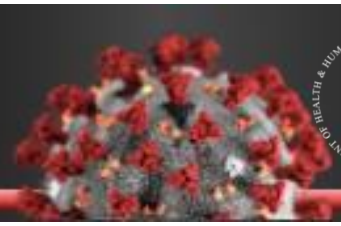
Indian Health Service
National Pharmacy and Therapeutics Committee

COVID-19 Emerging Treatments Update



December 21, 2020

Emergency Use Authorization

Moderna COVID-19 Vaccine (mRNA-1273)

Vaccine Platform & Mechanism of Action[1]: Messenger RNA (mRNA)-based vaccine that encodes a disease-specific antigen, the SARS-CoV-2 spike protein, and leverages the host cells' protein synthesis machinery to produce antigens that elicit an immune response. The production of this viral antigen within the body prepares the immune system to recognize this viral antigen so it can combat future infections caused by the virus with the same antigen.

Current Status[2]: On December 18, 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for mRNA-1273 (the Moderna COVID-19 Vaccine) for prevention of COVID-19 in individuals 18 years of age and older. It is not currently FDA-approved for any indication.

Availability[3,4]: In August 2020, the US Government pre-purchased 100 million doses of the Moderna COVID-19 Vaccine. In December 2020, the HHS acquired an additional 100 million doses of the vaccine, bringing the total doses owned by the US Government to 200 million. The additional doses will provide for continuous delivery through June 2021. The IHS, as a jurisdiction, is expected to receive ~46,000 doses in the initial allocation.

Recommended Administration & Storage[5]: The Moderna COVID-19 Vaccine (100 micrograms) is administered intramuscularly (IM) as a series of two doses (0.5 mL each), given 28 days apart.

The Moderna COVID-19 Vaccine is provided as a frozen suspension [stored between -25º to -15ºC (-13º to 5ºF)] multi-dose vial containing 10 doses. The vaccine must be thawed prior to administration. After thawing, a maximum of 10 doses (0.5 mL each) can be withdrawn from each vial. Vials can be stored refrigerated between 2° to 8°C (36° to 46°F) for up to 30 days prior to first use. Unopened vials may be stored between 8° to 25°C (46° to 77°F) for up to 12 hours. After the first dose has been withdrawn, the vial should be held between 2° to 25°C (36° to 77°F) and discarded after 6 hours. The vaccine does not contain a preservative.

Clinical Efficacy[2,5]: Study mRNA-1273-P301 is an ongoing Phase 3, randomized, placebo-controlled clinical trial to evaluate the efficacy, safety and immunogenicity of the Moderna COVID-19 vaccine administered in 2 doses 28 days apart in adults 18 years of age and older, at 99 sites in the US. Participants (N=30,351) were randomized to receive IM injections of either 100 micrograms of vaccine (n=15,181) or placebo (n=15,170) on Day 1 and Day 29. The study included 24,907 (82.1%) participants considered at risk for acquiring SARS-CoV-2 infection, of whom 25.1% were healthcare workers. American Indians and Alaska Natives represented <1% of all study participants. Pregnant patients were excluded from phase III clinical trial participation.

Final efficacy analysis of the primary endpoint, vaccine efficacy (VE) against COVID-19 starting 14 days after the second dose, was 94.1% (95% CI: 89.3%, 96.8%) with 11 cases in the vaccine group vs. 185 cases in the placebo group. This was consistent with results obtained from the interim analysis. Of note, the VE in participants ≥65 years of age appears to be lower than in younger adults 18 to <65 years (86.4% vs. 95.6%). Thirty COVID-19 cases were reported as "severe"; all 30 cases (100%) were in the placebo group and nine resulted in hospitalization. Vaccine efficacy was >93% in the group of participants *with or without* prior Infection. Efficacy outcomes across demographic subgroups were consistent with the efficacy seen in the overall study population.

Reactogenicity & Adverse Events (AEs)[2,5]: The proportions of vaccine and placebo participants with serious AEs (0.6% vs. 0.6%), death (<0.1% vs. <0.1%), and withdrawals due to AEs (0.3% vs. 0.5%) were balanced across study groups. Local site reactions and systemic solicited events after vaccination were frequent and mostly mild to moderate. The most common solicited adverse reactions were injection site pain, fatigue, headache, muscle pain, joint pain, and chills; 0.2% to 9.7% were reported as severe, with severe AEs being more frequent after dose 2 than after dose 1 and less frequent in adults ≥65 years of age as compared to younger participants.

Among AEs of clinical interest, lymphadenopathy was reported in 173 participants (1.14%) in the vaccine group and 95 participants (0.63%) in the placebo group. Additionally, there was a numerical imbalance in hypersensitivity adverse events (injection site rash, injection site urticaria, etc.) across study groups, with 1.5% of vaccine recipients and 1.1% of placebo recipients reporting such events. There were no anaphylactic or severe hypersensitivity reactions with close temporal relation to the vaccine.

There have been three reports of Bell's palsy (facial paralysis) in the vaccine group and one in the placebo group. Currently available information is insufficient to determine a causal relationship with the vaccine. The FDA recommends surveillance for cases of Bell's palsy following deployment of the vaccine into larger populations. There were no other notable patterns of imbalance between the treatment and placebo groups for specific categories of adverse events (including neurologic, neuro-inflammatory, and thrombotic events) that would suggest a causal relationship with the Moderna COVID-19 Vaccine. No specific safety concerns were identified in subgroup analyses by age, race, ethnicity, medical comorbidities, or prior SARS-CoV-2 infection.

CDC Advisory Committee of Immunization Practices (ACIP)[6,7,8]: On December 19, 2020, after a transparent, evidence-based review of available data, the ACIP issued an interim recommendation for use of the Moderna COVID-19 vaccine in persons aged ≥18 years for the prevention of COVID-19. The review included clinical considerations, including the lack of interchangeability between the Moderna and Pfizer-BioNTech vaccines.

The ACIP also provided recommendations for expanded vaccination group priorities, adding that next priority group, Phase 1b, should consist of front-line essential workers and adults aged 75 years and older. Next up, Phase 1c would include adults aged 65-74 years, adults aged 16-64 years with high-risk medical conditions, and essential workers who did not qualify for inclusion in Phase 1b.

Vaccine Safety & Monitoring[9,10]: **===>>>> CDC V-safe[SM] after vaccination health tracker <<<<===**
Following FDA authorization, expanded use of pharmaceuticals and/or vaccines into broader populations can identify safety signals not detected in clinical trials and warrants vigilant monitoring to ensure safe utilization in understudied demographic groups. Last week, 2 British individuals receiving the Pfizer-BioNTech vaccine reported serious allergic reactions minutes after taking the vaccine. Soon after, two individuals in Alaska reported similar adverse reactions. Further investigation of these cases is underway and management strategies are available. *The potential for serious unanticipated AEs underscores the need for both clinicians and patients to be knowledgeable and attentive to possible vaccine-related AEs and how best to report these events*. The CDC's smartphone-based tool "v-safe" offers a convenient method for patients to directly communicate AEs to the CDC.

Patient Educational Items[11]: *****Key Points and Materials to Share with Patients*****

1. Per IHS Policy, every COVID-19 vaccine recipient should be provided a completed COVID-19 vaccination card. Each COVID-19 vaccine shipment will include COVID-19 vaccination record cards. Completed vaccination cards may be given to the recipient, the adult caregiver accompanying the recipient (if applicable), or other legal representative (if applicable).
2. Discuss and provide the enrollment process for the CDC's "v-safe" after vaccination health checker
3. Various patient education documents are available from the CDC including:

- COVID-19 Vaccination Communication Toolkit (for Medical Centers, Clinics, and Clinicians)
- Talking to Patients about COVID-19 Vaccines
- Understanding mRNA COVID-19 Vaccines
- Making a Strong Recommendation for COVID-19 Vaccination
- ***(NEW!)*** NIH COVID-19 Vaccination* Communication: Addressing Vaccine Hesitancy & Fostering Confidence

References:

1. Li, Yingzhu. American Chemical Society blog. Meet the mRNA vaccine rookies aiming to take down COVID-19. Accessed Nov 30, 2020.
2. U.S. Food and Drug Administration. Fact Sheet for Health Care Providers. Emergency Use Authorization of the Moderna COVID-19 Vaccine.
3. Department of Health & Human Services. Operation Warp Speed. Fact Sheet: Explaining Operation Warp Speed. Assessed Dec 15, 2020.
4. Internal email. RADM Michael Weahkee, Director, IHS. IHS Week in Review of the week of December 6, 2020. Sent Dec 12, 2020 @ 9:03am.
5. FDA Briefing Document. Vaccines and Related Biological Products Advisory Committee Meeting December 20, 2020 Moderna COVID-19 Vaccine.
6. CDC MMWR. ACIP Interim Recommendation for Use of Moderna COVID-19 Vaccine — United States, December 20, 2020
7. CDC Interim Considerations. Use of mRNA COVID-19 Vaccines Currently Authorized in the United States. Accessed Dec 20, 2020.
8. Medscape Medical News. CDC Identifies Next Priority Groups for COVID Vaccine - Medscape - Dec 20, 2020.
9. Medscape Medical News. Alaskan Has Allergic Reaction After Getting Pfizer's COVID-19 Vaccine – Medscape. Dec 16, 2020
10. CDC Interim Considerations: Preparing for the Potential Management of Anaphylaxis at COVID-19 Vaccination Sites. Accessed Dec 18,2020.
11. Indian Health Service. IHS Manual. COVID-19 Vaccination Card. Indian Health Service Circular No. 20-17. Accessed Dec 17, 2020.