



COVID-19 Vaccines Approved by the US Food and Drug Administration

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1. Introduction

Coronavirus disease 2019 (COVID-19) vaccines are therapeutics produced to provide acquired immunity against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus responsible for COVID-19. COVID-19 vaccines are broadly accepted as an effective approach for lowering the severity and mortality rate of this infectious disease. This is why at the beginning of the vaccination era after the outbreak, countries prioritized vaccination for those at higher risk for severe disease and mortality, such as elderly people, people with underlying health-related conditions, and healthcare professionals who are at the center of disease transmission.

The SARS-CoV-2 genetic sequence data was completely discovered and shared through Global Initiative on Sharing All Influenza Data (GISAID) on January 10 2020. Two months later, the global pharmaceutical industry emphasized their commitment to addressing the COVID-19 pandemic as soon as possible. The primary focus of the global pharmaceutical industry for developing SARS-CoV-2 vaccines was on preventing symptomatic illness in infected individuals and avoiding the disease from becoming more severe and harder to manage.

The United States (US) Food and Drug Administration (FDA) is responsible for protecting and promoting public health through the control, management, and regulation of various food and drug-related fields. Any therapeutics approved by the US FDA are globally considered safe and effective in terms of clinical applications. This is because of the stringent and rigorous pathway a nominated drug

or any type of therapeutics should pass to be approved by the FDA.

In the case of public health emergencies, such as the pandemic of viral infectious diseases, including the Zika virus epidemic, the Ebola virus epidemic, and the COVID-19 pandemic, the US FDA uses a process called emergency use authorization (EUA). This process has been proposed to facilitate and expedite the availability and medical application of various types of therapeutics such as vaccines and personal protective equipment in emergencies. In the case of the COVID-19 pandemic, the same process was required to lower the mortality rate and control the pandemic and its critical consequences on different aspects of societies. According to the US FDA officials, this organization started receiving EUA requests for the first COVID-19 vaccine in early December 2020 (almost a year after the outbreak). In this regulatory process, COVID-19 vaccines must meet the FDA's rigorous scientific standards to be granted EUA.

2. Arguments

On August 23, 2021, the US FDA approved the first COVID-19 vaccine for medical applications. The vaccine has been known as the Pfizer-BioNTech COVID-19 vaccine (BNT162b2) (1, 2). This anti-COVID-19 vaccine is also marketed as Comirnaty (1, 2). The Pfizer-BioNTech COVID-19 vaccine is approved for medical use in individuals 16 years of age and older, and it is administered with the purpose of COVID-19 prevention (1, 2). The technology of Comirnaty is based on nucleoside-modified mRNA (modRNA) (1, 2). In

detail, this modRNA encodes a mutated form of the full-length spike protein present on the surface of SARS-CoV-2 (1, 2). Therefore, the production of this mutated form of SARS-CoV-2 spike protein in the body of the recipient triggers an immune response against SARS-CoV-2 (1, 2). In terms of side effects, most adverse effects are mild to moderate in severity and are resolved a few days following vaccination (1, 2). These side effects include pain at the injection site, fatigue, and headaches. Of note, no long-term complications related to this vaccine have been reported yet (1, 2). In terms of efficacy, according to an interim analysis, the Pfizer-BioNTech COVID-19 vaccine demonstrates a potential efficacy of 91.3% in the prevention of symptomatic infection following seven days of the second dose of vaccination (1, 2).

On January 31, 2022, the FDA granted approval to the second COVID-19 vaccine known as the Moderna COVID-19 vaccine (3). This vaccine, which is also known by its market name Spikevax, is approved for the prevention of COVID-19 in individuals 18 years of age and older (3). The technology of the Spikevax vaccine is similar to that of the Pfizer-BioNTech COVID-19 vaccine (3). In detail, Spikevax contains a modRNA (named mRNA-1273) encoding a spike protein of SARS-CoV-2 encapsulated in PEGylated lipid nanoparticle drug delivery (LNP) vehicles (3). The adverse effects of this COVID-19 vaccine include anaphylaxis and rash-like erythemas at the injection site (3). Moreover, myocarditis or pericarditis are also among other observed side effects of the Spikevax vaccine, both of which are rare (13 cases in one million young individuals) (4). In terms of effectiveness, the efficacy of the Moderna COVID-19 vaccine is similar to that of the Pfizer-BioNTech COVID-19 vaccine. In detail, an efficacy rate of 94.1% has been reported two weeks after the second dose of vaccination (3). The efficacy of this COVID-19 vaccine in the prevention of COVID-19 infection and severe disease has been described as astonishing and borderline historic (3).

Janssen COVID-19 vaccine is the third FDA-approved COVID-19 prevention vaccine (5-8). It is available under EUA as a single primary vaccination dose for people at least 18 years old (5-8). This vaccine is also available as a single booster dose for people at least 18 years old at least two months after completing primary vaccination with this vaccine (5-8). The Janssen COVID-19 vaccine is based on a human adenovirus viral vector carrying the encoding gene for the spike protein of the SARS-CoV-2 (5-8). After vaccination, the spike protein is produced in the body of the recipient, which results in the formation of immunizing antibodies (5-8). The Janssen COVID-19 vaccine requires only one dose, and it does not require freezing conditions for storage (5-8). The most common side effects of this COVID-19 vaccine include injection site pain, headache, fatigue,

muscle pain, and nausea. Moreover, hypersensitivity (allergy) and itchy rash are among the rare side effects of this vaccine (occurring in less than 0.1% of the individuals) (5-8). Limited cases of blood clotting after vaccination with this vaccine have also been reported (5). In terms of efficacy, the developer company has announced that a one-dose regimen of this vaccine is 66% effective in preventing symptomatic COVID-19, 85% effective in preventing severe COVID-19, and 100% effective in preventing hospitalization or death caused by COVID-19 (6-8).

3. Conclusions

The FDA-approved COVID-19 vaccines can be considered as the most effective and innovative ones in the market. These vaccines are also safe and reliable in terms of medical application. A recent study by Alden et al. demonstrated that BNT162b2 mRNA is reverse transcribed intracellularly into the DNA of the human liver cell line Huh7 in vitro upon BNT162b2 exposure (9). However, Alden et al. stated that there are various factors that should be considered (10). First, Huh7 cells respond to INF stimulation and are known as an ideal cell line for experiments regarding viral infection and replication in vitro (10). However, these cells do not resemble the complex in vivo environment of human subjects, and specifically, they do not have the broad cellular and humoral immune responses (10). Second, the vaccine dose used in the study by Alden et al. is much higher than its in vivo dose (10). Furthermore, the in vitro setting of these researchers for cell density and volume is much lower than the in vivo hepatic distribution volume in human subjects. Third, Alden et al. utilized cultured hepatocellular carcinoma cells that are remarkably different from primary human hepatocytes (10). In a nutshell, in vivo vaccine mRNA transfection to hepatocytes is not impossible; however, further studies are needed to determine whether hepatocyte transfection can stimulate the acquired immune system to remove infected cells without complications or lead to autoimmunity.

On the other hand, there are various limitations in terms of vaccine distribution worldwide. For instance, ultracold freezers are required for the shipping and distribution of mRNA-based COVID-19 vaccines. This equipment is not available in developing countries. Therefore, such vaccines may not be easily available in such areas of the world. Innovative solutions are required to overcome these limitations. As an example, Pfizer-BioNTech is investigating a freeze-dried version of its COVID-19 vaccine that does not require ultracold storage. Collectively, long-term evaluations are required to determine the long-term safety and efficacy of these FDA-approved vaccines. Moreover, finding strategies for overcoming the briefly mentioned limi-

tation of these vaccines can help greater populations benefit from these vaccines.

Footnotes

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