

Janssen Ad26.COVS COVID-19 Vaccine – Johnson & Johnson FDA Phase 3 Review and Analysis

Submitted by TeamHealth Emerging Infectious Disease Task Force (EIDT)

The Janssen Ad26.COVS COVID-19 Vaccine Concept

The Janssen Ad26.COVS vaccine (Janssen COVID-19 Vaccine – parent company Johnson & Johnson) uses a different technology than the Pfizer or Moderna products. Janssen employs a proprietary adenovirus (type 26 [Ad26]) that has been genetically engineered so that the virus itself cannot reproduce in living cells. The genetic code for segments of the SARS-CoV-2 spike protein (S) has been added to the genome of the adenovirus. This virus “infects” human cells and introduces the S protein genetic material – causing the cell to produce multiple copies of the spike antigen. The antigen is then processed by the human immune system creating a robust response to the SARS-CoV-2 virus.

There is experience using this adenovirus vector in previous vaccines. As example the Ad26.ZEBOV/MVA-BN-Filo Ebola vaccine is considered to be safe and highly effective by most clinicians – having been used during recent Ebola outbreaks. In addition, investigational vaccines for Zika, filovirus, HIV, HPV, malaria, and respiratory syncytial virus are under various stages of study. As of the end of 2020, almost 200,000 individuals have participated in clinical trials and vaccination programs using the Ad26 adenovirus platform. Overall, these vaccines seem to have an acceptable clinical safety profile.

The Janssen COVID-19 vaccine is administered as a single intramuscular injection of 0.5ml – potentially giving it a logistical and acceptance advantage over dual dose vaccines. The vaccine is supplied as a multidose vial (5 doses). It has a shelf life of 3 months when stored at 2° C (35.6°F) to 8° C (46.4°F). The specifics on dosing protocols are found in the Food and Drug Administration Emergency Use Authorization data document linked in this paper.

Janssen COVID-19 Vaccine Phase 3 Trial Effectiveness Results

- 49,000 initial participants were randomized (1:1) to receive either the vaccine or placebo with 39,351 reported on in this initial data.
- At 14 days post vaccination there were 116 COVID-19 cases in the vaccine group, and 348 in the placebo group. By 28 days there were another 66 and 193 respectively.
- An overall efficacy of about 66.9% (95%CI 59-73.4) at 14 days and 66.1% (95%CI 55.0-74.8) at 28 days was reported in preventing COVID-19.
- The benefits held through all genders, racial, and ethnic groups as well as patients with comorbidities.
- The data suggest an efficacy in prevention of severe and critical COVID-19 noted due to an observed reduction of hospitalizations and deaths in the vaccine cohort.
- Compared in context to the highly effective seasonal influenza vaccines (52% (95%CI 41-61) in a well-matched year, to 32% (95%CI 22-48) in a less well-matched year.

Janssen COVID-19 Vaccine Phase 3 Trial Safety Results

- The most common Adverse Events (AE) were local injection site pain/erythema/swelling (48.6%), headache (38.9%), fatigue (38.2%), and myalgia (33.2%).
- Although there were some unsolicited reports of nonspecific urticaria in both the vaccine and placebo cohorts, no anaphylaxis was reported.
- In general, AEs were mild to moderate in severity and transient lasting one to two days.
- AEs tended to be more frequent in younger participants (18-59 years of age).
- Severe Adverse Events (SAEs) were uncommon – about 0.4% with both vaccine and placebo.
- There were 19 reported deaths (three vaccine and 16 placebo) none deemed to be vaccine related.
 - Fatality causes for the three people in the vaccine group included two non-COVID pulmonary infections in immune compromised patients, and one sudden death with shortness of breath of undetermined etiology.
 - Since the initial report cutoff date, an additional six deaths have been reported in the study (two vaccine cohort and four placebo cohort). None of the deaths are vaccine related.

- Other more critical SAEs were reported at a rate of 0.06% in vaccine and 0.05% in the placebo groups. These included thromboembolic events such as deep venous thrombosis, pulmonary embolism, cerebral vascular accidents, carotid occlusion, and acute myocardial infarction.
- The reported safety profile is mostly consistent across all ages, gender, ethnic, and racial groups as well as comorbidities.

Janssen COVID-19 Vaccine Use in Pregnancy and/or Lactation

Patients who were pregnant or intended to become pregnant were excluded from this study. However eight participants became pregnant during the study with outcomes of; spontaneous abortion (1 vaccine, 0 placebo), incomplete abortion (0 vaccine, 1 placebo), elective abortion (0 vaccine, 2 placebo) and ectopic pregnancy (1 vaccine, 0 placebo) and three outcomes still pending. In addition, there is no sufficient human experience or available studies on widespread use of the Ad26 adenovirus vector platform for any vaccine in pregnancy. The Janssen Ad26 vaccine should probably not be recommended to pregnant patients or patients planning to become pregnant or patients breast feeding. This is in light of the lack of clinical outcome evidence for either the Ad26 adenovirus vector platform, or the Janssen COVID-19 vaccine itself in pregnancy or lactation. This maintains consistency with not using live attenuated viral vaccines during pregnancy or lactation. Admittedly, the Ad26 adenovirus should not be considered a classically “attenuated virus” but rather a “replication-incompetent adenovirus” genetically neutered to prevent replication. It is however still equipped with much of the functions of a “live” virus – about which we still have much to learn. This is particularly true when one considers the availability of other FDA EUA vaccines in the United States. As noted in previous reports, ACOG recommends that with appropriate education and counsel – the Pfizer and Moderna vaccines should not be withheld from recommendation for patients during pregnancy and lactation.

Janssen COVID-19 Vaccine Use in Pediatric Patients

There are no data on the safety or efficacy of the Janssen COVID-19 vaccine in children under the age of 18 years. However, pediatric studies are being initiated and registered with the National Institutes of Health.

Activity Against SARS-CoV-2 Virus Variants

Of great interest and importance in vaccinology are the efficacy of the currently available COVID-19 vaccines against emerging SARS-CoV-2 variants. The efficacy of the Janssen COVID-19 vaccine against specific SARS-CoV-2 variants cannot be estimated at this time due to insufficient data. However it is known that the following variants were detected within the study groups; Wuhan-H1 D614G, South Africa B.1.351, and Brazil P.2. Missing from the list are the United Kingdom B1.1.7 and the Brazil P.1 variants. There was a lower efficacy observed geographically in South Africa against moderate, 52.0% (95%CI 30.3-67.4) and severe, 64.0% (95%CI 41.2-78.7) COVID-19 disease respectively. It is unclear if this was due to a higher viral resistance due to more of the South African variant in that geographic location, or because of multiple other confounders impacting the results. These data are still being collected and analyzed.

Key Findings and Considerations

- The general efficacy of the Janssen COVID-19 vaccine to prevent moderate to severe/critical COVID-19 occurring 14 days after vaccination was 66.9% (95% CI 59.0; 73.4), and at 28 days 66.1% (95% CI 55.0; 74.8) in participants without prior evidence of SARS-CoV-2 infection.
- This is a strong efficacy when compared to the context of the highly effective seasonal influenza vaccines (52% (95%CI 41-61) in a well matched year, to 32% (95%CI 22-48) in a less well-matched year.
- The Janssen COVID-19 vaccine effectively reduces the risk of severe COVID-19 and associated hospitalizations.
- Even in the less effective years the seasonal influenza vaccine prevents 7.5 million influenza infections, 3.7 million outpatient visits, >100,000 hospitalizations, and > 6,000 deaths. The Janssen COVID-19 vaccine likely will have a similar impact regarding COVID-19.
- The overall lower efficacy reported for the Janssen COVID-19 vaccine when compared to the lipid-nanoparticle Pfizer and Moderna vaccines should not be interpreted as the Janssen COVID-19 vaccine being a less “effective” product clinically.
- The safety profile of the Janssen COVID-19 vaccine is consistent with other COVID-19 vaccines currently available under FDA EUAs in the United States and abroad.
- The single dose nature of the Janssen COVID-19 vaccine, along with reasonable efficacy still being reported, is a potential advantage over the logistics of two-dose vaccine regimens. This is particularly true in the context of vaccine supply shortfalls expected to continue over the next few months.
- In addition, the Janssen COVID-19 vaccine could be a reasonable solution to “getting more people vaccinated sooner” with a reasonably effective vaccine – as opposed to decreasing the efficacy of the Pfizer and Moderna by changing their protocols.
- Protocols are underway investigating various dual-dose regimens of the Janssen COVID-19 vaccine for safety and efficacy. This could alter the vaccine protocols and procedures by increasing vaccination options in the future. People receiving a single dose, could opt for a second “booster” dose if increased efficacy is determined from studies currently underway.
- Vaccines are a critical part of managing the COVID-19 pandemic as it has not been well mitigated by masking, social distancing, or other public health strategies alone for various reasons.
- There are insufficient data in our opinion to recommend the Janssen COVID-19 in pregnant, lactating, or pediatric (<18 years of age) patients.

Recommendations

- *The EIDT recommends vaccination with the Janssen Ad26.COV2.S vaccine (Janssen COVID-19 Vaccine) for all adults 18 years of age and above in every racial and ethnic demographic regardless of COVID-19 risk factors, prior COVID-19 infection, or other underlying health conditions, unless there are existing contraindications to receiving any vaccine. The EIDT would not recommend this vaccine for pregnant or lactating individuals due to a current paucity of safety data regarding both the vaccine and the Ad26 viral vector platform in this population, particularly when the Pfizer and Moderna vaccines are available for these individuals at this time.*
- *The EIDT would not support offering the Janssen COVID-19 vaccine to our pregnant providers (or patients), who are a group at increased risk from COVID-19. Particularly since the Pfizer and Moderna vaccines are available under their current FDA EUAs.*
- *The EIDT would not recommend the use of the Janssen COVID-19 vaccine in providers (or patients) who are lactating.*
- *Due to the unclear duration of immunity and risk of reinfection in individuals previously infected with SARS-CoV-2, limited data from the Janssen study (similar to the Pfizer and Moderna products) suggests that previously infected individuals should also benefit from vaccination with this vaccine.*
- *The EIDT recommend staggering administration of the Janssen COVID-19 vaccine to groups of providers by about 7 days, when possible, to minimize the impact that systemic adverse effects may have on staffing and operations.*
- *Insufficient data currently exist to recommend the Janssen COVID-19 vaccine to individuals less than 18 years of age, but pediatric vaccine trials have been underway since January 2021.*

This literature is endorsed unanimously by the team health EIDT. It is considered current as of March 2, 2021. 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 Center for Disease Control and Prevention or the World Health Organization.

Primary References

Janssen. Vaccines and Related Biological Products Advisory Committee Meeting. February 26, 2021 FDA Briefing Document. Janssen Ad26.COV2.S Vaccine for the Prevention of COVID-19 ([HERE](#))

FDA. **Janssen COVID-19 Vaccine** ([HERE](#))