Review article

SEMANTIC SCHOLAR REVIEW IN THE CLINICAL SUCCESS OF DIFFERENTLY ENGINEERED VACCINES TO NEUTRALIZE SARS-CoV-2

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Abstract
COVID-19 pandemic from 2019 to present, dramatically affects the human lifestyle with strict challenges to pause the SARS corona virus transmission globally. The appearance of SARS-CoV-2 leads to the development of various efficient WHO-approved novel corona vaccines like Ad26.COV2.S/Janssen, Ad5-Ncov/CanSino, Sputnik V, AZD1222/Covishield, mRNA-1273/Moderna, BNT162b1-2/Pfizer-BioNTech, BBV152/Covaxin, NVX-CoV2373/Novavax, ZyCoV-D/Zydus candila, CoronaVac/Sinovac, etc. by countries based on mRNA, DNA, protein, and recombinant vector immunogens. Vaccines are routed in ID, IM with 0.5mL with two or three doses maximum apart 28 days has a different rate of efficacy. Immune response and vaccine neutralising rate are affected by the occurrence of a new mutant SARS-CoV-2 strain with a new antigen epitope.

Introduction

SARS has the global power of novel diseases in western communities (Lederberg *et al*., 2003). People with COVID-19 have reported a wide range of symptoms, ranging from mild Revised: JAN/11/2022 symptoms to severe illness. Symptoms may appear 2 to 14 days after exposure to the virus. Symptoms may include fever or chills; cough; shortness of breath; fatigue; muscle or body aches; headache; new loss of taste or smell; sore throat; congestion or runny nose; nausea or vomiting; diarrhoea. Interspecies transmission of SARS-CoV-2 to human-to-human transmission and the nonstop international traveller exploded the local outbreak of an emerging novel disease into a hygienic pandemic. The most recent emerging zoonotic origin of novel diseases Nipah virus, Hendra virus, and SARS-CoV that have a wildlife reservoir cause threats to human health (Peiris *et al*., 2004). The disease "infectious atypical pneumonia" first emerged in Guangdong, 2002 due to contact with the live-game trade (Zhong *et al*., 2003; Xu *et al*., 2004). SARS was identified as a novel coronavirus (Peiris *et al*., 2003; Ksiazek *et al*., 2003; Drosten *et al*., 2003) with its propensity to cause clusters of disease in families and healthcare workers (Zhong *et al*., 2003; Peiris *et al*., 2004). The global scale of the disease SARS-CoV-2 resembles the human immunodeficiency virus. Tis SARS outbreak illustrates the potential health effects by the risk of the re-emergence of the disease that may derive from an animal reservoir or infections transmitted in the laboratory (Guan *et al*., 2003; http://www.moh.gov.sg/sars/pdf/ Report_SARS_Biosafety.pdf). SARS has the potential survival ability to skip off any of the uncertain seasonal duration in the host as the asymptomatic condition, brings attention for the continuation of detection and diagnosis. As active surveillance for severe respiratory disease inclusive of health care workers, the rapid diagnosis and prevention of other respiratory viruses must be preferential (Peiris *et al*., 2003). SARS is an acute lung alveolar disease that has a significant impact on morbidity and mortality in a cohort of zoonotic (Lee *et al*., 2003) within a period of fewer than two months, SARS has become a global health problem, prompting the WHO to issue a global alert for the first time in more than a decade (http://www.who.int/csr/ sarscountry/2003_03_27; Lee *et al*., 2003).

Corona virus

The finding of infectious coronavirus in the respiratory tract supports epidemiological data to suggest that the virus is spread by direct and indirect contact (Ksiazek *et al*., 2003). The SARS-CoV-2 was first reported in samples of Broncho-alveolar lavage fluid from three patients in Wuhan Jinyintan hospital and was confirmed as the cause of COVID-19 on January 24, 2020 (Huang *et al*., 2019). The similarity of clinical symptoms between corona virus-19 and beta-corona virus suggest that the incidence of severity and mortality of

COVID-19 is beyond chronic diseases had an impression on age distribution, daily lifestyle, and dietary habits of the Human population (Hu *et al*., 2019). The different age group has a different rate of infection. Many of the biomarkers and responsive factors like as oxygenation index, bilateral lung plaque shadow, and biochemical indexes (decreased lymphocyte count, increased C-reactive protein, increased aspartate aminotransferase, increased lactate dehydrogenase and creatine kinase appear to refer to the presence of coronavirus in that human host (Zheng *et al*., 2020). Coronaviruses have a different variant of infectious viruses in humans and may transmit through animals to humans or human to human out of them Rats, Cats, Bats, and Camels are the main host (Du *et al*., 2009). Coronavirus found with different rate of mortality with respect of country to country, as reported by WHO dated 29 March 2020 (Advice for public [Internet]. Who.int. 2018 [cited 2020 Jun 3], Sajed *et al*., 2020).

SARS-CoV-2

The International Committee on Taxonomy of Viruses termed corona virus as SARS-CoV-2 while COVID-19 coined by the world health organization (WHO) that have an adverse effect of the severe acute respiratory syndrome (Mesev *et al*., 2019). SARS-CoV-2 genomic sequence is 70% identical to SARS-CoV and 50% with the Middle Eastern respiratory syndrome coronavirus (MERS-CoV) (Lu *et al*., 2020). COVID-19 virus is a ribonucleo-particle that contains a positive sense single-strand RNA sequence as a genetic material composed of protein capsules (Hoffmann *et al*., 2020). Protein capsule embedded the spike glycoprotein (S) majorly that's the major immunogen particle in coronavirus to bind with human angiotensin-converting enzyme-2 (hACE2) to initiate infection.4 Spike glycoprotein has 2 subunits which are the main antibody targets (Roush *et al*., 2007; Verhees *et al*., 2018). 2019-nCoV prevalence is much more but the severity rate is higher of MERS and SARS. Clinical suggestion to minimize the COVID-19 is early screening, diagnosis, isolation, and treatment are necessary to prevent spread (Sajed *et al*., 2020). Taxonomy suggest that corona virus belongs to family Coronaviridae, order Nidovirales and classified into four genera, coronavirus-a, coronavirus-b, coronavirus-g, and lastly coronavirus-d that have many mutant strains (Li *et al*., 2016). Coronaviruses-b have a most privileged strain of COVID-19 are Severe Acute Respiratory Syndrome (SARS-CoV) and Middle East Respiratory Syndrome (MERS-CoV) (Bakkers *et al*., 2017). So SARS-CoV-2 is identified as that of b- coronavirus (Chen *et al*., 2020). The crown-shaped appearance of spike protein (S) is termed the name of COVID-19 as corona in Latin (corona- a crown) virus (Siddell *et al*., 1995; Coutard *et al*., 2020). Another study of microscopic imaging of SARS-CoV-2 presenting crown-like

outgrowth indicates again belongs to a family of coronaviruses (Prasad *et al*., 2020). Four classes of enveloping protein S, N, M, E maintain the surface structure that involves in the life cycle of the viral particles (Satarker *et al*., 2020). The appearance of SARS-CoV-2 in 2019 has more affinity to the receptor to enter into host cell making it more infectious rather than SARS coronavirus 2003 (Berry et. al., 2004).

Vaccine

Vaccines are the most widely accepted and effective treatment to control any of the viral or bacterial or fungal pandemic to restore the global economy (Richner *et al*., 2017; Pardi *et al*., 2017). To develop a vaccine needed of genetic information of that parasite so the viral pandemic by the coronavirus in 2019 sequenced in January 2020, With-in months of emergence, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is composed of a positive-stranded RNA genome of 29891 nucleotides with 9860 amino acids (Chan *et al*., 2020). World Health Organization (WHO) declared the COVID-19 infection as pandemic on 11 March 2020 (https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020). SARS infection results in activation of T-helper (Th1) cell-mediated immunity and hyper innate inflammatory 872 Hui & Zumla response. Delayed or less active innate and acquired immune response enable the coronavirus and mild disease to leads to cytokine dysregulation, viral cytopathic effects, down-regulation of lung ACE 2, abnormal immune responses, and autoimmune mechanisms may be jumped moderate to the severe stage and caused death (Nicholls *et al*., 2003; Peiris *et al*., 2003). Rhesus Macaques trial of SARS-CoV-specific immune responses of the adenoviral-based vaccine against COVID-19 could be applied on humans (Gao *et al*., 2003). A DNA-based vaccine immunity production in mice found a seroconversion of 3 doses of immunization is 75% (Zhao *et al*., 2004). Spike protein gene-containing plasmid DNA vector leads to humoral immune responses which reduce viral multiplication (Yang *et al*., 2004). Antigenicity and receptor-binding ability can be developed by recombinant Spike protein, while specific antibodies against SARS-CoV S protein might provide by synthetic peptides eliciting another approach for further developing SARS vaccine (Hui *et al*., 2019).

Live strain imprint of coronavirus could longer of time at room temperature (Lai *et al*., 2005). To detection of coronavirus, we found monoclonal antibodies antibody against the surface structural N protein was found to be a sensitive assay for the diagnosis of SARS furthermore EIA detection of SARS N was performed using a panel of three monoclonal antibodies (Che *et al*., 2005). Passive immunization is done by plasma donors who are procured by COVID-19 infection, with high titers of neutralizing antibody with no side effects (Cheng *et al*., 2005;

Yeh *et al*., 2005). A recent view of researcher suggests hyperimmune globulin which is produced from severe patients and equine plasma by immunization with inactivated SARS-CoV are available for prophylactic trials in humans (Lu *et al*., 2005; Zhang *et al*., 2005). A potent cross-reactive monospecific polyclonal antibodies against the spike protein conservative sequences, able to neutralize epidemic SARS-CoV-2 of 2019 (He *et al*., 2006; Zhu *et al*., 2007). A chimeric form of attenuated parainfluenza virus–SARS-CoV virus resulted in better immune response and decreases the duplication of SARS-CoV-2 in the upper and lower respiratory tract (Bukreyev *et al*., 2007). Active immunization expected, the importance of the Spike protein was confirmed in the murine model of highly attenuated modified vaccinia virus Ankara carrying the S protein (Bisht *et al*., 2004). The above structural and transmission investigation of the COVID-19 virus suggest that the vaccines could develop by several types of immunogen listed below (table-1) with respective selected widely efficient vaccine by WHO.

S. No.	Desirable vaccine immunogen	Derived vaccine against immunogen
1.	Adenoviral vector based	Ad26.COV2.S /Johanson & Johanson, Ad5-Ncov/CanSino, Sputnik V /Gam-Covid-Vac, AZD1222 /Covishield
2.	mRNA based	mRNA-1273 /Moderna, BNT162b1/ BNT162b2 /Pfizer-BioNTech
3.	Spike protein based	BBV152/Covaxin, NVX-CoV2373 /Novavax
4.	DNA based	ZyCoV-D/Zydus candila
5.	Inactivated SARS-CoV-2 virion based	CoronaVac/ Sinovac

Table-1: Specific selected WHO-approved various immunogen-based, COVID-19 pandemic developed vaccines to neutralise SARS-CoV-2 virus, are listed with their trade name.

Covishiled/AZD1222

Instead of covishield AZD1222 (Astra Zeneca, ChAdOx1) 48 more COVID-19 immune booster doses are under clinical progress. Out of the 11 are possess good immunogen in respect to immune response efficiency currently being evaluated in the third stage of clinical investigation (https://www.who.int/blueprint/priority-diseases/key-action/novel-coronavirus-landscape-ncov.pdf?ua=1). Oxford University research intelligence was successfully establish a COVID-19 specific antibody by using a replication-deficient chimpanzee that containing an adenoviral vector with spike glycoprotein; (nCoV-19) gene (Voysey *et al*., 2021). Adenoviral vector is taken for the development of covishield for better expression of

antigen-presenting cells CD4+ and CD8+ even in the absence of an adjuvant, that intense a strong cellular immune power (Ura *et al*., 2014). On April 23, 2020, has started the clinical trial in phase 1 across the UK(COV001), later randomise in the UK, Brazil, and South Africa, named COV002, COV003, COV005 respectively. In phase 1/2 clinical trial (NCT04324606) 5 adult COV001 and 6 older COV002 specimen are selectively published with safety features after the incubation of trial doses. Phase 3 clinical trial raised number of volunteers seems to be the perfection of immunogenicity and belief system in the population (Folegatti *et al*., 2020; Ramasamy *et al*., 2020; Barrett *et al*., 2021). The IgG antibody response peaked at end of the month which is multiplied by a second dose seen to neutralization response 91% in the first dose and 100% after the second booster dose (Folegatti *et al*., 2020). The maximum efficacy obtained was 90% by lowering the first dose followed by a full of the second dose of 0.5mL. In the next trial full amount of 0.5mL of both doses lowered the immune response to 62.1%. Thus overall efficacy amount incubated individuals seem to be 70.4%. Instant of this result Astra Zeneca has assigned with the US, EU, UK, India, China, Thailand, The Philippines, and Australia (Prüβ *et al*., 2021).

Covaxin/BBV152

COVID-19 strain NIV-2020-770, spike protein is sufficient to develop BBV152 Covaxin vaccine. Bharat Biotech is developed BBV152 vaccine in collaboration with the Indian Council of Medical Research (ICMR)-National Institute of Virology (NIV). Substitution of aspartic into glycine amino acid at locus 614 results in increased immunogenicity of the spike protein. *In-vivo* isolation of coronavirus strain NIV-2020-770 occurred in 'Vero CCL-81' cells genetic information with nucleotide sequence submitted to GISAID (EPI_ISL_420545) (Sarkale *et al*., 2020). In this vaccine, drive founds the development of a functionally inactive virion dependent vaccine against SARS-CoV-2 named BBV152 has a neutralizing antibody immune response to hCoV-19/India/2020770 (homologous), and two heterologous strains hCoV-19/India/2020Q111 and hCoV-19/India/2020Q100 in phase 1 clinical trial (Ella *et al*., 2021). They were also found a substitution mutation L3606F at locus 3606 of functional gene "open reading frame 1ab5" in both above mentioned homologous and heterologous strains (Sapkal *et al*., 2020). Plaque reduction neutralization (PRNT50)-based assay, the test of neutralizing antibodies immune response being 98.6% after incubation of first 6 microgram and second 3 microgram doses within 28 days interval with imidazoquinoline (Ella *et al*., 2020). Vaccine efficacy against all variant related COVID-19 disease 71% and further differ for a different types of corona variant. The sera test of vaccine recipients could find potential

escape by neutralization of all existing UK variant strains with recent mutation 501Y leads to advantage of the indigenous BBV152/COVAXIN (Sapkal *et al*., 2020).

Janssen/Ad26.COV2.S

Recombinant vector-based stable immune booster dose developed by a replication-incompetent recombinant adenovirus type 26 (Ad26) vector expressing the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) spike (S) protein (Winslow *et al*., 2017). It is colorless, visible particulates, and opalescent sterile vaccine route into intramuscular. The Ad26 vector expressing the SARS-CoV-2 S protein is grown in PER.C6 TetR cells, into amino acids containing culture media. In next the vaccine is processed through several purification steps, formulated with inactive ingredients: citric acid monohydrate (0.14 mg), trisodium citrate dehydrate (2.02 mg), ethanol (2.04 mg), 2-hydroxypropyl-β-cyclodextrin (HBCD) (25.50 mg), polysorbate-80 (0.16 mg), sodium chloride (2.19 mg) and filled into vials. Due to high immunogenicity efficiency, there is only a single dose incubated into the recipient. Janssen COVID-19 Vaccine does not contain a preservative. Adenovirion Vector expresses the SARS-CoV-2 spike (S) protein that's enough to work as a strong immunogen result human body immune response protects against COVID-19. Vaccine efficacy against severe/critical COVID-19 at least 14 days after vaccination was 76.7% (95% CI: 54.6; 89.1) and 85.4% (95% CI: 54.2; 96.9) at least 28 days after vaccination. The concordance vaccine efficacy rate into a subgroup of all existing SARS-CoV-2 variants against moderate to severe/critical COVID-19 and severe/critical COVID-19 for Brazil, South Africa, and the United States were conducted up to the data cut-off date between the PCR results from the local laboratory and the central laboratory was observed 90.3%. Janssen COVID-19 Vaccine also work as the heterologous booster vaccine dose. A 0.5 mL dose of Janssen COVID-19 Vaccine is applied to incubation, formulated to contain 5×1010 virus particles (VP). It contains the wild-type signal peptide that exhibits potent neutralizing immunity with single immunization administered intranasal or intratracheally minimizes the number of COVID-19 in hamsters and rhesus macaques (Bos *et al*., 2020; Tostanoski *et al*., 2020; Mercado *et al*., 2020).

Moderna/mRNA-1273

On November 30, 2020, ModernaTX was launched by FDA for an investigational COVID-19 mRNA-1273-P301 based vaccine intended to prevent COVID-19 caused by SARS-CoV-2. This vaccine has incubated both doses with an interval of four weeks in 0.5mL quantity in the United States. The Moderna COVID-19 Vaccine is a white to off-white, sterile, preservative-

free frozen suspension for intramuscular injection. The vaccine contains a genetically engineered m-RNA-1273-P301 encoding the pre-fusion stabilized spike glycoprotein (S) of SARS-CoV-2 virus against antibody is developed (Corbett *et al*., 2020). The vaccine following ingredients: lipids (SM-102, 1,2-dimyristoyl-rac-glycero3-methoxypolyethylene glycol-2000 [PEG2000-DMG], cholesterol, and 1,2-distearoyl-snglycero-3-phosphocholine [DSPC]), tromethamine, tromethamine hydrochloride, acetic acid, sodium acetate, and sucrose make it more susceptible (Richner *et al*., 2017; Hassett *et al*., 2019). N1-methyl-pseudouridine replaces the uridine to increase the stability of RNA (Anderson *et al*., 2011). The Moderna COVID-19 Vaccine, mRNA-1273 (100 µg) is administered intramuscularly as a series of two doses (0.5 mL each), given 28 days apart within 6 hours of opening. FDA has determined that the Sponsor has provided adequate information to ensure the vaccine's quality and consistency for authorization of the product under EUA (Ledford *et al*., 2020). Efficacy of the vaccine to prevent COVID-19 occurring at least 14 days after dose 2 was 94.5%, (95% CI 86.5%; 97.8%) in participants without prior evidence of SARS-CoV-2 infection across demographic subgroups were consistent in the overall study population. The major outcome of MODERNA vaccine is to stand hygienic rate to reduce the risk of confirmed COVID-19 within 14 days of the second dose.

Sputnik V/Gam-Covid-Vac

Adenovirus (rAd) type 26 and rAd5 are combined to form a shuttle vector to develop Sputnik V (Gam-COVID-Vac) vector vaccine (Logunov *et al*., 2020). It was developed by the Gamaleya National Center of Epidemiology and Microbiology. Virus-neutralizing antibodies and SARS-CoV-2 spike immunoglobulin G (IgG) were measured using wild-type (WT) SARS-CoV-2 and a pseudotyped vesicular stomatitis virus (VSV) spike-expressing GFP and enzyme-linked immunosorbent assay respectively (Ojeda *et al*., 2021; Case *et al*., 2020). Quantification is done followed by WHO International Standard protocol via different laboratories' data comparative study (Kristiansen *et al*., 2021). Specific anti-spike antibody response of 94% and WT virus-neutralizing capacity of 90% leads to 91.6% efficacy against coronavirus disease 2019 (COVID-19) (Logunov *et al*., 2021; Rossi *et al*., 2021). A high seroconversion rate just after 21 days of the first dose in naive individuals is a unique feature of Sputnik V. There are two doses of intramuscular Sputnik V routed in 21 days interval leads a fast and robust immune response in seropositive participants. The second dose increases antibody by binding and neutralizing and the T-cell response for CD4+ and CD8+ were observed moderative (Logunov *et al*., 2020). These initial immune response of the Sputnik V vaccine get approved on 11 August 2020, by Russia to become the first country

before third phase trial of vaccine to register a COVID-19 vaccine. This decision was questioned in most of the articles in high-impact journal (Burki *et al*., 2020; Callaway *et al*., 2020; Bucci *et al*., 2020).

Zydus Candila/ZyCoV-D

The most privileged surface protein spike-S gene ligated into plasmid DNA which coded for unit gene only able to establish DNA vaccine Zydus Candila (ZyCoV-D) of SARS-CoV-2. A transformation process is applied to the entry of DNA vector into E-coli host. The spike(S) region of surface protein includes a domain for receptor binding to bind with the human angiotensin-converting enzyme (ACE)-2 receptor and mediates the entry of virus inside the cell (Dey *et al*., 2021). Intradermal route of DNA vaccine in mice, guinea pig, and rabbit specimen of different doses found to be a potential immunogenic induces antibody response including neutralizing antibodies (NAB) against SARS-CoV-2 and same for MERS ((Dey *et al*., 2021; Modjarrad *et al*., 2019; Martin *et al*., 2008). Instead of SARS DNA vaccine, MERS DNA vaccine is 14% more susceptible in the sense of seroconversion. Zydus Candila is the first DNA vaccine that was tolerated by healthy adults with 66% efficacy. This DNA vaccine incubate immunization with three doses administration within 28 days apart make it first. There are currently several COVID-19 candidate vaccines undergoing pre-clinical, clinical trials globally, including mRNA vaccines, replicating or non-replicating viral vector vaccines, DNA vaccines, autologous dendritic cell-based vaccines, and inactive virus vaccines [7]. The results of Phase 1 and 2 trials of several vaccines have been published and a few of phase 3 trials have also been published now (Baden *et al*., 2021; Polack *et al*., 2020). The primary endpoint was the adverse reactions within 7 days after each of the vaccination and the 28th day as safety endpoints. The secondary endpoints included seroconversion based on IgG antibodies and IFN-g cellular immune responses after 3 doses of vaccine (Momin *et al*., 2021).

Novavax/NVX-CoV2373

NVX-CoV2373 is a recombinant SARS-CoV-2 vaccine developed by Novavax. A complete surface spike glycoprotein of SARS-CoV-2 (prototype Wuhan-Hu-1 sequence) was used and introduced into a baculovirus instead of adenovirus. MothSpodoptera frugiperda infected by baculovirus to evaluate spike protein and processed followed by chromatographic purification. The NVX-CoV2373 has an adverse effect on CD+ T-cell and induce a neutralising-antibody immune response four-time multiple after 2 dose route intramuscularly in 21 days apart (Keech *et al*., 2020). The NVX-CoV2373 vaccine efficacy was measured against Covid-19 under the transmission of B.1.351 SARS variant in South Africa (Cele *et*

al., 2021, Tegally et al., 2020). Vaccine efficacy of 49.4% among participants who were seronegative for SARS-CoV-2 at baseline regardless of HIV and 94% of participants without HIV infection, fulfilled the primary objective of the vaccine. Cases of Covid-19 among vaccine recipients were predominantly mild to moderate, with a reported overall vaccine efficacy of 22% (95% CI, −50 to 60) and an efficacy of 10% (95% CI, −77 to 55) against the B.1.351 variant, with the B.1.351 variant making up 95% of cases.25 NVX-CoV2373 SARS vaccine was found as the preliminary source of protection against B.1.351 variant (Shinde et al., 2021).

Pfizer-BioNTech/BNT162b1-2

RNA remains unplugged with host genetic material making RNA an efficient marker for any of them during designing (Sahin et al., 2021; Feldman et al., 2019). Two companies BioNTech and the US pharmaceutical giant Pfizer developed mRNA-based vaccines BNT162b1 and BNT162b2 are widely accepted. Modification of uridine into 1-methylpseudouridine facilitates more sustainable antibody production and protection of itself another reason to accept globally (Pardi et al., 2017). A two-dose regimen of BNT162b2 conferred 95% protection against Covid-19 in persons 16 years of age or older. Safety over a median of 2 months was similar to that of other viral vaccines. German-based BioNTech command on the production of BNT162b1 product that translates the receptor-binding domain (RBD) of the spike protein and BNT162b2 leads prefusion stabilized membrane-anchored full-length spike protein, which is a modified product of point mutation in two proline amino acids to maintain prefusion conformation. Out of them instead of BNT162b2, BNT162b1 product is preferentially considered a prime target for virus-neutralizing antibodies (Brouwer et al., 2020). BNT162b1 produced IgG antibody and antigen-presenting T cell CD8+ and CD4+ response while BNT162b2 was associated with less systemic reactogenicity with a similar response as BNT162b1 particularly in the 65–85 year age group (Walsh et al., 2020). A two-dose regimen of BNT162b2 was found to be safe and 95% effective against Covid-19. BioNTech/Pfizer has recently received emergency use authorization (EUA) from the FDA and approval by the UK (Tanne et al., 2020; Mahase et al., 2020). Pfizer has contracts with the US, EU, UK, Japan, Canada, and Australia. The rollout of the vaccine has started (Tanne et al., 2020). Pfizer was responsible for the design and conduct of the trial, data collection, data analysis, data interpretation, and the writing of the manuscript. BioNTech was the sponsor of the trial, manufactured the BNT162b2 clinical trial material, and contributed to the interpretation of the data and the writing of the manuscript (Polack et al., 2020).

CoronaVac/ Ad5-nCOV

The first human adenovirus-based two vaccines CanSino Biologics, China and the Ad5-nCOV vaccine by Beijing Institute of Biotechnology China are updated. The Ad5 vector was ligated with the mutant spike glycoprotein gene and the plasminogen activator signal peptide gene (Zhu *et al*., 2020). Mucosal vaccination trial on mice and ferrets was successful in protecting respiratory tract infection (Wu *et al*., 2020). The phase 1st trial NCT04313127 of the vaccine has an appropriate immune response to produce antibody and T-cell activation between 2 or 4 weeks (Zhu *et al*., 2020). The phase 2nd trial NCT04341389 administrated an intramuscular injection with a high dose rather than earlier, (5×1010 virus particles) found to be an effective immune response (Zhu *et al*., 2020). The phase 3rd trial NCT04540419 of a single vaccination with the same dose as phase 2nd leads to the severeness of disease progression, immunogenicity, adverse effects, serum chemistry, and blood counts. The Corona Vac vaccine proposed by Sinovac Biotech is contains inactivated SARS CoV-2 virus with aluminum hydroxide adjuvant. Two doses are routed with 0.5mL apart 14 days. The measurable fact is the titer of neutralizing antibodies and adverse immune effects. A research paper on the Coronavac vaccine published the protocol for an additional phase 3rd trial (NCT04456595) in Brazil (Palacios *et al*., 2020). Ad5-nCOV and CoronaVac vaccine has 63.7% and 51% efficacy overall while 100% in severe.

Vaccine	Company	Amount of dose (mL)	No. of dose	Implement site	Immunogen	Efficacy (%)	Country
AZD1222 /Covishield	University Oxford/ Astra Zeneca	0.5	2	IM	Adenoviral vector	91	UK
BBV152 /Covaxin	Bharat Biotech	0.5	2	IM	Spike protein	70.4%	India
Ad26.COV2.S /Johanson & Johanson	Janssen	0.5	1	IM	Adenovirus vector	85.4	The Netherland/US
mRNA-1273 /Moderna	Moderna	0.5	2	IM	m-RNA	94.5	US
Sputnik V /Gam-Covid-Vac	Gamaleya Nat. Center of Epidemic and Microbiol	0.5	2	IM	Adenovirus vector	91.6	Russia

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ZyCoV-D /Zydus candila	Candila Healthcare Ltd.	0.5	3	ID	DNA	66	India
NVX-CoV2373 /Novavax	Novavax	0.5	2	IM	Spike protein	94	US
BNT162b1/ BNT162b2 /Pfizer-BioNTech	Pfizer-BioNTech	0.5	2	IM	m-RNA	95	Germany/US
Ad5-nCOV	CanSino Biologics	0.5	2	IM	Adenovirus vector	63.7	China
CoronaVac	Sinovac Biotech	0.5	2	IM	Inactivated virion	51	China

Table-2: An indigenous summary of the above detail described most wide accepted WHO listed specific COVID-19 corona vaccine with their name, manufacturing company, amount or number of doses, route site, production country, etc. essential health worker parameters.

Conclusion

At present scenario of COVID-19 due to SARS has continued to threaten due to their ecological insensitive and unstable mutant variant continuously affecting humans with no age restriction. Even after successful genome sequencing and efficient vaccines development, scientist can't overcome the worldwide SARS-CoV-2 pandemic. Different biomarker-based mRNA-1273, BNT162b1/2, Sputnik V vaccines are found superior as their role of immune response after booster doses. Currently, most of the vaccines are under phase 3rd clinical trial which was routed intradermal and intramuscularly is sufficient to understand corona reaction and incomplete efficacy of the developed vaccine. This study refers to the need to focus on similar or percentages of similarity in different mutant corona variant basis vaccine development with another site of the route may stop reoccurrences of COVID-19 infection and regular economic losses. This could be applied to all upcoming or existing strains of coronavirus with near 100% efficacy.

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