Pfizer/BioNTech COVID-19 mRNA vaccine

Overview for ACIP Meeting

Dr Nicholas Kitchin, Pfizer Vaccine Clinical Research & Development

Note: The information contained in this document, including scientific approaches, assumptions regarding potential safety and efficacy, clinical trial and manufacturing plans and timing estimates, are subject to change based on emerging data, regulatory guidance, and manufacturing and technical developments, among other risks.
Pfizer/BioNTech COVID-19 mRNA vaccine program overview

Two Vaccine Antigens

- Spike Protein
  - Receptor Binding Domain (RBD)

- Spike-Antigen Whole Protein

Four Vaccine Candidates

<table>
<thead>
<tr>
<th>Variant</th>
<th>Target</th>
<th>RNA construct</th>
<th>Immunization</th>
</tr>
</thead>
<tbody>
<tr>
<td>162a1</td>
<td>RBD subunit</td>
<td>uRNA</td>
<td>prime / boost</td>
</tr>
<tr>
<td>162b1</td>
<td>RBD subunit</td>
<td>modRNA</td>
<td>prime / boost</td>
</tr>
<tr>
<td>162b2</td>
<td>P2-mutated full spike protein</td>
<td>modRNA</td>
<td>prime / boost</td>
</tr>
<tr>
<td>162c2</td>
<td>P2-mutated full spike protein</td>
<td>saRNA</td>
<td>single injection</td>
</tr>
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</table>

Focus of large-scale development

SARS-CoV-2 (3D Model)

SARS-COV-2 Spike Protein 3D Structure
(Wrapp et al., 2020, Science)
Two clinical studies assessed the safety, tolerability, and immunogenicity of ascending dose levels of BNT162 modRNA vaccine candidates

**US Phase 1/2/3 Study***  
(C4591001 / NCT04368728)  
- 15 healthy participants (18-55 or 65-85 years of age) per dose level  
[12 active vaccine recipients and 3 placebo recipients]  
- 10 µg, 20 µg, 30 µg, 100 µg  
- Immunized on Day 1 and a boost dose on Day 21 [No boost for 100µg cohort]

**Germany Phase 1/2 Study**  
(BNT162-01 / NCT04380701)  
- 12 healthy participants (18-55 or 56-85 years of age) per dose level  
- 1 µg, 10 µg, 30 µg, 50 µg, 60 µg  
- Immunized on Day 1 and a boost dose on Day 22 ± 2 [No boost for 60 µg cohort]

- **Human COVID-19 convalescent sera (HCS)**  
  - 38 human SARS-CoV-2 infection/COVID-19 convalescent sera from subjects 18-83 years of age  
    - N=29, 18-55 years of age  
    - N=9, 56-83 years of age  
  - Collected at least 14 days after PCR-confirmed diagnosis, and at a time when subjects were asymptomatic  
  - Serum donors predominantly had symptomatic infections (35/38), and one had been hospitalized

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US Phase 1/2/3 study overview (C4591001 / NCT04368728)

### Phase 1 (N=195)

<table>
<thead>
<tr>
<th>BNT162b1</th>
<th>N=15/group (4:1 randomization active:placebo)</th>
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<tbody>
<tr>
<td>18-55 yrs</td>
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To describe the safety and tolerability profiles of prophylactic BNT162 vaccines:
- E-diary (local reactions, systemic events incl. fever, use of analgesics/antipyretics)
- Adverse events
  - All up to 1 month after last dose
  - Serious AEs up to 6 months after last dose
- Hematology & chemistry

To describe the immune responses elicited by prophylactic BNT162 vaccines:
- SARS-CoV-2 neutralizing titers
- S1-binding IgG levels
- RBD-binding IgG levels

### Phase 2/3 (N=360/29,286)

<table>
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<tr>
<th>BNT162b2</th>
<th>N=180/14,643 group (1:1 randomization active:placebo)</th>
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<tr>
<td>18-55 yrs</td>
<td>~60% 30 µg</td>
</tr>
<tr>
<td>56-85 yrs</td>
<td>~40% 30 µg</td>
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To define the safety profile of, and immune responses to, prophylactic BNT162b2 vaccine in Phase 2 participants

To evaluate the efficacy of prophylactic BNT162b2 against confirmed COVID-19 in Phase 2/3 participants:
- Without evidence of infection before vaccination
- With and without evidence of infection before vaccination

To define the safety profile of prophylactic BNT162b2 vaccine in Phase 2/3 participants
- E-diary (local reactions, systemic events incl. fever, use of analgesics/antipyretics) – in a subset of at least 6000 participants
- Adverse events
  - All up to 1 month after last dose
  - Serious AEs up to 6 months after last dose

Additional secondary & exploratory objectives
To maximize a vaccine’s potential to prevent COVID-19, the following key criteria were evaluated in the selection of the final vaccine candidate and dose level:

- Acceptable safety and reactogenicity
- SARS-CoV-2 neutralizing titers at or above a human convalescent serum panel (HCS)
- Strong $T_H^1$-type CD4$^+$ and CD8$^+$ T cell responses

Both BNT162b1 and BNT162b2 looked strong as vaccine candidates

However, the totality of data favored the selection of BNT162b2 based on the following findings:

- A reactogenicity profile that is more favorable than BNT162b1 in both younger and older adults
- A trend towards stronger CD8$^+$ T cell responses
- Earlier clearance of SARS-CoV-2 RNA in the nose of BNT162b2 immunized and challenged rhesus

Based on the totality of data, we chose to advance BNT162b2 at the 30µg dose level
BNT162b2 reactogenicity data from C4591001 Phase 1
BNT162b2 shows favorable local reactogenicity profile in Phase 1 (both age groups)

**18-55 years**

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<th>Dose 2</th>
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</tr>
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**65-85 years**

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**Note:** 1-3 days follow-up for 10 µg group
BNT162b2 shows favorable systemic reactogenicity profile in Phase 1 (18-55 years)
BNT162b2 shows favorable systemic reactogenicity profile in Phase 1 (65-85 years)

Note: 1-3 days follow-up for 10 µg group
Immunogenicity data from C4591001 Phase 1
Robust SARS-CoV-2 50% neutralization titers after 2 doses of BNT162b2 in Phase 1 exceed those in a human convalescent panel (HCS*)
Strong T cell responses shown in German study BNT162-01
BNT162b1 induces strong CD4⁺ and CD8⁺ T cell responses with TH₁ dominance
German Trial, Phase 1, Day 29 (post-dose 2) analysis

Human Convalescent Sera (HCS)
Phase 1 demonstrated encouraging safety & immunogenicity for BNT162b2, supporting advancement to Phase 2/3

• Reactogenicity:
  – Lower after first vaccination compared to second
  – Lower in younger than older participants
  – Profile appears at least as good as approved adult vaccines

• Immunogenicity:
  – Neutralizing antibody responses 7 days after second dose are robust and exceed those observed in a panel of human convalescent sera (38 human SARS-CoV-2 infection/COVID-19 convalescent sera)
  – Strong CD4\(^+\) and CD8\(^+\) T cell responses with T\(_H1\) dominance
Overview of Phase 2/3
US Phase 1/2/3 study overview (C4591001 / NCT04368728)

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Additional secondary & exploratory objectives
Phase 2/3 efficacy schema – started 27 July, 2020

Vaccination period

21 days apart

Follow-up period

Up to 2 years

Active surveillance for potential COVID-19 symptoms – triggering telehealth or in-person visit and nasal swab

Cases defined based on:
- Presence of symptom(s); and
- Positive SARS-CoV-2 NAAT

Efficacy analyses in participants:
- Without evidence of infection before vaccination; and
- With and without evidence of infection before vaccination