CLINICAL STUDY REPORT SYNOPSIS

SYNOPSIS

Study Title: Final Report: A Phase 2/3, Placebo-Controlled, Randomized, Observer-Blind Study to Evaluate the Safety, Tolerability, and Immunogenicity of a SARS-CoV-2 RNA Vaccine Candidate (BNT162b2) Against COVID-19 in Healthy Pregnant Women 18 Years of Age and Older

Study Number: C4591015

Regulatory Agency or Public Disclosure Identifier Number:

European Union Drug Regulating Authorities Clinical Trials Database (EudraCT) Number: 2020-005444-35

ClinicalTrials.gov ID: NCT04754594

Study Phase: Phase 2/3

Name of Study Intervention: PF-07302048 (BNT162b2)

Trade Name: Comirnaty®

Name of Sponsor/Company: BioNTech SE

Clinical Study Report (CSR) Version and Report Date: Version 1.0 (22 May 2024)

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

This study was conducted at 41 sites in Brazil (3), South Africa (5), Spain (6), the UK (6), and the US (21). A list of study centers and investigators involved in this study is provided in Appendix 16.1.4.1.

Publications:

Not Applicable.

Study Period:

Study Initiation Date (first participant first visit [FPFV]): 16 February 2021

Study Completion (last participant last visit [LPLV]) Date: 15 July 2022

CLINICAL STUDY REPORT SYNOPSIS

Enrollment in this study was terminated on 25 October 2021 due to changes in the universal recommendations for coronavirus disease 2019 (COVID-19) vaccination of pregnant women with approximately 350 participants enrolled.

Rationale:

The purpose of the study was to describe the safety, tolerability, and immunogenicity of BNT162b2 ribonucleic acid (RNA)-based COVID-19 vaccine against COVID-19 in healthy pregnant women.

Pregnant women are at risk of acquiring SARS-CoV-2 infection, developing COVID-19 and COVID-19–associated complications. Given the global crisis of COVID-19 and fast expansion of the disease globally, the rapid development of an effective vaccine for use in this population is of utmost importance.

Objectives, Endpoints, and Statistical Methods:

Objectives, estimands, and endpoints for maternal participants and infants born to maternal participants are listed in Table S1 below:

Table S1. Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints
Primary Safety	**Primary Safety**	**Primary Safety**
To describe the safety and tolerability of prophylactic BNT162b2 when administered to maternal participants 18 years of age or older vaccinated at 24 to 34 weeks' gestation.	In maternal participants receiving at least 1 dose of study intervention from each vaccine group, the percentage of maternal participants reporting: • Local reactions for up to 7 days following each dose • Systemic events for up to 7 days following each dose adverse events (AEs) from Dose 1 through 1 month after Dose 2 • Serious adverse events (SAEs) from Dose 1 through 1 month after delivery	• Prompted local reactions (redness, swelling, and pain at the injection site) • Prompted systemic events (fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain) • AEs • SAEs

CLINICAL STUDY REPORT SYNOPSIS

Table S1. Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints
Primary Immunogenicity	**Primary Immunogenicity**	**Primary Immunogenicity**
To describe the immune response to prophylactic BNT162b2 in maternal participants 18 years of age or older vaccinated at 24 to 34 weeks' gestation and reference to the immune response in nonpregnant women 18 years of age or older from the C4591001 study without evidence of past severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection.	In female participants complying with the key protocol criteria (evaluable participants) and no serological or virological evidence (up to 1 month after receipt of the second dose) of past SARS-CoV-2 infection: • Geometric mean ratio (GMR), estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in pregnant women to those in nonpregnant women 1 month after Dose 2	• SARS-CoV-2 neutralizing titers
To describe the immune response to prophylactic BNT162b2 in maternal participants 18 years of age or older vaccinated at 24 to 34 weeks' gestation and reference to the immune response in nonpregnant women 18 years of age or older from the C4591001 study with and without evidence of prior SARS-CoV-2 infection.	In female participants complying with the key protocol criteria (evaluable participants): • GMR, estimated by the ratio of the geometric mean of SARS-CoV-2 neutralizing titers in pregnant women to those in nonpregnant female participants 1 month after Dose 2	• SARS-CoV-2 neutralizing titers
Secondary	**Secondary**	**Secondary**
To describe the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 7 days after Dose 2 through 1 month after delivery in maternal participants 18 years of age or older vaccinated at 24 to 34 weeks' gestation without evidence of prior SARS-CoV-2 infection.	In maternal participants complying with the key protocol criteria (evaluable participants) and no serological or virological evidence (prior to 7 days after receipt of Dose 2) of past SARS-CoV-2 infection: • 100 × (1 – incidence rate ratio [IRR]) [ratio of active vaccine to placebo]	• COVID-19 incidence per 1000 person-years of blinded follow-up based on central laboratory or locally confirmed nucleic acid amplification test (NAAT)
To describe the efficacy of prophylactic BNT162b2 against confirmed COVID-19 occurring from 7 days after Dose 2 through 1 month after delivery in maternal	In maternal participants complying with the key protocol criteria (evaluable participants):	• COVID-19 incidence per 1000 person-years of blinded follow-up based on central

CLINICAL STUDY REPORT SYNOPSIS

Table S1. Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints
participants 18 years of age or older vaccinated at 24 to 34 weeks' gestation with and without evidence of prior SARS-CoV-2 infection.	• 100 × (1 – IRR) [ratio of active vaccine to placebo]	laboratory or locally confirmed NAAT
To describe the efficacy of prophylactic BNT162b2 against asymptomatic SARS-CoV-2 infection through 1 month after delivery in maternal participants 18 years of age or older vaccinated at 24 to 34 weeks' gestation without evidence of prior SARS-CoV-2 infection.	In evaluable maternal participants without serological or virological evidence of prior SARS-CoV-2 infection: • 100 × (1 – IRR) [ratio of active vaccine to placebo]	• Incidence of asymptomatic infection of SARS-CoV-2 based on N-binding antibody seroconversion
To describe the immune response over time and persistence of prophylactic BNT162b2 when administered to maternal participants 18 years of age or older vaccinated at 24 to 34 weeks' gestation.	In maternal participants complying with the key protocol criteria (evaluable maternal participants) from each vaccine group: • Geometric mean concentrations (GMCs)/geometric mean titers (GMTs), at baseline (before Dose 1), 2 weeks after Dose 2, 1 month after Dose 2, at delivery, and 6 months after delivery • Geometric mean fold rises (GMFRs) from baseline through 2 weeks after Dose 2, 1 month after Dose 2, at delivery, and 6 months after delivery	• Full-length S-binding IgG levels • SARS-CoV-2 neutralizing titers
To assess the safety of maternal immunization in infants born to maternal participants 18 years of age or older who were vaccinated with BNT162b2 during pregnancy.	In infants born to maternal participants receiving at least 1 dose of study intervention from each vaccine group, the percentage of infants with: • Specific birth outcomes • AEs from birth through 1 month of age • SAEs and AESIs (major congenital anomalies, developmental delay) through 6 months of age	• Specific birth outcomes • AEs from birth through 1 month of age • SAEs and adverse events of special interest (AESIs) (major congenital anomalies, developmental delay) through 6 months of age

CLINICAL STUDY REPORT SYNOPSIS

Table S1. Objectives, Estimands, and Endpoints

Objectives[a]	Estimands	Endpoints
To describe the immune response in infants born to maternal participants vaccinated with prophylactic BNT162b2 during pregnancy.	In infants born to evaluable maternal participants from each vaccine group: • GMCs and GMFRs, at birth and 6 months after delivery	• Full-length S-binding IgG levels

a. Human immunodeficiency virus (HIV)-infected participants will not be included in analyses of the objectives, but in separate exploratory analyses. Analyses among HIV-infected women and their infants will be summarized separately.

Methodology:

This was a global Phase 2/3, randomized, placebo-controlled, observer-blind study to evaluate the safety, tolerability, and immunogenicity of 30 µg of BNT162b2 or placebo administered in 2 doses, 21 days apart, in approximately 350 healthy pregnant women 18 years of age or older vaccinated at 24 to 34 weeks' gestation. Participants were randomized 1:1 to receive BNT162b2 or placebo (saline).

The Phase 2 portion of the study included approximately 200 pregnant women enrolled at 27 to 34 weeks' gestation. The IRC reviewed safety data through 7 days after the second dose for all Phase 2 participants.

The Phase 3 portion of this study assessed the safety, tolerability, and immunogenicity of BNT162b2 in approximately 150 pregnant women enrolled at 24 to 34 weeks' gestation. Phase 3 proceeded after the first 200 maternal participants had been enrolled in Phase 2.

Maternal participants who originally received placebo could receive BNT162b2 at the 1 month postdelivery visit.

Enrollment in this study was terminated on 25 October 2021 due to changes in the universal recommendations for COVID-19 vaccination of pregnant women with approximately 350 participants enrolled. Enrollment was terminated due to enrollment challenges into a placebo-controlled study as a result of universal recommendations for COVID-19 vaccination of pregnant women and the increased global availability of COVID-19 vaccines. Participant enrollment numbers were modified accordingly (~200 in Phase 2, and ~150 in Phase 3).

It was planned that each maternal participant would participate in the study for up to approximately 10 months, depending on the vaccine group to which she was randomized. Her infant would participate in the study for approximately 6 months. The planned study duration was approximately 14 months.

CLINICAL STUDY REPORT SYNOPSIS

The BNT162b2 dose of 30 µg in this study is the same as that for Study C4591001 Phase 2/3 evaluation of safety, immunogenicity, and efficacy. A placebo was used as the control.

Number of Participants (planned and analyzed):

Maternal Participants

A total of 174 maternal participants were randomized to receive 2 doses of BNT162b2 30 µg and 174 were randomized to receive 2 doses of placebo. In total, 97.7% of maternal participants received both doses and 92.0% completed the 1-month postdelivery visit. Across groups, 5.5% of participants were withdrawn from the study; the most frequent reason was withdrawal by the participant.

Per protocol, participants originally randomized to placebo could receive BNT162b2 after being unblinded at the 1-month postdelivery visit. Among these participants, 152 (93.8%) received a first dose of BNT162b2 and 148 (91.4%) received a second dose of BNT162b2. Of these, 4 participants were withdrawn after the first dose of BNT162b2 and 1 after the second dose of BNT162b2.

Safety Population

The safety population for maternal participants included 173 participants in the BNT162b2 group and 173 participants in the placebo group; 2 maternal participants were excluded from the safety population because they did not receive the study intervention. Most maternal participants included in the safety population were breastfeeding, and 12 in the BNT162b2 group and 10 in the placebo group were HIV-positive.

CLINICAL STUDY REPORT SYNOPSIS

Immunogenicity Populations

The evaluable immunogenicity population for Study C4591015 maternal participants included 111 participants in the BNT162b2 group and 115 participants in the placebo group, and for Study C4591001 nonpregnant females included 114 participants in the BNT162b2 group and 124 participants in the placebo group. Exclusions from the evaluable immunogenicity population were balanced across BNT162b2 and placebo groups among C4591015 participants and among C4591001 participants; the most common reason for exclusion for C4591015 participants was due to a lack of at least 1 valid and determinate immunogenicity result within 28-42 days after Dose 2.

The evaluable immunogenicity population without evidence of SARS-CoV-2 infection prior to 1 month after Dose 2 for Study C4591015 maternal participants included 59 participants (33.9%) in the BNT162b2 group and 58 participants (33.3%) in the placebo group; for Study C4591001 nonpregnant females included 107 participants (87.0%) in the BNT162b2 group and 113 participants (85.0%) in the placebo group. Of note, the proportions of participants without evidence of prior infection for the C4591015 and C4591001 study participants reflect varying conditions of the COVID-19 pandemic, as the studies were conducted in different times and countries.

Efficacy Populations

The proportions of maternal participants included in the efficacy populations were balanced between the BNT162b2 and placebo groups. The evaluable efficacy population included 161 participants in the BNT162b2 group and 163 participants in the placebo group. Exclusions from the evaluable efficacy population were similar across groups; the most common reason was due to other protocol deviation(s) as determined by the clinician.

The evaluable efficacy population without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2 included 91 participants in the BNT162b2 group and 94 participants in the placebo group.

Infant Participants

A total of 167 infants were born to maternal participants in the BNT162b2 group and 168 were born to maternal participants in the placebo group. Most (86.9%) infant participants completed the 6-months-of-age follow-up visit. Withdrawal from the study was more frequently reported among infants whose mothers were randomized to placebo (17.3%) than those whose mothers were randomized to BNT162b2 (9.0%); the most frequent reasons for withdrawal during the study was withdrawal by parent/guardian and lost to follow-up. Two infant participants (1 in the BNT162b2 and 1 in the placebo group) died during the study due to SAEs that were assessed as unrelated to study vaccination, and were subsequently withdrawn from the study.

CLINICAL STUDY REPORT SYNOPSIS

Safety Population

The safety population for infant participants included 167 born to mothers in the BNT162b2 group and 168 born to mothers in the placebo group. Infants whose mothers were HIV-positive included 11 in the BNT162b2 group and 9 in the placebo group.

Immunogenicity Populations

The proportions of infant participants included in the immunogenicity populations were balanced between the BNT162b2 and placebo groups. The evaluable immunogenicity population for infant participants included 109 participants in the BNT162b2 group and 105 participants in the placebo group.

The proportion of participants excluded from the evaluable immunogenicity population was 34.7% and 37.5% for the BNT162b2 group and the placebo group, respectively. The most frequent reason for exclusion of infant participants from the evaluable immunogenicity populations was because the mother was not considered to be an evaluable immunogenicity maternal participant.

Efficacy Populations

The proportions of infant participants included in the efficacy populations were balanced between the BNT162b2 and placebo groups. The evaluable efficacy population included 167 participants in the BNT162b2 group and 168 participants in the placebo group.

For infants born to mothers in the BNT162b2 and placebo groups, most (88.0% and 90.5%, respectively) were breastfed and few (6.6% and 5.4%, respectively) were born to mothers who were HIV-positive.

Diagnosis and Main Criteria for Inclusion and Exclusion:

Enrolled in this study were participants who were healthy pregnant women ≥18 years of age and their infants, once born. Enrollment was monitored to help ensure distribution of vaccination across the gestational age ranges of 27 0/7 to 34 0/7 weeks for Phase 2 and ≥24 0/7 and ≤34 0/7 weeks for Phase 3.

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

Details of the study interventions, administered intramuscularly, are provided below:

- BNT162b2 (BNT162 RNA-lipid nanoparticle [LNP] vaccine utilizing modified ribonucleic acid [modRNA] and encoding the SARS-CoV-2 full-length, P2 mutant, prefusion spike glycoprotein [P2 S]): 30 µg

- Normal saline (0.9% sodium chloride solution for injection)

CLINICAL STUDY REPORT SYNOPSIS

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

Table S2. Study Intervention Lot Numbers

Study Intervention	Manufacturer	Vendor Lot Number (Manufacturer)	Lot Number[a] (Pfizer)
BNT162b2	BioNTech	ER5832 EE3813	PA2094601/P222676-0003L NC2075485/P222676-0001L
Diluent (normal saline, 0.9% sodium chloride solution)	Pfizer	EE4253 DK2074 EX2624	PA2091593/P222676-0005L 20-002221 21-AE-00230
Placebo (normal saline, 0.9% sodium chloride solution)	Pfizer	EE4253 DK2074;20-002221	PA2091593/P222676-0004L PA2069407/P222676-0002L

a. Lot number assigned to the study intervention by Pfizer Global Clinical Supply.
Protocol C4591015 Study Intervention Lot Numbers Table –Final, Version 1.0, 08Mar2024.

Duration of Study Intervention:

The Study C4591001 vaccine candidate selected for Phase 2/3 evaluation was BNT162b2 at a dose of 30 µg. Study C4591015 evaluated 2 doses of BNT162b2 30 µg or placebo administered 21 days apart (Visits 1 and 2). At 1 month after delivery, maternal participants who originally received placebo could receive 1 dose of BNT162b2 at Visits 101 and 102.

Summary of Results:

Demographic and Other Baseline Characteristics:

Maternal Participants

Safety Population

Demographic and baseline characteristics for the safety population of maternal participants were well balanced between the BNT162b2 and placebo groups. Overall, the majority of participants were White (67.9%), non-Hispanic/non-Latino (61.6%), and located in the United States (48.3%) or South Africa (23.7%). A total of 127 (36.7%) participants had a positive baseline SARS-CoV-2 status. The median age of participants at Dose 1 was 30.0 years, and the median gestational age at Dose 1 was 30.4 weeks. Both groups were similar with regards to HIV status and pre-pregnancy body mass index (BMI).

Medical history and obstetric history were generally similar for maternal participants in the BNT162b2 and placebo groups.

Baseline Charlson Comorbidities were reported for few maternal participants in the BNT162b2 and placebo groups (21 [12.1%] and 14 [8.1%], respectively). Across groups, the

CLINICAL STUDY REPORT SYNOPSIS

most common comorbidities reported were HIV-positive (6.4%) and chronic pulmonary disease (2.6%).

Immunogenicity Populations

Of note, a greater proportion of C4591015 participants identified as Black or African American (≥27.0% compared with ≥5.3% in C4591001) and a higher percentage were enrolled from South African sites (≥24.3% compared with ≥0.8% in C4591001). Additionally, the proportion of C4591015 maternal participants with positive baseline SARS-CoV-2 status (≥37.8%) was higher than what was observed among C4591001 participants (≥3.5%), which could have been due to the different timepoints at which participants were enrolled in each study relative to the progression of the COVID-19 pandemic. The majority of participants identified as non-Hispanic/non-Latino (63.7%). The median age of participants at Dose 1 was 30.0 years, and the median gestational age at Dose 1 for the BNT162b2 and placebo groups was 28.9 weeks and 29.1 weeks, respectively. Both groups were similar with regards to HIV status. Pre-pregnancy BMIs for C4591015 maternal participants were generally higher than those observed in C4591001 nonpregnant female participants.

Infant Participants

Safety Population

Demographics and baseline characteristics for the safety population of infant participants were balanced for the BNT162b2 and placebo groups. The majority of participants were White (65.4%), non-Hispanic/non-Latino (60.3%), and located in the United States (48.7%) or South Africa (23.9%). The majority of infants were born between ≥37 weeks to 41 weeks 6 days, and 89.3% of infant participants were breastfed. Both groups were similar with regards to HIV status.

Immunogenicity Populations

The demographics for the immunogenicity population of infant participants were generally similar to those of the safety population.

Exposure:

Most (≥97.7%) maternal participants were administered Dose 1 and Dose 2 as randomized. For participants who were originally randomized to placebo, 87.4% and 85.1% received a first dose and second dose of BNT162b2, respectively, following unblinding at the 1-month postdelivery visit.

In all randomized maternal participants, the majority (≥87.9%) in the BNT162b2 and placebo groups received Dose 2 in the protocol-defined window of 19 to 23 days after Dose 1. For the 152 (87.4%) maternal participants who were originally randomized to placebo and received a

CLINICAL STUDY REPORT SYNOPSIS

first dose of BNT162b2 after unblinding, the majority (127 [73.0%]) received a second dose of BNT162b2 in the protocol-defined window of 19 to 23 days after the first dose.

Vaccine administration timing was similar for Study C4591015 maternal participants and Study C4591001 nonpregnant female participants in the evaluable immunogenicity population across both vaccine groups.

Overall, important PDs were balanced among maternal participants in both the BNT162b2 and placebo groups. Important PDs in maternal participants were most frequently reported in the category of inclusion/exclusion criteria. One PD in the concomitant medications category was reported among infant participants in the placebo group. No PDs were reported among infants born to maternal participants in the BNT162b2 group.

Concomitant medications used after Dose 1 were reported similarly among maternal participants in the BNT162b2 and placebo groups (27.3% and 28.8%, respectively). The number of participants who received nonstudy vaccines after Dose 1 was also similar (16.1% and 20.9%, respectively). Concomitant medications received after birth were reported similarly among infants born to maternal participants in the BNT162b2 and placebo groups (13.5% and 14.5%, respectively).

In all randomized maternal participants, for each of the visits at which blood draws occurred the proportions were generally similar for the BNT162b2 and placebo groups through the delivery visit. For both groups, the majority (≥52.9%) of blood draws were within the protocol-defined window through the delivery visit. In infant participants, the majority had blood samples drawn at birth (≥89.9%) and in the protocol-defined window of 160 to 200 days (≥63.1%) for the 6-months of age follow-up visit.

For maternal participants, transmission of reactogenicity e-diary data for each day during the 7 days after Dose 1 of BNT162b2 ranged from 86.7% to 94.8%. After Dose 2 of BNT162b2, transmission of e-diary data ranged from 73.5% to 87.6% for Day 1 through Day 7.

Immunogenicity Results:

Primary Immunogenicity Analyses – Maternal Participants

GMR of Neutralizing Titers

Among participants without prior evidence of SARS-CoV-2 infection up to 1 month after Dose 2 (evaluable immunogenicity population), the ratio of the neutralizing GMT (GMR) in Study C4591015 maternal participants in the BNT162b2 (30 µg) group to that of Study C4591001 nonpregnant females who received BNT162b2 30 µg was 0.67 (95% confidence interval [CI]: 0.50, 0.90).

For participants with or without prior evidence of SARS-CoV-2 infection up to 1 month after Dose 2 (evaluable immunogenicity population), the model-adjusted ratio of the neutralizing GMT (adjusted GMR) in Study C4591015 maternal participants in the BNT162b2 (30 µg)

CLINICAL STUDY REPORT SYNOPSIS

group to that of Study C4591001 nonpregnant females who received BNT162b2 30 µg was 0.95 (95% CI: 0.69, 1.30). The adjusted GMT and GMR were calculated based on a regression model with vaccine group, age at Dose 1 and baseline neutralizing titers as the independent variables to minimize the confounding effect from imbalanced distribution of baseline SARS-CoV-2 infection.

Secondary Immunogenicity Analyses – Maternal Participants

Neutralizing GMTs and Full-length Spike Protein (S-binding) Immunoglobulin G (IgG) GMCs

For the evaluable immunogenicity population without evidence of infection, at 1 month after Dose 2 there was a substantial increase in SARS-CoV-2 50% neutralizing GMTs in maternal participants in the BNT162b2 group (1099.4 [95% CI: 820.6, 1473.0]) compared to the placebo group (43.5 [95% CI: 43.5, 43.5]), for which change from baseline was negligible; these results are consistent with those in nonpregnant females in Study C4591001. In maternal participants in the BNT162b2 group, GMTs were substantially increased, compared to the placebo group, peaked at 2 weeks after Dose 2 and remained elevated through the 6-month postdelivery visit. Results for participants in the evaluable immunogenicity population with or without evidence of infection followed a similar trend.

For the evaluable immunogenicity population without evidence of infection, at 2 weeks after Dose 2 there was a substantial increase in GMCs of full-length S-binding IgG in maternal participants in the BNT162b2 group (7639.0 [95% CI: 6403.0, 9113.6]) compared to the placebo group (1.7 [95% CI: 1.2, 2.6]), for which change from baseline was negligible. In the BNT162b2 group, GMCs were substantially increased, compared to the placebo group, peaked at 2 weeks after Dose 2 and remained elevated through the 6-month postdelivery visit. Results for participants in the evaluable immunogenicity population with or without evidence of infection followed a similar trend.

HIV-Positive Participants

Among HIV-positive maternal participants, SARS-CoV-2 50% neutralizing titers in maternal participants in the BNT162b2 group were generally higher compared to those in the placebo group at 1 month after Dose 2, and remained elevated at 6 months after Dose 2.

Overall, full-length S-binding IgG levels in HIV-positive maternal participants in the BNT162b2 group were substantially higher than those observed in the placebo group at 1 month after Dose 2, and remained elevated at 6 months after Dose 2. As this subgroup included a limited number of participants, these results should be interpreted with caution.

Subgroup Analyses

GMTs at prevaccination (Dose 1) and 1 month after Dose 2 were evaluated by race, ethnicity, and baseline SARS-CoV-2 status in Study C4591015 maternal participants and

CLINICAL STUDY REPORT SYNOPSIS

Study C4591001 nonpregnant females. Among participants with or without evidence of infection, higher baseline and post-vaccination titers were observed in Black/African American participants as compared to other race groups. Higher GMTs were also observed in participants with positive baseline SARS-CoV-2 status at both baseline and 1 month after Dose 2 timepoints compared to those observed in participants with negative baseline status. Overall, GMTs for the BNT162b2 groups for both studies were generally similar and did not identify any clinically meaningful differences for any other race subgroup or ethnicity. As several subgroups included a limited number of participants, these results should be interpreted with caution.

Neutralizing Titer and Full-length S-binding IgG GMFRs

In maternal participants in the evaluable immunogenicity population without evidence of infection, the SARS-CoV-2 NT GMFR at 1 month after Dose 2 was substantially higher in the BNT162b2 group (25.3 [95% CI: 18.9, 33.9]) compared to the placebo group (1.0 [95% CI: 1.0, 1.0]), for which change from baseline was negligible. In maternal participants in the BNT162b2 group, the GMFR peaked at 2 weeks after Dose 2 and remained elevated through the delivery visit and 6-month postdelivery timepoints. Results for participants in the overall evaluable immunogenicity population followed a similar trend.

In maternal participants in the evaluable immunogenicity population without evidence of infection, the full-length S-binding IgG GMFR at 1 month after Dose 2 was substantially higher in maternal participants in the BNT162b2 group (2276.4 [95% CI: 1545.5, 3352.9]) compared to the placebo group (0.9 [95% CI: 0.8, 1.1]), for which change from baseline was negligible. In maternal participants in the BNT162b2 group, the GMFR peaked at 2 weeks after Dose 2 and remained elevated compared to the placebo group through the delivery visit and 6-month postdelivery timepoints. Results for participants in the overall evaluable immunogenicity population followed a similar trend.

Secondary Immunogenicity Analyses – Infant Participants

Full-length S-binding IgG GMCs

Maternal vaccination with BNT162b2 30 µg yielded substantially higher GMCs of full-length S-binding IgG in infants compared to placebo. For the evaluable immunogenicity population, at birth and 6 months of age GMCs were 5576.4 (95% CI: 4246.2, 7323.2) and 311.1 (95% CI: 235.8, 410.5), respectively, for infants whose mothers received BNT162b2, compared to 19.4 (95% CI: 10.2, 37.0) and 22.0 (95% CI: 11.4, 42.7) for infants whose mothers received placebo.

Infants Born to HIV-Positive Maternal Participants

Among infants born to HIV-positive maternal participants, full-length S-binding IgG levels at birth and 6 months of age were higher among infants born to vaccinated participants (with ranges of 406.32-39970 at birth and 169.12-5029.4 at 6 months) than those born to

CLINICAL STUDY REPORT SYNOPSIS

participants in the placebo group (with ranges of 4.92-1561.33 at birth and 7.01-653.18 at 6 months). As this subgroup included a limited number of participants, these results should be interpreted with caution.

Exploratory Subgroup Analyses

GMCs of full-length S-binding IgG in infants in the evaluable immunogenicity population were evaluated by breastfeeding status. GMCs for breastfed infants were generally higher than those observed for infants who were not breastfed. GMCs for breastfed or not breastfed infants whose mothers received BNT162b2 were substantially higher at birth compared to infants whose mothers received placebo, and remained elevated at 6 months of age. As the not breasted subgroup included a limited number of participants, these results should be interpreted with caution.

GMFRs

In infants in the evaluable immunogenicity population whose mothers received BNT162b2, the GMFR of full-length S-binding IgG from birth to 6 months of age was 0.1 [95% CI: 0.0, 0.1], indicating a decline in antibody titers during this period.

Exploratory Subgroup Analyses

GMFRs of full-length S-binding IgG in infants in the evaluable immunogenicity population were evaluated by breastfeeding status. GMFRs by breastfeeding status were generally similar to those observed in the overall population. As the not breastfed subgroup included a limited number of participants, these results should be interpreted with caution.

Efficacy Results:

Secondary Efficacy Analyses – Maternal Participants

Vaccine Efficacy Against Confirmed COVID-19

Due to the very small sample size, and hence number of COVID-19 cases, vaccine efficacy (VE) results are uninterpretable; nevertheless, they are described below:

For confirmed COVID-19 based on the protocol definition, in maternal participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2 in the evaluable efficacy population, the VE during the blinded follow-up period was observed as 3.8% (95% CI: -1227.8%, 93.0%) based on 2 cases in the BNT162b2 group and 2 cases in the placebo group confirmed from at least 7 days after Dose 2 through 1 month after delivery.

For confirmed COVID-19 based on the protocol definition, in maternal participants with or without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2 in the evaluable efficacy population, the VE during the blinded follow-up period was observed as 35.1%

CLINICAL STUDY REPORT SYNOPSIS

(95% CI: -466.5%, 94.6%), with 2 cases reported in the BNT162b2 group and 3 cases in the placebo group confirmed from at least 7 days after Dose 2 through 1 month after delivery.

For confirmed COVID-19 based on the Centers for Disease Control and Prevention (CDC) definition, in maternal participants without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2 in the evaluable efficacy population, the VE during the blinded follow-up period was observed as 36.2% (95% CI: -456.5%, 94.7%) based on 2 cases in the BNT162b2 group and 3 cases in the placebo group confirmed from at least 7 days after Dose 2 through 1 month after delivery.

For confirmed COVID-19, based on the CDC definition, in maternal participants with or without evidence of SARS-CoV-2 infection prior to 7 days after Dose 2 in the evaluable efficacy population, the observed VE during the blinded follow-up period was generally higher at 51.1% (95% CI: -241.0%, 95.6%), with 2 cases reported in the BNT162b2 group and 4 cases in the placebo group confirmed from at least 7 days after Dose 2 through 1 month after delivery.

Vaccine Efficacy Against Asymptomatic SARS-CoV-2 Infection Based on Seroconversion (Nucleoprotein Binding [N-Binding])

For asymptomatic infection, based on N-binding antibody seroconversion, in the evaluable efficacy population of maternal participants without evidence of SARS-CoV-2 infection prior to the first post-Dose 2 N-binding test, the VE during the blinded follow-up period was observed as 40.9% (95% CI: -104.9%, 86.5%) based on 4 cases in the BNT162b2 group and 10 cases in the placebo group confirmed from after Dose 2 through 1 month after delivery. As this subgroup included a limited number of participants, these results should be interpreted with caution.

Additional VE analyses for asymptomatic infection had similar results, with most cases occurring in the placebo group.

Safety Results:

Local Reactions – Maternal Participants

In maternal participants in the BNT162b2 group, pain at the injection site was the most frequently reported local reaction, and frequency was similar after Dose 1 and after Dose 2 (82.6% vs 75.0%). In the placebo group, pain at the injection site after each dose was less frequently reported compared to the BNT162b2 group and was reported more frequently after Dose 2 (16.4%) than Dose 1 (9.8%). Redness and swelling after either Dose 1 or Dose 2 were reported in ≤6.8% and ≤0.7% of participants in the BNT162b2 and placebo groups, respectively.

Most local reactions were mild or moderate in severity. A severe event of swelling was reported in 1 participant in the BNT162b2 group after Dose 1, and a severe event of pain at

the injection site was reported in 1 participant in the same group after Dose 2. No Grade 4 local reactions were reported in either group.

Across both groups, median onset for all local reactions was between Day 1 and Day 2.5 after Dose 1 or Dose 2, and all events resolved with median durations between 1 to 2 days.

HIV-Positive Participants

Among HIV-positive participants, frequencies of local reactions within 7 days after Dose 1 and Dose 2 were generally reported at higher frequencies among participants in the BNT162b2 group compared to those in the placebo group. Of note, pain at the injection site was more frequently reported after each dose in the BNT162b2 group (≤50.0% after either Dose 1 or Dose 2) than in the placebo group (≤20.0% after Dose 1 and ≤22.2% after Dose 2). No severe or Grade 4 local reactions were reported in either group. As this subgroup included a limited number of participants, these results should be interpreted with caution.

Subgroup Analyses

Local reactions reported within 7 days after vaccination were evaluated by race, ethnicity, and baseline SARS-CoV-2 status. Overall, for these subgroups, local reactions were reported at higher frequencies among participants in the BNT162b2 group after both doses compared to those in the placebo group. Among vaccinated participants, no clinically meaningful differences were observed by race or ethnicity in either group. For participants with baseline negative SARS-CoV-2 status, higher frequencies of pain at the injection site were reported after each dose in both the BNT162b2 and placebo groups as compared to baseline positive participants. As several subgroups included a limited number of participants, these results should be interpreted with caution.

Systemic Events – Maternal Participants

In maternal participants, systemic events were generally similar frequencies in the placebo group compared to the BNT162b2 group after Dose 1; however, systemic events were observably higher after Dose 2 among participants in the BNT162b2 group. Fatigue and headache were most frequently reported after each dose in the BNT162b2 (≤50.0% reported fatigue and ≤41.2% reported headache) and placebo groups (≤42.9% reported fatigue and ≤35.6% reported headache). Fever was reported in few participants after each dose in both the BNT162b2 (≤2.7%) and placebo groups (≤1.8%).

Most systemic events were mild or moderate in severity. In both the BNT162b2 and placebo groups, the most frequently reported severe events after any dose were fatigue (2.0% and 0.6%, respectively) and headache (1.9% and 0.6%, respectively). No Grade 4 systemic events were reported in either group.

Across both groups, median onset for all systemic events was between Day 1 and Day 4 after Dose 1 or Dose 2, and all events resolved with median durations between 1 to 4.5 days.

CLINICAL STUDY REPORT SYNOPSIS

The reported frequencies of participants with baseline systemic events were similar for the BNT162b2 and placebo groups, with the baseline fatigue most frequently reported (29.7% and 33.8%, respectively).

HIV-Positive Participants

Among HIV-positive participants, systemic events were reported at numerically higher frequencies after Dose 1 in the placebo group compared to the BNT162b2 group; however, systemic events were reported at generally similar frequencies after Dose 2 in the two vaccine groups. In both the BNT162b2 and placebo groups, the most frequently reported systemic events after any dose were fatigue (≤66.7% and ≤60.0%, respectively) and headache (≤41.7% and ≤60.0%, respectively). No Grade 4 systemic events were reported in either group. As this subgroup included a limited number of participants, these results should be interpreted with caution.

Subgroup Analyses

Systemic events reported within 7 days after vaccination were evaluated by race, ethnicity, and baseline SARS-CoV-2 status. Among vaccinated participants, no clinically meaningful differences were observed by race, ethnicity, or SARS-CoV-2 status in either group. As several subgroups included a limited number of participants, these results should be interpreted with caution.

Adverse Events – Maternal Participants

From Dose 1 to 1 month after Dose 2 during the blinded follow-up period, the proportion of participants reporting any AE was similar in the BNT162b2 (23.6%) and placebo (22.7%) groups. Across both groups, any related, severe, or serious AEs were reported in ≤0.6%, ≤4.9%, and ≤5.6%, respectively. In the placebo group, life-threatening AEs were reported in 1.8% of participants.

No maternal participants had any AEs leading to withdrawal and none died from Dose 1 to 1 month after Dose 2 during the blinded follow-up period.

In maternal participants originally randomized to placebo who received BNT162b2 after unblinding at 1 month postdelivery, the frequency of AEs reported among participants who originally received placebo and then received BNT162b2 after unblinding (22.2%) was similar to that in the BNT162b2 group during the blinded follow-up period (23.6%), and overall the results did not suggest any meaningful differences in types of AEs reported.

From vaccination with BNT162b2 to 1 month after the second dose of BNT162b2 for original placebo participants who then received BNT162b2 after unblinding, there were no reported SAEs, life-threatening AEs, AEs leading to withdrawal, or deaths. Except for 1 participant, all AEs were mild or moderate in severity. Related AEs were reported in 12.5%

CLINICAL STUDY REPORT SYNOPSIS

of participants. The most frequently reported AEs in these participants unblinded at 1 month postdelivery were reactogenicity events.

HIV-Positive Participants

Among HIV-positive participants, AEs were reported in 16.7% of participants in the BNT162b2 group and 40.0% of participants in the placebo group. Most AEs were mild or moderate in severity (1 severe event was reported in the BNT162b2 group), and none were assessed as related. SAEs were reported in ≤10.0% between both groups. No life-threatening AEs were reported.

Subgroup Analyses

AEs reported in maternal participants from Dose 1 to 1 month after Dose 2 were evaluated by race, ethnicity, and SARS-CoV-2 status. Overall, results for both the BNT162b2 and placebo groups suggested no clinically meaningful differences across subgroups. As several subgroups included a limited number of participants, these results should be interpreted with caution.

Adverse Events – Infant Participants

The proportions of infant participants with any AEs reported from birth to 1 month of age were similar in the BNT162b2 (35.3%) and placebo (37.1%) groups. Most AEs were mild or moderate in severity (≤6.3% were severe between both groups), and none were assessed by the investigator as related. Between both groups, SAEs were reported in ≤13.8% and life-threatening AEs were reported in and ≤3.1% of infants.

One infant participant in the placebo group was withdrawn due to a fatal SAE of neonatal pneumonia that was assessed by the investigator as unrelated to study intervention. Additionally, 1 infant born to an HIV-positive maternal participant in the BNT162b2 group was withdrawn due to a fatal SAE of pneumonia that was also assessed as unrelated to study intervention by the investigator.

Conclusions:

In this study, the reactogenicity, safety, and tolerability profile of BNT162b2 at 30 μg was found to be satisfactory in maternal participants.

BNT162b2 (30 μg) elicited robust immunogenicity responses in healthy pregnant women 18 years of age and older, with SARS-CoV-2 neutralizing titers that were notably higher compared to placebo; however, among those without SARS-CoV-2 infection, numerically lower GMTs were observed in the maternal participants compared to the selected nonpregnant female participants from Study C4591001. A similar pattern was shown in those with or without SARS-CoV-2 infection after adjusting the baseline neutralizing titers.

CLINICAL STUDY REPORT SYNOPSIS

Infants born to vaccinated maternal participants had higher S-binding IgG concentrations at birth and at 6 months after delivery when compared to infants born to maternal participants from the placebo group. Breastfed infants had marginally higher antibody levels at 6 months after delivery than non-breastfed infants. No safety issues attributable to BNT162b2 exposure were identified in infants born to maternal participants who were vaccinated during pregnancy.

Overall, the data from this study support a favorable benefit risk profile in pregnant women and their infants.