

Comparing the Efficacy and Safety of the Pfizer BNT162b2 Vaccine with Other Alternatives Under COVID-19

Jingdong Tan

Department of Biochemistry and Microbiology, University of Victoria, Victoria, British Columbia, Canada

jingdongtan@uvic.ca

Abstract. In an epidemic or pandemic caused by a pathogen that has never been encountered, scientists have to compete against time to develop new vaccines. Vaccination effectively prevents the spread of the disease and saves lives. Under the COVID-19 crisis, several types of vaccines were developed and authorized as Emergency Use Authorization (EUA), including the first mRNA vaccine product ever approved by FDA, the BNT162b1. The transiently expressed mRNA does not encounter the problem of genome integration with the host and it takes less time to develop, which differentiates it from alternative types such as inactivated and subunit vaccines. This paper attempts to present the difference of the BNT162b2 mRNA vaccine from the Novavax subunit vaccine, and the Sinovac inactivated vaccine, in terms of COVID-19 prevention and adverse events, therefore attempts to provide a better understanding of the behaviors of mRNA vaccines under COVID-19.

Keywords: COVID-19, Vaccines, Pfizer BNT162b2, Vaccine effectiveness and safety.

1. Introduction

COVID-19 has been a global health emergency for the past years. The first case of the disease was identified in Wuhan, China in 2019 winter, and until August 2023 COVID-19 continues to pose a risk to public health. Until 2023 summer, 768,983,095 cases have been confirmed with 6,953,743 deaths, therefore, scientists are still fighting against the virus by developing effective vaccines to save lives. Until 2023, there are 13,492,099,754 doses of vaccine have been administered globally, those vaccines reduced the transmission of the disease, prevented ICU admissions, and protected individuals who are vulnerable to the virus, such as elders, children, and women in pregnancy [1].

Vaccine development is usually a slow process, the five stages of vaccine development can take up to at least 10 years. During the long time of pre-clinical and clinical trials, the effectiveness and adverse effects of potential vaccines are tested, and eventually, only the appropriate vaccine dose will be delivered to the public. However, under the stress of the COVID-19 pandemic, it is a pressing necessity to compete against the virus and develop vaccines fast to protect global health. The pandemic brought sufficient funding, numbers of researchers, and volunteers which significantly increased the development speed of vaccines, and thus, Pfizer got their BNT162b2 mRNA vaccine manufactured and authorized in less than a year [2].

BNT162b2 mRNA vaccine, also known as COMIRNATY is the first mRNA dose ever approved by the FDA. mRNA vaccine development is relatively different from old vaccine types, it is usually faster because the manufacturing process does not encounter any cell or tissue culturing. In 2020, Pfizer and BioNTech's decided to work together on the mRNA vaccine program BNT162 to prevent COVID-19 diseases; they carried out Phase I and II trials in March 2020 and presented the readout in July. After then, they carried out Phase III studies until the same year October and November, and the mRNA vaccine, BNT162b2 was submitted to UK and US for authorization. One month later, UK and U.S. approved BNT162b2 as EUA. Until 2023, even though the original dose is no longer authorized and instead, an updated dose is being used, there are still more than 366 million of BNT162b2 vaccine doses that were introduced and delivered in the U.S. excluding booster-dose counts [3, 4].

Other vaccine types are also taken place during the COVID-19 pandemic, such as the subunit vaccine from Novavax, and the inactivated vaccine Sinovac-CoronaVac. Subunit vaccines are

protein-based vaccines that contain virulence protein subunits aiming to trigger immune responses. Inactivated vaccines are a collection of physically or chemically killed pathogens that also build up immune memories. The different concepts and manufacturing processes of vaccine types resulted in different outcomes of efficacy and safety.

This article aims to present the difference of the original Pfizer-BioNTech mRNA vaccine from Novavax and Sinovac by (1) differentiating vaccine types and mechanisms; (2) comparing and contrasting the vaccine effectiveness, and (3) analyzing observed adverse events on different individuals.

2. The Pfizer-BioNTech (BNT162b2) COVID-19 Vaccine

The Pfizer-BioNTech mRNA vaccine BNT162b2 is the first mRNA product approved by FDA, it is also one of the major vaccines applied to the public worldwide. Generally, three doses are required for all age groups from 6 months and older to gain a high efficacy preventing the SARS-CoV-2, however, as the arose of Omicron BA.4/BA.5 variant, on April 18th, 2023, the original (monovalent) Pfizer-BioNTech mRNA vaccine is revoked with an updated bivalent dose presented. The updated dose is recommended for all individuals and the efficacy of protection against COVID-19 new variants is still under study [5].

2.1. Background Concepts of mRNA Vaccines

Messenger RNA vaccine is one of the advanced technologies in the vaccine field. During a normal infection, the pathogen introduces its genetic information to host cells, gives instructions, and uses the host cell mechanism for reproduction. The mRNA vaccine functions in a similar way; instead of introducing the complete genome encodes for the pathogen, mRNA segments are introduced. Those mRNA segments only encode for the virulence factor, in terms of BNT162b2 is the spike protein; after the mRNA is introduced to the body, the host cell will produce the virulence protein and triggers a strong immune response causing no diseases. mRNA vaccines are very adaptable between pathogenic variants because the genome encodes the virulence factor can be formulated easily, speeding up the vaccine manufacturing process and allowing the public to have a quicker response to disease threats [6].

2.2. The Compositions and Mechanism of BNT162b2

BNT162b2 contains single-stranded 5' capped mRNA that encodes for the P.2 variant of the spike protein from SARS-CoV-2. The mRNA is carried in lipid nanoparticles (LNPs), within the vaccine solution, there are sugar and buffers such as sucrose and tromethamine to keep the vaccine molecule stable and prevent degradation. There are two sets of different additional stabilizer ingredients depending on the version of the vaccine, however, the mRNA segment and LNPs are the same.

The delivery mode of BNT162b2 is intramuscular injection; capillaries in muscles help with the releasement of vaccine molecules. After injection, LNPs will interact and fuse with the host cells where the lipid will be dissolved to release the mRNA molecules. After the mRNA is translated into spike proteins, it is degraded into peptides and brought out to the membrane of dendritic cells with the binding of the Major Histocompatibility Complex II. After that, the antigen presented on dendritic cells which activates Helper T cells and induces the adaptive immune responses specifically against the spike protein. Therefore, a defensive immune memory against COVID-19 is built [5, 6].

2.3. BNT162b2 Effectiveness on COVID-19

Studies suggested BNT162b2 has a high efficacy in COVID-19 prevention after the second dose, this effect is observed between various individuals.

The C4591001 clinical trial group presented a Phase III study in 2020 with 43,448 participants. Among all participants, half were injected with BN162b2 and the other half with a placebo, and the majority race is Caucasians with few other races. This study aimed to investigate the vaccine

effectiveness of 16 years older individuals after taking two doses of BN162b2 21 days apart. In terms of prevention, 8 cases of COVID-19 infection were observed after the second dose under the condition of 36,523 participants with no previous SARS-CoV-2 infections. The clinical trial is carried into subgroups of individuals with different health indexes, such as age, sex, race, and body mass. The overall vaccine effectiveness on COVID-19 prevention after the second dose is 95% (95%CI: 90.3%-97.6%), and generally in subgroups are 90% to 100% regarding individual differences, and only one participant acquired a severe symptom of COVID-19, and it was after the first dose [7].

Along with the spread of the pandemic, COVID-19 mutant Delta and Omicron arose, another study ended in 2022 suggested the effectiveness of BNT162b2 in preventing variant infections. The result reported an efficacy of 89.4% (95%CI: 86.2%-91.9%) on preventing the Delta variant after two doses of BNT162b2; and 28.4 % (95%CI: 7.1%-44.8%) against Omicron after three doses. The effect of BNT162b2 on the prevention of the SARS-CoV-2 variants has decreased contrasting to the original SARS-CoV-2 virus, one of the reasons might be the mutation of the amino acid sequence of spike protein which altered its structure and chemical properties [8].

2.4. Observed Adverse Events and the Safety of BNT162b2

In the same C4591001 clinical trial group study in 2020, the adverse events of BNT162b2 are compared with the placebo. Generally, there are more observed adverse events on BNT162b2; the solicited adverse events after the first and second doses are 71% and 66% respectively, and the unsolicited (for all 43,252 participants) adverse event and specifically vaccine-related events are 27% and 21% respectively, compared to the placebo which is only 12% and 5%. BNT162b2-related lymphadenopathy is also observed in 64 participants, which takes 0.3% of all. Few developed serious adverse events such as injection-related shoulder injuries, arrhythmia, and lymphadenopathy under the right armpit. Two of the participants were recorded dead from arteriosclerosis and cardiac arrest after being introduced to BNT162b2, and four were recorded dead from placebo participants, the cause of death of two people was unknown, however, there was no death caused by COVID-19 reported. All observed adverse event cases were under the stopping rules [7].

Another study in 2021 aimed to present a detailed study on different symptoms after injecting BNT162b2. All symptoms were self-reported by health care workers (HCWs) and among 803 HCWs, 695 females, and 108 males, 92.9% completed two doses of BNT162b2. From the report, 75.97% of HCWs had generalized symptoms such as headaches, fever with chills, or dizziness. 45.70% had muscle pain. In terms of serious adverse events, 12.83% found difficulties or have symptoms that affected normal daily living; however, those serious symptoms are recorded only to be temporary [9].

3. The Novavax (NVX-CoV2373) COVID-19 Vaccines

NVX-CoV2373 recombinant subunit-based vaccine contains spike protein molecules and adjuvants. It is approved by the technical advisory group as EUA on December 20th, 2021, and approved by FDA as EUA for ages above 18 on July 13th, 2022. The two names of Nuvaxovid and Covovax indicate the different manufacturing locations of this vaccine. Novavax is an American company that chose to manufacture NVX-CoV2373 in Europe and India, and this resulted in two different names, however, Nuvaxovid and Covovax are biologically and chemically the same. Novavax requires 2 doses of the original vaccines and an additional updated bivalent booster dose just like BNT162b2 [10].

3.1. Comparisons on Background Concepts of subunit Vaccines and mRNA Vaccines

Subunit vaccine is a general term for protein-based vaccines, usually, subunit vaccine is also called recombinant vaccines. Unlike the mRNA vaccine which uses the genome to produce the virulence protein in host cells, subunit vaccines contain prior biochemically purified proteins, in terms of Novavax just like BNT162b2, it is the spike protein, therefore, an additional culturing step is required in subunit vaccine. To get the protein product, a DNA genome encoding for the spike protein has to

be integrated either into bacteria, mammalian cells, or insects; the NVX-CoV2373 vaccine integrated COVID DNA into baculovirus, and utilize baculovirus to induce infections to Sf9 cells in *Spodoptera frugiperda*, then the spike protein is purified and collected from the cell membrane [10]. Thus, this biochemistry step takes a much longer time than the mRNA construction step in BNT162b2.

3.2. Compositions of NVX-CoV2373 is Entirely Different from BNT162b2

NVX-CoV2373 from Novavax is a fully different type of vaccine from BNT162b2, it does not require lipid vesicles to transport RNAs; instead, it contains purified spike proteins, inactive ingredients, and an adjuvant Matrix-M. Recombinant subunit vaccines require adjuvants to elicit a strong immune response by inducing inflammation and activating the internalization of protein subunits by macrophages. In terms of NVX-CoV2373, each dose contains 5ug of fully structured SARS-CoV-2 spike proteins, inactive ingredients such as disodium hydrogen phosphate dibasic heptahydrate to keep the vaccine nontoxic, and 50ug per dose of Matrix-M that biasedly induce innate immunity and T helper 1 cell responses to amplify immune reactions against the spike protein [10].

Even though BNT162b2 and NVX-CoV2373 both apply the spike protein to build immune memories against COVID-19, however, the mechanisms are different, BNT162b2 does not require an adjuvant to boost immune responses because it uses the host cell machinery to produce spike proteins.

3.3. The Differences in Vaccine Effectiveness between NVX-CoV2373 and BNT162b2

The 2019nCoV-302 Study Group reported a phase III study in 2021 with 15,187 randomized participants with age from 18 to 84 years old, half were introduced with NVX-CoV2373 and the rest with placebo. The majority of this population are Caucasians and a few other races, there were 48.4% women which balanced the sex of participants. Compared to the phase III study of BNT162b2, the population size is smaller, however, the composition of different races, sexes, and ages is highly alike, which made the result of the two studies comparable [11].

In the NVX-CoV2373 study, there were 10 recorded COVID-19 cases in at least 7 days after two doses of vaccination, which presented a vaccine effectiveness of 89.7% (95% CI: 80.2%-94.6%), specifically, there is an 86.3% (95% CI: 71.3%-93.5%) efficacy specifically against the Alpha variant [11].

As a reference to the Delta variant, a new study reported from the same study group in 2022 suggested an 82.0% (95% CI: 32.4%-95.2%) efficacy on infection prevention, this result is similar to BNT162b2 which was 89.4% (95%CI: 86.2%-91.9%) [7, 12].

The NVX-CoV2373 vaccine and the BNT162b2 vaccine are both very effective in preventing SARS-CoV-2, in contrast, the VE of NVX-CoV2373 is relatively lower, however, the difference is not huge. The comparison of only two studies is also limited, the reasons for the difference in VE between BNT162b2 and NVX-CoV2373 caused by random noise have to be considered.

3.4. The differences in Vaccine Safeties between NVX-CoV2373 and BNT162b2

The same phase III study in 2021 also reported adverse events of NVX-CoV2373, 2310 participants were recorded for any of their specific symptoms. The reported solicited local and systemic symptoms after the first dose are 57.6% and 45.7%; and after the second doses are 79.6% and 64%. Symptoms such as local pain or tenderness, and systemic headache, fatigue, or vomiting were reported. In terms of five severe symptoms, 3 of grade-4 fevers were reported, and two reported deaths were COVID-19 related.

The frequency of unsolicited adverse events was much lower, which is 25.3%, with 0.5% of developed serious symptoms in all 15,139 participants [11].

To analyze the difference between NVX-CoV2373 and BNT162b2, the unsolicited AEs are similar between NVX-CoV2373 (25.3%) and BNT162b2 (27%). However, the solicited AEs of NVX-CoV2373 are different from BNT162b2 referring to the two doses. After the first dose, NVX-CoV2373 has much lower AEs (57.6% and 45.7%) compared to BNT162b2 (71%); and the second

dose of NVX-CoV2373 reported similar frequency (79.6% and 64%) compared to BNT162b2 (66%). Combining the result of all observed AEs in this study, NVX-CoV2373 reported a lower ratio of adverse events [7, 11].

4. The Sinovac-CoronaVac Inactivated COVID-19 Vaccine

The Sinovac-Coronavac vaccine was presented by the Chinese company Sinovac during the COVID-19 pandemic. Sinovac-Coronavac is an inactivated vaccine that is safer to introduce to immunocompromised populations such as children, elders, and women in pregnancy. Sinovac-Coronavac was first authorized in China on June 5th, 2021 for younger populations, and it was authorized by FDA much later on March 11th, 2022 for EUA. Data collected on January 31st, 2022 reported 2.47 billion produced doses of the Sinovac-Coronavac inactivated vaccine [13, 14].

4.1. Comparisons on Background Concepts of Inactivated Vaccine and mRNA Vaccines

Unlike the BNT162b2 mRNA vaccine contains the genomic information of the spike protein, the Sinovac-Corona inactivated vaccine contains killed pathogens that elicit immune responses causing no diseases. Generally, pathogens have to be treated for inactivation, Sinovac-Corona is Vero-cell and β -propiolactone-inactivated from the CZ02 variant from SARS-CoV-2, which is a beta-alike variant. By culturing SARS-CoV-2 in Vero cells over time, it gains adaptations on infecting the Vero cell and loses its invasiveness towards humans, in another term the virus is weakened. β -propiolactone (BPL) is an organic compound that induces alkylations on nucleic acids and disrupts the protein-protein interaction through acetylation. Therefore, SARS-CoV-2 cannot perform a normal protein-protein interaction with host cells, and its genome cannot be replicated or transcribed [13].

Overall, inactivated vaccines are completely different from mRNA vaccines. The factor that elicits the immune responses is not genomic and protein subunit-based and like BNT162b2, but instead of killed pathogens. Therefore, the immune response from the Sinovac-Corona inactivated vaccine is weaker and requires one more booster dose (total of three doses) than BNT162b2. The development of Sinovac-Coronavac was also much slower because it contains a cell culturing step and a chemical treatment step.

4.2. Sinovac-CoronaVac Has Different Composition Compared to BNT162b2

The Sinovac-CoronaVac vaccine does not contain any genomic materials that take the function of the vaccine and it does not require any lipid nano-particles to be delivered like BNT162b2. Sinovac-CoronaVac contains 3 μ g of inactivated SARS-CoV-2 with aluminum hydroxide as an adjuvant in saline solution; disodium hydrogen phosphate was also included to keep the ingredient nontoxic [13].

4.3. The difference in Vaccine Effectiveness between Sinovac-CoronaVac and BNT162b2

A Phase III study carried out in Turkey between 2020 to 2021 on Sinovac-CoronaVac involved 10,214 participants, and 6,646 of them were introduced to the Sinovac-CoronaVac vaccine with the rest to placebo. All participants were aged between 18-59 years old with no prior SARS-CoV-2 infections, individuals with different body mass and comorbidities were randomized, and sex are balanced equally. Comparing the Sinovac-CoronaVac participants with BNT162b2, the major difference is the variability of races, which is not illustrated in this study, however, other factors are still consistent and thus, the VE result is comparable [15].

The result reported 9 cases of COVID-19 from confirmation of PCR tests in at least 14 days after receiving two doses of Sinovac-CoronaVac. The resulting vaccine effectiveness is 83.5% (95% CI: 65.4%-92.1%) on COVID-19 prevention, and 100% on hospitalization [15].

Another paper reported the vaccine effectiveness of Sinovac-CoronaVac against Omicron; among 1050 participants who received all three doses, the VE of Sinovac-CoronaVac on Omicron prevention is 32.4% (95%CI: 9.0%-49.8%) [16].

Generally compared to BNT162b2 after taking both doses, Sinovac-CoronaVac is weaker on preventing the infection of SARS-CoV-2, the VE contrast is 83.5% vs. 95%, the result is somewhat expected because Sinovac-CoronaVac requires a third booster dose which was not developed in 2021. On the prevention of SARS-CoV-2 omicron, Sinovac-CoronaVac reported a higher VE than two doses of BNT162b2, which are 32.4% vs. 28.4 %, however, both vaccines are not efficacious in preventing Omicron infections, the BNT162b2 updated bivalent dose is still under study, so results could not yet to be compared [7, 16].

4.4. The Difference in Vaccine Safeties between Sinovac-CoronaVac and BNT162b2

In the same phase III study from Turkey, adverse events were reported to be much lower than BNT162b2. There was a total of 18.9% of AEs in the vaccine group, in terms of solicited AE is 17.3%, and 4.6% for unsolicited. The frequency of local AE was 2.7% with most symptoms of pains around injection sites; the systemic AE has a frequency of 17.7%, major symptoms reported were fatigue, headaches, and myalgia, and 1.81% had a fever. No death cases were recorded in this study [16].

Sinovac-CoronaVac inactivated vaccine takes advantage on safeties, the mechanism of inactivated vaccine resulted in much lower AEs than BNT162b2. There were three times more frequent (66%) solicited AEs observed in the BNT162b2 Phase III study, the reported fever was also significantly lower. In terms of the symptoms, there was no lymphadenopathy after Sinovac-CoronaVac, participants in both studies had headaches as the major reaction of systemic AEs, however, Sinovac-CoronaVac has less headache frequency in terms of all participants who experienced an adverse event [7, 16].

5. Conclusion

During a pandemic time is essential for developing vaccines and protecting public health. BNT162b2 mRNA vaccine has an advantage in the manufacturing process, it is faster to produce than NVX-CoV2373 or Sinovac-CoronaVac because it does not require any cell culturing step. BNT162b2 can easily be updated against new variants by adding a new mRNA referring to the new virulence protein structure (bivalent), which NVX-CoV2373 and Sinovac-CoronaVac will perform a slower process.

On the seccusfullness of COVID-19 prevention, BNT162b2, NVX-CoV2373, and Sinovac-CoronaVac all reported high vaccine effectiveness (95%, 89.7%, and 83.5%) that distribute immunity across participants. However, BNT162b2 has the highest VE suggesting a better performance than the other two vaccines.

BNT162b2 reported a higher frequency of adverse events than NVX-CoV2373 and Sinovac-CoronaVac, with 66% of unsolicited AE compared to 64% and 4.6%. There are also more serious AEs and various reactions after BNT162b2 injection such as injection-related shoulder injuries, arrhythmia, and lymphadenopathy in unusual sites, which were not observed in either NVX-CoV2373 or Sinovac-CoronaVac.

To conclude, all vaccines are designed to protect the global health and provide a safer environment; the conclusion of this paper is not drawn for distinguishing the best vaccine, but to attempt to provide a better understanding of how BNT162b2 behaves differently from other alternative types, and possible consideration on future vaccine developments.

References

- [1] World Health Organization. Coronavirus disease (COVID-19) pandemic. World Health Organization. 2023. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019>.
- [2] World Health Organization. The effects of virus variants on COVID-19 vaccines. World Health Organization. 2021-03-01. <https://www.who.int/news-room/feature-stories/detail/the-effects-of-virus-variants-on-covid-19-vaccines>.

- [3] Thorn C R, Sharma D, Combs R, et al. THE JOURNEY OF A LIFETIME – DEVELOPMENT OF PFIZER’S COVID-19 VACCINE. *Current Opinion in Biotechnology*, 2022, 78: 102803.
- [4] Mikulic M. COVID-19 vaccinations administered number by manufacturer U.S. 2021. Statista. 2023-05-02. <https://www.statista.com/statistics/1198516/covid-19-vaccinations-administered-us-by-company/>.
- [5] Vaccine Information Fact Sheet for Recipients and Caregivers about Comirnaty. Pfizer-BioNTech COVID-19 Vaccine. Food and Drug Administration. 2022-12-08.
- [6] Background document on the mRNA vaccine BNT162b2 (Pfizer-BioNTech) against COVID-19. World Health Organization. 2021-01-14.
- [7] Polack F P, Thomas S J, Kitchin N, et al. Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine. *New England Journal of Medicine*, 2020, 383 (27): 2603–2615.
- [8] Chatzilena A, Hyams C, Challen R, et al. Effectiveness of BNT162b2 COVID-19 vaccination in prevention of hospitalisations and severe disease in adults with SARS-CoV-2 Delta (B.1.617.2) and Omicron (B.1.1.529) variant between June 2021 and July 2022: a prospective test negative case–control study. *The Lancet regional health, Elsevier BV*, 2023, 25: 100552.
- [9] Kadali R A K, Janagama R, Peruru S, et al. Side effects of BNT162b2 mRNA COVID-19 vaccine: A randomized, cross-sectional study with detailed self-reported symptoms from healthcare workers. *International Journal of Infectious Diseases*, 2021, 106: 376–381.
- [10] Background document on the Novavax (NVX-CoV2373) vaccine against COVID-19. World Health Organization. 2021-12-20.
- [11] Heath P T, Galiza E P, Baxter D N, et al. Safety and Efficacy of NVX-CoV2373 Covid-19 Vaccine. *New England Journal of Medicine*, 2021, 385.
- [12] Toback S, Galiza E, Cosgrove C, et al. Safety, immunogenicity, and efficacy of a COVID-19 vaccine (NVX-CoV2373) co-administered with seasonal influenza vaccines: an exploratory substudy of a randomised, observer-blinded, placebo-controlled, phase 3 trial. *The Lancet Respiratory Medicine*, 2021.
- [13] Background document on the inactivated vaccine Sinovac-CoronaVac against COVID-19. World Health Organization. 2021-05-24.
- [14] Zhang W. Sinovac: COVID-19 vaccine production figures 2022. Statista. 2022-05-10/2023-08-18. <https://www.statista.com/statistics/1306710/sinovac-covid19-vaccine-production-figures/>.
- [15] Tanriover M D, Doğanay H L, Akova M, et al. Efficacy and safety of an inactivated whole-virion SARS-CoV-2 vaccine (CoronaVac): interim results of a double-blind, randomised, placebo-controlled, phase 3 trial in Turkey. *The Lancet*, 2021, 398 (10296): 213–222.
- [16] Tsang N N Y, So H C, Cowling B J, et al. Effectiveness of BNT162b2 and CoronaVac COVID-19 vaccination against asymptomatic and symptomatic infection of SARS-CoV-2 omicron BA.2 in Hong Kong: a prospective cohort study. *The Lancet Infectious Diseases*, 2022, 23 (4): 421-434.