lymphoma or other cancer. A follow-up visit with oncology (and possible repeat ultrasound) was planned for 3 months' time.

- 1 participant in the younger age group had an SAE of shoulder injury related to vaccine administration (SIRVA; erroneously administered into or near the shoulder joint capsule) after Dose 2, which lasted 153 days and resolved.

- 1 participant in the older age group with a past medical history significant for AV block with pacemaker, sinus node dysfunction, atrial fibrillation, and supraventricular tachycardia had an SAE of ventricular arrhythmia that occurred 1 day after Dose 2 and lasted for 8 days and resolved.

Table 68. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	127 (0.6)	(0.5, 0.7)	116 (0.5)	(0.4, 0.6)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Lymphadenopathy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Neutropenia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Thrombocytopenia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
CARDIAC DISORDERS	20 (0.1)	(0.1, 0.1)	21 (0.1)	(0.1, 0.1)
Atrial fibrillation	2 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Acute myocardial infarction	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Acute coronary syndrome	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Coronary artery disease	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Myocardial infarction	0	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Aortic valve incompetence	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Bradycardia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cardiac arrest	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cardiac failure congestive	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Acute left ventricular failure	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Angina pectoris	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Angina unstable	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Arrhythmia supraventricular	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Arteriospasm coronary	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cardiac failure acute	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 68. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Coronary artery dissection	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Coronary artery occlusion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Junctional ectopic tachycardia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Myocardial ischaemia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pericarditis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Tachyarrhythmia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tachycardia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Ventricular arrhythmia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Congenital bladder neck obstruction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Heart disease congenital	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
EAR AND LABYRINTH DISORDERS	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Vertigo	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
EYE DISORDERS	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Choroidal neovascularisation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Diplopia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Retinal artery occlusion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Visual impairment	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
GASTROINTESTINAL DISORDERS	9 (0.0)	(0.0, 0.1)	12 (0.1)	(0.0, 0.1)
Small intestinal obstruction	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pancreatitis acute	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Abdominal adhesions	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Abdominal pain	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Abdominal pain upper	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Colitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Diarrhoea	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Diverticular perforation	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Gastrointestinal haemorrhage	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Gastrointestinal mucosa hyperaemia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Incarcerated inguinal hernia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Inguinal hernia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Intestinal obstruction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Obstructive pancreatitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Oesophageal food impaction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Oesophageal varices haemorrhage	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pancreatitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Salivary gland calculus	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 68. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Umbilical hernia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Volvulus	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	4 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Non-cardiac chest pain	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Chest pain	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Death	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Influenza like illness	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Shoulder injury related to vaccine administration	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Vascular stent occlusion	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
HEPATOBILIARY DISORDERS	6 (0.0)	(0.0, 0.1)	2 (0.0)	(0.0, 0.0)
Cholecystitis acute	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Cholelithiasis	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Bile duct stone	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cholecystitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
IMMUNE SYSTEM DISORDERS	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Anaphylactic reaction	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Anaphylactic shock	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Drug hypersensitivity	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
INFECTIONS AND INFESTATIONS	27 (0.1)	(0.1, 0.2)	21 (0.1)	(0.1, 0.1)
Appendicitis	7 (0.0)	(0.0, 0.1)	3 (0.0)	(0.0, 0.0)
Pneumonia	2 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Cellulitis	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Urinary tract infection	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Appendicitis perforated	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
COVID-19	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Diverticulitis	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Peritonsillar abscess	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Postoperative wound infection	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pyelonephritis	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Abdominal abscess	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Abscess	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Abscess intestinal	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Anal abscess	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Bacterial sepsis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Brain abscess	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Complicated appendicitis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 68. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Empyema	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Meningitis bacterial	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Osteomyelitis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Peritoneal abscess	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Peritonitis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pyelonephritis acute	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Shigella sepsis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Staphylococcal infection	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Subacute endocarditis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Subcutaneous abscess	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Suspected COVID-19	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Upper respiratory tract infection	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Urosepsis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	8 (0.0)	(0.0, 0.1)	15 (0.1)	(0.0, 0.1)
Overdose	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Facial bones fracture	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Road traffic accident	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Alcohol poisoning	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cervical vertebral fracture	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Colon injury	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Fall	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Femur fracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Flail chest	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Foot fracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Forearm fracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Head injury	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hip fracture	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Humerus fracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Lower limb fracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Multiple injuries	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Procedural haemorrhage	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Rib fracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Spinal column injury	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Spinal cord injury cervical	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Subdural haematoma	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Toxicity to various agents	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Traumatic haemothorax	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Traumatic intracranial haemorrhage	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 68. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Ulna fracture	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
INVESTIGATIONS	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Blood glucose abnormal	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cardiac stress test abnormal	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hepatic enzyme increased	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
METABOLISM AND NUTRITION DISORDERS	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Diabetic ketoacidosis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Fluid retention	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypoglycaemia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hypokalaemia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	7 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Intervertebral disc protrusion	3 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Osteoarthritis	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Arthralgia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Back pain	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Muscular weakness	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Osteochondritis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	13 (0.1)	(0.0, 0.1)	10 (0.0)	(0.0, 0.1)
Prostate cancer	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Malignant melanoma	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Uterine leiomyoma	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Adenocarcinoma gastric	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Adenocarcinoma pancreas	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Adrenal gland cancer	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Biliary cancer metastatic	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Breast cancer	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Chronic myeloid leukaemia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Intraductal proliferative breast lesion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Invasive ductal breast carcinoma	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Leydig cell tumour of the testis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Meningioma	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Metastases to central nervous system	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Metastases to liver	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Oropharyngeal squamous cell carcinoma	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pancreatic carcinoma	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 68. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Penile neoplasm	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Prostate cancer metastatic	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Thyroid cancer	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
NERVOUS SYSTEM DISORDERS	14 (0.1)	(0.0, 0.1)	15 (0.1)	(0.0, 0.1)
Subarachnoid haemorrhage	4 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Syncope	1 (0.0)	(0.0, 0.0)	4 (0.0)	(0.0, 0.0)
Cerebrovascular accident	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Ischaemic stroke	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Transient ischaemic attack	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Amnesia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Amyotrophic lateral sclerosis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cerebral infarction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cervicogenic headache	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dizziness	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Haemorrhagic stroke	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Hemiplegic migraine	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Idiopathic intracranial hypertension	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Paraesthesia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Spinal cord compression	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Transient global amnesia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Uraemic encephalopathy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
PREGNANCY, PUERPERIUM AND PERINATAL CONDITIONS	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Abortion spontaneous	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Abortion spontaneous incomplete	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
PSYCHIATRIC DISORDERS	3 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Suicidal ideation	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Bipolar disorder	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Depression suicidal	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Disorientation	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Mental disorder	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Psychotic disorder	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Suicide attempt	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
RENAL AND URINARY DISORDERS	5 (0.0)	(0.0, 0.1)	1 (0.0)	(0.0, 0.0)
Nephrolithiasis	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Acute kidney injury	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Renal colic	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Subcapsular renal haematoma	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 68. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Urinary bladder polyp	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	2 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Breast hyperplasia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Ovarian cyst	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Ovarian mass	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Uterine prolapse	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	7 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Pulmonary embolism	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Acute respiratory failure	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pneumonia aspiration	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Chronic obstructive pulmonary disease	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypoxia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Interstitial lung disease	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pneumonitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pneumothorax	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pulmonary mass	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Respiratory arrest	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
VASCULAR DISORDERS	7 (0.0)	(0.0, 0.1)	5 (0.0)	(0.0, 0.1)
Deep vein thrombosis	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Hypertension	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Orthostatic hypotension	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Aortic stenosis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Arteriosclerosis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypertensive crisis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Hypertensive urgency	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Note: MedDRA (v23.1) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
c. Exact 2-sided CI based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:10)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA/adae s130 ser all pd2 p3 saf

HIV+ Participants

No participants with confirmed stable HIV disease reported an SAE from Dose 1 to 1 month after Dose 2.

2.5.5.5.5.2. Blinded Follow-Up Period from Dose 1 to the Unblinding Date

SAEs reported from Dose 1 to the unblinding date during the blinded placebo-controlled follow-up period are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Supplemental Table 14.166.

From Dose 1 to the unblinding date, IRs of at least 1 SAE were similar in the BNT162b2 group (3.2 per 100 PY) and in the placebo group (3.3 per 100 PY). The IR was lower in the younger age groups (2.1 per 100 PY and 2.4 per 100 PY for the BNT162b2 and placebo groups, respectively) than in the older age groups (4.9 per 100 PY and 4.6 per 100 PY for the BNT162b2 and placebo groups respectively).

Four SAEs in the BNT162b2 group and 1 in the placebo group were assessed by the investigator as related to study intervention. In addition to 3 related SAEs in the BNT162b2 group described in Section 2.5.5.5.5.1, 2 related SAEs occurred from 1 month after Dose 2 to the unblinding date:

- 1 participant in the BNT162b2 younger age group with a medical history significant for occipital neuralgia, and migraines had an SAE of paresthesia (right leg) 47 days after Dose 2 which was recovering/resolving at the data cutoff date.

- 1 participant in the placebo younger age group had an SAE of psoriatic arthropathy 38 days after Dose 2 which was continuing at the data cutoff date.

Subgroup Analyses

Overall, no clinically meaningful differences in IRs of SAEs were observed by baseline SARS-CoV-2 status, ethnicity, race, or sex subgroups.

Baseline SARS-CoV-2 Status

IRs of SAEs were similar by baseline SARS-CoV-2 status in the BNT162b2 and placebo groups for baseline positive (4.0 per 100 PY [95% CI: 1.9, 7.3] and 1.9 per 100 PY [95% CI: 0.6, 4.4]) and baseline negative (3.2 per 100 PY [95% CI: 2.8, 3.6] and 3.3 per 100 PY [95% CI: 2.9, 3.7]) participants. IRs of SAEs in the baseline positive BNT162b2 group were similar (4.0 per 100 PY [95% CI: 1.9, 7.3]) to those in the baseline negative BNT162b2 group (3.2 per 100 PY [95% CI: 2.8, 3.6]), and similar to what was observed in the overall SAE analysis irrespective of baseline status (Table 60).

While there are differences in exposure (2.5 vs 80.4) by baseline SARS-CoV-2 positive and negative status, respectively, IRs were numerically low or similar by baseline SARS-CoV-2 status, so there is no evidence that individuals who are positive at baseline report AEs at a higher frequency than those who are negative at baseline.

Race/Ethnicity

IRs of SAEs were similar in the BNT162b2 and placebo groups for Hispanic/Latino participants (3.5 per 100 PY [95% CI: 2.8, 4.3] and 3.6 per 100 PY [95% CI: 2.9, 4.5]), Non-Hispanic/Non-Latino participants (3.1 per 100 PY [95% CI: 2.7, 3.6] for each), and not reported (2.4 per 100 PY [95% CI: 0.1, 13.1] and 2.3 per 100 PY [95% CI: 0.1, 12.7]) participants.

IRs of SAEs were similar in the BNT162b2 and placebo groups for White participants (3.3 per 100 PY [95% CI: 2.9, 3.8] and 3.5 per 100 PY [95% CI: 3.1, 4.0]), Black or African American participants (2.5 per 100 PY [95% CI: 1.6, 3.9] and 2.6 per 100 PY [95% CI: 1.6, 4.0]), and greater in the BNT162b2 group for All Other participants compared to placebo (2.7 per 100 PY [95% CI: 1.6, 4.3] and 1.4 per 100 PY [95% CI: 0.6, 2.7]).

Sex

IRs of SAEs were similar by sex in the BNT162b2 and placebo groups for male participants (3.5 per 100 PY[95% CI: 3.0, 4.1] and 3.4 per 100 PY [95% CI: 2.8, 4.0]) and female participants (2.9 per 100 PY [95% CI: 2.4, 3.5] and 3.2 per 100 PY [95% CI: 2.6, 3.7]).

HIV+ Participants

From Dose 1 to the unblinding date, IRs of at least 1 SAE in participants with stable HIV disease were similar in the BNT162b2 group (6.6 per 100 PY [95% CI: 0.8, 23.9]) and the placebo group (6.9 per 100 PY [95% CI: 0.8, 25.1]) with 2 participants reporting at least 1 SAE in each group.

- 1 participant in the BNT162b2 group had an SAE of pneumonia 86 days after Dose 2 which lasted 8 days and resolved
- 1 participant in the BNT162b2 group had a fatal SAE of road traffic accident (b) (6) days after Dose 2
- 1 participant in the placebo group had an SAE of breast cancer 71 days after Dose 2 that was continuing at the data cutoff date.
- 1 participant in the placebo group had an SAE of diabetes mellitus 68 days after Dose 2, and then had COVID-19 pneumonia 72 days after Dose 2 which lasted (b) (6) days and resulted in death (see Section 2.5.5.5.4.1). The participant had a history of asthma, HIV, hypertension, and obesity and then was diagnosed with diabetes mellitus 68 days after Dose 2; 4 days after the diagnosis, the participant presented in the emergency room with an elevated blood glucose level and was admitted. Laboratory tests on the following day included a SARS-CoV-2 PCR test, which was positive; 2 days later, a second test confirmed the COVID-19 positive diagnosis. The following day (b) (6) days after Dose 2), the participant died due to disease progression and COVID-19 pneumonia. The investigator concluded that the events of diabetes mellitus and COVID-19 pneumonia were not related to study intervention. Note, this participant had COVID-19 diagnosed based on a local test that could not be confirmed as protocol-approved and was not subsequently confirmed by a test result from the central laboratory (therefore not included in efficacy analyses).

2.5.5.5.5.3. Open-Label Follow-Up Period – Original BNT162b2 Participants

SAEs reported from the unblinding date to the data cutoff date for the originally randomized BNT162b2 group during the open-label follow-up period are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Supplemental Table 14.180.

From the unblinding date to the data cutoff date, the IR of at least 1 SAE was 2.0 per 100 PY (95% CI: 1.5, 2.6) in original BNT162b2 participants.

One younger participant with no past medical history had a life-threatening SAE of myocardial infarction 71 days after Dose 2 that was assessed by the investigator as related to study intervention, which lasted 1 day and resolved the same day.

2.5.5.5.5.4. Cumulative Blinded and Open-Label Follow-Up Periods from Dose 1 to 6 Months After Dose 2 – BNT162b2 Group

From Dose 1 to 6 months after Dose 2, during the blinded and open-label follow-up periods, 190 (1.6%) participants in the BNT162b2 group reported at least 1 SAE (Table 69).

Two of the SAEs in the BNT162b2 group (SIRVA and paresthesia; see Section 2.5.5.5.5.1 and Section 2.5.5.5.5.2, respectively) were assessed by the investigator as related to study intervention (Table 60).

The number of participants who reported at least 1 SAE was 73 (1.1%) and 117 (2.2%) in the younger and older age groups, respectively.

Comparison of SAEs reported from Dose 1 to 1 month after Dose 2 to SAEs reported from 1 month after Dose 2 to 6 months after Dose 2 shows that the frequency of SAEs increased from 0.5% to 1.1%, respectively. The following SOCs had the largest increase in SAEs (from Dose 1 to 1 month after Dose 2 vs 1 month after Dose 2 to 6 months after Dose 2):

- Neoplasms, benign, malignant, unspecified including cysts and polyps: 4 (0.0%) vs 21 (0.2%)
- Injury, poisoning, and procedural complications: 2 (0.0%) vs 14 (0.1%)
- Infections and infestations: 14 (0.1%) vs 22 (0.2%)
- Gastrointestinal disorders: 4 (0.0%) vs 10 (0.1%)
- Respiratory, thoracic, and mediastinal disorders: 2 (0.0%) vs 8 (0.1%)
- Hepatobiliary disorders: 3 (0.0%) vs 8 (0.1%)

Table 69. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Any event	190 (1.6)	(1.4, 1.8)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.0)	(0.0, 0.0)
Pancytopenia	1 (0.0)	(0.0, 0.0)
CARDIAC DISORDERS	27 (0.2)	(0.1, 0.3)
Acute myocardial infarction	4 (0.0)	(0.0, 0.1)
Atrial fibrillation	4 (0.0)	(0.0, 0.1)
Myocardial infarction	4 (0.0)	(0.0, 0.1)
Angina pectoris	3 (0.0)	(0.0, 0.1)
Angina unstable	2 (0.0)	(0.0, 0.1)
Cardiac failure congestive	2 (0.0)	(0.0, 0.1)
Acute coronary syndrome	1 (0.0)	(0.0, 0.0)
Arrhythmia supraventricular	1 (0.0)	(0.0, 0.0)
Atrial flutter	1 (0.0)	(0.0, 0.0)
Bradycardia	1 (0.0)	(0.0, 0.0)
Cardiac arrest	1 (0.0)	(0.0, 0.0)
Coronary artery disease	1 (0.0)	(0.0, 0.0)
Coronary artery occlusion	1 (0.0)	(0.0, 0.0)
Pericarditis	1 (0.0)	(0.0, 0.0)
Ventricular tachycardia	1 (0.0)	(0.0, 0.0)
EAR AND LABYRINTH DISORDERS	1 (0.0)	(0.0, 0.0)
Vertigo	1 (0.0)	(0.0, 0.0)
EYE DISORDERS	4 (0.0)	(0.0, 0.1)
Choroidal neovascularisation	1 (0.0)	(0.0, 0.0)
Diplopia	1 (0.0)	(0.0, 0.0)
Ophthalmic vein thrombosis	1 (0.0)	(0.0, 0.0)
Retinal tear	1 (0.0)	(0.0, 0.0)
GASTROINTESTINAL DISORDERS	14 (0.1)	(0.1, 0.2)
Colitis	2 (0.0)	(0.0, 0.1)
Gastritis	2 (0.0)	(0.0, 0.1)
Small intestinal obstruction	2 (0.0)	(0.0, 0.1)
Abdominal pain upper	1 (0.0)	(0.0, 0.0)
Food poisoning	1 (0.0)	(0.0, 0.0)
Gastrointestinal haemorrhage	1 (0.0)	(0.0, 0.0)
Haematemesis	1 (0.0)	(0.0, 0.0)
Haemorrhoids	1 (0.0)	(0.0, 0.0)

Table 69. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Impaired gastric emptying	1 (0.0)	(0.0, 0.0)
Intestinal obstruction	1 (0.0)	(0.0, 0.0)
Obstructive pancreatitis	1 (0.0)	(0.0, 0.0)
Pancreatitis	1 (0.0)	(0.0, 0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	7 (0.1)	(0.0, 0.1)
Chest pain	2 (0.0)	(0.0, 0.1)
Non-cardiac chest pain	2 (0.0)	(0.0, 0.1)
Asthenia	1 (0.0)	(0.0, 0.0)
Shoulder injury related to vaccine administration	1 (0.0)	(0.0, 0.0)
Vascular stent occlusion	1 (0.0)	(0.0, 0.0)
HEPATOBILIARY DISORDERS	11 (0.1)	(0.0, 0.2)
Cholecystitis acute	3 (0.0)	(0.0, 0.1)
Cholelithiasis	3 (0.0)	(0.0, 0.1)
Bile duct stone	2 (0.0)	(0.0, 0.1)
Biliary colic	2 (0.0)	(0.0, 0.1)
Cholecystitis	1 (0.0)	(0.0, 0.0)
Cholelithiasis obstructive	1 (0.0)	(0.0, 0.0)
Portosplenomesenteric venous thrombosis	1 (0.0)	(0.0, 0.0)
IMMUNE SYSTEM DISORDERS	2 (0.0)	(0.0, 0.1)
Anaphylactic reaction	1 (0.0)	(0.0, 0.0)
Drug hypersensitivity	1 (0.0)	(0.0, 0.0)
INFECTIONS AND INFESTATIONS	36 (0.3)	(0.2, 0.4)
Appendicitis	10 (0.1)	(0.0, 0.2)
Diverticulitis	3 (0.0)	(0.0, 0.1)
Pneumonia	3 (0.0)	(0.0, 0.1)
Cellulitis	2 (0.0)	(0.0, 0.1)
Pyelonephritis	2 (0.0)	(0.0, 0.1)
Abscess	1 (0.0)	(0.0, 0.0)
Appendicitis perforated	1 (0.0)	(0.0, 0.0)
Arthritis bacterial	1 (0.0)	(0.0, 0.0)
Bacteraemia	1 (0.0)	(0.0, 0.0)
Bacterial sepsis	1 (0.0)	(0.0, 0.0)
Clostridium difficile colitis	1 (0.0)	(0.0, 0.0)
Device related infection	1 (0.0)	(0.0, 0.0)
Empyema	1 (0.0)	(0.0, 0.0)

Table 69. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Endocarditis	1 (0.0)	(0.0, 0.0)
Escherichia urinary tract infection	1 (0.0)	(0.0, 0.0)
Gangrene	1 (0.0)	(0.0, 0.0)
Gastroenteritis	1 (0.0)	(0.0, 0.0)
Herpes zoster oticus	1 (0.0)	(0.0, 0.0)
Meningitis bacterial	1 (0.0)	(0.0, 0.0)
Penile infection	1 (0.0)	(0.0, 0.0)
Peritoneal abscess	1 (0.0)	(0.0, 0.0)
Peritonitis	1 (0.0)	(0.0, 0.0)
Peritonsillar abscess	1 (0.0)	(0.0, 0.0)
Postoperative abscess	1 (0.0)	(0.0, 0.0)
Sepsis	1 (0.0)	(0.0, 0.0)
Subcutaneous abscess	1 (0.0)	(0.0, 0.0)
Urinary tract infection	1 (0.0)	(0.0, 0.0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	16 (0.1)	(0.1, 0.2)
Ankle fracture	2 (0.0)	(0.0, 0.1)
Road traffic accident	2 (0.0)	(0.0, 0.1)
Wrist fracture	2 (0.0)	(0.0, 0.1)
Burns second degree	1 (0.0)	(0.0, 0.0)
Burns third degree	1 (0.0)	(0.0, 0.0)
Cervical vertebral fracture	1 (0.0)	(0.0, 0.0)
Craniocerebral injury	1 (0.0)	(0.0, 0.0)
Facial bones fracture	1 (0.0)	(0.0, 0.0)
Fall	1 (0.0)	(0.0, 0.0)
Head injury	1 (0.0)	(0.0, 0.0)
Humerus fracture	1 (0.0)	(0.0, 0.0)
Patella fracture	1 (0.0)	(0.0, 0.0)
Pelvic fracture	1 (0.0)	(0.0, 0.0)
Procedural dizziness	1 (0.0)	(0.0, 0.0)
Spinal cord injury cervical	1 (0.0)	(0.0, 0.0)
Tibia fracture	1 (0.0)	(0.0, 0.0)
Traumatic intracranial haemorrhage	1 (0.0)	(0.0, 0.0)
Upper limb fracture	1 (0.0)	(0.0, 0.0)
INVESTIGATIONS	1 (0.0)	(0.0, 0.0)
Cardiac stress test abnormal	1 (0.0)	(0.0, 0.0)

Table 69. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
METABOLISM AND NUTRITION DISORDERS	3 (0.0)	(0.0, 0.1)
Diabetic ketoacidosis	1 (0.0)	(0.0, 0.0)
Hypoglycaemia	1 (0.0)	(0.0, 0.0)
Hypokalaemia	1 (0.0)	(0.0, 0.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	9 (0.1)	(0.0, 0.1)
Osteoarthritis	4 (0.0)	(0.0, 0.1)
Arthritis	1 (0.0)	(0.0, 0.0)
Intervertebral disc compression	1 (0.0)	(0.0, 0.0)
Intervertebral disc degeneration	1 (0.0)	(0.0, 0.0)
Intervertebral disc protrusion	1 (0.0)	(0.0, 0.0)
Osteochondritis	1 (0.0)	(0.0, 0.0)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	25 (0.2)	(0.1, 0.3)
Breast cancer	2 (0.0)	(0.0, 0.1)
Invasive ductal breast carcinoma	2 (0.0)	(0.0, 0.1)
Prostate cancer	2 (0.0)	(0.0, 0.1)
Acute myeloid leukaemia	1 (0.0)	(0.0, 0.0)
Adenocarcinoma pancreas	1 (0.0)	(0.0, 0.0)
Adrenal gland cancer	1 (0.0)	(0.0, 0.0)
Benign hydatidiform mole	1 (0.0)	(0.0, 0.0)
Bladder cancer	1 (0.0)	(0.0, 0.0)
Borderline serous tumour of ovary	1 (0.0)	(0.0, 0.0)
Brain cancer metastatic	1 (0.0)	(0.0, 0.0)
Breast cancer in situ	1 (0.0)	(0.0, 0.0)
Carcinoid tumour of the stomach	1 (0.0)	(0.0, 0.0)
Colon adenoma	1 (0.0)	(0.0, 0.0)
Gallbladder cancer stage II	1 (0.0)	(0.0, 0.0)
Gastric cancer	1 (0.0)	(0.0, 0.0)
Malignant melanoma	1 (0.0)	(0.0, 0.0)
Non-small cell lung cancer stage IV	1 (0.0)	(0.0, 0.0)
Skin cancer	1 (0.0)	(0.0, 0.0)
Squamous cell carcinoma	1 (0.0)	(0.0, 0.0)
Thyroid cancer	1 (0.0)	(0.0, 0.0)
Transitional cell carcinoma	1 (0.0)	(0.0, 0.0)
Uterine cancer	1 (0.0)	(0.0, 0.0)

Table 69. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
NERVOUS SYSTEM DISORDERS	23 (0.2)	(0.1, 0.3)
Subarachnoid haemorrhage	3 (0.0)	(0.0, 0.1)
Cerebrovascular accident	2 (0.0)	(0.0, 0.1)
Dizziness	2 (0.0)	(0.0, 0.1)
Optic neuritis	2 (0.0)	(0.0, 0.1)
Syncope	2 (0.0)	(0.0, 0.1)
Transient ischaemic attack	2 (0.0)	(0.0, 0.1)
Carpal tunnel syndrome	1 (0.0)	(0.0, 0.0)
Idiopathic intracranial hypertension	1 (0.0)	(0.0, 0.0)
Intracranial aneurysm	1 (0.0)	(0.0, 0.0)
Ischaemic stroke	1 (0.0)	(0.0, 0.0)
Paraesthesia	1 (0.0)	(0.0, 0.0)
Peripheral nerve lesion	1 (0.0)	(0.0, 0.0)
Seizure	1 (0.0)	(0.0, 0.0)
Toxic encephalopathy	1 (0.0)	(0.0, 0.0)
Transient global amnesia	1 (0.0)	(0.0, 0.0)
Uraemic encephalopathy	1 (0.0)	(0.0, 0.0)
PREGNANCY, PUERPERIUM AND PERINATAL CONDITIONS	2 (0.0)	(0.0, 0.1)
Abortion spontaneous	2 (0.0)	(0.0, 0.1)
PSYCHIATRIC DISORDERS	1 (0.0)	(0.0, 0.0)
Suicide attempt	1 (0.0)	(0.0, 0.0)
RENAL AND URINARY DISORDERS	9 (0.1)	(0.0, 0.1)
Nephrolithiasis	5 (0.0)	(0.0, 0.1)
Acute kidney injury	2 (0.0)	(0.0, 0.1)
Renal colic	1 (0.0)	(0.0, 0.0)
Subcapsular renal haematoma	1 (0.0)	(0.0, 0.0)
REPRODUCTIVE SYSTEM AND BREAST DISORDERS	3 (0.0)	(0.0, 0.1)
Breast hyperplasia	1 (0.0)	(0.0, 0.0)
Endometrial thickening	1 (0.0)	(0.0, 0.0)
Endometriosis	1 (0.0)	(0.0, 0.0)
Ovarian cyst	1 (0.0)	(0.0, 0.0)
Uterine prolapse	1 (0.0)	(0.0, 0.0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	10 (0.1)	(0.0, 0.2)
Pulmonary embolism	4 (0.0)	(0.0, 0.1)
Chronic obstructive pulmonary disease	2 (0.0)	(0.0, 0.1)

Table 69. Number (%) of Subjects Reporting at Least 1 Serious Adverse Event From Dose 1 to 6 Months After Dose 2, by System Organ Class and Preferred Term – Subjects With at Least 6 Months of Follow-up Time After Dose 2 – Phase 2/3 Subjects ≥16 Years of Age (Subjects Who Originally Received BNT162b2) – Safety Population

	Vaccine Group (as Administered)	
	BNT162b2 (30 µg) (N[a]=12006)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])
Dyspnoea	1 (0.0)	(0.0, 0.0)
Dyspnoea exertional	1 (0.0)	(0.0, 0.0)
Interstitial lung disease	1 (0.0)	(0.0, 0.0)
Pneumonitis	1 (0.0)	(0.0, 0.0)
SOCIAL CIRCUMSTANCES	1 (0.0)	(0.0, 0.0)
Miscarriage of partner	1 (0.0)	(0.0, 0.0)
SURGICAL AND MEDICAL PROCEDURES	1 (0.0)	(0.0, 0.0)
Finger amputation	1 (0.0)	(0.0, 0.0)
VASCULAR DISORDERS	6 (0.0)	(0.0, 0.1)
Aortic aneurysm	3 (0.0)	(0.0, 0.1)
Deep vein thrombosis	2 (0.0)	(0.0, 0.1)
Arterial occlusive disease	1 (0.0)	(0.0, 0.0)
Hypertension	1 (0.0)	(0.0, 0.0)

Note: MedDRA (v23.1) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
c. Exact 2-sided CI based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:16)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA/adae s130 pd2 ser p3 saf

2.5.5.5.5.5. Open-Label Follow-Up Period – Original Placebo Participants Who Received BNT162b2

From Dose 3 (first dose of BNT162b2) to the data cutoff date, the IR of at least 1 SAE in original placebo participants who then received BNT162b2 was 2.7 per 100 PY (95% CI: 2.1, 3.5) (Table 70).

One SAE was assessed by the investigator as related to study intervention (Table 65). This participant in the younger age group had an ongoing medical history of seasonal and food allergies and drug hypersensitivity, had an anaphylactoid reaction 2 days post Dose 3, with

an event duration of 1 day; the event was reported as an SAE, reported as resolved, and the participant withdrew from the study (also described in Section 2.5.5.5.7.1).

Table 70. Incidence Rates of at Least 1 Serious Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Any event	65	2.7	(2.1, 3.5)
CARDIAC DISORDERS	8	0.3	(0.1, 0.7)
Acute myocardial infarction	1	0.0	(0.0, 0.2)
Arrhythmia	1	0.0	(0.0, 0.2)
Arteriospasm coronary	1	0.0	(0.0, 0.2)
Atrial fibrillation	2	0.1	(0.0, 0.3)
Cardiac failure congestive	1	0.0	(0.0, 0.2)
Cardio-respiratory arrest	1	0.0	(0.0, 0.2)
Cardiovascular disorder	1	0.0	(0.0, 0.2)
Ischaemic cardiomyopathy	1	0.0	(0.0, 0.2)
Myocardial infarction	1	0.0	(0.0, 0.2)
CONGENITAL, FAMILIAL AND GENETIC DISORDERS	1	0.0	(0.0, 0.2)
Hypertrophic cardiomyopathy	1	0.0	(0.0, 0.2)
EAR AND LABYRINTH DISORDERS	1	0.0	(0.0, 0.2)
Vertigo	1	0.0	(0.0, 0.2)
EYE DISORDERS	1	0.0	(0.0, 0.2)
Diplopia	1	0.0	(0.0, 0.2)
GASTROINTESTINAL DISORDERS	8	0.3	(0.1, 0.7)
Anal prolapse	1	0.0	(0.0, 0.2)
Gastrointestinal haemorrhage	1	0.0	(0.0, 0.2)
Gastrointestinal necrosis	1	0.0	(0.0, 0.2)
Gastrooesophageal reflux disease	1	0.0	(0.0, 0.2)
Intestinal obstruction	1	0.0	(0.0, 0.2)
Intestinal ulcer perforation	1	0.0	(0.0, 0.2)
Pancreatitis acute	2	0.1	(0.0, 0.3)
Small intestinal obstruction	1	0.0	(0.0, 0.2)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	3	0.1	(0.0, 0.4)
Drug withdrawal syndrome	1	0.0	(0.0, 0.2)
Fatigue	1	0.0	(0.0, 0.2)
Pelvic mass	1	0.0	(0.0, 0.2)

Table 70. Incidence Rates of at Least 1 Serious Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
HEPATOBILIARY DISORDERS	2	0.1	(0.0, 0.3)
Cholecystitis	1	0.0	(0.0, 0.2)
Hepatitis acute	1	0.0	(0.0, 0.2)
IMMUNE SYSTEM DISORDERS	1	0.0	(0.0, 0.2)
Anaphylactoid reaction	1	0.0	(0.0, 0.2)
INFECTIONS AND INFESTATIONS	4	0.2	(0.0, 0.4)
Appendicitis perforated	1	0.0	(0.0, 0.2)
COVID-19 pneumonia	1	0.0	(0.0, 0.2)
Clostridium difficile infection	1	0.0	(0.0, 0.2)
Focal peritonitis	1	0.0	(0.0, 0.2)
Pelvic abscess	1	0.0	(0.0, 0.2)
Pneumonia	1	0.0	(0.0, 0.2)
Urosepsis	1	0.0	(0.0, 0.2)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	6	0.3	(0.1, 0.5)
Ankle fracture	1	0.0	(0.0, 0.2)
Fall	1	0.0	(0.0, 0.2)
Lower limb fracture	1	0.0	(0.0, 0.2)
Postoperative ileus	1	0.0	(0.0, 0.2)
Scapula fracture	1	0.0	(0.0, 0.2)
Spinal fracture	1	0.0	(0.0, 0.2)
Traumatic intracranial haemorrhage	1	0.0	(0.0, 0.2)
METABOLISM AND NUTRITION DISORDERS	1	0.0	(0.0, 0.2)
Diabetes mellitus inadequate control	1	0.0	(0.0, 0.2)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	4	0.2	(0.0, 0.4)
Myalgia	1	0.0	(0.0, 0.2)
Osteoarthritis	3	0.1	(0.0, 0.4)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	5	0.2	(0.1, 0.5)
Brain neoplasm	1	0.0	(0.0, 0.2)
Breast cancer	1	0.0	(0.0, 0.2)
Breast cancer stage II	1	0.0	(0.0, 0.2)
Hepatic cancer	1	0.0	(0.0, 0.2)
Non-small cell lung cancer stage III	1	0.0	(0.0, 0.2)
NERVOUS SYSTEM DISORDERS	9	0.4	(0.2, 0.7)
Brachial plexopathy	1	0.0	(0.0, 0.2)

Table 70. Incidence Rates of at Least 1 Serious Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Cerebrovascular accident	4	0.2	(0.0, 0.4)
Seizure	1	0.0	(0.0, 0.2)
Syncope	1	0.0	(0.0, 0.2)
Transient ischaemic attack	2	0.1	(0.0, 0.3)
PSYCHIATRIC DISORDERS	5	0.2	(0.1, 0.5)
Alcohol withdrawal syndrome	1	0.0	(0.0, 0.2)
Anxiety	1	0.0	(0.0, 0.2)
Bipolar disorder	1	0.0	(0.0, 0.2)
Completed suicide	1	0.0	(0.0, 0.2)
Depression	1	0.0	(0.0, 0.2)
Major depression	1	0.0	(0.0, 0.2)
Suicide attempt	1	0.0	(0.0, 0.2)
RENAL AND URINARY DISORDERS	2	0.1	(0.0, 0.3)
Nephrolithiasis	1	0.0	(0.0, 0.2)
Urinary tract obstruction	1	0.0	(0.0, 0.2)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	8	0.3	(0.1, 0.7)
Acute respiratory failure	2	0.1	(0.0, 0.3)
Chronic obstructive pulmonary disease	1	0.0	(0.0, 0.2)
Dyspnoea	1	0.0	(0.0, 0.2)
Pulmonary embolism	4	0.2	(0.0, 0.4)
VASCULAR DISORDERS	5	0.2	(0.1, 0.5)
Aortic stenosis	1	0.0	(0.0, 0.2)
Deep vein thrombosis	2	0.1	(0.0, 0.3)
Hypertension	1	0.0	(0.0, 0.2)
Thrombosis	1	0.0	(0.0, 0.2)

Table 70. Incidence Rates of at Least 1 Serious Adverse Event From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])

Note: Dose 3 = First dose of BNT162b2 (30 µg).
Note: MedDRA (v23.1) coding dictionary applied.
a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 3 to data cutoff date. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:16)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA/adae_s131_sae_exp_p3x_saf

Subgroup Analyses

Two participants reported SAEs among baseline SARS-CoV-2 positive original placebo participants who then received BNT162b2. Based on this small number, meaningful comparison with baseline negative participants is not possible.

Open-Label Follow-Up Period – Original Placebo Participants who had COVID-19 Occurrence After Dose 1 and Then Received BNT162b2

SAEs reported among original placebo participants who had COVID-19 occurrence after Dose 1 and then received BNT162b2 in the open-label follow-up period are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Supplemental Table 14.186.

For original placebo participants who had COVID-19 occurrence after Dose 1 and then received BNT162b2, the IR for at least 1 SAE was 3.4 per 100 PY (95% CI: 0.7, 10.0). These SAEs occurred in 3 participants.

- 1 participant with a significant past medical history of deep vein thrombosis and COVID-19 in the placebo-controlled follow-up period, and had a grade 3 SAE of

pulmonary embolism 6 days post Dose 4, which lasted 2 days and resolved with sequelae. The SAE was assessed as not related to the study intervention by the investigator.

- 1 participant with a past medical history of hypertension, hypercholesterolemia, coronary artery disease, and a coronary artery bypass in 2006, had a grade 3 SAE of myocardial infarction 16 days post Dose 3, which lasted 4 days and resolved with sequelae. The SAE was assessed and not related to the study intervention by the investigator.

- 1 participant in the older age group had 4 SAEs, all assessed by the investigator as not related to study intervention:

  - 2 grade 3 SAEs of urosepsis and acute hypoxic respiratory failure; both occurred 7 days post Dose 3, lasted 5 days, and resolved.

  - grade 3 SAE of non-small cell lung cancer (stage III), occurred 31 days post Dose 4, and was continuing at the data cutoff date.

  - grade 2 SAE of *Clostridium difficile* infection occurred 47 days post Dose 4 and was continuing at the data cutoff date.

2.5.5.5.6. Adverse Events Leading to Withdrawal – Phase 2/3

Note, several participants remain in the study but were erroneously reported as withdrawn because of AEs, which was subsequently queried and corrected as described in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Errata.

2.5.5.5.6.1. Blinded Follow-Up Period from Dose 1 Through 1 Month After Dose 2

From Dose 1 to 1 month after Dose 2, few participants in the BNT162b2 group (0.1%) and in the placebo group (0.2%) were withdrawn because of AEs (Table 71).

There were 32 participants in the BNT162b2 group and 36 participants in the placebo group had an AE leading to withdrawal (Table 71). The most common SOCs with PTs leading to withdrawal in either vaccine group included:

- 6 participants in the BNT162b2 group and 2 participants in the placebo group who withdrew from the study due to AEs in the SOC of general disorders and administration site conditions (BNT162b2 group: injection site pain [2 participants] and chills, facial pain, injection site dermatitis, injection site swelling, pyrexia, and swelling face [1 participant each]; placebo group: death and fatigue [1 participant each]).

- 5 participants in the BNT162b2 group and 6 participants in the placebo group withdrew from the study due to AEs in the SOC of injury, poisoning and procedural complications (BNT162b2 group: exposure during pregnancy, maternal exposure during pregnancy [2 participants each] and alcohol poisoning [1 participant]; placebo group: exposure during pregnancy [5 participants] and overdose [1 participant].

- 3 participants in the BNT162b2 group and 5 participants in the placebo group withdrew from the study due to AEs in the SOC cardiac disorders (BNT162b2 group: cardiac

arrest, coronary artery disease and tachycardia [1 participant each]; placebo group: atrial fibrillation [2 participants], cardiac failure congestive, coronary artery occlusion, and myocardial infarction [1 participant each]).

- 3 participants in the BNT162b2 group and 6 participants in the placebo group withdrew from the study due to AEs in the SOC of nervous system disorders (BNT162b2 group: headache [3 participants]; placebo group: dizziness [2 participants], amnesia, cerebral infarction, hemorrhagic stroke, paraparesis, and Parkinsonism [1 participant each]).

- 3 participants in the BNT162b2 group and 6 participants in the placebo group withdrew from the study due to AEs in the SOC of gastrointestinal disorders (BNT162b2 group: abdominal pain upper, gastrointestinal hemorrhage, and paresthesia oral [1 participant each]; placebo group: diarrhea [2 participants], diverticular perforation, dry mouth, dysphagia, and nausea [1 participant each]).

No clinically meaningful differences in AEs leading to withdrawal were observed by age subgroups.

Table 71. Number (%) of Subjects Withdrawn Because of Adverse Events From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
Any event	32 (0.1)	(0.1, 0.2)	36 (0.2)	(0.1, 0.2)
BLOOD AND LYMPHATIC SYSTEM DISORDERS	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Lymphadenopathy	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
CARDIAC DISORDERS	3 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Atrial fibrillation	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Cardiac arrest	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Cardiac failure congestive	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Coronary artery disease	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Coronary artery occlusion	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Myocardial infarction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Tachycardia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
EAR AND LABYRINTH DISORDERS	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Deafness unilateral	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Vertigo	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 71. Number (%) of Subjects Withdrawn Because of Adverse Events From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
EYE DISORDERS	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Eye pain	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Visual impairment	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
GASTROINTESTINAL DISORDERS	3 (0.0)	(0.0, 0.0)	6 (0.0)	(0.0, 0.1)
Diarrhoea	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Abdominal pain upper	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Diverticular perforation	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dry mouth	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Dysphagia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Gastrointestinal haemorrhage	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Nausea	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Paraesthesia oral	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	6 (0.0)	(0.0, 0.1)	2 (0.0)	(0.0, 0.0)
Injection site pain	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Chills	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Death	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Facial pain	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Fatigue	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Injection site dermatitis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Injection site swelling	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Pyrexia	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Swelling face	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
IMMUNE SYSTEM DISORDERS	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Drug hypersensitivity	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
INFECTIONS AND INFESTATIONS	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Shigella sepsis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	5 (0.0)	(0.0, 0.1)	6 (0.0)	(0.0, 0.1)
Exposure during pregnancy	2 (0.0)	(0.0, 0.0)	5 (0.0)	(0.0, 0.1)
Maternal exposure during pregnancy	2 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Alcohol poisoning	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Overdose	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
INVESTIGATIONS	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Heart rate irregular	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Myalgia	1 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)

Table 71. Number (%) of Subjects Withdrawn Because of Adverse Events From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	3 (0.0)	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Adenocarcinoma gastric	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Biliary cancer metastatic	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Lymphoproliferative disorder	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Metastases to central nervous system	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Metastases to liver	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
NERVOUS SYSTEM DISORDERS	3 (0.0)	(0.0, 0.0)	6 (0.0)	(0.0, 0.1)
Headache	3 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Dizziness	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Amnesia	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Cerebral infarction	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Haemorrhagic stroke	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Paraparesis	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Parkinsonism	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
PSYCHIATRIC DISORDERS	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Depression	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Depression suicidal	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Panic attack	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Suicide attempt	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
RESPIRATORY, THORACIC AND MEDIASTINAL DISORDERS	0	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Pulmonary embolism	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Respiratory arrest	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	2 (0.0)	(0.0, 0.0)	3 (0.0)	(0.0, 0.0)
Urticaria	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Diabetic foot	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)
Eczema	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Pruritus	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
Rash maculo-papular	0	(0.0, 0.0)	1 (0.0)	(0.0, 0.0)
VASCULAR DISORDERS	2 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Hypertension	1 (0.0)	(0.0, 0.0)	2 (0.0)	(0.0, 0.0)
Arteriosclerosis	1 (0.0)	(0.0, 0.0)	0	(0.0, 0.0)

Table 71. Number (%) of Subjects Withdrawn Because of Adverse Events From Dose 1 to 1 Month After Dose 2, by System Organ Class and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)			
	BNT162b2 (30 µg) (N[a]=21926)		Placebo (N[a]=21921)	
System Organ Class Preferred Term	n[b] (%)	(95% CI[c])	n[b] (%)	(95% CI[c])

Note: MedDRA (v23.1) coding dictionary applied.
a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
c. Exact 2-sided CI based on the Clopper and Pearson method.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 27MAR2021 (02:10)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA/adae s130 1md2 wd p3 saf

2.5.5.5.6.2. Blinded Follow-Up Period from Dose 1 to the Unblinding Date

AEs leading to withdrawal reported from Dose 1 to the unblinding date during the blinded placebo-controlled follow-up period are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Supplemental Table 14.189.

From Dose 1 to the unblinding date, the IRs of participants withdrawn because of AEs were 0.5 per 100 PY in the BNT162b2 group and 0.6 per 100 PY in the placebo group.

There were 45 participants in the BNT162b2 group and 51 participants in the placebo group had an AE leading to withdrawal, which included:

- 9 participants in the BNT162b2 group and 8 participants in the placebo group withdrew from the study due to AEs in the SOC cardiac disorders (BNT162b2 group: cardiac arrest [4 participants], cardiac failure congestive, cardio-respiratory arrest, coronary artery disease, hypertensive heart disease and tachycardia [1 participant each]; placebo group: atrial fibrillation [2 participants], cardiac arrest, cardiac failure congestive, cardio-respiratory arrest, coronary artery occlusion, [1 participant each] and myocardial infarction [2 participants]).

- 3 participants in the BNT162b2 group and 6 participants in the placebo group withdrew from the study due to AEs in the SOC of gastrointestinal disorders (BNT162b2 group: abdominal pain upper, gastrointestinal hemorrhage, and paresthesia oral [1 participant each]; placebo group: diarrhea [2 participants], diverticular perforation, dry mouth, dysphagia, and nausea [1 participant each]).

- 7 participants in the BNT162b2 group and 2 participants in the placebo group withdrew from the study due to AEs in the SOC of general disorders and administration site conditions (BNT162b2 group: injection site pain [2 participants], chills, facial pain, injection site dermatitis, injection site swelling, pyrexia, sudden cardiac death and swelling face [1 participant each]; placebo group: death and fatigue [1 participant each]).

- 4 participants in the BNT162b2 group and 3 participants in the placebo group withdrew from study due to AEs in the SOC infections and infestations (BNT162b2 group: COVID-19 pneumonia, emphysematous cholecystitis, sepsis, septic shock and Shigella sepsis [1 participant each]; placebo group: COVID-19, pneumonia, and septic shock [1 participant each]).

No clinically meaningful differences in IRs of AEs leading to withdrawal were observed in the younger and older age groups.

2.5.5.5.6.3. Open-Label Follow-Up Period – Original BNT162b2 Participants

AEs leading to withdrawal in the originally randomized BNT162b2 group reported from the unblinding date to the data cutoff date during open-label follow-up are presented in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Supplemental Table 14.192.

From the unblinding data to the data cutoff date, IRs of original BNT162b2 participants withdrawn because of AEs were 0.1.

2.5.5.5.6.4. Cumulative Blinded and Open-Label Follow-Up Periods from Dose 1 to 6 Months After Dose 2 – BNT162b2 Group

From Dose 1 to 6 months after Dose 2 during the blinded and open-label follow-up period, 1 participant in the older BNT162b2 group was reported as withdrawn because of AEs (dermatitis). However, this participant remains in the study as the withdrawal was subsequently queried and corrected, as described in Module 5.3.5.1 C4591001 6-Month Update Interim CSR Errata.

2.5.5.5.6.5. Open-Label Follow-Up Period – Original Placebo Participants Who Received BNT162b2

From unblinding to receive BNT162b2 (Dose 3) up to the data cutoff date, IR of original placebo participants withdrawn because of AEs was 0.8 per 100 PY (Table 72).

Table 72. Incidence Rates of Subjects Withdrawn Because of Adverse Events From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Any event	19	0.8	(0.5, 1.2)
CARDIAC DISORDERS	2	0.1	(0.0, 0.3)
Angina pectoris	1	0.0	(0.0, 0.2)
Cardio-respiratory arrest	1	0.0	(0.0, 0.2)
GASTROINTESTINAL DISORDERS	2	0.1	(0.0, 0.3)
Diarrhoea	1	0.0	(0.0, 0.2)
Gastrointestinal haemorrhage	1	0.0	(0.0, 0.2)
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS	7	0.3	(0.1, 0.6)
Chills	2	0.1	(0.0, 0.3)

Table 72. Incidence Rates of Subjects Withdrawn Because of Adverse Events From Dose 3 to Data Cutoff Date (13MAR2021), by System Organ Class and Preferred Term – Open-Label Follow-up Period – Subjects Who Originally Received Placebo and Then Received BNT162b2 After Unblinding – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)		
	BNT162b2 (30 µg) (N[a]=19525, TE[b]=23.8)		
System Organ Class Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])
Fatigue	2	0.1	(0.0, 0.3)
Injection site pain	3	0.1	(0.0, 0.4)
Pain	1	0.0	(0.0, 0.2)
IMMUNE SYSTEM DISORDERS	2	0.1	(0.0, 0.3)
Allergy to vaccine	1	0.0	(0.0, 0.2)
Anaphylactoid reaction	1	0.0	(0.0, 0.2)
INJURY, POISONING AND PROCEDURAL COMPLICATIONS	3	0.1	(0.0, 0.4)
Maternal exposure during pregnancy	3	0.1	(0.0, 0.4)
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS	1	0.0	(0.0, 0.2)
Myalgia	1	0.0	(0.0, 0.2)
NEOPLASMS BENIGN, MALIGNANT AND UNSPECIFIED (INCL CYSTS AND POLYPS)	1	0.0	(0.0, 0.2)
Hepatic cancer	1	0.0	(0.0, 0.2)
NERVOUS SYSTEM DISORDERS	2	0.1	(0.0, 0.3)
Headache	2	0.1	(0.0, 0.3)
PSYCHIATRIC DISORDERS	1	0.0	(0.0, 0.2)
Completed suicide	1	0.0	(0.0, 0.2)
SKIN AND SUBCUTANEOUS TISSUE DISORDERS	1	0.0	(0.0, 0.2)
Angioedema	1	0.0	(0.0, 0.2)
Urticaria	1	0.0	(0.0, 0.2)

Note: Dose 3 = First dose of BNT162b2 (30 µg).
Note: MedDRA (v23.1) coding dictionary applied.
a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 3 to data cutoff date. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified event. For "any event," n = number of subjects reporting at least 1 occurrence of any event.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 31MAR2021 (18:33)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File: ./nda2_unblinded/C4591001_BLA1/adae_s131_wd_exp_p3x_saf

Open-Label Follow-Up Period – Original Placebo Participants who had COVID-19 Occurrence After Dose 1 and Then Received BNT162b2

The subset of participants originally randomized to placebo, who had a COVID-19 case after Dose 1 of placebo and were later unblinded to receive BNT162b2 (Dose 3), were evaluated. Three participants in this group had AEs leading to withdrawal that were assessed as related to BNT162b2 (also summarized in Section 2.5.5.5.3.5.1): 1 participant with an AE of allergy to vaccine, 1 participant with an AE of pain, and 1 participant with 5 AEs (chills, injection site pain, myalgia, headache, and diarrhea).

2.5.5.5.7. Other Significant Adverse Events – Phase 2/3

AEs of clinical interest were evaluated based on regulatory agency feedback and sponsor medical review. Terms requested for analysis by the FDA were summarize and detailed for any such cases reported. Other terms of clinical interest, such as the CDC's list of AESIs for COVID-19 vaccines, which both include terms potentially indicative of severe COVID-19 or serious autoimmune and neuroinflammatory disorders, were considered in the review of reported events. Numerical imbalances for AESIs were based on the evaluation of AEs in the blinded placebo-controlled period. These safety evaluations are summarized below.

Narratives were prepared for a defined set of events as described in Section 2.5.5.1.2.3.

2.5.5.5.7.1. FDA-Requested Adverse Events of Clinical Interest

Safety evaluations were conducted for AEs of clinical interest: anaphylaxis, Bell's Palsy, lymphadenopathy, and appendicitis based on feedback from the FDA.

Participants ≥16 years of age reporting these terms during blinded placebo-controlled follow-up (unless otherwise noted as occurring during open-label follow-up) are summarized below.

Hypersensitivity/Anaphylaxis

During the blinded placebo-controlled follow-up period of Study C4591001 in participants ≥16 years of age, there were 3 allergic reactions reported as SAEs (all reported at the time of the 14 November 2020 data cutoff date). All 3 cases of allergic reaction were considered by the investigator as not related to study treatment.

- Anaphylactic reaction following a bee sting in a BNT162b2 recipient (8 days after Dose 2)
- Drug hypersensitivity to an antibiotic in a BNT162b2 recipient (9 days after Dose 2)
- Anaphylactic shock due to an ant bite in a placebo recipient (18 days after Dose 2).

During the open-label follow-up period, 1 participant who received BNT162b2 as Dose 3 (after originally being randomized to placebo and unblinded to receive BNT162b2) had an SAE of anaphylactoid reaction, which was assessed as related to study intervention. This participant was a female adolescent with a medical history significant for multiple allergies since infancy. Two days after Dose 3, she experienced hives on the left arm (deltoid) and self-administered an epinephrine pen 24 minutes later (given the history of anaphylaxis to

multiple allergens). Six minutes after injection, she experienced shortness of breath. Hives and shortness of breath resolved within 10 and 30 minutes, respectively, of epinephrine treatment. The participant did not seek additional medical attention. As a result of the anaphylactoid reaction, the participant was permanently withdrawn from the study.

Hypersensitivity is also assessed as a CDC-defined AESI in Section 2.5.5.5.7.2.

Bell's Palsy/Facial Paralysis

During the blinded placebo-controlled follow-up period, 6 participants developed one-sided facial paralysis (Bell's palsy): 4 were randomized to BNT162b2 (all male) and 2 were randomized to placebo (1 male; 1 female). Regarding the 4 vaccinated participants (previously reported at 14 November 2020 cutoff date), their ages ranged from 40 to 70 years of age (compared to 71 to 73 years of age in placebo participants). Events began from 3 to 48 days after their last dose, were mild to moderate in severity (moderate in the placebo participants), and duration ranged from 3 to 68 days (15 days in 1 placebo participant and ongoing in the other). Of the 4 cases in participants randomized to BNT162b2, 2 were considered by the investigator to be related to study intervention. The remaining 4 cases (2 in participants originally randomized to BNT162b2 and 2 in participants originally randomized to placebo) were assessed as not related to study intervention.

During the open-label follow-up period, 3 participants who received BNT162b2 as Dose 3 or Dose 4 (after originally being randomized to placebo) experienced facial paralysis. All were female and their ages ranged from 19 to 34 years. Events began 2 to 8 days after Dose 3 and were mild to severe in severity. One case involved a duration of 12 days while the other 2 were ongoing as of the data cutoff date. All these events of facial paralysis were considered by the investigator as related to study intervention.

During the open-label follow-up period for participants originally randomized to BNT162b2, a male participant 51 years of age developed Bell's palsy 154 days after receiving Dose 2.

Bell's palsy is also assessed as an AESI in Section 2.5.5.5.7.3.

Lymphadenopathy

In participants ≥16 years of age, during the blinded placebo-controlled follow-up period, lymphadenopathy was reported in 87 participants (1.0 per 100 PY) in the BNT162b2 group compared to 8 participants (0.1 per 100 PY) in the placebo group. The majority of events were mild to moderate; only 3 severe events of lymphadenopathy were reported (all in the BNT162b2 group). The median onset of lymphadenopathy after Dose 1 and before Dose 2 was 5.5 days in the BNT162b2 group and 5.0 days in the placebo group; median onset after Dose 2 was shorter in the BNT162b2 group versus the placebo group (2.0 days vs 7.0 days). The median duration of lymphadenopathy was 5.5 days in the BNT162b2 group and 4.0 days in the placebo group. One case (previously reported at 14 November 2020 cutoff date) was reported as a related SAE (see Section 2.5.5.5.5.1).

Appendicitis

Cases of appendicitis were examined in the placebo-controlled follow-up period of the study including PTs of appendicitis perforated and complicated appendicitis). There were 14 cases of appendicitis and 1 case of appendicitis perforated in the BNT162b2 group; and 9 cases of appendicitis, 2 cases of complicated appendicitis, and 1 appendicitis perforated in the placebo group. Appendicitis cases were all reported as SAEs (see Section 2.5.5.5.5.1 and Section 2.5.5.5.5.2), and none of the cases were considered related to study intervention.

2.5.5.5.7.2. CDC-Defined Adverse Events of Special Interest

CDC-defined AESIs associated with COVID-19 vaccination were evaluated in the blinded placebo-controlled follow-up period, where reported in the Phase 2/3 safety population.

After a review of AEs using the CDC's AESI list, the following terms were not found reported in the study: acute disseminated encephalomyelitis, transverse myelitis, multiple sclerosis, chronic inflammatory demyelinating polyneuropathy, encephalitis, myelitis, encephalomyelitis, meningoencephalitis, ataxia, narcolepsy, cataplexy, immune thrombocytopenia, thrombotic thrombocytopenic purpura, disseminated intravascular coagulation, Kawasaki disease, multisystem inflammatory syndrome in children (MIS-C) and in adults (MIS-A), and acute respiratory distress syndrome.

There were 2 cases of bacterial meningitis reported but they were not analyzed further as there is an immediate and self-evident cause to their illness.

Terms that were present in the safety population are summarized below. For a given SMQ, if there was no imbalance in the BNT162b2 group versus placebo, the PTs within the SMQ were not further examined. In the case of an imbalance, the PTs responsible for the imbalance are further described and the nature of the events characterized with regard to plausible associated with vaccination.

Overall, the number and percentage of participants with any unsolicited AEs within the selected SMQs was similar in the BNT162b2 (224 [1.02%]) and placebo (217 [0.99%]) groups from Dose 1 to the unblinding date (Table 73). From analysis of terms corresponding to AESIs from the CDC's list, individual SMQs are discussed below.

Table 73. Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Subjects with any unsolicited adverse events within SMQ	224 (1.02)	217 (0.99)
Angioedema (SMQ)	Any unsolicited adverse events within Angioedema (SMQ)	30 (0.14)	29 (0.13)
	Eye disorders	2 (0.01)	2 (0.01)
	Conjunctival oedema	0	1 (0.00)
	Eye swelling	0	1 (0.00)
	Eyelid oedema	1 (0.00)	0
	Swelling of eyelid	1 (0.00)	0
	Gastrointestinal disorders	6 (0.03)	3 (0.01)
	Gingival swelling	0	1 (0.00)
	Lip oedema	1 (0.00)	0
	Lip swelling	2 (0.01)	1 (0.00)
	Swollen tongue	2 (0.01)	1 (0.00)
	Tongue oedema	1 (0.00)	0
	General disorders and administration site conditions	4 (0.02)	7 (0.03)
	Face oedema	2 (0.01)	0
	Swelling face	2 (0.01)	7 (0.03)
	Respiratory, thoracic and mediastinal disorders	1 (0.00)	3 (0.01)
	Pharyngeal swelling	1 (0.00)	3 (0.01)
	Skin and subcutaneous tissue disorders	21 (0.10)	18 (0.08)
	Angioedema	3 (0.01)	2 (0.01)
	Urticaria	18 (0.08)	15 (0.07)
	Urticaria papular	0	1 (0.00)
Arthritis (SMQ)	Any unsolicited adverse events within Arthritis (SMQ)	35 (0.16)	48 (0.22)
	Infections and infestations	1 (0.00)	0
	Arthritis bacterial	1 (0.00)	0
	Metabolism and nutrition disorders	5 (0.02)	3 (0.01)
	Gout	5 (0.02)	3 (0.01)
	Musculoskeletal and connective tissue disorders	29 (0.13)	45 (0.21)
	Arthritis	6 (0.03)	6 (0.03)
	Arthritis reactive	1 (0.00)	0
	Osteoarthritis	15 (0.07)	23 (0.10)
	Patellofemoral pain syndrome	0	1 (0.00)

Table 73. Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Periarthritis	4 (0.02)	1 (0.00)
	Polyarthritis	0	1 (0.00)
	Rheumatoid arthritis	0	2 (0.01)
	Spinal osteoarthritis	2 (0.01)	4 (0.02)
	Spondylitis	1 (0.00)	1 (0.00)
	Synovitis	0	2 (0.01)
	Temporomandibular joint syndrome	1 (0.00)	4 (0.02)
Convulsions (SMQ)	Any unsolicited adverse events within Convulsions (SMQ)	2 (0.01)	2 (0.01)
	Nervous system disorders	2 (0.01)	2 (0.01)
	Generalised tonic-clonic seizure	0	1 (0.00)
	Seizure	2 (0.01)	1 (0.00)
Demyelination (SMQ)	Any unsolicited adverse events within Demyelination (SMQ)	2 (0.01)	1 (0.00)
	Nervous system disorders	2 (0.01)	1 (0.00)
	Guillain-Barre syndrome	0	1 (0.00)
	Optic neuritis	2 (0.01)	0
Hypersensitivity (SMQ)	Any unsolicited adverse events within Hypersensitivity (SMQ)	182 (0.83)	161 (0.73)
	Ear and labyrinth disorders	0	1 (0.00)
	Allergic otitis media	0	1 (0.00)
	Eye disorders	5 (0.02)	5 (0.02)
	Conjunctival oedema	0	1 (0.00)
	Conjunctivitis allergic	3 (0.01)	2 (0.01)
	Eye allergy	0	1 (0.00)
	Eye swelling	0	1 (0.00)
	Eyelid oedema	1 (0.00)	0
	Swelling of eyelid	1 (0.00)	0
	Gastrointestinal disorders	6 (0.03)	3 (0.01)
	Gingival swelling	0	1 (0.00)
	Lip oedema	1 (0.00)	0
	Lip swelling	2 (0.01)	1 (0.00)
	Swollen tongue	2 (0.01)	1 (0.00)
	Tongue oedema	1 (0.00)	0

Table 73. Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	General disorders and administration site conditions	8 (0.04)	9 (0.04)
	Application site rash	0	1 (0.00)
	Face oedema	2 (0.01)	0
	Injection site dermatitis	1 (0.00)	0
	Injection site rash	2 (0.01)	1 (0.00)
	Injection site urticaria	1 (0.00)	0
	Swelling face	2 (0.01)	7 (0.03)
	Immune system disorders	10 (0.05)	13 (0.06)
	Anaphylactic reaction	1 (0.00)	0
	Anaphylactic shock	0	1 (0.00)
	Drug hypersensitivity	7 (0.03)	7 (0.03)
	Hypersensitivity	2 (0.01)	5 (0.02)
	Infections and infestations	5 (0.02)	1 (0.00)
	Dermatitis infected	0	1 (0.00)
	Pustule	3 (0.01)	0
	Rash pustular	2 (0.01)	0
	Injury, poisoning and procedural complications	3 (0.01)	0
	Administration related reaction	2 (0.01)	0
	Stoma site rash	1 (0.00)	0
	Investigations	1 (0.00)	0
	Blood immunoglobulin E increased	1 (0.00)	0
	Respiratory, thoracic and mediastinal disorders	19 (0.09)	21 (0.10)
	Allergic respiratory disease	0	1 (0.00)
	Allergic sinusitis	2 (0.01)	0
	Bronchospasm	3 (0.01)	3 (0.01)
	Pharyngeal swelling	1 (0.00)	3 (0.01)
	Rhinitis allergic	13 (0.06)	14 (0.06)
	Skin and subcutaneous tissue disorders	134 (0.61)	119 (0.54)
	Angioedema	3 (0.01)	2 (0.01)
	Dermatitis	5 (0.02)	4 (0.02)
	Dermatitis acneiform	1 (0.00)	0
	Dermatitis allergic	3 (0.01)	5 (0.02)
	Dermatitis atopic	0	1 (0.00)

Table 73. Selected Standard MedDRA Queries From Dose 1 to Unblinding Date – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

		Vaccine Group (as Administered)	
		BNT162b2 (30 µg) (N[a]=21926)	Placebo (N[a]=21921)
SMQ	Overall SMQ System Organ Class Preferred Term	n[b] (%)	n[b] (%)
	Dermatitis bullous	0	1 (0.00)
	Dermatitis contact	14 (0.06)	21 (0.10)
	Dermatitis exfoliative	1 (0.00)	0
	Drug eruption	0	2 (0.01)
	Eczema	7 (0.03)	3 (0.01)
	Erythema nodosum	1 (0.00)	0
	Fixed eruption	1 (0.00)	0
	Hand dermatitis	2 (0.01)	2 (0.01)
	Perioral dermatitis	0	1 (0.00)
	Pruritus allergic	0	2 (0.01)
	Rash	62 (0.28)	52 (0.24)
	Rash erythematous	2 (0.01)	3 (0.01)
	Rash maculo-papular	7 (0.03)	4 (0.02)
	Rash papular	1 (0.00)	0
	Rash pruritic	8 (0.04)	6 (0.03)
	Urticaria	18 (0.08)	15 (0.07)
	Urticaria contact	0	1 (0.00)
	Urticaria papular	0	1 (0.00)
Peripheral neuropathy (SMQ)	Any unsolicited adverse events within Peripheral neuropathy (SMQ)	3 (0.01)	6 (0.03)
	Nervous system disorders	3 (0.01)	6 (0.03)
	Guillain-Barre syndrome	0	1 (0.00)
	Neuralgia	1 (0.00)	1 (0.00)
	Neuritis	0	1 (0.00)
	Neuropathy peripheral	1 (0.00)	3 (0.01)
	Peripheral sensory neuropathy	1 (0.00)	0

a. N = number of subjects in the specified group. This value is the denominator for the percentage calculations.
b. n = Number of subjects reporting at least 1 occurrence of the specified event category. For "any event," n = the number of subjects reporting at least 1 occurrence of any event.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 14APR2021 (10:22)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA RR/adae smq nzud 16 saf

Angioedema

Overall, the number and percentage of participants with any unsolicited AE within the SMQ of angioedema were low and similar in the BNT162b2 group (30 [0.14%]) and placebo group (29 [0.13%]) (Table 73). AEs were most frequently reported in the SOC of skin and subcutaneous tissue disorders (21 [0.10%] BNT162b2 vs 18 [0.08%] placebo) with urticaria the most frequently reported PT.

In the SOC of gastrointestinal disorders within the SMQ of angioedema, lip edema, or lip swelling was observed in 3 participants in the BNT162b2 group versus 1 participant in the placebo group. Swollen tongue or tongue edema was observed in 3 participants in the BNT162b2 group versus 1 participant in the placebo group. Lip swelling in 1 participant in the BNT162b2 group and swollen tongue in 1 participant in the placebo group were considered as related to the study intervention:

- In the BNT162b2 group, 1 participant experienced mild upper and lower lip swelling 14 and 19 days after Dose 1 which lasted 2 days before resolving and was considered as related to the study intervention. This same participant also experienced upper lip swelling and drug hypersensitivity 2 days after Dose 2, which were recovering/resolving as of the data cutoff date and were considered related to study intervention by the investigator.

- In the placebo group, 1 participant experienced moderate swollen tongue as well as moderate pharyngeal swelling 21 days after Dose 2; both resolved after 9 days; this participant also experienced moderate drug hypersensitivity and mild rash (on chin, elbows, knees, neck and back) 2 days after Dose 2 which lasted for 28 days and 30 days, respectively, and resolved. Swollen tongue as well as these other AEs were all considered related to the study intervention by the investigator.

Angioedema events in the other SMQs were all reported at low percentages in the BNT162b2 (≤0.02) and placebo groups (≤0.03%) (Table 73).

Arthritis

Overall, the number and percentage of participants with any unsolicited AE within the SMQ of arthritis was lower in the BNT162b2 group (35 [0.16%]) than in placebo group (48 [0.22%]) (Table 73). AEs were most frequently reported in the SOC of musculoskeletal and connective tissue disorders (0.13% BNT162b2 vs 0.21% placebo) with osteoarthritis the most frequently reported PT.

Convulsions

Overall, the number and percentage of participants with any unsolicited AE within the SMQ of convulsions was low and equal in the BNT162b2 group and placebo group (2 participants [0.01%] in each group) (Table 73). All events were in the SOC of nervous system disorders: seizure (2 participants in the BNT162b2 group) and generalized tonic-clonic seizure (1 participant in the placebo group).

Demyelination

Overall, the number and percentage of participants with any unsolicited AE within the SMQ of demyelination was low: 2 (0.01%) participants in the BNT162b2 group and 1 (0.00%) participant in the placebo group. All events were in the SOC of nervous system disorders.

Optic neuritis was observed in 2 participants in the BNT162b2 group and none in the placebo group; 1 case occurring in a male participant and 1 case occurring in a female participant. Both participants were in the younger age group. These events occurred 79 and 81 days after their last vaccination of BNT162b2. Both were considered not related to BNT162b2. Both events were reported as SAEs.

Guillain-Barre syndrome was reported as an SAE in 1 participant in the placebo group.

These events of optic neuritis and Guillain-Barre syndrome are also included in AESI analyses in Section 2.5.5.5.7.3.

Hypersensitivity

Overall, the number and percentage of participants with any unsolicited AE within the SMQ of hypersensitivity was higher in the BNT162b2 group (182 [0.83%]) than in the placebo group (161 [0.73%]) (Table 73). The difference was mainly due to skin and subcutaneous tissue disorders (134 [0.61%] BNT162b2 vs 119 [0.54%] placebo):

- rash (62 [0.28%] BNT162b2 vs 52 [0.24%] placebo)
- rash maculo-papular (7 [0.03%] BNT162b2 vs 4 [0.02%] placebo)
- rash papular (1 [0.00%] BNT162b2 vs 0 placebo).

Rash was assessed as related to study intervention at a higher IR in the BNT162b2 group (0.3) than in the placebo group (0.1).

In the SMQ of hypersensitivity in the SOC of infections and infestations: pustule and rash pustular were reported only in the BNT162b2 group by 3 participants (0.01%) and 2 participants (0.01%), respectively. In the SOC of injury, poisoning and procedural complications, administration related reaction (2 participants) and stoma site rash (1 participant) were reported only in the BNT162b2 group.

Additionally, in the SMQ of hypersensitivity in the SOC of gastrointestinal disorders, lip edema, lip swelling, swollen tongue, and tongue edema were observed more frequently in the BNT162b2 group versus the placebo group. Refer to the Angioedema section above for details.

Anaphylactic reaction was observed in 1 participant in the BNT162b2 group (refer to Section 2.5.5.5.7.1 for more detail).

In the SMQ of hypersensitivity in the SOC of investigations, increased blood IgE was observed in 1 participant in the BNT162b2 group.

Peripheral Neuropathy

Overall, the number and percentage of participants with any unsolicited AE within the SMQ of peripheral neuropathy was lower in the BNT162b2 group (3 [0.01%]) than in the placebo group (6 [0.03%]). All PTs were in the SOC of nervous system disorders (Table 73).

2.5.5.5.7.3. Other Sponsor-Identified Adverse Events of Special Interest

Additional terms beyond those designated by the CDC as AESIs were evaluated to assess potential imbalances in the BNT162b2 and placebo groups, and further characterized such an imbalance. PTs associated with these AE categories and by SOC/PT were identified during the blinded placebo-controlled follow-up period and presented (Table 74). These events are summarized below.

One death in the placebo group was captured as a potential AESI as there was no reported primary cause of death at the time of the data cutoff. This death is also captured in Table 67 in the analysis of deaths reported from Dose 1 to the unblinding date (Section 2.5.5.5.4.1).

From analysis of additional designated AESIs, individual categories are discussed below.

Table 74. Incidence Rates of at Least 1 Adverse Event Category of Special Interest From Dose 1 to Unblinding Date, by Adverse Event Category and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)							
	BNT162b2 (30 µg) (N[a]=21926, TE[b]=83.4)			Placebo (N[a]=21921, TE[b]=82.2)			Difference	
Adverse Event Category Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])	IRD (/100 PY)[f]	(95% CI[g])
ACUTE MYOCARDIAL INFARCTION								
Acute coronary syndrome	1	0.0	(0.0, 0.1)	4	0.0	(0.0, 0.1)	-0.04	(-0.09, 0.02)
Acute myocardial infarction	6	0.1	(0.0, 0.2)	4	0.0	(0.0, 0.1)	0.02	(-0.05, 0.10)
Coronary artery occlusion	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
Myocardial infarction	4	0.0	(0.0, 0.1)	8	0.1	(0.0, 0.2)	-0.05	(-0.13, 0.03)
ANAPHYLAXIS								
Anaphylactic reaction	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)	0.01	(-0.01, 0.04)
Anaphylactic shock	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
APPENDICITIS								
Appendicitis	14	0.2	(0.1, 0.3)	9	0.1	(0.1, 0.2)	0.06	(-0.06, 0.17)
Appendicitis perforated	1	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)	-0.00	(-0.03, 0.03)
Complicated appendicitis	0	0.0	(0.0, 0.0)	2	0.0	(0.0, 0.1)	-0.02	(-0.06, 0.01)

Table 74. Incidence Rates of at Least 1 Adverse Event Category of Special Interest From Dose 1 to Unblinding Date, by Adverse Event Category and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)							
	BNT162b2 (30 µg) (N[a]=21926, TE[b]=83.4)			Placebo (N[a]=21921, TE[b]=82.2)			Difference	
Adverse Event Category Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])	IRD (/100 PY)[f]	(95% CI[g])
ARTHRITIS/ARTHRALGIA								
Arthralgia	281	3.4	(3.0, 3.8)	122	1.5	(1.2, 1.8)	1.88	(1.41, 2.36)
Arthritis	6	0.1	(0.0, 0.2)	6	0.1	(0.0, 0.2)	-0.00	(-0.08, 0.08)
Arthritis reactive	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)	0.01	(-0.01, 0.04)
BELL'S PALSY								
Facial paralysis	4	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)	0.04	(-0.02, 0.09)
Facial paresis	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
COVID-19 DISEASE								
COVID-19	0	0.0	(0.0, 0.0)	13	0.2	(0.1, 0.3)	-0.16	(-0.24, -0.07)
COVID-19 pneumonia	1	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)	-0.00	(-0.03, 0.03)
DEATH								
Death	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
ENCEPHALOPATHY								
Toxic encephalopathy	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)	0.01	(-0.01, 0.04)
Uraemic encephalopathy	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)	0.01	(-0.01, 0.04)
GUILLAIN-BARRE SYNDROME								
Guillain-Barre syndrome	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
MULTISYSTEM INFLAMMATORY SYNDROME IN CHILDREN (MIS-C) AND IN ADULTS (MIS-A)								
Multiple organ dysfunction syndrome	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
MYOCARDITIS								
Myocarditis	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
NON-ANAPHYLACTIC ALLERGIC REACTIONS								
Angioedema	3	0.0	(0.0, 0.1)	2	0.0	(0.0, 0.1)	0.01	(-0.04, 0.06)
Hypersensitivity	2	0.0	(0.0, 0.1)	5	0.1	(0.0, 0.1)	-0.04	(-0.10, 0.03)
Lip swelling	2	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)	0.01	(-0.03, 0.05)
Pruritus	24	0.3	(0.2, 0.4)	20	0.2	(0.1, 0.4)	0.04	(-0.11, 0.20)
Rash	62	0.7	(0.6, 1.0)	52	0.6	(0.5, 0.8)	0.11	(-0.14, 0.36)
Rash pruritic	8	0.1	(0.0, 0.2)	6	0.1	(0.0, 0.2)	0.02	(-0.07, 0.11)

Table 74. Incidence Rates of at Least 1 Adverse Event Category of Special Interest From Dose 1 to Unblinding Date, by Adverse Event Category and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)							
	BNT162b2 (30 µg) (N[a]=21926, TE[b]=83.4)			Placebo (N[a]=21921, TE[b]=82.2)			Difference	
Adverse Event Category Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])	IRD (/100 PY)[f]	(95% CI[g])
Swelling face	2	0.0	(0.0, 0.1)	7	0.1	(0.0, 0.2)	-0.06	(-0.13, 0.01)
Swollen tongue	2	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)	0.01	(-0.03, 0.05)
Urticaria	18	0.2	(0.1, 0.3)	15	0.2	(0.1, 0.3)	0.03	(-0.10, 0.17)
OPTIC NEURITIS								
Optic neuritis	2	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)	0.02	(-0.01, 0.06)
PERICARDITIS								
Pericarditis	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)	0.01	(-0.01, 0.04)
PULMONARY EMBOLISM								
Pulmonary embolism	8	0.1	(0.0, 0.2)	8	0.1	(0.0, 0.2)	-0.00	(-0.10, 0.09)
SEIZURE/CONVULSION								
Generalised tonic-clonic seizure	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
Seizure	2	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)	0.01	(-0.03, 0.05)
STROKE, HEMORRHAGIC								
Haemorrhagic stroke	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
Intraventricular haemorrhage	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
Subarachnoid haemorrhage	4	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)	0.04	(-0.02, 0.09)
STROKE, ISCHEMIC								
Cerebellar infarction	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
Cerebral infarction	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
Cerebrovascular accident	4	0.0	(0.0, 0.1)	1	0.0	(0.0, 0.1)	0.04	(-0.02, 0.09)
Ischaemic stroke	2	0.0	(0.0, 0.1)	2	0.0	(0.0, 0.1)	-0.00	(-0.05, 0.05)
Transient ischaemic attack	2	0.0	(0.0, 0.1)	3	0.0	(0.0, 0.1)	-0.01	(-0.07, 0.04)
THROMBOCYTOPENIA								
Platelet count decreased	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)	0.01	(-0.01, 0.04)
Thrombocytopenia	1	0.0	(0.0, 0.1)	2	0.0	(0.0, 0.1)	-0.01	(-0.05, 0.03)
VACCINATION DURING PREGNANCY AND ADVERSE PREGNANCY OUTCOMES								
Abortion incomplete	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
Abortion spontaneous	2	0.0	(0.0, 0.1)	3	0.0	(0.0, 0.1)	-0.01	(-0.07, 0.04)
Abortion spontaneous incomplete	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
Exposure during pregnancy	30	0.4	(0.2, 0.5)	42	0.5	(0.4, 0.7)	-0.15	(-0.35, 0.05)

Table 74. Incidence Rates of at Least 1 Adverse Event Category of Special Interest From Dose 1 to Unblinding Date, by Adverse Event Category and Preferred Term – Blinded Placebo-Controlled Follow-up Period – Phase 2/3 Subjects ≥16 Years of Age – Safety Population

	Vaccine Group (as Administered)							
	BNT162b2 (30 µg) (N[a]=21926, TE[b]=83.4)			Placebo (N[a]=21921, TE[b]=82.2)			Difference	
Adverse Event Category Preferred Term	n[c]	IR (/100 PY)[d]	(95% CI[e])	n[c]	IR (/100 PY)[d]	(95% CI[e])	IRD (/100 PY)[f]	(95% CI[g])
Retained products of conception	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
VENOUS THROMBOEMBOLISM								
Coagulopathy	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)	0.01	(-0.01, 0.04)
Deep vein thrombosis	7	0.1	(0.0, 0.2)	7	0.1	(0.0, 0.2)	-0.00	(-0.09, 0.09)
Ophthalmic vein thrombosis	1	0.0	(0.0, 0.1)	0	0.0	(0.0, 0.0)	0.01	(-0.01, 0.04)
Penile vein thrombosis	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)
Venous thrombosis limb	0	0.0	(0.0, 0.0)	1	0.0	(0.0, 0.1)	-0.01	(-0.04, 0.01)

Note: MedDRA (v23.1) coding dictionary applied.
Note: The 95% confidence interval quantifies the precision of the incidence rate difference estimate. Confidence intervals are not adjusted for multiplicity. They should only be used to identify potentially important adverse events.
a. N = number of subjects in the specified group.
b. TE = total exposure time in 100 person-years across all subjects in the specified group. Exposure time for a subject is the time from Dose 1 to the end of blinded follow-up. This value is the denominator for the incidence rate calculation.
c. n = Number of subjects reporting at least 1 occurrence of the specified event.
d. Incidence rate (IR) is calculated as number of subjects reporting the event/total exposure time in 100 person-years (PY) across all subjects in the specified group.
e. 2-sided CI based on Poisson distribution.
f. Difference in incidence rate (BNT162b2 [30 µg] - placebo).
g. 2-sided Wald CI for the incidence rate difference.
PFIZER CONFIDENTIAL SDTM Creation: 25MAR2021 (20:15) Source Data: adae Table Generation: 16APR2021 (13:49)
(Cutoff Date: 13MAR2021, Snapshot Date: 25MAR2021) Output File:
./nda2 unblinded/C4591001 BLA1/adae s131 aesi cat p3 saf

Acute Myocardial Infarction

Acute myocardial infarctions were searched with the PTs of acute myocardial infarction, acute coronary syndrome, coronary artery occlusion, and myocardial infarction. A total of 11 events were identified in the BNT162b2 group (6 acute myocardial infarctions, 4 myocardial infarctions group, and 1 acute coronary syndrome) and a total of 17 event were identified in the placebo group (4 acute myocardial infarctions, 8 myocardial infarctions, 4 acute coronary syndromes, and 1 coronary artery occlusion). Most of these events had onset distant (ie, >30 days following) to receipt of vaccine or placebo. None of these events were assessed by the investigator as related to study intervention. Outcome was resolved in all participants in the BNT162b2 group; in the placebo group, outcome was fatal in 2 participants and resolved in remaining participants.

Anaphylaxis

Overall, the category of anaphylaxis included 1 participant with anaphylactic reaction in the BNT162b2 group and 1 participant with anaphylactic shock in the placebo group. These events are further described in Section 2.5.5.5.7.1.

Appendicitis

Overall, the category of appendicitis (including appendicitis perforated and complicated appendicitis) included 15 participants in the BNT162b2 group and 12 participants in the placebo group. These events are further described in Section 2.5.5.5.7.1.

Arthritis/Arthralgia

Arthralgia not associated with reactogenicity was evaluated starting from Day 8 after either dose of BNT162b2. The IR of arthralgia assessed from Day 8 (ie, beyond the 7-day reactogenicity period in which arthralgia is recorded in e-dairies for the reactogenicity subset) after each dose was lower in the BNT162b2 group (0.6) than in the placebo group (0.8).

Autoimmune Disease

There are no search term SMQ that would reliably capture all potential autoimmune diseases. Hence a comprehensive manual medical review of all reported AEs in the blinded placebo-controlled period was undertaken to identify PTs potentially indicative of autoimmune disease. These PTs are summarized by vaccine group.

In the BNT162b2 group there were 10 autoimmune disease cases identified. There were 1 case each in the BNT162b2 group: autoimmune thyroiditis, ulcerative colitis, Crohn's disease, reactive arthritis, fibromyalgia, systemic lupus erythematosus, alopecia areata, psoriasis, and 2 cases of psoriatic arthropathy.

In the placebo group there were 15 autoimmune cases identified. There were 1 case each in the placebo group: autoimmune thyroiditis, celiac disease, alopecia areata, psoriasis, Raynaud's phenomenon, and 2 cases of psoriatic arthropathy, 2 cases of psoriasis, 2 cases of ulcerative colitis, 2 cases of rheumatoid arthritis, 3 cases of fibromyalgia.

Bell's Palsy/Facial Paralysis

Overall, the category of Bell's Palsy (facial paralysis and facial paresis) included 4 participants in the BNT162b2 group and 2 participants in the placebo group during blinded placebo-controlled follow-up. These events are further described in Section 2.5.5.5.7.1.

Multiple Cases of COVID-19

There were 5 participants, all randomized to placebo, who developed 2 separate and clinically symptomatic instances of COVID-19 confirmed by NAAT at the central laboratory. All of the second confirmed COVID-19 cases occurred during the blinded period before their first dose of BNT162b2 (Dose 3), except for 1 participant who had a second COVID-19 diagnosis 4

days after receiving their second dose of BNT162b2. All participants were N-binding antibody negative prior to their first instance of COVID-19. The time interval between the first and second COVID-19 episode generally varied from 1 to 3 months.

Death

One death (placebo group) was captured as a potential AESI as there was no reported primary cause of death at the time of the data cutoff. This death is also captured in Table 67 in the analysis of deaths reported from Dose 1 to the unblinding date (Section 2.5.5.5.4.1).

Encephalopathy

Overall, the category of encephalopathy included 2 participants in the BNT162b2 group and none in the placebo group. One participant reported an SAE of toxic encephalopathy 64 days after Dose 2 in the setting of diverticulosis and a urinary tract infection, which resolved 8 days later, and the other participant reported an SAE of uremic encephalopathy 36 days after Dose 2, which resolved 3 days later. Both events were assessed by the investigator as not related to study intervention.

Guillain-Barre Syndrome

One participant in the placebo group reported an SAE of Guillain-Barre syndrome. This case was also captured as a CDC AESI in Section 2.5.5.5.7.2..

Multisystem Inflammatory Syndrome

One participant in the placebo group reported an SAE of multiple organ dysfunction syndrome.

Myocarditis

One case in the placebo group was reported.

Non-Anaphylactic Allergic Reactions

Overall, there was no imbalance in each of the PTs in non-anaphylactic allergic reactions (123 in the BNT162b2 group and 109 in the placebo group). Selected events are also captured as CDC AESIs under SMQ of Angioedema and Hypersensitivity in Section 2.5.5.5.7.2.

Optic Neuritis

Two participants in the BNT162b2 group reported an SAE each of optic neuritis. This case was also captured as a CDC AESI in Section 2.5.5.5.7.2.

Pericarditis

There was 1 participant in the older BNT162b2 age group with pericarditis. The event had an onset of 28 days after Dose 2, was ongoing at the data cutoff date, and was assessed by the investigator as not related to the study intervention.

Pulmonary Embolism

PTs associated with pulmonary embolism were searched in the blinded placebo-controlled period: pulmonary embolism, pulmonary thrombosis, pulmonary venous thrombosis, and pulmonary artery thrombosis. There were 8 cases of pulmonary embolism in the BNT162b2 group and 8 cases in the placebo group.

Stroke, Hemorrhagic

PTs associated with hemorrhagic stroke were searched in the blinded placebo-controlled follow-up period: hemorrhagic stroke, cerebral hemorrhage, hemorrhagic cerebral infarction, basal ganglia hemorrhage, brain stem hemorrhage, cerebellar hemorrhage, subarachnoid hemorrhage, and intraventricular hemorrhage.

Overall, there were 4 hemorrhagic strokes in the BNT162b2 and 3 in the placebo group. In the BNT162b2 group there were 4 subarachnoid hemorrhages and in the placebo group there was 1 subarachnoid hemorrhage, 1 intraventricular hemorrhage, and 1 hemorrhagic stroke.

Stroke, Ischemic

PTs associated with ischemic stroke were searched in the blinded placebo-controlled follow-up period: ischemic stroke, ischemic cerebral infarction, cerebral infarction, lacunar infarction, cerebral ischemia, cerebellar stroke, brain stem stroke, vertebrobasilar stroke, embolic stroke, thrombotic stroke, thrombotic and cerebral infarction, cerebral vascular accident, transient ischemic attack, and cerebellar infarction.

There were a total of 8 of these PTs in the BNT162b2 group and 8 in the placebo group. There were 2 ischemic strokes, 4 cerebral vascular accidents, 2 transient ischemic attacks identified in the BNT162b2 group. In the placebo group there are 2 ischemic strokes, 3 transient ischemic attacks, 1 cerebral vascular accident, 1 cerebral infarction and 1 cerebellar infarction.

Thrombocytopenia

PTs associated with thrombocytopenia were searched in the blinded placebo-controlled period and included thrombocytopenia and platelet count decreased. The BNT162b2 group had 1 case of thrombocytopenia and 1 case of platelet count decreased, and the placebo group had 2 cases of thrombocytopenia.

Vaccination During Pregnancy and Pregnancy Outcomes

There was no imbalance in the BNT162b2 group versus the placebo group with regard to pregnancy and maternal exposure. Pregnancy and maternal exposure reported during the study is discussed in Section 2.5.5.7.2.

Venous Thromboembolism

PTs associated with venous thromboembolism were searched in the blinded placebo-controlled period: cerebral venous sinus thrombosis, cerebral venous thrombosis, cerebral

thrombosis, superior sagittal sinus thrombosis, deep vein thrombosis, venous thrombosis limb, retinal vein thrombosis, retinal vein occlusion, mesenteric vein thrombosis, thrombosis mesenteric vessel, splenic thrombosis, splenic vein thrombosis, splenic embolism, visceral venous thrombosis, hepatic vein thrombosis, hepatic vein embolism, vena cava thrombosis, vena cava embolism, renal vein thrombosis, renal vein embolism, venous thrombosis, thrombosis, embolism, and thrombotic microangiopathy.

Overall, there were 9 thrombotic events in the BNT162b2 group and 9 in the placebo group. In the BNT162b2 group included 7 deep vein thromboses, 1 coagulopathy, and 1 ophthalmic vein thrombosis; and in the placebo group included 7 deep vein thromboses, 1 penile vein thrombosis, and 1 venous thrombosis limb (Table 74). None of the venous events were associated with thrombocytopenia.

2.5.5.6. Clinical Laboratory Evaluations

Clinical laboratory evaluations were conducted routinely during the Phase 1 part of Studies BNT162-01 and C4591001. No post-dose laboratory abnormalities were associated with clinical findings.

2.5.5.6.1. Clinical Laboratory Evaluations in Study BNT162-01

Details of clinical laboratory evaluations are provided in Module 5.3.5.1 BNT162-01 Interim CSR Section 12 and Module 2.7.4 and summarized below.

Clinical laboratory evaluations were performed in the Phase 1 part of Study BNT162-01 after Dose 1 and after Dose 2 for each vaccine candidate and dose level.

Clinical Chemistry

Clinical chemistry abnormalities were observed infrequently. No clinically relevant abnormalities were observed, except for slight elevations in C-reactive protein reported on Day 2 by 1 participant each in the 30 µg and 50 µg dose groups for BNT162b1 and on Day 8 by 1 participant in the 1 µg dose group for BNT162b2. These values returned to normal at the subsequent visit without any clinical consequences.

Hematology

The most commonly observed hematologic laboratory changes were transient decreases in lymphocytes noted 1-2 days after Dose 1. These decreases returned to normal by the subsequent study visit (by Day 8), without any clinical consequences or sequelae. Overall, the incidence of decreased lymphocyte counts was lower for BNT162b2 recipients compared with BNT162b1 recipients.

No additional clinically relevant hematologic laboratory changes were observed, except for a high lymphocyte count reported on Day 29 by 1 participant in the 1 µg dose group for BNT162b1, which was assessed as an AE considered as related to study intervention and as a clinically significant event. The event resolved 8 days after the second dose without any medication.

2.5.5.6.2. Clinical Laboratory Evaluations in Study C4591001

Details of clinical laboratory evaluations are provided in Module 5.3.5.1 C4591001 Efficacy Final Analysis Interim CSR Section 12.1.5 and Module 2.7.4 and summarized below.

Clinical laboratory evaluations were performed in the Phase 1 part of Study after Dose 1 and after Dose 2 for each vaccine candidate, dose level, and age group. Note that the younger group of participants (18 to 55 years of age) who received BNT162b1 at the 100 µg dose level did not receive a second dose at this level per IRC decision due to reactogenicity. This group instead received a second dose of 10 µg, and the 100 µg dose level was discontinued.

Clinical Chemistry

Clinical chemistry abnormalities were observed infrequently. No abnormalities were observed for BNT162b1, and only one abnormality was observed for BNT162b2: one younger participant in the 10 µg group had a grade 2 bilirubin abnormality at screening that was noted as grade 3 at 1 to 3 days after Dose 1 and then recovered to grade 1 by 6 to 8 days.

Hematology

The most commonly observed hematology laboratory changes were transient decreases in lymphocytes (<0.8 × LLN) noted 1 to 3 days after Dose 1. These decreases returned to normal by the next measurement, within 6 to 8 days of the first dose. Overall, the incidence of decreased lymphocyte counts was lower for BNT162b2 recipients compared with BNT162b1 recipients, and most decreases in lymphocyte counts were grade 1 or 2.

2.5.5.7. Other Safety Assessments

Details of other safety analysis results in Study C4591001 are provided in Module 2.7.4 and summarized below.

2.5.5.7.1. Severe COVID-19 Illness

Cases of COVID-19, both overall and those considered as severe, were evaluated per criteria described in Section 2.5.4.1.1.3. A description of severe COVID-19 cases evaluated for efficacy in Phase 2/3 is presented in Section 2.5.4.3.1.3.2 (interim analysis), Section 2.5.4.3.2.1.3.2 (final analysis), and Section 2.5.4.3.3 (updated analysis). The protocol had prespecified stopping rules that included monitoring of severe COVID-19 cases, and these stopping criteria were not met. These data show confinement of severe cases predominantly to the placebo group, suggesting no evidence for vaccine-associated enhanced disease (VAED) including vaccine-associated enhanced respiratory disease (VAERD).

2.5.5.7.2. Pregnancies

At the time of the data cutoff date (13 March 2021), a total of 50 participants who had received BNT162b2 had reported pregnancies, including 42 participants originally randomized to the BNT162b2 group and 8 participants originally randomized to the placebo group who then received BNT162b2. In total, 12 participants (n=6 each in the randomized BNT162b2 and placebo groups) withdrew from the blinded placebo-controlled vaccination period of the study due to pregnancy, and 4 participants originally randomized to placebo

who then received BNT162b2 withdrew from the open-label vaccination period due to pregnancy (Table 54). These participants continue to be followed for pregnancy outcomes. No births have been reported from individuals who have become pregnant in Study C4591001 as of the time of this submission.

2.5.5.7.3. Adverse Drug Reactions

Adverse reactions (ADRs) were identified from Study C4591001 Phase 2/3 safety data and are detailed in Module 2.7.4. ADRs are defined as AEs for which there is reason to conclude the vaccine was the cause of the event; this ADR review also included reactogenicity terms.

The CIOMS frequency categories for adverse reactions are as follows:

- Very common: ≥10%
- Common: ≥1% and <10%
- Uncommon: ≥0.1% and <1%
- Rare: ≥0.01% and <0.1%
- Very rare: <0.01%.

Reactogenicity ADRs that occurred with a very common frequency, based on any dose in the BNT162b2 group from the reactogenicity subset of data as of 13 March 2021, are:

- Injection site pain: 4153/4924 (84.3%)
- Fatigue: 3185/4924 (64.7%)
- Headache: 2814/4924 (57.1%)
- Muscle pain: 1980/4924 (40.2%)
- Chills: 1707/4924 (34.7%)
- Joint pain: 1232/4924 (25.0%)
- Fever: 749/4924 (15.2%)
- Injection site swelling: 546/4924 (11.1%).

A reactogenicity ADR that occurred with a common frequency, based on any dose in the BNT162b2 group from the reactogenicity subset of data as of 13 March 2021, was:

- Injection site redness: 486/4924 (9.9%)

ADRs considered as common (nausea) and uncommon (lymphadenopathy and malaise) in the BNT162b2 group were identified from AE data in the safety population as of 13 March 2021, compared to placebo for reference:

- Nausea: 274/21,926 (1.2%) in BNT162b2 vs 87/21,921 (0.4%) in placebo
- Lymphadenopathy: 83/21,926 (0.4%) in BNT162b2 vs 7/21,921 (0.0%) in placebo
- Malaise: 130/21,926 (0.6%) in BNT162b2 vs 22/21,921 (0.1%) in placebo

The following additional ADRs were identified in the post-authorization setting. Frequencies for these ADRs were obtained from clinical study data (Study C4591001) when possible, as per labeling guidance.

- Diarrhea (very common)
- Vomiting (common)
- Pain in Extremity (uncommon)
- Rash (uncommon)
- Pruritus (uncommon)
- Urticaria (uncommon)
- Angioedema (rare)
- Anaphylaxis (unknown).

It should be noted that at the time of conditional approval of BNT162b2 by the EMA, the sponsor was requested to include the following as ADRs in the Summary of Product Characteristics (SmPC) even though they were not considered ADRs in the Core Data Sheet (CDS). The frequencies in the initial EMA-approved SmPC reflected data from the initial conditional approval submission (data cutoff date: 14 November 2020):

- Acute peripheral facial paralysis 3/18801 = 0.02% (rare)
- Injection site pruritus 27/18801 = 0.1% (uncommon)
- Insomnia 23/18801 = 0.1% (uncommon).

The following ADRs have been identified from the clinical study data and are supported by reports in the post-authorization setting; the CIOMS frequency category for these reactions is uncommon (based on clinical data from Study C4591001): lethargy, asthenia, decreased appetite, hyperhidrosis, and night sweats. These ADRs will be added to the CDS and subsequently proposed for all BNT162b2 labels. The additional ADRs further characterize the safety profile of BNT162b2 but do not impact its favorable risk:benefit profile.

2.5.5.8. Safety in Special Groups and Situations

Details of safety in special groups and situations are provided in Module 2.7.4 and summarized below.

2.5.5.8.1. Geriatric Use

Clinical studies of BNT162b2 (30 µg) include participants ≥65 years of age whose data contribute to overall assessment of safety and efficacy. The clinical data have demonstrated a predominantly mild reactogenicity profile in older adults, overall and compared with younger adults. This is coupled with evidence of robust immune response following the two-dose vaccination regimen, and overwhelming efficacy comparable to younger adults (>90%).

2.5.5.8.2. Pediatric Use

Further study of pediatric use of the vaccine and/or immunobridging study will be undertaken to characterize the vaccine response in children.

2.5.5.8.3. Use During Pregnancy and Lactation

Women who were pregnant or breastfeeding were not eligible to participate in Studies BNT162-01 or C4591001.

There were no pregnancies reported in Study BNT162-01 as of the data cutoff date for the BNT162-01 Phase 1 Interim CSR. At the time of the most recent data cutoff in Study C4591001 (13 March 2021), a total of 50 participants had reported pregnancies in the safety database (Section 2.5.5.7.2). These participants continue to be followed for pregnancy outcomes.

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. Available data on BNT162b2 administered to pregnant women are insufficient to inform vaccine-associated risks in pregnancy. In a DART study, no vaccine-related adverse effects on female fertility, fetal development, or postnatal development were reported.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for vaccination with BNT162b2 and any potential adverse effects on the breastfed child from BNT162b2 or from the underlying maternal condition. For preventive vaccines, the underlying maternal condition is susceptibility to disease prevented by the vaccine.

2.5.5.8.4. Use in Immunocompromised Individuals

Individuals who are immunocompromised or taking immunosuppressive therapy at the time of vaccine administration may have diminished response to immunization. Study C4591001 included enrollment of individuals with medical history of immunocompromised condition or immunosuppressive therapy (Section 2.5.5.5.1). There are limited data on the safety and effectiveness of the vaccine in this patient population at the time of this submission.

2.5.5.8.5. Other Safety Considerations

Overdose

In Study C4591001, any dose of study intervention exceeding 30 µg within a 24-hour time period was considered an overdose (refer to Module 5.3.5.1 C4591001 Protocol Section 8.4). An error in dilution during the study resulted in 52 participants receiving a higher than intended dose of BNT162b2: instead of receiving 30 µg, an actual dose of 58 µg BNT162b2 was administered. These participants did not report an increase in reactogenicity or AEs.

Drug Abuse and Withdrawal and Rebound

Not applicable for BNT162b2.

Effects on Ability to Drive or Operate Machinery or Impairment of Mental Ability

BNT162b2 has no or negligible influence on the ability to drive and use machines.

2.5.5.9. Post-Authorization Safety Summary

Post-authorization safety data are continually monitored by Pfizer and BioNTech for pharmacovigilance and risk management purposes. Pfizer's safety database contains cases of AEs reported spontaneously to Pfizer, cases reported by the health authorities, cases published in the medical literature, cases from Pfizer-sponsored marketing programs, non-interventional studies, and cases of serious AEs reported from clinical studies regardless of causality assessment. Through 28 February 2021, there were a total of 42,086 case reports

(25,379 medically confirmed and 16,707 non-medically confirmed) containing 158,893 events. Cases were received from 63 countries.

Consistent with events in Phase 2/3 of Study C4591001, most reported AEs were in SOCs with reactogenicity events: general disorders and administration site conditions (51,335), nervous system disorders (25,957), musculoskeletal and connective tissue disorders (17,283), and gastrointestinal disorders (14,096). Post-authorization data have also informed the addition of ADRs related to the experience of reactogenicity to product labeling (see Section 2.5.5.7.3 for additional information regarding ADRs).

Aside from addition of anaphylaxis and hypersensitivity, the analyses of cumulative post-authorization safety data, including a review of AESIs, are consistent with the analysis of the pivotal clinical study (C4591001). Review of post-authorization data has not revealed any novel safety concerns except for anaphylaxis and has confirmed the favorable benefit-risk profile of the vaccine.

Further details regarding the cumulative analysis of post-authorization safety data are presented in Module 5.3.6.

2.5.5.10. Safety Conclusions

Phase 1

Based on Phase 1 data from the FIH Study BNT162-01, BNT162b1 and BNT162b2 were safe and well-tolerated in healthy adults 18 to 55 years of age, with no unanticipated safety findings. Reactogenicity and AEs tended to increase in incidence and/or severity with increasing dose of BNT162b2. Reactogenicity was mostly mild to moderate and short-lived after dosing (eg, arose and resolved within the first 1 to 2 days after dosing), and the AE profile and clinical laboratory results did not suggest any safety concerns.

Based on Phase 1 data from Study C4591001 and Study BNT162-01, BNT162b1 and BNT162b2 were safe and well-tolerated in younger healthy adults 18 to 85 years of age, with no unanticipated safety findings. Reactogenicity and AEs were generally milder and less frequent in participants in the older group compared with the younger group and overall tended to increase with increasing BNT162b2 dose. Reactogenicity was mostly mild to moderate and short-lived after dosing, and the AE profile did not suggest any safety concerns, including up to approximately 6 months after Dose 2 for BNT162b2 30 µg groups. Clinical laboratory evaluations showed a transient decrease in lymphocytes that was observed in all age and dose groups after Dose 1, which resolved within approximately 1 week, were not associated with any other clinical sequelae, and were not considered clinically relevant.

RNA vaccines are known to induce type I interferon,[22] and type I interferons regulate lymphocyte recirculation and are associated with transient migration and/or redistribution of lymphocytes.[23] This rapid rebound of lymphocytes supports that the lymphocytes are not depleted, but temporarily migrated out of the peripheral blood, and subsequently re-entered the bloodstream by the time of the next assessment.

Phase 2/3

Based on Phase 2/3 data from approximately 44,000 participants ≥16 years of age with up to at least 6 months of follow-up after Dose 2 in Study C4591001, BNT162b2 at 30 µg was safe and well-tolerated across age groups. Reactogenicity and AEs were generally milder and less frequent in participants in the older group (>55 years of age) compared with the younger group (≤55 years of age). Reactogenicity was mostly mild to moderate and short-lived after dosing for both younger and older age groups (ie, median onset between 1 to 4 days after dosing and resolution within 1 to 2 days after onset), and the AE profile did not suggest any serious safety concerns. The incidence of SAEs and deaths were low in the context of the number of participants enrolled and comparable in BNT162b2 and placebo. The incidence of discontinuations due to AEs was also generally low and similar between BNT162b2 and placebo groups.

Cumulative safety follow-up to at least 6 months after Dose 2 for approximately 12,000 Phase 2/3 participants originally randomized to BNT162b2, comprising the combined blinded and open-label periods, showed no new safety signals or suggested and new safety concerns arising from this period of follow-up.

Similarly, open-label follow-up of participants originally randomized to placebo from the time of unblinding to receive BNT162b2 until the data cutoff date showed no new safety signals or concerns.

Safety analysis results for subgroups based on demographics (age, race, ethnicity, and sex) and by baseline SARS-CoV-2 status (positive vs negative) have not shown any clinically important differences in the BNT162b2 safety profile. Analysis of the subset of individuals with stable HIV did not suggest any safety concerns in this population. Analysis of participants originally randomized to placebo who then received BNT162b2 (Dose 3) by demographic subgroups and based on prior evidence of SARS-CoV-2 infection or prior COVID-19 illness did not suggest any safety concerns.

Phase 2/3 safety data were generally concordant with safety data in Phase 1 of the study, both overall and with regard to younger and older participants.

2.5.6. Benefits and Risks Conclusions

2.5.6.1. Benefits

COVID-19 is a serious and potentially fatal or life-threatening human infection. Based on clinical data to date, it is expected that BNT162b2 (30 µg) will elicit an immune response that is likely to protect against COVID-19. The total duration of any such protection is currently unknown.

Vaccine Efficacy

Efficacy of BNT162b2 (30 µg) to prevent COVID-19 was overwhelmingly demonstrated at the first interim analysis of 94 cases (data cutoff date: 04 November 2020), with a VE of 95.5% (with a 2-sided 95% credible interval of 88.8% to 98.4%) in pivotal Study C4591001 Phase 3 participants who had no prior evidence of SARS-CoV-2 infection, which met the

protocol prespecified success criteria for the first primary endpoint. This was confirmed in the final analyses of 170 cases reported in participants without evidence of past SARS-CoV-2 infection before or during the vaccination regimen, with VE of 95.0% (data cutoff date: 14 November 2020).

Overall, the observed VE in each demographic subgroup in the final analysis, as defined by age, sex, race, ethnicity, and country, was >90% in the interim and final analyses, and additional post hoc analyses of at-risk subgroups also showed high VE, consistent with broad effectiveness of BNT162b2 to protect vaccinees against COVID-19. Severe cases were predominantly confined to the placebo group.

In the final analysis, among participants without evidence of past SARS-CoV-2 infection before and during the 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 after Dose 2 in the study.

In the all-available population of the final analysis, 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. Efficacy against severe COVID-19 was similar when applying the CDC definition of severe, which includes a general criterion of hospitalization.

Efficacy final analyses counting COVID-19 occurring at least 14 days after Dose 2 resulted in similar efficacy estimates as the 7-day efficacy analyses. Moreover, the analyses of efficacy using CDC-defined symptoms gave similar efficacy estimates as the definition used in other primary and secondary endpoints.

Duration of Protection

Updated analyses of efficacy for cases occurring confirmed from at least 7 days after Dose 2 and accrued up to the submission cutoff date (13 March 2021), which represents up to approximately 6 months of blinded follow-up after Dose 2, included estimated VE of 91.3% and 91.1% for evaluable efficacy populations without and with or without past evidence of SARS-CoV-2 infection before or during the vaccination regimen. During this same follow-up period, VE against severe COVID-19 occurring at least 7 days after Dose 2 was 95.3% in participants with or without prior evidence of SARS-CoV-2 infection when applying FDA criteria for severe disease and was 100.0% when applying the CDC definition of severe disease.

High VE (>90%) has continued to be observed for participants across most subgroups defined by demographics, at-risk status (including obesity and Charlson comorbidities), and geography (including in countries where SARS-CoV-2 variants are in predominant circulation). Note that sequencing of SARS-CoV-2 strains from breakthrough cases in the BNT162b2 group is in progress to determine which strains were the cause of COVID-19 as compared to the placebo group and will be submitted at a later time. Few confirmed cases

were reported in the subgroup of baseline SARS-CoV-2 positive participants, precluding a meaningful determination of VE in this subset.

Vaccine-Elicited Immune Response

Immunogenicity data from Phase 1 and Phase 2 participants have shown robust humoral and T cell-mediated immune responses after vaccination with 2 doses of BNT162b2 at 30 µg in both younger and older adults. This immunogenicity has been shown to be maintained up to 6 months after the second dose for Phase 1 participants inclusive of functional neutralizing and antigen-binding antibodies and T cell responses and was evident up to 1 month after Dose 2 in Phase 2 adult participants. Analyses of Phase 2 participants included a small number of individuals with evidence of prior SARS-CoV-2 infection, for whom vaccine induced neutralizing and antigen-binding antibodies were substantially further boosted after BNT162b2 vaccination.

Overall Benefits

Taken together, efficacy and immunogenicity data suggest the BNT162b2 (30 µg) 2-dose regimen induces a strong immune response and provides durable protection from COVID-19 across a spectrum of individuals representative of the population at large for individuals ≥16 years of age: those with or without prior exposure to SARS-CoV-2 and those in higher risk categories based on age, race, ethnicity, and/or comorbidity.

2.5.6.2. Risks

Reactogenicity Profile

The Phase 2/3 reactogenicity profile was typically mild to moderate, arose within the first 1 to 4 days after dosing, and reactions were short-lived. The most common prompted local reaction was injection site pain. The most common prompted systemic events reported in Phase 2/3 included fatigue, headache, muscle and joint pain, and chills.

Adverse Event Profile

The AE profile among approximately 44,000 participants ≥16 years of age enrolled to date as of the most recent safety cutoff date (13 March 2021), was mostly reflective of reactogenicity events with low incidences of severe and/or related events. The incidence of SAEs was low and similar in the vaccine and placebo groups. Few participants withdrew from the study due to AEs. Few deaths occurred overall in both the vaccine and placebo groups with no imbalance. Review of AEs of clinical interest have suggested no clear patterns or safety concerns.

Safety analyses up to at least 6 months after Dose 2 for participants who were randomized to BNT162b2, inclusive of cumulative blinded and open-label data, showed no new safety findings or signals over a longer duration of follow-up.

For participants randomized to placebo and then unblinded to receive BNT162b2 vaccination, open-label data from the time of unblinding to the data cutoff date (13 March 2021) showed no new safety findings or signals. Open-label safety data for participants originally

randomized to placebo who were unblinded to receive BNT162b2 followed generally similar patterns relative to those who were originally randomized to BNT162b2 during blinded follow-up. This supports the overall consistency of the safety profile of the BNT162b2 30 µg two-dose vaccination regimen across study phases and follow-up periods.

Safety analyses of study participants across various demographic subgroups, by baseline SARS-CoV-2 prior infection status, and with stable HIV have not shown any clinically important differences in the BNT162b2 safety profile for the duration of blinded follow-up.

Study participants will continue to be followed for 2 years or end of study.

Severe Disease

As of the most recent safety cutoff date (13 March 2021), representing up to 6 months of follow-up after Dose 2, the reported cases of COVID-19 considered per FDA criteria as severe from Dose 1 onwards included 1 case in the BNT162b2 group and 30 cases in the placebo group; according to CDC criteria, from Dose 1 onwards this included 1 case in the BNT162b2 group and 45 cases in the placebo group. The case split between the study groups using either definition for severe disease suggests no evidence of VAED or VAERD.

Post-Authorization Safety

From December 2020 until April 2021, >100 million doses of BNT162b2 have been administered to individuals ≥16 years of age in the US under EUA.[24,25] It is reassuring that the most commonly reported AEs in the post-authorization review (which includes global reporting; see Section 2.5.5.9) reflect the same profile observed in the blinded placebo-controlled follow-up period of the pivotal clinical study, primarily reflecting short-lived and resolving reactogenicity events. Further, the same pattern was observed for pivotal study participants originally randomized to the placebo group who were unblinded (per protocol) to receive BNT162b2: these participants, in the open-label setting, also reported mostly reactogenicity events similar to those in the blinded follow-up. AEs of clinical interest were not reported frequently in the controlled clinical study and continue to be evaluated in the post-authorization setting.

Overall Safety Profile

Overall, BNT162b2 recipients had a similar or more favorable systemic reactogenicity profile compared with other vaccines that are widely used in clinical settings. Local reactions for BNT162b2 are comparable or less than those seen with other licensed vaccines (eg, Shingrix®, Trumenba®, pneumococcal polysaccharide and pneumococcal conjugate vaccines) in matching age groups; systemic events, particularly chills and fever, were observed more frequently after BNT162b2 compared to the other vaccines, but in a tolerable range with very few withdrawals related to such events (see Section 2.5.5.5.2).

2.5.6.3. Benefit-Risk Conclusions

The available clinical evidence for BNT162b2 (30 µg) effectiveness includes induction of strong immune responses and overwhelmingly high vaccine efficacy, suggesting the vaccine confers protection against COVID-19 in individuals ≥16 years of age.

The potential risks are based on the observed safety profile to date, which shows mostly mild reactogenicity, low incidence of severe or serious events, and no clinically concerning safety observations or safety concerns. The vaccine appears to be safe and well-tolerated across the safety population comprising approximately 44,000 study participants ≥16 years of age, among whom approximately 12,000 have been followed for at least 6 months after completing the two-dose regimen. Safety analyses have also included demographic subgroups based on age, sex, race, ethnicity, and baseline SARS-CoV-2 status and the subset with stable HIV. The confinement of severe cases of COVID-19 predominantly to the placebo group versus the BNT162b2 group suggests no evidence of VAED. Post-authorization safety review reinforces that BNT162b2 is safe and tolerable.

Vaccine efficacy was remarkably high, ≥95% for participants without prior evidence of SARS-CoV-2 infection and >94% for those with or without prior infection, in the prespecified interim and/or final analyses. Updated analyses with all confirmed cases accrued up to approximately 6 months after Dose 2 showed persistence of protection with estimated VE of ≥91.1%. Overall, observed VE was >90% across subgroups identified by age, sex, race, ethnicity, country, and risk factors and remained high in the updated analysis. Severe cases have been confined overwhelmingly to the placebo group in all efficacy analyses. Efficacy data suggest highly effective protection against COVID-19 in a broad population of individuals across demographic characteristics, with durable immune responses and protection from COVID-19 disease observed up to approximately 6 months after completing the vaccination regimen.

Mass immunization with a safe and effective vaccine against COVID-19 can dramatically alter the trajectory of the pandemic. According to policy briefing by the Institute for Health Metrics and Evaluation published on 31 March 2021, COVID-19 remains a leading cause of death in the US with up to 100,000 additional deaths per month projected in the US between March and July 2021, many of which can likely be prevented with COVID-19 vaccination.[26,27]

Vaccination against COVID-19 began with EUA/conditional approvals in December 2020, in a phased rollout defined by national/regional guidance. However, there continue to be concerning trends that may counteract the impacts of this vaccination effort, including:

- limitations in access to obtaining a vaccine due to infrastructure challenges (ie, clinic and appointment capacity and systems)[28]
- increasing viral transmission fueled by relaxed compliance with mitigations as the pandemic surpasses the 1-year mark (ie, masks, physical distancing, limiting travel)[26,28]
- increasing circulation of emerging variants of concern (which are currently driving continued spread of viral infection in Europe despite extensive mitigation mandates).[26,28]

A vaccine program must be implemented expediently and rapidly expanded to have a significant impact on the pandemic course.[27,29] Licensure of BNT162b2 is likely to enhance vaccine uptake by facilitating supply of vaccine from Pfizer/BioNTech directly to pharmacies and healthcare providers/facilities. The greatest impact of BNT162b2 licensure may be direct supply to healthcare providers who serve vulnerable populations such as elderly patients and those who live in rural and underserved communities (ie, individuals who might be unable to navigate the challenges of securing vaccine access using the systems in place for EUA). Expansion of vaccine via licensure would ultimately improve the prospect of achieving population herd immunity to bring the pandemic under control.[30]

Overall, the potential risks and benefits, as assessed by the safety profile and the efficacy and immunogenicity of BNT162b2 (30 µg), are balanced in favor of the potential benefits to prevent COVID-19 in immunized individuals. Likewise, the BNT162b2 30 µg benefit and risk profile supports further development in pediatric, maternal, and other at-risk populations.

2.5.7. References

1 Virus Pathogen Database and Analysis Resource (ViPR). Available at: https://www.viprbrc.org/brc/viprStrainDetails.spg?ncbiAccession=MN908947&decorator=corona. Accessed 11 August 2020.

2 Zhu N, Zhang D, Wang W, et al. A novel coronavirus from patients with pneumonia in China, 2019. N Engl J Med 2020;382:727-33.

3 Johns Hopkins University Coronavirus Resource Center. Available at: https://coronavirus.jhu.edu/map.html. Accessed 23 April 2021.

4 Wiersinga WJ, Rhodes A, Cheng AC, et al. Pathophysiology, transmission, diagnosis, and treatment of Coronavirus Disease 2019 (COVID-19). JAMA 2020; [ePub]doi:10.1001/jama.2020.12839.

5 Centers for Disease Control and Prevention (CDC). Coronavirus Disease (COVID-19). Available at: https://www.cdc.gov/coronavirus/2019-ncov/symptoms-testing/symptoms.html. Accessed 11 August 2020.

6 Onder G, Rezza G, Brusaferro S. Case-fatality rate and COVID-19 death characteristics in Italy. JAMA 2020;[ePub]:doi:10.1001/jama.2020.4683.

7 Wu Z, McGoogan JM. Characteristics of and important lessons from the Coronavirus Disease 2019 (COVID-19) outbreak in China. JAMA 2020; [ePub]:doi:10.1001/jama.2020.2648.

8 Infectious Diseases Society of America Guidelines on the Treatment and Management of Patients with COVID-19. Available at: https://www.idsociety.org/practice-guideline/covid-19-guideline-treatment-and-management. Accessed 02 March 2021.

9 Vogel AB, Lambert L, Kinnear E, et al. Self-amplifying RNA vaccines give equivalent protection against influenza to mRNA vaccines but at much lower doses. Mol Ther 2018;26(2):446-55.

10 Moyo N, Vogel AB, Buus S, et al. Efficient induction of T cells against conserved HIV-1 regions by mosaic vaccines delivered as self-amplifying mRNA. Mol Ther Methods 2019;12:32-46.

11 Pardi N, Hogan MJ, Pelc RS, et al. Zika virus protection by a single low-dose nucleoside-modified mRNA vaccination. Nature 2017;543(7644):248-51.

12 Kirchdoerfer RN, Wang N, Pallesen J, et al. Stabilized coronavirus spikes are resistant to conformational changes induced by receptor recognition or proteolysis. Sci Rep 2018;8(1):15701.

13 Wrapp D, Wang N, Corbett KS, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science 2020;367(6483):1260-63.

14 Pallesen J, Wang N, Corbett KS, et al. Immunogenicity and structures of a rationally designed prefusion MERS-CoV spike antigen. Proc Natl Acad Sci 2017;114(35):E7348-57.

15 Lambert, P-H, Ambrosino DM, Andersen SR, et al. Consensus summary report for CEPI/BC March 12-13, 2020 meeting: Assessment of risk of disease enhancement with COVID-19 vaccines. Vaccine 2020; 38:4783-91; doi:10.1016/j.vaccine.2020.05.064.

16 Vogel AB, Kanevsky I, Che Y, et al. A prefusion SARS-CoV-2 spike RNA vaccine is highly immunogenic and prevents lung infection in non-human primate. 2020; published online at https://www.biorxiv.org/content/10.1101/2020.09.08.280818v1.

17 US Food and Drug Administration. Development and Licensure of Vaccines to Prevent COVID-19. Guidance for Industry. June 2020. Available at: https://www.fda.gov/media/139638/download

18 Centers for Disease Control and Prevention (CDC). Coronavirus Disease (COVID-19). Available at: https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-with-medical-conditions.html. Accessed 09 December 2020.

19 Walsh EE, Frenck RW Jr, Falsey AR, et al. Safety and immunogenicity of two RNA-based Covid-19 vaccine candidates. N Engl J Med. 2020;[ePub]:doi: 10.1056/NEJMoa2027906.

20 Mulligan MJ, Lyke KE, Kitchin N, et al. Phase I/II study of COVID-19 RNA vaccine BNT162b1 in adults. Nature 2020;586(7830):589-93. [ePub]doi:10.1038/s41586-020-2639-4.

21 US Food and Drug Administration, Guidance for Industry Toxicity Grading Scale for Healthy Adult and Adolescent Volunteers Enrolled in Preventive Vaccine Clinical Trial. Available at: https://www.fda.gov/media/73679/download

22 Kranz LM, Diken M, Haas H, et al. Systemic RNA delivery to dendritic cells exploits antiviral defence for cancer immunotherapy. Nature 2016;534, 396-401.

23 Kamphuis E, Junt T, Waibler Z, et al. Type I interferons directly regulate lymphocyte recirculation and cause transient blood lymphopenia. Blood 2006;108(10):3253-61.

24 Centers for Disease Control and Prevention (CDC). COVID-19 Data Tracker. Available at: https://covid.cdc.gov/covid-data-tracker/#vaccinations. Accessed 23 April 2021.

[25] Coronavirus (COVID-19) Vaccinations – Statistics and Research – Our World in Data. Available at: https://ourworldindata.org/covid-vaccinations#which-vaccines-have-been-administered-in-each-country. Accessed 23 April 2021.

[26] Institute for Health Metrics and Evaluation. COVID-19 policy briefings: United States of America COVID-19 results briefing. 31 March 2021. Available at: http://www.healthdata.org/sites/default/files/files/Projects/COVID/2021/102_briefing_United_States_of_America_11.pdf. Accessed 07 April 2021.

[27] Biggerstaff M. Oct 2020 ACIP meeting. Available at: https://www.cdc.gov/vaccines/acip/meetings/slides-2020-10.html

[28] Coronavirus (COVID-19) Vaccinations – Statistics and Research – Our World in Data. Available at: https://ourworldindata.org/covid-vaccinations#vaccination-policies. Accessed 07 April 2021.

[29] Biggerstaff M, Reed C, Swerdlow D, et al. Estimating the potential effects of a vaccine program against an emerging influenza pandemic—United States. Clinical Infectious Diseases 2015;60(S1):S20-9.

[30] Anderson R, Vegvari C, Truscott J, Collyer BS. Challenges in creating herd immunity to SARS-CoV-2 infection by mass vaccination. Lancet 2020;[ePub]:doi.org/10.1016/S0140-6736(20)32318-7.

Document Approval Record

Document Name:	COVID-19 Vaccine 2.5 Clinical Overview - Initial Adult BLA Submission (2021)
Document Title:	COVID-19 Vaccine 2.5 Clinical Overview - Initial Adult BLA Submission (2021)

Signed By:	Date(GMT)	Signing Capacity
Perez, John	30-Apr-2021 20:12:52	Final Approval