Proceedings of the Pakistan Academy of Sciences: B. Life and Environmental Sciences 58(S): 11-17 (2021)

ISSN (Print): 2518-4261; ISSN (Online): 2518-427X
http://doi.org/10.53560/PPASB(58-sp1)652

Pakistan Academy of Sciences

Review Article

COVID-19 Vaccines: Pakistan's Perspective

Sidra Rahman[1*], Misbahud Din[1], Sahrish Khan[1], Lubna Yar[1], Fatima Zia[1], Muhammad Idrees[2], and Muhammad Ali[1,3]

[1]Department of Biotechnology, Quaid-i-Azam University, Islamabad, Pakistan
[2]Centre of Excellence in Molecular Biology, University of the Punjab, Lahore-53700, Pakistan
[3]Pakistan Academy of Sciences, Islamabad, Pakistan

Abstract: The pandemic of COVID-19 has affected millions of individuals around the globe. Its impact on the world has made essential progress in the research sector to develop safe and effective vaccines. Several vaccines for COVID-19 have been made utilizing the SARS-CoV-2's spike protein. Presently, Moderna's COVID-19 vaccine, Pfizer-BioNTech COVID-19 vaccine, and Johnson & Johnson's Janssen vaccine are approved and suggested by CDC to prevent the COVID-19. Five vaccines (till April 2021) have been approved by WHO on emergency basis which are AstraZeneca, Pfizer-BioNTech, Moderna, Sinopharm, and Johnson & Johnson. The Food and Drug Administration approve the scientific standard of drugs and vaccine such as their efficacy, safety, and quality. Currently, ambiguous information regarding COVID-19 vaccine are being circulated globally. During health crisis, rumours roll out and generate fear, psychosis, and anxiety. On the other hand, the variants of SARS-CoV-2 are continuously emerging across the globe. Different platforms are being utilized for the development of whole virus-based vaccine, nucleic acid-based vaccine, and proteins sub-unit vaccine; all displayed good efficacy where few were further proceeded to clinical trials. The current article provide an overview on the COVID-19 vaccines, their efficacy, and discuss the possible reduction in vaccine efficacy due to the emergence of new variants.

Keywords: COVID-19, Vaccine, New Variants, Pandemic, Efficacy, Mutations.

1. INTRODUCTION

The COVID-19 pandemic caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) has affected millions of individuals around the globe [1, 2]. Scientists across the globe are trying to develop vaccines that are both effective and safe to prevent COVID-19. Several candidate vaccines are in the pipeline or already in the clinical trial developmental stages while some or clinically available and have been approved. Studies from animal models along with human trials already indicated potential trends to achieve a high level of neutralizing antibodies [3]. Promising results have been revealed by the antibodies of SARS-CoV-2 spike proteins in terms of inducing high titers in preclinical models.

A proteins-based recombinant vaccine such as CoV-RBD219N1 and chemically inactivated virus vaccines i.e PiCoVacc have reported a high level of protective immunity in animal models such as mice and rhesus macaques [4, 5]. Other studies have reported adenovirus vectored vaccines as inducing high-level of antibodies for SARS-CoV-2 [6,7]. The mentioned vaccine of COVID-19 (ChAdOx1-nCoV-19) has shown antibodies titers ranging from 5-40 in the rhesus macaques [6]. A human adenovirus 5-vactored COVID-19 vaccines in trial phase-I induced both live virus-neutralizing antibodies titers and pseudovirus neutralizing antibodies titers in healthy individuals in 28 days post-vaccination [7]. The reported titers of antibodies induced by adenovirus vectored COVID-19 vaccines were lower than the reported human convalescent plasma [8, 9].

Efforts have been made to develop vaccines candidates particularly utilizing the SARS-CoV-2's spike protein [10]. Public health authorities across

Received: February 2021; Accepted: July 2021
*Corresponding Author: Sidra Rahman <sidrarahman1716@yahoo.com>

the globe have been mobilizing to deliver the biggest ever vaccination program to battle COVID-19. As of 25th May 2021, 5.3% of the world population has been fully vaccinated [11]. Presently, Moderna's COVID-19 vaccine, Pfizer-BioNTech, and Johnson & Johnson's Janssen COVID-19 vaccine are approved and suggested by CDC to prevent COVID-19 [12, 13]. As of 27th February 2021, there are almost 50 other COVID-19 vaccines still in developmental stages [11, 12]. Five vaccines have been approved by WHO on emergency basis which are AstraZeneca, Pfizer-BioNTech, Moderna, Sinopharm, and Johnson & Johnson's Janssen [14].

Vaccines could be based on live or attenuated viruses, virus-like particles, proteins sub-unit, viral vector, DNA, RNA, and/or conjugated nanoparticles [15]. The mRNA-based vaccines trigger an immune response as they teach the cells how to make a protein that could activate the immune response. The Pfizer-BioNTech which is an mRNA-based vaccine is recommended by CDC for people aged 16 years and older. Similarly, the Moderna vaccine is also a mRNA-based vaccine and is recommended for people aged 18 years and older. The BNT162b1vaccine is an mRNA vaccine that encodes for the SARS-CoV-2 RNA binding domain (optimized codon) which is an essential target for neutralizing antibodies. The vaccine immunogenicity has been enhanced by the addition of T4 fibritin-derived fold on trimerization domain to the RNA binding domain. The mRNA is efficiently delivered as it is encapsulated in 80nm ionizable cationic lipid nanoparticles. The clinical trials have revealed moderate to transient reactions with no obvious adverse side effects [16].

The mRNA-1273 is a synthetic mRNA vaccine encapsulated in the lipid nanoparticles encoding for spike proteins of SARS-CoV-2. This vaccine could activate the immune response to the spike protein and is considered safe because of its mRNA nature [17]. This vaccine was quickly approved by the food and drug administration (FDA) for clinical trials [18]. The vaccine was reported to be welltolerated and safe in 25-100 μg dose cohorts [19].

1.1. Vaccine Authorization and Policies

The FDA approve the scientific standard of drugs and vaccine such as their efficacy, safety, and quality. FDA also provides regulatory and scientific advices to researcher and vaccine developers and evaluate the information of clinical phases of vaccines [20]. FDA enhanced the process of the vaccine's approval due to the public health emergency and the importance of the urgent need and availability. The interim final rule with request for comments (IFC) discusses CMS implementation of section 3713 of the Coronavirus relief, Aid, and Economic-Security Act (CARES Act) which is recognized as Medicare Part-B coverage and payment for COVID-19 vaccine and its administration [20].

1.2. Vaccines in Pakistan

Pakistani health authroities have awarded emergency use authorization to COVID-19 vaccines particularly the Russian vaccine, Sputnik-V, or Gam COVID Vac to be administered in Pakistan. The authorities have also granted authorization to China's state-owned Sinopharm and British-Swedish-vaccine manufacturers Oxford AstraZeneca's AZD1222/ Covisheild vaccine [21, 22]. COVID-19 vaccination has been started in

Table 1. Vaccines that clinically approved or have entered to clinical trial (Phase III) [12]

S. No	Vaccines	Producer Company/ Organization
1	Ad5-nCoV	CanSino Biologicals
2	INO-4800	Inovio, Inc
3	mRNA-1273	Moderna
4	ChAdOx1	University of Oxford
5	Pathogen-specific aAPC	ShinzenGeno-Immune Medical Institute
6	BNT162b2	Pfizer, Inc., and BioNTech

Pakistan. The emergency use authorization was announced by the Drug Regulatory Authority on 22nd January of 2021 following which vaccines could be shifted to the country in the coming few days [22]. The 5 million doses of vaccine have been donated by China and 17 million vaccines have been donated by the UK to Pakistan.

2. MISINFORMATION ASSOCIATED WITH VACCINE IN PAKISTAN

Ambiguous information regarding COVID-19 are being circulated across the globe. Keeping vaccines at the center of conflict, many myths and rumors have been spread. Vaccines associated with infertility were the most heard rumor following by vaccines ingredients and their composition used for vaccine harming the person who inject it. A huge part of the world suffering from this pandemic has faced the hardest challenges to coping with the loss of loved ones [23]. The reason for the uncertainty associated with the use of vaccination is also due to certain factual cases related to COVID-19 vaccination e.g., the certain patient developed thrombotic thrombocytopenia (blood clotting) after receiving the AstraZeneca vaccine. More than 20 million people have been vaccinated (as per April 2021) with the AstraZeneca vaccine in the UK and about 79 cases of rare blood clots with low platelets have been reported along with 19 deaths. However, the WHO and the European Medicines Agency recommended that there is no increased risk of blood clots with the vaccine and vaccinations should be continued [24]. People also urged that the vaccine-based immunity is not long-lasting, hence there could be chances of reinfections and vaccination is not an appropriate option.

During a health crisis, rumors roll out and generate fear, psychosis, and anxiety. Patients with HIV, cancer, organ transplants, bone marrow recipients with the suppressed immune system are not willing to get vaccines [25]. Other misconception also exists according to which tracking device/chip is implanted in the human body [26]. The spread of coronavirus rumors gives rise to serious menace not only for the effectiveness of vaccine campaigns but also to public health. Vaccines are only a part of efforts to put pandemics under control, adding that it is also important for the authority to increase testing, tracing, and treatment [27].

2.1 New Variants Reported from Pakistan

Fearfully, VOC-202012/01 (Variant of Concern, the year 2020, month 12, variant 01) formerly known as VUI-202012/01, was recognized in United Kingdom, South Africa, and Brazil [28]. About 31 countries of the world have reported the new variants till 30 December 2020 [29]. It is thought that new virus might be up to 70% more transmissible and threaten than old virus strain, which could cause another wave of the same pandemic. According to a newly published study, a new coronavirus variant moved from the UK to the US rapidly [30]. In Pakistan's first case of the UK variant was reported in Sindh province. On 29th December 2020 in Karachi, three samples of UK returnees show 95% similarity in the first phase of genotyping to new coronavirus variants from the UK. It has been documented that three patients of UK returnees have a new variant of SARS-CoV-2 in the first phase, 12 samples were genotyped in which six were detected positive. Besides, the National Command and Operation Centre (NCOC) reported two positive cases of the UK variant in Islamabad on 4th, January 2021. The individuals had recently returned from the UK while the variant was confirmed via whole-genome sequencing. Pakistan has extended the travel restrictions on several countries, including the UK, till February 28 to minimize the spread of the deadly variant of the coronavirus amidst the second wave of infections [31].

3. EFFICACY OF VACCINE COVID-19

It has been documented that the vaccine formed by the Chinese (Cansino Biologic's COVID-19 vaccine) was 65.7% effective in averting the symptomatic cases and 90.1% in severe disease [29]. The percentage was based on analysis of multiple countries' phase-III clinical trials of the Cansino vaccine, however, the Pakistani sub-set with 30,000 contestants exhibited 74.8% defense against symptomatic cases and 100% in serious illnesses. In addition to Pakistan, Cansino has analyzed its vaccine in Chile, Mexico, Russia, and Argentina. Neither the Cansino nor Pakistani government announced further information on the efficacy statistics, suggesting that Cansino joins other Chinese vaccine manufacturers Sinopharm and Sinovac in publishing little data beyond

headline efficacy figures [30]. The early trials showed that Cansino's vaccine induced only a limited immune response that was surpassed by Pfizer and Moderna. After rising in the vaccine run, foreign vaccine manufacturers like Moderna and Pfizer also defeated Cansino in completing Phase-III clinical trials, obtaining approvals from the government. Cansino also fell behind its Chinese counterparts Sinovac and Sinopharm, which are now distributing hundreds of millions of doses across at least a dozen foreign countries. Sinopharm's vaccine is 79% effective while Sinovac's vaccine is between 50% and 90% effective [32].

Cansino's shot is based on similar viral-vector vaccine technology that Johnson & Johnson is using for its one-shot vaccine. Cansino's 65% efficacy rate also appears on par with Johnson & Johnson's 66% figure. Cansino's 65% efficacy figure would pass the WHO's recommended threshold of 50%, but it still lags the 94.1% and 95% figures posted by Moderna and Pfizer, respectively [33]. Like the Johnson & Johnson single-dose vaccine, Cansino may have distinct advantages in distributing its jabs to poor and middle-income countries. Unlike mRNA vaccines from Pfizer and Moderna, Cansino's vaccine does not require sub-zero storage; it can be transported in less expensive supply-chain networks at normal refrigerated temperatures (2 to 8 degrees Celsius) [32,34]. Its administration in a single dose could boost efforts to distribute vaccines to more rural areas, where it may be difficult to send supplies and set up follow-up appointments. Cansino's vaccine has not been officially approved in Pakistan or any other country, but it has been distributed to members of China's military and other high-risk population groups in China on an emergency basis since at least June 2020. In November 2020, Cansino has the potential benefits of having a viable one-shot COVID-19 vaccine. In the pandemic environment, what you need is a vaccine that can quickly provide protection. If we can make a single dose work, it will stop the spread of the virus [32, 35].

3.1 Possible Reduction in Vaccine Efficacy due to Variation

The Oxford-AstraZeneca vaccine shows good efficacy against the UK's dominant variant (new corona-virus variant). Vaccine designers declare it is a comparatively simple process to adjust the existing formula to target any new variants. Scientists behind the Moderna and Pfizer-BioNTech vaccines also suggest their vaccines seem to protect against UK's dominant new variant. Now that more than 10 million people have been vaccinated, these are the first indications that the vaccine even now defends maximum people with COVID-19. Oxford investigators reveal similar levels of efficacy against "Kent" B117 (74.6%) and the old variant (84%). It is now present across the UK and in other countries. In what way variants impact the severity of COVID-19 disease and how variants impact the efficacy of vaccines and therapeutics. Surveillance of emergent variants can assist detection of the variant with the ability to circulate more rapidly in people, capability to evade detection by specific diagnostic tests, ability to produce either moderate or more serious disease in people, ability to evade natural or vaccine-induced immunity, and reduced susceptibility to therapeutics that utilize monoclonal antibodies [36]. It has been stated that vaccines could work efficiently to avert COVID-19 and could not be affected by variations or the emergence of new SARS-CoV-2 variants. The report also reveals the vaccine may decrease the spread of the disease as well as preventing severe infection and death from COVID-19. The necessity for a new vaccine had always been estimated. "Corona-viruses are less disposed to mutation than influenza viruses, but due to continuing pandemic situation, we have always expected that new variants will begin to dominate and that ultimately need a new version of the vaccine for the updated spike protein. It would be essential to sustain vaccine efficacy at the highest possible level. There is a need for continuous monitoring on the emergence of new variants and work with AstraZeneca to make changes to the vaccine if compulsory [37].

The lineage carries many mutations in the SARS-CoV-2 spike protein, the immune system's prime target, which allows the virus to identify and infect host cells including some changes linked to weakened antibody activity against the virus. The rapid spread of variants could be its ability to elude previously established immune responses [38, 39]. To investigate this, a virologist isolated the new variant from infected people. Then they tested the variant samples against serum the antibody-containing portion of blood taken from six people who had recovered from COVID-19 caused by other versions of the virus. This convalescent serum tends to contain neutralizing, or virus-

blocking, antibodies that can prevent infection. The researchers found that the convalescent serum was much worse at neutralizing new variants than at neutralizing variants that circulated earlier in the pandemic [38]. Some people's plasma performed better against new variants than others, but in all cases, the neutralizing power was substantially weakened. The researcher probed the effects of convalescent serum on several groupings of spike mutations observed in variants. They did this using a 'pseudo-virus' a mutated form of HIV that infects cells using the spike protein of SARS-CoV-2. These experimentations demonstrated that variant contains mutations that blunt the effects of neutralizing antibodies that recognize two key regions of spike: its N-terminal domains and receptor-binding. Pseudo-viruses with the full package of new variants mutations were fully resistant to convalescent serum from 21 out of 44 participants and were partly resistant to the serum of many people [38, 40].

Mutations in the receptor-binding domain of variant caused a modest drop in the potency of antibodies from people who had received either the Pfizer or Moderna mRNA vaccines. Most COVID-19 vaccines elicit high levels of antibodies that target diverse regions of the spike protein, so some of the molecules are likely to be able to block variants of the virus. And other components of the immune response, such as T cells, might not be affected by new variants [38].

4. CONCLUSION

The development of a vaccine against COVID-19 was an important aspect and a challenging job. Presently, Moderna's COVID-19 vaccine and Pfizer-BioNTech COVID-19 vaccine are approved and suggested by CDC to prevent COVID-19. The vaccine formed by the Chinese resarchers was 65.7% effective in averting the symptomatic cases and 90.1% in severe disease. The emergence of new variants are due to the variation that occurs in the spike protein of SARS-CoV-2 and mutation in the receptor-binding domain which may causes a reduction in vaccine efficacy.

5. CONFLICT OF INTEREST

The authors declare no conflict of interest.

6. REFERENCES

1. World Health Organization. WHO Coronavirus Disease (COVID-19) Dashboard (2020). https://covid19.who.int/ (accessed 24 January 2021)
2. M. Din., H. Ali., M. Khan., A. Waris., S. Ullah., M. Kashif, and M. Ali. Impact of COVID-19 on polio vaccination in Pakistan: a concise overview. *Reviews in medical virology* 31(4): e2190 (2020).
3. K. Dhama., K. Sharun., R. Tiwari., M. Dadar., Y. S. Malik., K. P. Singh, and W. Chaicumpa. COVID-19, an emerging coronavirus infection: advances and prospects in designing and developing vaccines, immunotherapeutics, and therapeutics. *Human vaccines & immunotherapeutics* 16(6): 1232-1238 (2020).
4. Q. Gao., L. Bao., H. Mao., L. Wang., K. Xu., M. Yang, and Qin. C. Development of an inactivated vaccine candidate for SARS-CoV-2. *Science* 369(6499): 77-81 (2020).
5. W. H. Chen., X. Tao., A. S. Agrawal., A. Algaissi., B. H. Peng., J. Pollet, and C. T. K. Tseng. Yeast-expressed SARS-CoV recombinant receptor-binding domain (RBD219-N1) formulated with aluminum hydroxide induces protective immunity and reduces immune enhancement. *Vaccine* 38(47): 7533-7541 (2020).
6. N. van Doremalen., T. Lambe., A. Spencer., S. Belij-Rammerstorfer., J. N. Purushotham., J. R. Port, and V. J. Munster. ChAdOx1 nCoV-19 vaccine prevents SARS-CoV-2 pneumonia in rhesus macaques. *Nature* 586(7830): 578-582 (2020).
7. F. C. Zhu., Y. H. Li., X. H. Guan., L. H. Hou., W. J. Wang., J. X. Li, and W. Chen. Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial. *The Lancet* 395(10240): 1845-1854 (2020).
8. D. F. Robbiani., C. Gaebler., F. Muecksch., J. C. Lorenzi., Z. Wang., A. Cho, and M. C. Nussenzweig. Convergent antibody responses to SARS-CoV-2 in convalescent individuals. *Nature* 584(7821): 437-442 (2020).
9. J. Yu., L. H. Tostanoski., L. Peter., N. B. Mercado., K. McMahan., S. H Mahrokhian, and D. H. Barouch. DNA vaccine protection against SARS-CoV-2 in rhesus macaques. *Science* 369(6505): 806-811 (2020).
10. K. Dhama., K. Sharun., R. Tiwari., M. Dadar., Y. S. Malik., K. P. Singh, and W. Chaicumpa. COVID-19, an emerging coronavirus infection: advances and prospects in designing and developing vaccines,

immunotherapeutics, and therapeutics. *Human vaccines & immunotherapeutics* 16(6): 1232-1238 (2020).
11. Pharmaceutical Technology: Covid-19 Vaccination Tracker. Latest news, statistics, daily rates, and updates (2021) https://www.pharmaceutical-technology.com/covid-19-vaccination-tracker/ (accessed 27 May 2021)
12. WHO. Draft landscape of COVID-19 candidate vaccines. *World Health Organisation* (2020).
13. CDC: Different COVID-19 Vaccines (2021) https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines.html (accessed 27 May 2021)
14. WHO: Status of COVID-19 Vaccines within WHO EUL/PQ evaluation process (2021).
15. N. Wang., J. Shang., S. Jiang, and L. Du. Subunit vaccines against emerging pathogenic human coronaviruses. *Frontiers in microbiology* 11: 298 (2020).
16. M. J. Mulligan., K. E. Lyke., N. Kitchin., J. Absalon., A. Gurtman., S. Lockhart, and K. U. Jansen. Phase 1/2 study to describe the safety and immunogenicity of a COVID-19 RNA vaccine candidate (BNT162b1) in adults 18 to 55 years of age: interim report. *Nature* 586(7830):589-593 (2020).
17. Tu. Y. F., Chien. C. S., Yarmishyn. A. A., Lin. Y. Y., Luo. Y. H., Lin. Y. T, and Chiou. S. H. A review of SARS-CoV-2 and the ongoing clinical trials. *International journal of molecular sciences* 21(7): 2657 (2020).
18. C. NCT04283461. Safety and Immunogenicity Study of 2019-nCoV Vaccine (mRNA-1273) for Prophylaxis SARS CoV-2 Infection. *Clinical Trials. gov* (2020).
19. moderna: Moderna Announces Positive Interim Phase 1 Data for its mRNA Vaccine (mRNA-1273) Against Novel Coronavirus (2020) https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-positive-interim-phase-1-data-its-mrna-vaccine (2020).
20. Central of Disease Control and Prevention (2020). https://www.cdc.gov/coronavirus/2019-ncov/vaccines/different-vaccines/Pfizer-BioNTech.html (accessed 24 January 2021)
21. COVID-19 Vaccine Policies & Guidance. https://www.cms.gov/COVIDvax (2021).
22. The News: https://www.thenews.com.pk/print/779104-russian-covid-19-vaccine-allowed-in-pakistan (accessed 24 January 2021)
23. Cincinnati Children's. Coronavirus (COVID-19) Vaccines | Myths and Truths (2020) https://www.cincinnatichildrens.org/patients/coronavirus-information/vaccines/busting-myths (accessed 20 February 2021)
24. J. Wise. Covid-19: Rare immune response may cause clots after AstraZeneca vaccine, say researchers *British medical journal* 373: n954 (2021).
25. World health Organization: Episode #24 - Vaccine myths vs science (2021). https://www.who.int/emergencies/diseases/novel-coronavirus-2019/media-resources/science-in-5/episode-24---vaccine-myths-vs-science (accessed 5 February 2021)
26. Reuters: Fact check: RFID microchips will not be injected with the COVID-19 vaccine, altered video features Bill and Melinda Gates and Jack Ma (2020) https://www.reuters.com/article/uk-factcheck-vaccine-microchip-gates-ma-idUSKBN28E286 (accessed 5 February 2021)
27. I. Ali. The covid-19 pandemic: Making sense of rumor and fear: Op-ed. *Medical anthropology* 39(5): 376-379 (2020).
28. U. A. Awan., A. A. Khattak., M. S. Afzal., N. Iqbal, and M. F. Nadeem. Emergence of SARS-CoV-2 Variant: A Wake-Up Call for Pakistan's overburdened Healthcare System. *Journal of Medical Virology.* 93(5): 2595-2598 (2021).
29. M. Chand. Investigation of novel SARS-COV-2 variant: Variant of Concern 202012/01 (PDF). *Public Health England* (2020).
30. BBC NEWS: UK coronavirus variant spreading 'rapidly' through US, study finds (2021) https://www.bbc.com/news/world-us-canada-55986819 (accessed 14 February 2021)
31. Wionews: Pakistan extends travel restrictions on six countries including UK till Feb 28 https://www.wionews.com/south-asia/pakistan-extends-travel-restrictions-on-six-countries-including-uk-till-feb-28-360266 (accessed 15 February 2021)
32. NEWS.CGTN: China's drug regulator accepts CanSinoBIO COVID-19 vaccine application https://news.cgtn.com/news/2021-02-24/China-s-drug-regulator-accepts-CanSinoBIO-COVID-19-vaccine-application-Y8RbcYHxra/index.html (accessed 25 February 2021)
33. Fortune: It's not just Johnson & Johnson: China has a single-dose COVID-19 vaccine that's 65% effective (2021). https://fortune.com/2021/02/09/china-covid-vaccine-single-dose-cansino-johnson-johnson/ (accessed 14 February 2021)

34. news-medical life sciences: Study shows real-world effectiveness of Moderna and Pfizer/BioNtech vaccines (2021). https://www.news-medical.net/news/20210221/Study-shows-real-world-effectiveness-of-Moderna-and-PfizerBioNtech-vaccines.aspx (accessed 22 February 2021)
35. China Briefing: China's COVID-19 Vaccine Development and Availability (2021). https://www.china-briefing.com/news/chinas-covid-19-vaccine-development-and-availability/ (accessed 14 February 2021)
36. BBC NEWS: Oxford-AZ vaccine 'effective against dominant UK variant' (2021). https://www.bbc.com/news/health-55951920 (accessed 15 February 2021)
37. CDC: Genomic Surveillance for SARS-CoV-2 Variants (2021). https://www.cdc.gov/coronavirus/2019-ncov/cases-updates/variant-surveillance.html (accessed 15 February 2021)
38. E. Callaway. Fast-spreading COVID variant can elude immune responses. *Nature* 589(7843): 500-501 (2021).
39. G. Salvatori., L. Luberto., M. Maffei., L. Aurisicchio., G. Roscilli., F. Palombo, and E. Marra. SARS-CoV-2 SPIKE PROTEIN: an optimal immunological target for vaccines. *Journal of translational medicine* 18: 1-3 (2020).
40. C. K. Wibmer., F. Ayres., T. Hermanus., M. Madzivhandila., P. Kgagudi., B. E. Lambson, and P. L. Moore. SARS-CoV-2 501Y. V2 escapes neutralization by South African COVID-19 donor plasma. Nature Medicine 27: 622–625 (2021).