Pfizer-BioNTech COVID-19 Vaccine (BNT-162b2) FDA Phase 3 Review and Analysis

Submitted by TeamHealth Emerging Infectious Disease Task Force (EIDT)

The Pfizer-BioNTech BNT-162b2 Vaccine (Pfizer Vaccine) Concept

The Pfizer vaccine is a piece of messenger RNA (mRNA) that informs the cell's own machinery to make portions of the SARS-CoV-2 virus called spike proteins. These spike proteins are produced by the cell in massive quantities which then drives the body to mount an immune response to the spike protein, directly conferring an immunity to the SARS-CoV-2 virus, protecting the recipient from getting COVID-19.

Previous vaccines have been composed of live virus infections (e.g., smallpox), disabled virus infections (e.g., measles), or sub-components of virus (yearly flu), all of which are designed to stimulate the immune system against a specific disease. The mRNA in the Pfizer vaccine is delivered into the cell in a lipid (fat) nanoparticle which results in less reaction to the vaccine itself.

Pfizer Vaccine Phase 3 Trial Effectiveness Results

- 38,000 patients were randomized to receive either the vaccine or a placebo.
- Of the 17,411 receiving the vaccine, only eight subsequently developed COVID-19 versus 162 in the 17,511 in the placebo group.
- *The vaccine trial demonstrated an average of 95% efficacy, meaning that the vaccine was effective in preventing COVID-19 infections in the vaccinated cohort with 95% effectiveness as compared with the placebo vaccine cohort.*
- There were 10 severe COVID-19 infections, one occurred in the vaccine cohort and nine in the placebo group. These data reveal an 88.9% efficacy in preventing severe COVID-19.
- Vaccine efficacy was 82% after dose one and 95% at least seven days after dose two. There is evidence of protection beginning on day 14 after the first vaccine dose.
- Comparatively, the flu vaccine is 40-60% effective on any given year. A more effective vaccine means that greater herd immunity is produced per vaccination. The Pfizer vaccine result is markedly better than expected.

Pfizer Vaccine Phase 3 Trial Safety Results

- The expected local vaccination reactions are pain, redness, and swelling at the vaccine site. The most common local reaction was pain at the injection site (80%), with redness or swelling occurring in about 5% of cases.
- The most common systemic adverse events and their frequencies (after the second dose) were: fatigue (59%), headache (52%), myalgia (37%), chills (35%), fever (31%), and arthralgia (22%). These adverse events were consistently worse after the second vaccination across all demographic groups.
- A total of six deaths occurred that were deemed unrelated to the vaccine during the study period, two in the vaccine cohort and four in the placebo. These were cardiac or stroke events occurring in the age > 55 population.
- Non-fatal serious adverse events (SAEs) occurred 0.6% in the vaccine group and 0.5% in the placebo group. The most common SAEs were appendicitis, cardiovascular, and stroke.
- Individuals with previous COVID-19 infections were included but at low numbers. No conclusion could be made, however, no SAEs were reported in this cohort. Pregnant patients were excluded. Patients younger than 16 were not studied.
- Recent media reports of a few allergic reactions in individuals with prior severe atopic conditions have caused the United Kingdom to recommend such individuals not receive the Pfizer vaccine. Although this issue is being carefully monitored, there is currently no evidence that the frequency of allergic reactions is higher than with other vaccines.

Summary Findings and EIDT Recommendations

Key Findings

- The Pfizer vaccine showed 95% effectiveness, which is better than expected, across all age and demographic groups studied. Groups receiving the vaccine can expect a 95% reduction in the likelihood of contracting COVID-19.
- The vaccine is safe with mild adverse effects after the first dose and moderate adverse effects after the second dose.
- The vaccine showed a promising severe adverse effect profile with only a minimal number of SAEs and deaths.
- The COVID-19 pandemic has not been well mitigated by masking, social distancing, or other public health strategies for various reasons.

Recommendations

- *The EIDT strongly recommends vaccination with the Pfizer-BioNTech COVID-19 vaccine for all adults above 16 years of age in every racial and ethnic demographic regardless of COVID-19 risk factors, prior COVID-19 infection or other underlying health conditions, unless there are clear, existing contraindications to receiving any vaccine.*
- Because the Pfizer vaccine is a novel approach using mRNA technology never previously employed in a vaccine, the long-term effects are unknown. More information will be gained as the vaccine is deployed over the coming months and years. mRNA-based therapies have been used in the treatment of cancer and certain hereditary disorders safely and effectively for decades.
- The EIDT supports offering the Pfizer vaccine to our pregnant clinicians, who are a group at increased risk from COVID-19. Our pregnant clinicians that choose to take the vaccine should understand the vaccine has not been studied during pregnancy, and we have no data on possible fetal impacts.
- Due to the unclear duration of immunity and risk of reinfection in individuals previously infected with SARS-CoV-2, limited data from the study suggests that previously infected individuals could benefit from vaccination.
- The EIDT recommends staggering administration of the Pfizer vaccine, to groups of clinicians by about seven days, when possible, to minimize the impact that systemic adverse effects may have on staffing and operations.
- Insufficient data currently exist to recommend the Pfizer vaccine in individuals less than 16 years of age, but pediatric vaccine trials have been underway since September 2020.

This literature is endorsed unanimously by the TeamHealth EIDT. It is considered current as of December 14, 2020, and changing frequently; this document is provided for informational and educational purposes; it is not intended to replace clinical judgement, information from relevant professional societies or any information from the Centers for Disease Control and Prevention or the World Health Organization.