**Pfizer COVID 19 Trial Document Highlights**

**A PHASE 1/2/3, PLACEBO-CONTROLLED, RANDOMIZED, OBSERVER-BLIND,DOSE-FINDING STUDY TO EVALUATE THE SAFETY, TOLERABILITY,IMMUNOGENICITY, AND EFFICACY OF SARS-COV-2 RNA VACCINE CANDIDATES AGAINST COVID-19 IN HEALTHY INDIVIDUALS**

6.5.1. Prohibited During the Study

Receipt of chronic systemic treatment with known immunosuppressant medications, or

radiotherapy, within 60 days before enrollment through conclusion of the study.

Receipt of systemic corticosteroids (≥20 mg/day of prednisone or equivalent) for ≥14 days is

prohibited from 28 days prior to enrollment to Visit 7 for Phase 1 participants, and Visit 3 for

Phase 2/3 participants).

1.3.2. Phase 2/3

An unplanned potential COVID-19 illness visit and unplanned potential COVID-19 convalescent visit are required at any time between Visit 1 (Vaccination 1) and Visit 6 (24-month follow-up visit) that potential COVID-19 symptoms are reported, including MIS-C. (page 23)

2. INTRODUCTION

The BNT162 RNA-based COVID-19 vaccines are currently being investigated for

prevention of COVID-19 in **healthy individuals**. (page 26)

2.1. Study Rationale

The purpose of the study is to rapidly describe the safety, tolerability, and immunogenicity of

2 BNT162 RNA-based COVID-19 vaccine candidates against COVID-19, and the efficacy

of 1 candidate, in healthy individuals. **There are currently no licensed vaccines to prevent**

**infection with SARS-CoV-2 or COVID-19**. Given the global crisis of COVID-19 and fast

expansion of the disease in the United States and elsewhere, the rapid development of an

effective vaccine is of utmost importance.

2.2. Background

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. Later in January, 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 another

coronavirus infecting humans, the Middle East respiratory syndrome (MERS) virus. (page 26)

2.3. Benefit/Risk Assessment

There is an ongoing global pandemic of COVID-19 with no preventative or therapeutic

options available. **While there were no data available from clinical trials on the use of**

**BNT162 vaccines in humans at the outset of this study**, available nonclinical data with these

vaccines, and data from nonclinical studies and clinical trials with the same or related RNA

components, or antigens, supported a favorable risk/benefit profile. Anticipated AEs after

vaccination were expected to be manageable using routine symptom-driven standard of care

as determined by the investigators and, as a result, the profile of these vaccine candidates

supported initiation of this Phase 1/2/3 clinical study. (page 27)

2.3.1. Risk Assessment

Potential Risk of Clinical

Significance

Summary of Data/Rationale for Risk Mitigation Strategy

Study Intervention: BNT162 RNA-Based COVID-19 Vaccine

Potential for local reactions (injection

site redness, injection site swelling,

and injection site pain) and systemic

events (fever, fatigue, headache,

chills, vomiting, diarrhea, muscle

pain, and joint pain) following

vaccination.

These are common adverse reactions seen

with other vaccines, as noted in the FDA

Center for Biologics Evaluation and

Research (CBER) guidelines on toxicity

grading scales for healthy adult volunteers

enrolled in preventive vaccine clinical

trials.8

The Phase 1 study design includes the use of controlled vaccination and

dose escalation to closely monitor and limit the rate of enrollment to ensure

participant safety. The study employs the use of a reactogenicity e-diary to

monitor local reactions and systemic events in real time. Stopping rules are

also in place. The first 5 participants in each group in Phase 1 will be

observed for 4 hours after vaccination to assess any immediate AEs. All

other participants will be observed for at least 30 minutes after vaccination.

Unknown AEs and laboratory

abnormalities with a novel vaccine.

**This study is one of the first 2**

**parallel-running clinical studies** with the

BNT162 vaccine candidates and as such

**there are no clinical data available for this**

**vaccine**.

The Phase 1 study design includes the use of controlled vaccination and

dose escalation to closely monitor and limit the rate of enrollment to ensure

participant safety. An IRC (in Phase 1) and DMC (throughout the study)

will also review safety data. Stopping rules are also in place. The first 5

participants in each group in Phase 1 will be observed for 4 hours after

vaccination to assess any immediate AEs. All other participants will be

observed for at least 30 minutes after vaccination.

**Potential for COVID-19**

**enhancement.**

**Disease enhancement has been seen**

**following vaccination with respiratory**

**syncytial virus (RSV), feline coronavirus,**

**and Dengue virus vaccines**.

Phase 1 excludes participants with likely previous or current COVID-19. In

Phase 2/3, temporary delay criteria defer vaccination of participants with

symptoms of potential COVID-19. All participants are followed for any

potential COVID-19 illness, including markers of severity, and have blood

samples taken for potential measurement of SARS-CoV-2 antigen-specific

antibody and SARS-CoV-2 neutralizing titers. (page 29)

8.2.6. Pregnancy Testing

A negative pregnancy test result will be required prior to the participant’s receiving the study intervention. Pregnancy tests may also be repeated if requested by IRBs/ECs or if required by local regulations. In the case of a positive confirmed pregnancy, the participant will be withdrawn from administration of study intervention but may remain in the study. (page 65)

8.3.1. Time Period and Frequency for Collecting AE and SAE Information

SAEs will be collected from the time the participant/parent(s)/legal guardian provides

informed consent to approximately 6 months after the last dose of study intervention (Visit 8

for Phase 1 participants, and Visit 4 for Phase 2/3 participants). (page 65)

If a participant definitively discontinues or temporarily discontinues study intervention

because of an AE or SAE, the AE or SAE must be recorded on the CRF and the SAE

reported using the Vaccine SAE Report Form.

Investigators are not obligated to actively seek AEs or SAEs after the participant has

concluded study participation. However, if the investigator learns of any SAE, including a

death, at any time after a participant has completed the study, and he/she considers the event

to be reasonably related to the study intervention, the investigator must promptly report the

SAE to Pfizer using the Vaccine SAE Report Form. (page 66)

8.3.2. Method of Detecting AEs and SAEs

The method of recording, evaluating, and assessing causality of AEs and SAEs and the

procedures for completing and transmitting SAE reports are provided in Appendix 3.

Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and

nonleading verbal questioning of the participant is the preferred method to inquire about

AE occurrences.

8.3.3. Follow-up of AEs and SAEs

After the initial AE/SAE report, the investigator is required to proactively follow each

participant at subsequent visits/contacts. For each event, the investigator must pursue and

obtain adequate information until resolution, stabilization, the event is otherwise explained,

or the participant is lost to follow-up (as defined in Section 7.3). (page 66)

8.3.5. Exposure During Pregnancy or Breastfeeding, and Occupational Exposure

Exposure to the study intervention under study during pregnancy or breastfeeding and

occupational exposure are reportable to Pfizer Safety within 24 hours of investigator

awareness.

8.3.5.1. Exposure During Pregnancy

An EDP occurs if:

• A female participant is found to be pregnant while receiving or after discontinuing

study intervention.

• A male participant who is receiving or has discontinued study intervention exposes a

female partner prior to or around the time of conception.

• A female is found to be pregnant while being exposed or having been exposed to

study intervention due to environmental exposure. Below are examples of

environmental exposure during pregnancy:

• A female family member or healthcare provider reports that she is pregnant after

having been exposed to the study intervention by inhalation or skin contact.

\*A male family member or healthcare provider who has been exposed to the study

intervention by inhalation or skin contact then exposes his female partner prior to

or around the time of conception.

The investigator must report EDP to Pfizer Safety within 24 hours of the investigator’s

awareness, irrespective of whether an SAE has occurred. The initial information submitted

should include the anticipated date of delivery (see below for information related to

termination of pregnancy).

• If EDP occurs in a participant or a participant’s partner, the investigator must report

this information to Pfizer Safety on the Vaccine SAE Report Form and an EDP

Supplemental Form, regardless of whether an SAE has occurred. Details of the

pregnancy will be collected after the start of study intervention and until 6 months

after the last dose of study intervention.

• If EDP occurs in the setting of environmental exposure, the investigator must report

information to Pfizer Safety using the Vaccine SAE Report Form and EDP

Supplemental Form. Since the exposure information does not pertain to the

participant enrolled in the study, the information is not recorded on a CRF; however,

a copy of the completed Vaccine SAE Report Form is maintained in the investigator

site file.

Follow-up is conducted to obtain general information on the pregnancy and its outcome for

all EDP reports with an unknown outcome. The investigator will follow the pregnancy until

completion (or until pregnancy termination) and notify Pfizer Safety of the outcome as a

follow-up to the initial EDP Supplemental Form. **In the case of a live birth, the structural**

**integrity of the neonate can be assessed at the time of birth**. In the event of a termination, the

reason(s) for termination should be specified and, if clinically possible, the structural

integrity of the terminated fetus should be assessed by gross visual inspection (unless

preprocedure test findings are conclusive for a congenital anomaly and the findings are

reported).

**Abnormal pregnancy outcomes are considered SAEs.** **If the outcome of the pregnancy meets**

**the criteria for an SAE (ie, ectopic pregnancy, spontaneous abortion, intrauterine fetal**

**demise, neonatal death, or congenital anomaly), the investigator should follow the procedures**

**for reporting SAEs.** Additional information about pregnancy outcomes that are reported to

Pfizer Safety as SAEs follows:

• Spontaneous abortion including miscarriage and missed abortion;

• Neonatal deaths that occur within 1 month of birth should be reported, without regard

to causality, as SAEs. In addition, infant deaths after 1 month should be reported as

SAEs when the investigator assesses the infant death as related or possibly related to

exposure to the study intervention. (page 68)

Additional information regarding the EDP may be requested by the sponsor. Further

follow-up of birth outcomes will be handled on a case-by-case basis (eg, follow-up on

preterm infants to identify developmental delays). In the case of paternal exposure, the

investigator will provide the participant with the Pregnant Partner Release of Information

Form to deliver to his partner. The investigator must document in the source documents that

the participant was given the Pregnant Partner Release of Information Form to provide to his

partner. (page 69)

8.3.5.2. Exposure During Breastfeeding

A female is found to be breastfeeding while being exposed or having been exposed to

study intervention (ie, environmental exposure). An example of environmental

exposure during breastfeeding is a female family member or healthcare provider who

reports that she is breastfeeding after having been exposed to the study intervention

by inhalation or skin contact.

The investigator must report exposure during breastfeeding to Pfizer Safety within 24 hours

of the investigator’s awareness, irrespective of whether an SAE has occurred. The

information must be reported using the Vaccine SAE Report Form. When exposure during

breastfeeding occurs in the setting of environmental exposure, the exposure information does

not pertain to the participant enrolled in the study, so the information is not recorded on a

CRF. However, a copy of the completed Vaccine SAE Report Form is maintained in the

investigator site file.

An exposure during breastfeeding report is not created when a Pfizer drug specifically

approved for use in breastfeeding women (eg, vitamins) is administered in accord with

authorized use. However, if the infant experiences an SAE associated with such a drug, the

SAE is reported together with the exposure during breastfeeding.

8.3.6. Cardiovascular and Death Events

Not applicable. ? (page 70)

10.4.2. Female Participant Reproductive Inclusion Criteria

A female participant is eligible to participate if she is not pregnant or breastfeeding, and at

least 1 of the following conditions applies:

• Is not a WOCBP (see definitions below in Section 10.4.3).

OR

• Is a WOCBP and using an acceptable contraceptive method as described below

during the intervention period (for a minimum of 28 days after the last dose of study

intervention). The investigator should evaluate the effectiveness of the contraceptive

method in relationship to the first dose of study intervention.

The investigator is responsible for review of medical history, menstrual history, and recent

sexual activity to decrease the risk for inclusion of a woman with an early undetected

pregnancy. (page 132)

10.4.4. Contraception Methods

5. Vasectomized partner:

• Vasectomized partner is a highly effective contraceptive method provided that the

partner is the sole sexual partner of the woman of childbearing potential and the

absence of sperm has been confirmed. If not, an additional highly effective method

of contraception should be used. The spermatogenesis cycle is approximately

90 days.

8. Sexual abstinence:

• Sexual abstinence is considered a highly effective method only if defined as

refraining from heterosexual intercourse during the entire period of risk associated

with the study intervention. The reliability of sexual abstinence needs to be evaluated

in relation to the duration of the study and the preferred and usual lifestyle of the

participant. (page 134)

10.5. Appendix 5: Liver Safety: Suggested Actions and Follow-up Assessments

Potential Cases of Drug-Induced Liver Injury

Rises in AST/ALT and TBili separated by more than a few weeks should be assessed

individually based on clinical judgment; any case where uncertainty remains as to whether it

represents a potential Hy’s law case should be reviewed with the sponsor.

The participant should return to the investigator site and be evaluated as soon as possible,

preferably within 48 hours from awareness of the abnormal results. This evaluation should

include laboratory tests, detailed history, and physical assessment. (page 137)

In addition to repeating measurements of AST and ALT and TBili for suspected cases of

Hy’s law, additional laboratory tests should include albumin, CK, direct and indirect

bilirubin, GGT, PT/INR, total bile acids, and alkaline phosphatase. Consideration should

also be given to drawing a separate tube of clotted blood and an anticoagulated tube of blood

for further testing, as needed, for further contemporaneous analyses at the time of the

recognized initial abnormalities to determine etiology. A detailed history, including relevant

information, such as review of ethanol, acetaminophen/paracetamol (either by itself or as a

coformulated product in prescription or over-the-counter medications), recreational drug,

supplement (herbal) use and consumption, family history, sexual history, travel history,

history of contact with a jaundiced person, surgery, blood transfusion, history of liver or

allergic disease, and potential occupational exposure to chemicals, should be collected.

Further testing for acute hepatitis A, B, C, D, and E infection and liver imaging (eg, biliary

tract) and collection of serum samples for acetaminophen/paracetamol drug and/or protein

adduct levels may be warranted.

All cases demonstrated on repeat testing as meeting the laboratory criteria of AST/ALT and

TBili elevation defined above should be considered potential DILI (Hy’s law) cases if no

other reason for the LFT abnormalities has yet been found**. Such potential DILI (Hy’s law)**

**cases are to be reported as SAEs, irrespective of availability of all the results of the**

**investigations performed to determine etiology of the LFT abnormalities**. (page 137)