

COVID-19 Vaccine Update

Deanna Moretz, PharmD, BCPS, Oregon State University Drug Use Research and Management Group

To date, three COVID-19 vaccines have received Emergency Use Authorization (EUA) by the Food and Drug Administration (FDA) for administration to the American population. Safety and efficacy for the two messenger ribonucleic acid (mRNA) vaccines were reviewed in the January 2021 edition of the Oregon State Drug Review.¹ Vaccines approved or currently being studied are presented in **Table 1**. As the mRNA vaccines became available in the United States (US), COVID-19 variants from the United Kingdom, South Africa, and Brazil emerged in North America. The mRNA vaccines were studied when virus variants were not widely circulating. This newsletter will review the evidence supporting the efficacy of the single-dose viral vector Janssen-Johnson & Johnson vaccine in preventing moderate to severe COVID-19 and address ongoing concerns related to COVID-19 vaccinations.

Table 1. COVID-19 Vaccines Authorized or Under Investigation in Phase 2 and 3 Trials²

Vaccine Manufacturer	Mechanism	Age	Dosing Schedule	EUA Status
Pfizer-BioNTech BNT162b2	mRNA	≥16 yo	0.3 mL IM for 2 doses (Days 0, 21)	Authorized 12/11/20
Moderna mRNA-1273	mRNA	≥18 yo	0.5mL IM for 2 doses (Days 0, 28)	Authorized 12/20/20
Janssen-Johnson & Johnson Ad26.COV2.S	Viral Vector	≥18 yo	0.5 ml IM for 1 dose (Day 0)	Authorized 2/27/21
AstraZeneca-Oxford AZD1222	Viral Vector	N/A	2 doses (Days 0, 28)	Anticipated 2021
Novavax NVX-CoV2373	Protein Subunit	N/A	2 doses (Days 0, 21)	Anticipated 2021
Sanofi-GSK	Protein Subunit	N/A	2 doses (Days 0, 21)	Anticipated 2022

Abbreviations: EUA = Emergency Use Authorization; IM = intramuscular; mL = milliliters; mRNA = messenger RNA; N/A = Not Available; yo = years old

Janssen COVID-19 Vaccine

The Janssen COVID-19 vaccine received EUA for use in persons aged 18 years and older for the prevention of COVID-19 on February 27, 2021.³ The Janssen COVID-19 vaccine is a recombinant, replication-incompetent adenovirus serotype 26 (Ad26) vector vaccine, encoding the stabilized prefusion spike glycoprotein of SARS-CoV-2.³ While adenoviruses are relatively common, Ad26 has been modified for this product so that it cannot replicate in the human body to cause illness. After vaccination, the body can temporarily make the spike protein,

which prompts an immune response against the SARS-CoV-2 virus. Viral vector vaccines have been studied since the 1970s. Two Ebola vaccines currently in use are both viral vector vaccines. The first of these vaccines was approved by the FDA in December 2019 following review of 12 clinical trials that included a total of 15,399 adults.⁴ Viral vector vaccines have also been used in clinical trials against viruses that include the Zika virus, human immunodeficiency virus (HIV) and influenza viruses.

Immunization with the Janssen COVID-19 vaccine consists of a single 0.5-mL dose administered intramuscularly.³ The vaccine may be stored refrigerated at 36° to 46° F (2° to 8°C) for up to 3 months. The Janssen vaccine was studied in geographic areas when COVID-19 virus variants were circulating, particularly in South Africa and Brazil.

The effectiveness data to support the Janssen COVID-19 vaccine EUA is based on results from an ongoing randomized, double-blind, placebo-controlled phase 3 study (ENSEMBLE) conducted in the US, South Africa, Brazil, Chile, Argentina, Columbia, Peru, and Mexico.⁵ Adults (n=44,325) who did not have evidence of SARS-CoV-2 infection prior to receiving the vaccine were eligible for enrollment in the trial.⁵ Participants were randomized 1:1 to receive vaccine (n=19,630) or saline placebo (n=19,691).⁵ Subjects were followed for a median of eight weeks after vaccination. Overall, 58.7% of participants were White, 45.3% were Hispanic or Latino, 19.4% were Black or African American, 9.5% were American Indian or Alaska Native, 3.5% were Asian, 0.2% were Native Hawaiian or other Pacific Islander, and 5.6% were multiracial.⁵ The median age of study participants was 52 years and 45% were female.⁵ Demographic characteristics were similar among individuals who received the Janssen COVID-19 vaccine and those who received saline placebo.⁵ Approximately 41% of enrolled patients had a least 1 coexisting condition.⁵

The co-primary endpoints for the ENSEMBLE trial were efficacy of a single dose of vaccine to prevent symptomatic, laboratory confirmed, moderate to severe/critical COVID-19 occurring 1) at least 14 days after vaccination and 2) at least 28 days after vaccination in study participants. Severe/critical COVID-19 was defined as: a severe systemic response requiring respiratory support, or evidence of shock, or significant organ damage, or admission to intensive care unit.³ Results from the trial are presented in **Table 2**.

Table 2. ENSEMBLE Trial Results⁵

Outcome	Number of Cases (N=19,630) Vaccine	Number of Cases (N =19,691) Placebo
COVID-19 Cases 14 days post-vaccination	116 (0.6%)	348 (1.8%)
COVID-19 Cases 28 days post-vaccination	66 (0.3%)	193 (0.90%)
Hospitalization 14 days post-vaccination	2 (0.01%)	29 (0.14%)
Hospitalization 28 days post-vaccination	0	16 (0.08%)

Overall, the vaccine was approximately 66.9% [95% Confidence Interval (CI) 59.0 to 73.4] effective in preventing moderate COVID-19 occurring at least 14 days after vaccination and 66.1% (95% CI 55 to 74.8) effective in preventing moderate COVID-19 occurring at least 28 days after vaccination.⁵ Additionally, the vaccine was approximately 76.7% (95% CI 54.6 to 89.1) effective in preventing severe/critical COVID-19 occurring at least 14 days after vaccination and 85.4% (95% CI 54.2 to 96.9) effective in preventing severe/critical COVID-19 occurring at least 28 days after vaccination.⁵ Vaccine efficacy varied geographically and was highest in the US (74.4%) and lowest in South Africa (52%), where the B.1.351 variant dominated.³ As of the primary analysis cutoff date of 1/22/21, there were no COVID-19-related deaths reported in the vaccine arm compared to 5 COVID-19-related deaths reported in the placebo arm.⁵

Safety Concerns

The safety subset population included 6,736 individuals. Geographically, the safety subset was limited to individuals from the US (51.4%), Brazil (38.5%) and South Africa (10.2%).⁶ The most commonly reported side effects were local adverse events such as pain at the injection site (48.6%), and systemic adverse events including headache (38.9%), fatigue (38.2%), myalgia (33.2%) and nausea (14.2%).⁵ Most of these side effects were mild to moderate in severity and lasted 1 to 2 days.⁵ Overall, symptoms were more frequent in younger people than individuals aged over 60 years of age.⁵

Viral vector vaccines have been associated with rare, but serious thrombosis-thrombocytopenia syndrome (TTS) reported in the first 2 weeks after vaccine administration.⁷ To date, 8 million doses of the Janssen vaccine have been administered in the U.S. and 15 cases of TTS have been reported.⁷ Most cases of TTS reported following the Janssen COVID-19 Vaccine have occurred in females ages 18 through 49 years; some have been fatal.⁷ The clinical course of these events shares features with autoimmune heparin-induced thrombocytopenia, which is why heparin should be avoided in patients exhibiting symptoms of TTS after COVID-19 vaccination.⁶ After a 10 day pause to

investigate the possible link between the vaccine and TTS, the CDC approved resuming administration of the Janssen vaccine on Friday, April 25, 2021.⁷ At this time, the available data suggest the chance of TTS occurring is very low, but the FDA and CDC will remain vigilant in continuing to investigate this risk.⁷

Health care providers should alert their patients to be aware of any symptoms of TTS, which include severe headache, vision changes such as blurry vision, extremity pain or swelling, chest pain, and shortness of breath. People should not be concerned about mild headaches and flu-like symptoms in the first few days after vaccination as these are commonly reported side effects. The Astra Zeneca vaccine has been associated with a similar hematologic disorder in European patients. The European Medicines Agency has determined the benefits of the AstraZeneca COVID-19 vaccine outweigh the risks. No reports of blood clots events have been reported with the mRNA vaccines manufactured by Pfizer and Moderna.

Comparative Vaccine Efficacy

The only way to accurately compare the effectiveness of vaccines is by direct comparison in head-to-head clinical trials, which did not occur for any of the COVID-19 vaccines. The clinical trials for these vaccines occurred in different geographic regions and at different points in time with varying incidence of COVID-19. In addition, the primary outcome for the mRNA vaccines was the efficacy in preventing symptomatic COVID-19 compared with placebo 7 days after the second dose (Pfizer) or 14 days after the second dose (Moderna). In contrast, the primary outcome for the Janssen vaccine stratified the severity of COVID-19 as moderate or severe disease and evaluated occurrence of infection 14 and 28 days post vaccination. All the COVID-19 vaccines the FDA has authorized for emergency use are at least 50% more effective than placebo in preventing COVID-19 (range 65 to 95%). According to FDA guidance, a vaccine with at least 50% efficacy would have a significant impact on disease, both at the individual and societal level.⁸

Vaccine Efficacy Against SARS-CoV-2 Variants

One reason SARS-CoV-2 variants are emerging is because relatively few people globally have been vaccinated.⁹ Current COVID-19 vaccines are based on the SARS-CoV-2 spike protein of the original Wuhan-hu-1 virus.⁹ Some emerging variants, which appear to be more transmissible or deadlier than the wild-type SARS-CoV-2, contain mutations in the spike protein, spurring vaccine efficacy concerns.⁹ Trials of the Novavax, Janssen, and AstraZeneca vaccines in South Africa, where the B.1.351 variant of concern represents virtually all of the circulating SARS-CoV-2, seemed to justify those concerns.⁹ Those trials found lower vaccine efficacy compared with trials in other countries where B.1.351 was not dominant.⁹

The pivotal trials of the Pfizer and Moderna vaccines were conducted mainly in the US before any cases of infection by B.1.351 or other variants of concern had been detected.⁹ Most of the current data on the mRNA vaccines' efficacy against SARS-CoV-2 variants has come from laboratory studies in which researchers exposed serum samples from immunized individuals to genetically engineered versions of concerning variants and then measured neutralizing antibody titers.⁹ These studies repeatedly have shown the vaccines elicit lower levels of neutralizing antibodies against SARS-CoV-2 variants than against older, more common isolates.⁹ However, that still might be sufficient to protect against COVID-19, or at least severe COVID-19.⁹ Although serum antibody levels correlate well with protection for many infectious diseases, protective levels have not yet been determined for SARS-CoV-2.⁹ In addition to neutralizing antibodies, mRNA vaccines also induce virus-specific helper T cells and cytotoxic T cells that might help protect against infection.⁹ Pfizer and Moderna have started evaluating the safety and immunogenicity of a third dose of the mRNA vaccine to see whether it would boost immunity to SARS-CoV-2 variants. Janssen is currently evaluating the efficacy of 2 doses, separated by 57 days, of its vaccine to improve outcomes in virus variants in a planned 30,000 patient study. Whether COVID-19 will join influenza as an infectious disease for which annual vaccination is required is not yet known.

Special Populations

The Centers for Disease Control and Prevention (CDC) and Advisory Committee on Immunization Practices (ACIP), in collaboration with the American College of Obstetricians and Gynecologists and the American Academy of Pediatrics, have issued guidance indicating that Covid-19 vaccines should not be withheld from pregnant persons.¹⁰⁻¹² A recent article published in the *New England Journal of Medicine* summarized preliminary data obtained from several surveillance systems to address the safety of mRNA COVID-19 vaccines in pregnant women.¹³ As of March 30, 2021, the vaccine-safety (v-safe) pregnancy registry call center attempted to contact 5230 persons who were vaccinated through February 28, 2021, and who identified during a v-safe survey as pregnant at or shortly after Covid-19 vaccination.¹³ Among enrolled participants, most were 25 to 44 years of age (98.8%), non-Hispanic White (79.0%), and, at the time of interview, did not report a Covid-19 diagnosis during pregnancy (97.6%).¹³ Receipt of a first dose of vaccine meeting registry-eligibility criteria was reported by 92 participants (2.3%) during the periconception period, by 1132 (28.6%) in the first trimester of pregnancy, by 1714 (43.3%) in the second trimester, and by 1019 (25.7%) in the third trimester.¹³

Among 827 participants who had a completed pregnancy, the pregnancy resulted in a live birth in 712 (86.1%), in a

spontaneous abortion in 104 (12.6%), in stillbirth in 1 (0.1%), and in other outcomes (induced abortion and ectopic pregnancy) in 10 (1.2%).¹³ A total of 96 of 104 spontaneous abortions (92.3%) occurred before 13 weeks of gestation, and 700 of 712 pregnancies that resulted in a live birth (98.3%) were among persons who received their first eligible vaccine dose in the third trimester.¹³ Adverse outcomes among 724 live-born infants — including 12 sets of multiple gestation — were preterm birth (60 of 636 among those vaccinated before 37 weeks [9.4%]), small size for gestational age (23 of 724 [3.2%]), and major congenital anomalies (16 of 724 [2.2%]); no neonatal deaths were reported at the time of interview.¹³ Calculated proportions of pregnancy and neonatal outcomes appeared similar to incidences published in the peer-reviewed literature.¹³

Key Oregon Health Authority Talking Points

- The COVID-19 vaccines will not end the pandemic, but vaccination will. It is important that everyone is vaccinated to achieve community immunity.
- COVID-19 vaccines have been extensively evaluated in large-scale clinical trials. These trials involved adults from a diverse and inclusive range of races, ethnicities, and ages.
- COVID-19 vaccines are vetted for safety and efficacy by three independent scientific groups.

Racial and Ethnic Inequities in Oregon

The COVID-19 pandemic has affected everyone in Oregon, but it has not disproportionately affected certain communities.¹⁴ In Oregon, the Latino community is experiencing the most pronounced inequities, compared to the white community:

- People who identify as white represent 75% of Oregonians. While they only comprise about half (48%) of COVID-19 cases, they account for 74% of vaccinations.¹⁴
- People who identify as Latino or Hispanic represent 13% of Oregonians. However, they comprise 26% of COVID-19 cases. Despite the disproportionate burden of COVID-19 cases in the Latino community, they account for only 5% of the vaccinations administered to date.¹⁴

Latino, Black, African Americans and Native American communities are also burdened by significant health inequities that enhance their risks from COVID-19. These health inequities are the product of systemic racism, toxic stress and other factors.¹⁴ Future outreach and education efforts need to provide clear, accurate messages about how to prevent COVID-19 in Spanish and for audiences with low literacy.¹⁵ These messages should be delivered by trusted messengers in community settings using appropriate media channels (e.g., Spanish television and radio).¹⁵ The OHA has also developed resources in Spanish at the [Vacnunacovid](#) page.

Addressing Vaccine Hesitancy

“COVID-19 vaccines were developed too fast to be safe.”

- The technology used to develop the new COVID-19 vaccines has been used to develop other vaccines and is not new.
- All COVID-19 vaccines have gone through rigorous studies to ensure they are as safe as possible. The Center for Disease control is continuing to watch for safety issues that are reported across the entire country.

“There were not enough participants in the clinical trials to declare the vaccines safe.”

- All 3 COVID-19 vaccines enrolled tens of thousands of participants, many of whom were followed for 2 months after receiving the final dose, as is common with other vaccines.

Conclusions

Although 3 vaccines are currently authorized for use in the US, the emergence of virus variants is concerning. It is important to maximize availability of COVID-19 vaccines to all Oregonians to reduce transmission of the SARS-CoV-2 virus and prevent additional viral mutations. All available vaccines have proven efficacy and safety from large randomized controlled trials. Educating the public is vital to overcoming concerns about receiving the vaccine.

Peer Reviewed By: Holly Villamagna, MD, Clinical Educator, Division of Infectious Disease, Oregon Health and Science University and Kendall Tucker, PharmD, MS, BCPS, BCIDP, Clinical Fellow Infectious Disease and Epidemiology/Outcomes, OSU College of Pharmacy

References:

1. The Oregon State Drug Review. Coronavirus Disease-2019 Vaccine Update. January 2021. https://www.orpdl.org/durm/newsletter/osdr_articles/volume1/1/osdr_v11_i1.pdf.
2. American Society of Health-Systems Pharmacists. <https://www.ashp.org/-/media/assets/pharmacy-practice/resource-centers/Coronavirus/docs/Vaccine-candidate-tracking-table.ashx?la=en&hash=445ED31EC216D4F4E33C920AE151530C986F9255>. Accessed March 18, 2021.
3. Janssen COVID-19 Vaccine Emergency Use Authorization. US Department of Health and Human Services, Food and Drug Administration. <https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/janssen-covid-19-vaccine> Accessed March 18, 2021.
4. Centers for Disease Control and Prevention. Ebola Vaccine: Information about Ervebo®. <https://www.cdc.gov/vhf/ebola/clinicians/vaccine/index.html> Accessed April 2.
5. Sadoff J, Gray G, Vandebosch A, et al. Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19. *N Engl J Med*. 2021.

6. Janssen COVID-19 Vaccine FDA Fact Sheet Horsham, PA; Janssen Biotech, Inc. 4/23/2021. <https://www.fda.gov/media/146304/download>. Accessed April 29, 2021.
7. U.S. Food and Drug Administration. Joint CDC and FDA Statement on Johnson & Johnson COVID-19 Vaccine. April 23, 2021. <https://www.fda.gov/news-events/press-announcements/fda-and-cdc-lift-recommended-pause-johnson-johnson-janssen-covid-19-vaccine-use-following-thorough>. Accessed April 29, 2021.
8. Food and Drug Administration. Emergency Use Authorization for Vaccines to Prevent COVID-19. February 2021 <https://www.fda.gov/media/142749> Accessed March 19, 2021.
9. Rubin R. COVID-19 Vaccines vs Variants—Determining How Much Immunity Is Enough. *Jama*. 2021.
10. Centers for Disease Control and Prevention. COVID-19 vaccines: interim clinical considerations for use of COVID-19 vaccines currently authorized in the United States. 2021 (<https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html>). Accessed April 28, 2021.
11. American College of Obstetricians and Gynecologists. Vaccinating pregnant and lactating patients against COVID-19: practice advisory. December 2020 (<https://www.acog.org/clinical/clinical-guidance/practice-advisory/articles/2020/12/vaccinating-pregnant-and-lactating-patients-against-covid-19>). Accessed April 28, 2021.
12. American Academy of Pediatrics. Interim guidance for COVID-19 vaccination in children and adolescents. 2021 (<https://services.aap.org/en/pages/2019-novel-coronavirus-covid-19-infections/clinical-guidance/interim-guidance-for-covid-19-vaccination-in-children-and-adolescents/>). Accessed April 28, 2021.
13. Shimabukuro TT, Kim SY, Myers TR, et al. Preliminary Findings of mRNA Covid-19 Vaccine Safety in Pregnant Persons. *N Engl J Med*. 2021.
14. Oregon Health Authority. COVID-19 Health Talking Points <https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/VACCINES/IMMUNIZATION/IMMUNIZATIONPROVIDERRESOURCES/Pages/COVIDvaccine.aspx> Accessed March 18, 2021.
15. Ornelas IJ, Ogedegbe G. Listening to Latinx Patient Perspectives on COVID-19 to Inform Future Prevention Efforts. *JAMA network open*. 2021;4(3):e210737-e210737.

