Comparisons Of Mrna Vaccine from Different Manufactures

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Abstract. The severe acute respiratory syndrome coronavirus 2, which is responsible for the COVID-19 pandemic, causes severe respiratory illness. The condition was initially discovered in December 2019 and spread all over to the world, causing 6724248 deaths by January 25th 2023 worldwide. Through the course of three years from 2019 to 2022, the virus has developed multiple variants from Alpha, Beta, Gamma, Delta and Omicrons. In response to a virus with such a rapidly mutating virus, the development of mRNA vaccines has been prioritized. The easiness of producing mRNA vaccine allowing less time can be spent on the development phase of a vaccine. Thus, mRNA vaccines can also be updated frequently to keep up the mutations in the virus. Three mRNA vaccines are described in this article (two of them are currently available and one is still developing) in terms of target protein, effectiveness, adverse effects and price and compare them to give recommendations for different cohorts.

Keywords: BNT162b2; mRNA vaccine; mRNA-1273; ARCoV.

1. Introduction

In 2019, the broke out of the COVID-19 disrupt the life of people. Billions of people die from this pandemic and all people around the world has affected by the pandemic. Under this circumstance, the vaccine was developed to fight against the virus. There are several types of vaccines: Live-attenuated vaccine, dead vaccine, mRNA vaccine and so on. We compare three different mRNA vaccine companies in this essay. For traditional vaccine such as DNA vaccine and Live-attenuated vaccines, people inject the whole virus into our bodies. But mRNA vaccine is not the same as the conventional vaccine as it only injects mRNA sequence into our body. The function of the mRNA is to translate spike protein of SARS-CoV-2 in our body and stimulate the immune response to fight against the COVID-19.

1.1. History

The attempt to inject mRNA molecules into human body was first developed in 1980s [1]. This technique was undergone several improvements in the following two decades [1]. In 1990s, researchers did some preclinical test which delivered RNA vectors into murine muscle and the results show that the mRNA vaccine will trigger the activation of cytotoxic T lymphocytes of the murine [1]. It will trigger the humoral response of B lymphocyte as well [1]. The activated B cells will secrete specific antibodies to fight against target disease.

1.2. Mechanism

To make mRNA vaccine, researchers select the desired spike protein and extract the mRNA to make the vaccine. After the mRNA inject into our body, the protective particle will fuse with our cell membrane so the mRNA is able to get into our cell. The mRNA translates the spike protein in cell cytoplasm using a ribosome. The spike protein then being placed on the cell surface. Our immune system will soon recognize them and B-cell will secrete antibodies to fight against it. Memory cells will remember them and the next time the real virus enter our body, our immune system will response quickly to erase them.

1.3. Advantage

Different from the conventional vaccine, mRNA vaccine is easier and quicker to make. It is much smaller than the whole cells and it is easy to extract. Thus, it is more available for the emergency use such as the suddenly outbreak COVID-19. The mRNA vaccine is safer than traditional vaccine too, it will not enter the cell nucleus but only present in cytoplasm. It will not affect the genome so it has high biosafety.

One of the advantages of mRNA vaccine is that it is safer and quickly to make as mentioned above. Another reason is that it will not cause any potential risk of infection as it only translates the spike protein but not the whole virus.

1.4. Disadvantage

In contrast, there are also some side effects. The mRNA is different to store. It needs to place in a very low temperature so it is not very convenient to store and transport. Besides, as the mRNA is single stranded, it is more likely to be recognized and destroy by our innate immune response. If it happens, the vaccine is useless. But we can solve this problem, protect the mRNA in the lipid nanoparticle or recode it sequence which can escape from the immune system. The basic funamental of BP neural network

2. Pfizer BioNTech

The German biotechnology business BioNTech created the mRNA vaccine known as BNT162b2, and they worked along with the American corporation Pfizer to conduct clinical studies both in the United States and everywhere else [2]. People aged 5 and older, those aged 12 and older, and those aged 16 and older may use the vaccination for various conditions [3-4] to protect against the infection of the virus [5]. Multiple approvals and authorized emergency use in different countries from the U.K. to Japan come with the success of the vaccine [5].

2.1. Target protein

BNT162b2 encodes for the full-length spike protein of SARS-CoV-2 which includes the both S1 and S2 subunits. Moreover, the developer used a 2P mutation strategy based on research on previous coronaviruses. By adopting this method, 2 prolines will replace 2 other amino acids at the top of S2 subunits to improve the prefusion conformation.

2.2. Effectiveness

In preventing patients without previous experience with any SARS-CoV-2 infection, the effectiveness of BNT162b is 95% with 95% confidence interval (90.3%-97.6%) 8 instances had COVID-19 symptoms after the second dose of vaccine, whereas 162 cases got placebo. In preventing patients mixed together (no evidence of whether or not infected before), the got placebo. In preventing patients mixed together (no evidence of whether or not infected before), the effectiveness of BNT162b is 94.6% with 95% confidence interval (89.9%-97.3%) in the sample of 9 cases with COVID-19 symptoms greater than 7 days with a consequent dose of BNT162b and 169 incidents received placebo. The efficiency of BNT162b is consistent regardless of the age, sex, race, ethnicity, obesity or previous infection [5].

2.3. After recovery from COVID

Researches shown among all eligible 149,032 recoveries from a precvious infection, 83,356 (56%) of the them received vaccination during 270 days period. 354 vaccinated patients and 2168 patients in unvaccinated group reoccurred signs of reinfection. Therefore, the effectiveness of BNT162b is estimated to be 82% with 95% confidence interval (80%-84%) among age between 16 to 64 years old and 60% with 95% confidence interval (36%-76%) for age greater than 64 years old [6].

2.4. Severe cases

Patients in the case group and 723 control patients. The results showed fully vaccinated patients range from age 12 to 18, BNT162b2 was 94% with 95% confidence interval (90%-96%) effective in preventing COVID-19 hospitalization. The effectiveness against ICU admission was 98% with 95 confidence interval (93%-99%). The vaccine effectiveness against life support is 98% with 95 confidence interval (92%-100%) (See Table 1) [7].

Table 1. The effectiveness of BNT162b2 against hospitalization

Subgroup	Vaccinated case patients	Vaccinated control patients	Vaccine effectiveness (95% CI)
Hospitalization	17/444	282/723	94 (90-96)
ICU admission	2/196	282/723	98 (93-99)
Life support	1/127	282/723	98 (92-100)

2.5. The third dose

A total sample of 10125 patients who had received to doses of BNT163b2 participated in the experiment with 5receivingived the third dose and 5044received a placebo. The mean age of all participants is 53 with 23.3% of them being 65 years of age or older and 1% being 16 or 17 years of age. The sample also contains different races (White, Black, Asian, Hispanic) with different coexisting conditions (obesity, chronic pulmonary diseases, diabetes). From 7 days to the final day, COVID-19 was found in 7 and 124 patients from the vaccinated and placebo groups, respectively. Therefore, BNT162b2 third dose was 94.6% effective with 95 confidence interval (88.5% to 97.9%) with no severe case [8].

2.6. Adverse effects

Some of the adverse effects have been reported by the manufacturer, including pain at the injection site, generalized fatigue, swelling etc. The frequency for some of the adverse effect is shown in Figure1. Pfizer-BioNTech Vaccine Frequency of adverse effects [9].

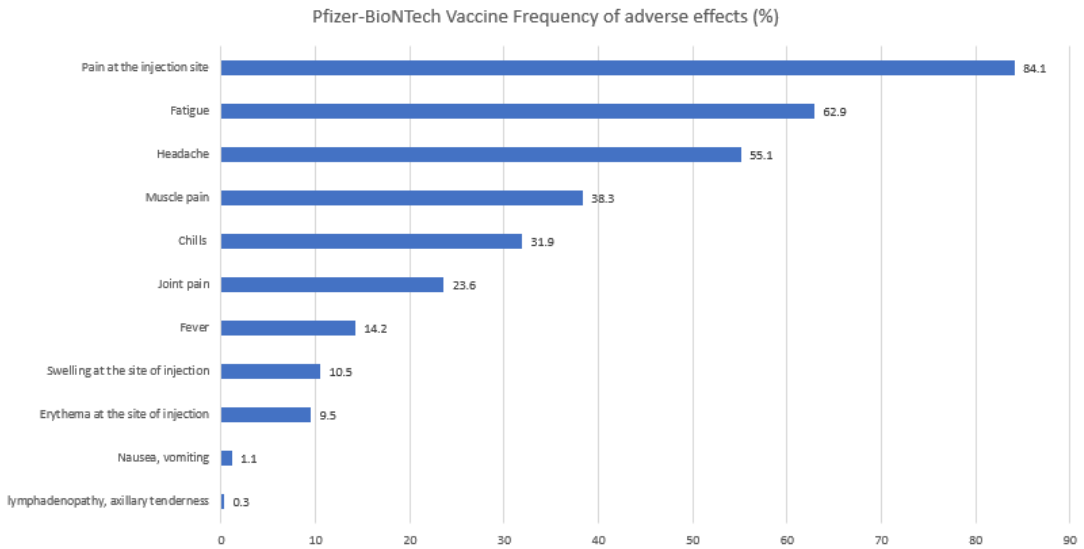

Figure 1. Pfizer-BioNTech Vaccine Frequency of adverse effects [3]

1245 medical professionals who had received one or more doses of the Pfizer-BioNTech vaccine were the subjects of the study on the negative effects of the BNT162b2 vaccination. Among all 803 BNT162b2 recipients, less than 10% of the people have aged 65 or above and over 65% of the participants were under 50. The result of the research showed with a moderate rate of localized and musculoskeletal symptoms, high rate of generalized symptom occurrence [10]. (See in Table 2.)

Table 2. Patients who experienced symptoms after BNT162b2 injection

Symptoms following either the first or second dose of the BNT162b2 vaccination	Percentage	Number
Universal symptom/s		
Fatigue	58.89%	391
Headache	45.48%	302
Fever	21.99%	146
Dizziness	9.04%	60
Regional symptom/s		
Arm soreness	88.04%	707
Itching	5.35%	43
Bleeding	0.37%	3
Muscle-related symptom/s		
Muscle ache	45.7%	367
joint pains	16.56%	133

2.7. Price

Since the COVID-19 epidemic first emerged, the federal government in the U.S. has provided the general public with free vaccines, COVID tests and treatments through funding from the Congress and other government programs [11]. At a cost of $25.3 billion, 200 million doses of mRNA vaccine from both Pfizer and Moderna were purchased by the federal government in the middle of 2020. The average price at the moment was $19.50 per dose [12]. However, the company plans to increase the vaccine list price to $110-130 per dose in the upcoming 2023 if the shots no longer have federal funding. Fortunately, people with Medicare or private health insurance will only have to pay a fraction, meaning people who have no such insurance above need to pay the list price [11].

3. Moderna

The mRNA vaccine called mRNA-1273 was created by the American company Moderna. In specific circumstances, individuals aged 6 months, 12 years, or 18 years or older may use the vaccine to prevent the viral infection. It is also authorized in the U.K., Switzerland, Australia, Canada and the European Union.

3.1. Target protein

The mRNA-1273 encodes for the full-length spike protein of SARS-CoV-2 which includes the both S1 and S2 subunits. Moreover, the developer used a 2P mutation strategy based on research on previous coronaviruses. By adopting this method, 2 prolines will replace 2 other amino acids at the top of S2 subunits to improve the prefusion conformation.

3.2. Effectiveness

With a sample of 30420 participants, 15210 participants in each group are receiving either two doses of mRNA-1273 or a placebo. Final participants for the main efficiency analysis were 14073 and 14134. In total, 196 patients of COVID-19 were found, with 11 participants associated with the vaccine group and 185 participants who received placebo, according to the results. The vaccine has a 94.1% effectiveness with a 95% confidence interval (89.3% to 96.8%) [13].

3.3. Severe cases

In the time period from August 19 to December 21, 2021, the IVY enrolled total of 4094 patients over age 18. After, 2952 patients were included in the investigation with 1385 case patients and 1567 controls. The mean age among the participants was 62 with 49% female. The result revealed the

effectiveness against hospitalization was 82% with 95% confidence interval (77% to 86%) for participants with no immunocompromising conditions, 69% with 95% confidence interval (57% to 78%) for participants with immunocompromising conditions and 65% with 95% confidence interval (49% to 76%) for the participants with moderately to severely immunocompromising conditions [14].

3.4. The third dose

In the experiment mention above, the participants who received the third dose showed a 97% effectiveness with 95% confidence interval (95% to 99%) for participants with no immunocompromising conditions, 88% with 95% confidence interval (81% to 93%) for participants with immunocompromising conditions and 87% with 95% confidence interval (78% to 92%) for the participants with moderately to severely immunocompromising conditions [14].

Another experiment was conducted among a group of U.S. veterans over the course of nearly 4 months from late 2021 to early 2022. mRNA-1273 or BNT162b2 was administered as a third dose to 2 groups totaling 65196 individuals. The results showed an excess 45.4 cases with 95% confidence interval 19.4% to 84.7% for infection, 3.7%, 2.2% to 14.1% (95% CI) having COVID-19 symptoms; 10.6%, 5.1% to 19.7% (95% CI), for COVID-19 hospitalization; 2.0%, −3.1% to 6.3% (95% CI), for COVID-19 special and extra care and 0.2%, −2.2% to 4.0% (95% CI), for COVID-19 death number per 10000 people for BNT162b2 compared to mRNA-1273 [15].

3.5. Adverse effects

The manufacturer has disclosed some of the side effects, including headache, generalized fatigue, swelling etc. People received the first dose of vaccine were having only moderate symptoms. People received the second may appear severe conditions. The frequency for some of the adverse effects is shown in Figure 2 Moderna Vaccine Frequency of adverse effects [9].

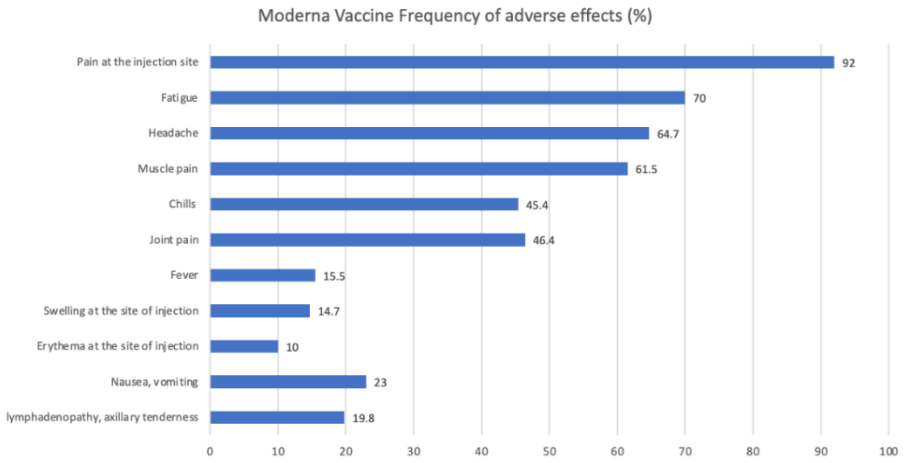

Figure 2. Moderna Vaccine Frequency of adverse effects [3]

3.6. Price:

In the middle of 2020, the federal government also ordered 100 million doses of mRNA vaccine from Moderna. The average price was $15.25 per dose [12]. Unfortunately, Moderna is also considering raising the shot price to $110-130 per dose [16].

4. Walvax biotechnology

Walvax biotechnology manufactured the first COVID mRNA vaccine in China. The vaccine is called ARCoV or AWcorna and it is already got approval by Indonesia. This vaccine codes for the RBD of SARS-CoV-2 Spike protein which is not same as the other mRNA COVID vaccines like Pfizer-BioNTech and Moderna. ARCoV was come out on 29th September 2022.

4.1. Target protein

Walvax biotechnology uses the mRNA which is only code for the receptor binding domain (RBD). For SARS-CoV-2 virus, there is a spike protein placed on the virus. When the virus enters our body, it is split by a specific enzyme into two subunits-S1 and S2. The RBD is placed on S1 and it will bind to the human angiotensin-converting enzyme 2 (ACE2). The way Walwax biotechnology use to fight against COVID-19 is to replicate the mRNA code of the RBD protein in the form of the vaccine.

4.2. Effectiveness

The preclinical studies showed that ARCoV develop a Th1-biased cellular response and intense antibodies against SARS-CoV-2[17]. There was a test on macaques to measure the efficiency of the ARCoV. The macaques were divided into three groups and they injected with 50 μg, 200μg and placebo (empty LNPs) respectively [18]. The degree of SARS-CoV-2 specific IgG were collected in 14 days, 21 days and 28 days respectively after the injection. They injected a booster 14 days after the first vaccination. The IgG antibody levels in animals injected with 50 or 200 μg of ARCoV reached 576,316 and 670,750 on day 28 after vaccination [18]. The Phase II trials also show that the vaccine trigger a strong immune response [19].

4.3. Adverse effects

In June 2020, the vaccine experienced its first Phase 1 test in Hangzhou [17]. A Phase I clinical trial to assess the safety, tolerability, and early immunogenicity of various doses of a SARS-CoV-2 mRNA vaccine in the population of people aged 18–59 and 60 and over. Fever is the common response to the vaccine but it can be cured about 2 days after vaccination. The Phase 1 had two trials. In Phase 1b, the age group changes to 18-59 years. The second Phase trial is based on the safety of different doses. From these three phases tests, it was shown that the vaccine may cause low lymphocyte count [17]. It is said that SARS-CoV-2 infection induces a decreased lymphocyte count so in the future we need to make sure that those people are not infected by the virus during vaccination [17]. But in the positive side, the researchers found that the levels of neutralizing antibodies that aim the Omicon after being injected with the ARCoV vaccine were four times higher than that after the injection of booster of CoronaVac [19].

4.4. Storage

The storage of the mRNA vaccine is a consistent challenge. The stability of ARCoV was improved under the manufacture condition of GMP conditions [18]. The vaccine purity held above 75.9% after storage for 6 months at 2-8 °C and the storage efficiency kept over 86% after 6 months storage [18]. The test showed that there is no much different between fresh and stored ARCoV so the stability of ARCoV is very ideal [18].

4.5. Price

Walvax biotechnology cost 325 million Yuan to manufacture the vaccine, which represent 50% of the total cost of Walvax biotechnology. As the vaccine is still during the third trials in China so the price is still uncertain. Although the price is not set, it may be between 50 Yuan and 60 Yuan.

5. Comparison

5.1. Target protein

In conclusion, the Pfizer and Moderna use the complete section of the spike protein but Walvax only uses the receptor binding domain to make the mRNA vaccine.For full-length spike protein, the 2p mutation is more stable. The cost of RBD is less than full-length protein as it only account for a small proportion of spike protein but full-length set up the whole. RBD has a higher supply volume too. So if people consider the price as the top, they can choose RBD vaccine like Walvax mRNA

vaccine. The full-length spike protein is more stable so the people who desire the stability of the vaccine can choose full-length spike protein vaccines such as BNT162b2 and mRNA-1273.

5.2. Economic strength

The economic level and technique of Pfizer and Moderna are much greater than Walvax. These companies were set up earlier and get more approval than Walvax so the vaccine of Pfizer and Moderna is more reliable and more people would choose them. People who do not want to take risks could choose Pfizer and Moderna. As the neutralizing antibody titer is all very high in those three companies so people can choose any one of the three.

5.3. Effectiveness

The effectiveness of three vaccines is all very high, with 95% in Pfizer, 95% in Moderna and very robust antibodies form in Walvax. Comparing the RBD and full-length spike protein, they both have high neutralizing antibody and B-cell memory [20]. Their antibody persistences are both high which can persist more than 6 months. What difference is RBD have less CD4+ epitopes but full-length spike protein with a very high volume of CD4+ epitopes.

5.4. Safety

For the weakness of the vaccine, Moderna and Pfizer is much serious than Walvax. Many people who vaccinated with BNT162b2 undergo pain, swelling, fever, fatigue and so on which in Moderna have the similar response. But in Walvax mRNA vaccine, the receivers have only fever and reduce in lymphocytes count which is much less severe than two of the companies above. Besides, the full-length spike protein has higher stability so it is safer to be vaccinated.

5.5. Price

People can receive three of the vaccine for free. For the government, the BNT162b2 cost $19.5 per dose in average, Moderna spend $15.25 for the vaccine. ARCoV is the cheapest which costs only 50 to 60 Yuan (around $8-9). There is a saying that at 2023, both Pfizer and Moderna will start to collect fee for the vaccine which is around $110-$130. It is very expensive for people who do not have medical card (consider the people have medical cards will pay less). Under this strategy, people better choose ARCoV for less price. For those three vaccines, ARCoV is the latest to come out. Although it had already got approval in Indonesia, it still remains in the Phase III trials.

6. Conclusion

BNT162b2, mRNA-1273 and ARCoV have their own strengths and weaknesses. In terms of effectiveness, BNT162b2 is the most effective (95%), followed by mRNA-1273 (94.1%). Those two mRNA vaccines have also proved to have high effectiveness against hospitalization and death. However, they will also introduce adverse effects on the recipients. The ARCoV, on the other hand, might not be as effective as BNT162b2 and mRNA-1273, it doesn't cause adverse effects in most cases or only mild fever to the recipients. The price for both BNT162b2 and mRNA-1273 are high in the future for the general public but the price of ARCoV will stay low. Therefore, healthy working-age people and the elderly are recommended to receive BNT162b2 and mRNA-1273 since they are more effective with acceptable adverse effects. For people with underlying medical conditions, ARCoV is recommended since it generates the least adverse effects with the highest safety. For financially disadvantaged groups, BNT162b2 and mRNA-1273 are recommended when the government still provides free vaccination or the list prices are still below $20.00. Otherwise, a cheaper ARCoV is a better choice.

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