ModernaTX COVID-19 Vaccine (mRNA-1273) FDA Phase 3 Review and Analysis

Submitted by TeamHealth Emerging Infectious Disease Task Force (EIDT)

The ModernaTX mRNA-1273 (Moderna Vaccine) Concept

The Moderna 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. The Moderna vaccine is intended for individuals 18 years and older and consists of two doses of 100 mcg intramuscular each administered one month apart.

Moderna Vaccine Phase 3 Trial Effectiveness Results

- 30,400 participants were randomized to receive either the vaccine or placebo.
- Only 11 patients in the vaccine group versus 185 patients in the placebo group developed COVID-19.
- *The vaccine trial demonstrated an average of 94% 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. This was slightly lower in the age cohort > 65 years old.*
- The benefits held through all genders, racial, and ethnic groups as well as patients with comorbidities. Included in this, are small numbers of individuals having had prior COVID-19 infections.
- There were 30 severe cases in the placebo arm and none in the vaccine arm, indicating significant protection from severe COVID-19 infection.

Moderna Vaccine Phase 3 Trial Safety Results

- The most common adverse reactions were injection site pain (91.6%), fatigue (68.5%), headache (63.0%), muscle pain (59.6%), joint pain (44.8%), and chills (43.4%). Local and regional adenopathy was reported in 1.1% of the vaccine and 0.63% of the placebo cohorts. Local hypersensitivity of the vaccinated arm was noted in 1.5% of the vaccine and 1.1% of the placebo cohorts.
- Severe Adverse Reactions (SAEs) were low: 1% in the vaccine cohort and 1% in the placebo group.
- The most common SAEs in the vaccine cohort included myocardial infarction (0.03%), cholecystitis (0.02%), and nephrolithiasis (0.02%). The numbers are insufficient to link causality to the vaccine.
- No anaphylaxis or severe hypersensitivity reactions were noted.
- Four cases of Bell's palsy were reported – three in the vaccine cohort and one in the placebo cohort with insufficient numbers to determine any relationship to the vaccine.
- The safety profile is generally consistent across all age, groups, gender, ethnic, racial groups and comorbidities.

Summary Findings and EIDT Recommendations

Key Findings

- The Moderna vaccine showed a 94.1% efficacy in preventing COVID-19 across all age and demographic groups studied. In general, individuals receiving the vaccine can expect a 94.1% reduction in the likelihood of contracting COVID-19.
- Based on this evidence, the vaccine is believed to be safe for use with mild adverse effects after the first dose and moderate adverse effects after the second dose. The numbers of SAEs were low and not statistically associated with the vaccine.
- 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 Moderna COVID-19 vaccine for all adults 18 years of age and above and 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.*
- Similar to the Pfizer vaccine, the Moderna COVID-19 vaccine is a novel approach using messenger RNA technology not previously employed in a vaccine. Because of this, long-term effects are unknown. More information will be obtained as the vaccine is deployed over the coming months and years. Messenger RNA based therapies have been used in the treatment of cancer and certain hereditary disorders safely and effectively for decades.
- The EIDT supports offering the Moderna 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 Moderna study suggests that previously infected individuals could benefit from vaccination.
- The EIDT recommends staggering administration of the Moderna 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 Moderna vaccine to individuals less than 18 years of age, but pediatric vaccine trials are currently underway.

This literature is endorsed unanimously by the TeamHealth EIDT. It is considered current as of December 17, 2020. This information changes frequently; this document is provided for informational and educational purposes; it is not intended to replace clinical judgment, information from the relevant professional societies or any information from the Centers for Disease Control and Prevention (CDC) or the World Health Organization (WHO).

Reference

FDA. Vaccines and Related Biological Products Advisory Committee Meeting, December 17, 2020 FDA Briefing Document Moderna COVID-19 Vaccine (HERE)