Study to Evaluate the Safety, Tolerability, and Immunogenicity of an RNA Vaccine Candidate Against COVID-19 in Healthy Children <12 Years of Age

ClinicalTrials.gov Identifier: NCT04816643

Recruitment Status : Recruiting
First Posted : March 25, 2021
Last Update Posted : May 19, 2021

See **Contacts and Locations**

Sponsor:
BioNTech SE

Collaborator:
Pfizer

Information provided by (Responsible Party):
BioNTech SE

Study Description

Go to

Brief Summary:

This is a Phase 1/2/3 study in healthy children <12 years of age.

Dependent upon safety and/or immunogenicity data generated during the course of this study, and the resulting assessment of benefit-risk, the safety, tolerability, and immunogenicity of BNT162b2 in participants <6 months of age may subsequently be evaluated.

Condition or disease	Intervention/treatment	Phase
SARS-CoV-2 Infection, COVID-19	Biological: Biological/Vaccine: BNT162b2 10mcg Biological: BNT162b2 20mcg Biological: BNT162b2 30mcg	Phase 1 Phase 2

Detailed Description:

Phase 1 is the open-label dose-finding portion of the study to evaluate safety, tolerability, and immunogenicity of BNT162b2 on a 2-dose (separated by approximately 21 days) schedule in up to 3 age groups (participants ≥5 to <12 years, ≥2 to <5 years, and ≥6 months to <2 years of age). Dose finding is being initiated in this study in participants ≥5 to <12 years of age based on the acceptable blinded safety assessment of the 30-µg dose in 12- to 15-year-olds in the C4591001 study.

The purpose of Phase 1 is to identify preferred dose level(s) of BNT162b2 from up to 3 different dose levels in each age group.

Phase 2/3 will evaluate the safety, tolerability, and immunogenicity in each age group at the selected dose level from Phase 1. Efficacy will be evaluated across all age groups in which immunobridging is successful, depending on accrual of a sufficient number of cases across those age groups.

All participants will have blood drawn at baseline prior to Dose 1 and 6 months after Dose 2. Immunobridging to participants 16 to 25 years of age in the C4591001 study will be based on immunogenicity data collected at baseline and 1 month after Dose 2. The persistence of the immune response will be based on immunogenicity data collected in participants at baseline and at 1, 6, 12 (original BNT162b2 group only), and 24 months after Dose 2 (original BNT162b2 group only). In addition, efficacy against confirmed COVID-19 and against asymptomatic infection will also be assessed.

At the 6-month follow-up visit, all participants will be unblinded. Participants who originally received placebo will be offered the opportunity to receive BNT162b2 as part of the study.

Approximately 450 participants (300 in the active vaccine group and 150 in the placebo group) randomized in each age group in this phase will contribute to the immunobridging analysis at 1 month after Dose 2 and will contribute to the overall analysis of the persistence of immune response at 6 months after Dose 2. These participants will be enrolled from both US and EU sites to ensure this subset is representative of the whole study.

For the persistence time points of 12 and 24 months after Dose 2, approximately 70 participants from each age group in the original BNT162b2 vaccine group will have an immunogenicity blood draw in order to contribute to the analysis. All approximately 4500 participants will contribute to the VE analysis for conditional VE and asymptomatic infection. Efficacy will be evaluated across all age groups in which immunobridging is successful, depending on accrual of a sufficient number of cases across those age groups.

Study Design

Go to

Study Type :

Interventional (Clinical Trial)

Estimated Enrollment :

4644 participants

Allocation:

Non-Randomized

Intervention Model:

Parallel Assignment

Masking:

None (Open Label)

Primary Purpose:

Prevention

Official Title:

A PHASE 1, OPEN-LABEL DOSE-FINDING STUDY TO EVALUATE SAFETY, TOLERABILITY, AND IMMUNOGENICITY AND PHASE 2/3 PLACEBO-CONTROLLED, OBSERVER-BLINDED SAFETY, TOLERABILITY, AND IMMUNOGENICITY STUDY OF A SARS-COV-2 RNA VACCINE CANDIDATE AGAINST COVID-19 IN HEALTHY CHILDREN <12 YEARS OF AGE

Actual Study Start Date :

March 24, 2021

Estimated Primary Completion Date :

March 4, 2022

Estimated Study Completion Date :

September 1, 2023

Arms and Interventions

Go to

Arm	Intervention/treatment
Experimental: Low-Dose, ≥5 to <12 Years old Low-Dose (10mcg), 2 doses 21 days apart	Biological: Biological/Vaccine: BNT162b2 10mcg BNT162b2 Low-Dose (10mcg) level
Experimental: Mid-Dose, ≥5 to <12 Years old Mid-Dose, (20mcg), 2 doses 21 days apart	Biological: BNT162b2 20mcg BNT162b2 Mid-Dose (20mcg) level

Arm	Intervention/treatment
Experimental: High-Dose, ≥5 to <12 Years old High-Dose (30mcg), 2 doses 21 days apart	Biological: BNT162b2 30mcg BNT162b2 High-Dose (30mcg) level
Experimental: Low-Dose, ≥2 to < 5 Years old Low Dose (10mcg), 2 doses 21 days apart	Biological: Biological/Vaccine: BNT162b2 10mcg BNT162b2 Low-Dose (10mcg) level
Experimental: Mid-Dose, ≥2 to <5 Years old Mid-Dose, (20mcg), 2 doses 21 days apart	Biological: BNT162b2 20mcg BNT162b2 Mid-Dose (20mcg) level
Experimental: High-Dose, ≥2 to <5 Years old High-Dose, (30mcg), 2 doses 21 days apart	Biological: BNT162b2 30mcg BNT162b2 High-Dose (30mcg) level
Experimental: Low-Dose, ≥6 Months to <2 years old Low-Dose, (10mcg), doses 21 days apart	Biological: Biological/Vaccine: BNT162b2 10mcg BNT162b2 Low-Dose (10mcg) level
Experimental: Mid-Dose, ≥6 Months to <2 years old Mid-Dose, (20mcg), doses 21 days apart	Biological: BNT162b2 20mcg BNT162b2 Mid-Dose (20mcg) level
Experimental: High-Dose, ≥6 Months to <2 years old High-Dose, (30mcg), 2 doses 21 days apart	Biological: BNT162b2 30mcg BNT162b2 High-Dose (30mcg) level

Outcome Measures

Go to

Primary Outcome Measures :

1. Percentage of participants in Phase 1 reporting local reaction in each dose level in each age group
   [Time Frame: for 7 days after Dose 1 and Dose 2]

   For participants in ≥5 to <12 years and ≥2 to <5 years of age:

   Pain at the injection site, redness and swelling as reported on electronic diaries.

   For participants in ≥6 months to <2 years of age:

   Tenderness at the injection site, redness, and swelling as reported on electronic diaries

2. Percentage of participants in Phase 1 reporting systemic events in each dose level in each age group
   [Time Frame: for 7 days after Dose 1 and Dose 2]

For participants ≥5 to <12 years and ≥2 to <5 years of age Fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened join pain as reported on electronic diaries

For Participants ≥6 months to <2 years of age Fever, decreased appetite drowsiness, and irritability as reported on electronic diaries

3. Percentage of participants in Phase 1 reporting adverse events in each dose level in each age group [Time Frame: from Dose 1 through 1 month after the last dose]

   As elicited by investigational site staff

4. Percentage of participants in Phase 1 reporting serious adverse events in each dose level in each age group [Time Frame: from Dose 1 through 6 months after the last dose]

   As elicited by investigational site staff

5. Percentage of participants in Phase 2/3 reporting local reaction in each dose level in each age group [Time Frame: for 7 days after Dose 1 and Dose 2]

   For participants in ≥5 to <12 years and ≥2 to <5 years of age:

   Pain at the injection site, redness and swelling as reported on electronic diaries.

   For participants in ≥6 months to <2 years of age:

   Tenderness at the injection site, redness, and swelling as reported on electronic diaries

6. Percentage of participants in Phase 2/3 reporting systemic events in each dose level in each age group [Time Frame: for 7 days after Dose 1 and Dose 2]

   For participants in ≥5 to <12 years and ≥2 to <5 years of age: fever, fatigue, headache, chills, vomiting, diarrhea, new or worsened muscle pain, and new or worsened joint pain as reported on electronic diaries.

   For participants in ≥6 months to <2 years of age:

   Fever, decreased appetite, drowsiness, and irritability as reported on electronic diaries

7. Percentage of participants in Phase 2/3 reporting adverse events in each dose level in each age group [Time Frame: from Dose 1 through 1 month after the last dose]

   As elicited by investigational site staff

8. Percentage of participants in Phase 2/3 reporting serious adverse events in each dose level in each age group [Time Frame: from Dose 1 through 6 months after the last dose]

   As elicited by investigational site staff

9. In Phase 2/3 participants, Geometric Mean Ratio of SARS-CoV-2 neutralizing titers in participants in each age group at selected dose level to those 16 to 25 years of age in study C4591001 [Time Frame: 1 month

after the second dose]

As measured at the central laboratory

Secondary Outcome Measures :

1. In Phase 1 participants in each age group at each dose level, Geometric Mean Titers of SARS-CoV-2 serum neutralizing antibody titers [Time Frame: Through 7 days after Dose 2]

   As measured at the central laboratory

2. In Phase 1 participants in each age group at each dose level, Geometric Mean Fold Ratio in SARS-CoV-2 serum neutralizing antibody titers from before vaccination to each subsequent time point [Time Frame: Up to 7 days after Dose 2]

   As measured at the central laboratory

3. In evaluable Phase 2/3 participants at selected dose level in each age group, Geometric Mean Titers of SARS-CoV-2 neutralizing titers with no serological or virological evidence of past SARS-CoV-2 infection [Time Frame: At baseline, and at 1, 6, 12(participants who originally received BNT162b2) and 24 months(participants who originally received BNT162b2) after dose 2]

   As measured at the central laboratory

4. In evaluable Phase 2/3 participants at selected dose level in each age group, Geometric Mean Fold Ratio in SARS-CoV-2 serum neutralizing titer from before vaccination to each subsequent time point [Time Frame: from before Dose 1 and at 1, 6, 12(participants who originally received BNT162b2) and 24 months(participants who originally received BNT162b2) after dose 2]

   As measured at the central laboratory

5. Ratio of confirmed COVID-19 illness, in all age groups of Phase 2/3 participants without evidence of prior SARS-CoV-2 infection for the active vaccine group to the placebo group [Time Frame: from 7 days after the second dose]

   Per 1001 person-years of follow-up if at least 22 cases are accrued across the age group

6. Ratio of confirmed COVID-19 illness, in all age groups of Phase 2/3 participants with and without evidence of prior SARS-CoV-2 infection for the active vaccine group to the placebo group [Time Frame: from 7 days after the second dose]

   Per 1001 person-years of follow-up if at least 22 cases are accrued across the age group

7. In the evaluable Phase 2/3 participants, Ratio of incidence of asymptomatic SARS-CoV-2 infection based on N-binding antibody seroconversion for the active vaccine group to the placebo group without evidence of past SARS-CoV-2 infection [Time Frame: Through 6 months after the second dose]

As measured at the central laboratory

Eligibility Criteria

Go to

Information from the National Library of Medicine

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the contacts provided below. For general information, Learn About Clinical Studies.

Ages Eligible for Study:

6 Months to 11 Years (Child)

Sexes Eligible for Study:

All

Accepts Healthy Volunteers:

Yes

Criteria

Inclusion Criteria:

- Male or female participants ≥6 months to <12 years of age, at the time of randomization, at Visit 1.
- Participants' parent(s)/legal guardian(s) and participants, as age appropriate, who are willing and able to comply with all scheduled visits, treatment plan, laboratory tests, lifestyle considerations, and other study procedures.
- Healthy participants who are determined by medical history, physical examination, and clinical judgment of the investigator to be eligible for inclusion in the study.
- Participants are expected to be available for the duration of the study and whose
- parent(s)/legal guardian can be contacted by telephone during study participation.
- Negative urine pregnancy test for female participants who are biologically capable of having children.
- Female participant of childbearing potential or male participant able to father children who is willing to use a highly effective method of contraception as outlined in this protocol for at least 28 days after the last dose of study intervention if at risk of pregnancy with her/his partner; or female participant not of childbearing potential or male participant not able to father children.
- The participant's parent(s)/legal guardian is capable of giving signed informed consent.

Exclusion Criteria:

- Phase 1 only: Past clinical (based on COVID-19 symptoms/signs alone, if a

- SARS-CoV-2 NAAT result was not available) or microbiological (based on COVID-19 symptoms/signs and a positive SARS-CoV-2 NAAT result) diagnosis of COVID-19.
- Phase 1 only: Known infection with HIV, HCV, or HBV.
- Receipt of medications intended to prevent COVID-19.
- Previous or current diagnosis of MIS-C.
- Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study.
- History of severe adverse reaction associated with a vaccine and/or severe allergic reaction (eg, anaphylaxis) to any component of the study intervention(s).
- Immunocompromised individuals with known or suspected immunodeficiency, as determined by history and/or laboratory/physical examination.
- Individuals with a history of autoimmune disease or an active autoimmune disease requiring therapeutic intervention, including but not limited to systemic lupus erythematosus.
- Bleeding diathesis or condition associated with prolonged bleeding that would, in the opinion of the investigator, contraindicate intramuscular injection.
- Female who is pregnant or breastfeeding.
- Previous vaccination with any coronavirus vaccine.
- Individuals who receive treatment with immunosuppressive therapy, including cytotoxic agents or systemic corticosteroids, eg, for cancer or an autoimmune disease, or planned receipt throughout the study. If systemic corticosteroids have been administered short term (<14 days) for treatment of an acute illness, participants should not be enrolled into the study until corticosteroid therapy has been discontinued for at least 28 days before study intervention administration. Inhaled/nebulized, intra-articular, intrabursal, or topical (skin or eyes) corticosteroids are permitted.
- Receipt of blood/plasma products, immunoglobulin, or monoclonal antibodies, from 60 days before study intervention administration, or receipt of any passive antibody therapy specific to COVID-19 from 90 days before study intervention administration, or planned receipt throughout the study.
- Participation in other studies involving study intervention within 28 days prior to study entry and/or during study participation.
- Previous participation in other studies involving study intervention containing LNPs.
- Participants who are direct descendants (child or grandchild) of investigational site staff members or Pfizer/BioNTech employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members.

Contacts and Locations

Go to

Information from the National Library of Medicine

To learn more about this study, you or your doctor may contact the study research staff using the contact information provided by the sponsor.

Please refer to this study by its ClinicalTrials.gov identifier (NCT number): ***NCT04816643***

Contacts

Contact: Pfizer CT.gov Call Center 1-800-718-1021 ClinicalTrials.gov_Inquiries@pfizer.com

Locations

▶ Show 67 study locations

Sponsors and Collaborators

BioNTech SE

Pfizer

Investigators

Study Director: Pfizer CT.gov Call Center Pfizer

More Information

Go to ▼

Additional Information:

To obtain contact information for a study center near you, click here. EXIT

Responsible Party:

BioNTech SE

ClinicalTrials.gov Identifier:

NCT04816643 History of Changes

Other Study ID Numbers:

C4591007

2020-005442-42 (EudraCT Number)

First Posted:

March 25, 2021 Key Record Dates

Last Update Posted:

May 19, 2021

Last Verified:

May 2021

Individual Participant Data (IPD) Sharing Statement:

Plan to Share IPD:

No

Plan Description:

Pfizer will provide access to individual de-identified participant data and related study documents (e.g. protocol, Statistical Analysis Plan (SAP), Clinical Study Report (CSR)) upon request from qualified researchers, and subject to certain criteria, conditions, and exceptions. Further details on Pfizer's data sharing criteria and process for requesting access can be found at: https://www.pfizer.com/science/clinical_trials/trial_data_and_results/data_requests.

Studies a U.S. FDA-regulated Drug Product:

Yes

Studies a U.S. FDA-regulated Device Product:

No

Keywords provided by BioNTech SE:

COVID-19
Coronavirus Vaccine
SARS-CoV-2
RNA Vaccine
mRNA Vaccine