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APPROVED COVID 19 VACCINES: A REVIEW

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ABSTRACT

The purpose of the review: To update the knowledge of nations regarding approved covid 19 vaccines by Emergency Use Authorization (EUA). To bring awareness in the community about the kind of vaccine, their mechanism of action, administration route, effective dosing, observed side effects and storage conditions. This article represents the essential data about covid 19 vaccines. COVID-19 has affected millions of people and put an unparalleled burden on healthcare systems as well as economies throughout the world. Currently, there is no decisive therapy for COVID-19 or related complications. The only hope to mitigate this pandemic is through vaccines. The COVID-19 vaccines are being developed rapidly, compared to traditional vaccines, and are being approved via Emergency Use Authorization (EUA) worldwide. So far, there are 232 vaccine candidates. One hundred and seventy-two are in preclinical development and 60 in clinical development, of which 10 are approved under EUA by different countries. This includes the United Kingdom (UK), United States of America (USA), Canada, Russia, China, Australia and India.[1] The article contains COVID-19 vaccines authorized/approved for emergence use as of February 28, 2021.

KEYWORDS: BNT162, mRNA-1273, AZD1222 by AstraZeneca, CoronaVac by Sinovac, Sinopharm and the Wuhan Institute of Virology China, Sputnik V, BBIBP-CorV, EpiVacCorona, covaxin, Janssen.

INTRODUCTION

Coronavirus disease-2019 (COVID-19), caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was declared a global pandemic on 11 March 2020, by the World Health Organisation.[26] The methods used to control the spread of the virus have been

the traditional social distancing, quarantine, use of disinfectant substances, and wearing of protective face masks. These measures have adverse consequences, both psychological and economic, and have resulted in substantial disagreement among the medical community and political decision-makers regarding their efficacy. In parallel with the imposed restrictions to prevent viral spread and the testing of (mainly) repurposed anti-viral treatments is the accelerated development of vaccines to prevent/restrict potential viral damage.[27] Safe and effective vaccines will be a gamechanger but for the foreseeable future we must continue wearing masks, physically distancing and avoiding crowds. Being vaccinated does not mean that we can throw caution to the wind and put ourselves and others at risk, particularly because it is still not clear the degree to which the vaccines can protect not only against disease but also against infection and transmission.[2]

Vaccine platforms used for SARS-CoV-2 vaccine development

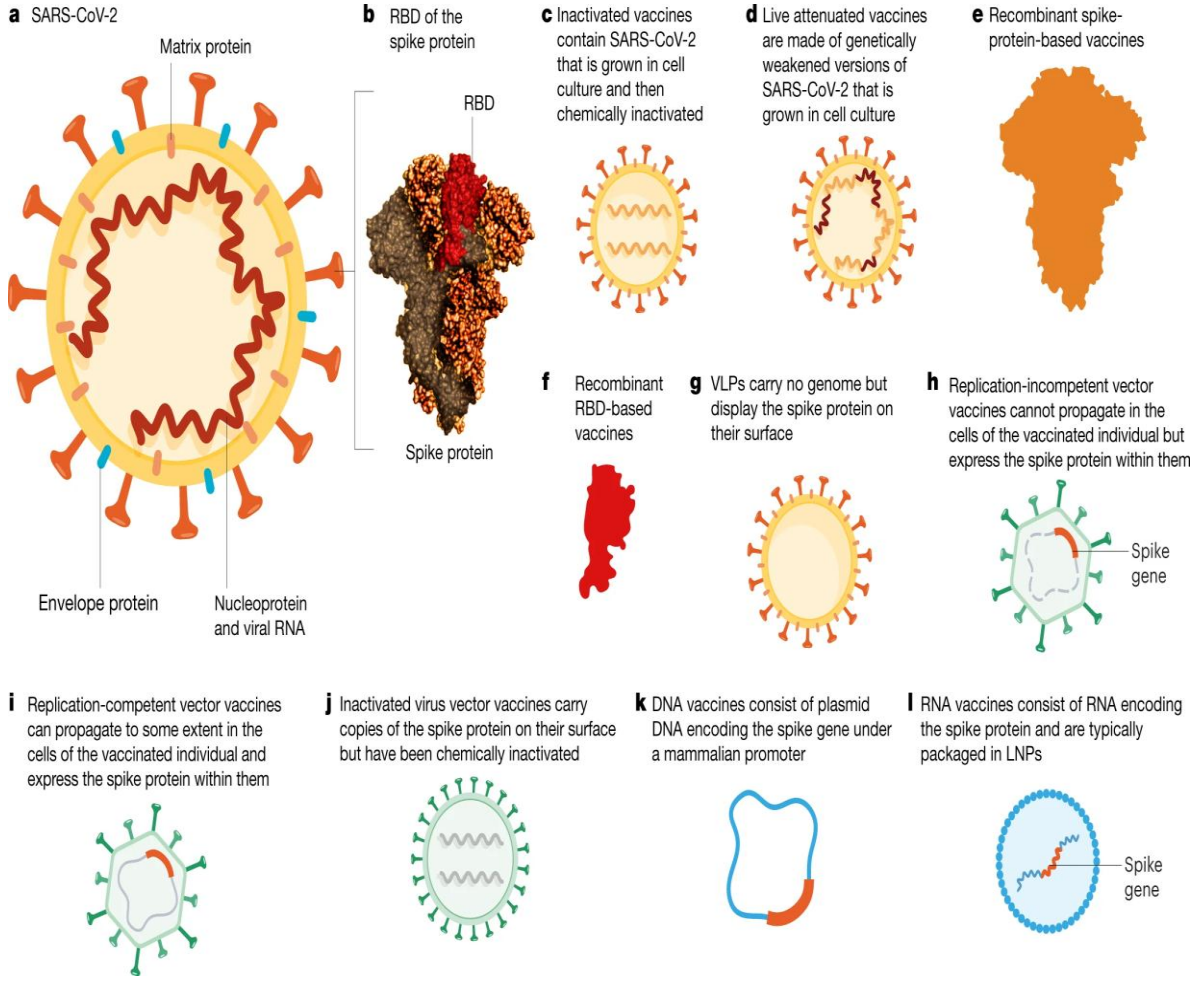

Fig. 1: A model showing the platforms used for SARS-CoV-2 vaccine development.[25]

COVID-19 vaccines Authorized/Approved for emergence use as of February 28, 2021:[4]

Name	Vaccine Type	Developer/sponsor	Country of Origin	Authorization/Approval
Vero cell	Inactivated vaccine	Wuhan Institute of Biological Products; Sinopharm	China	China
BBIBP-CorV	Inactivated vaccine	Beijing Institute of Biological Products; Sinopharm	China	China, Bahrain, United Arab Emirates, Egypt, Jordan, Iraq, Pakistan, Serbia
Covaxin	Inactivated vaccine	Bharat Biotech, ICMR	India	India
CoronaVac	Inactivated vaccine (formalin with alum adjuvant)	Sinovac	China	China, Bolivia, Turkey, Indonesia, Brazil
EpiVacCorona	Protein subunit	Federal Budgetary Research Institution State Research Center of Virology and Biotechnology "Vector"	Russia	Russia
AZD1222 (Covishield)	Non-replicating viral vector	AstraZeneca, University of Oxford, BARDA, OWS	UK	UK, Argentina, El Salvador, Dominican Republic, India, Bangladesh, Mexico, Nepal, Pakistan, Brazil, Saudi Arabia, Iraq, Hungary, Thailand
Sputnik V	Non-replicating viral vector	Gamaleya Research Institute of Epidemiology and Microbiology, Acellena Contract Drug Research and Development	Russia	Russia, Belarus, Argentina, Guinea (experimental use), Bolivia, Algeria, Palestine, Venezuela, Paraguay, Turkmenistan, Hungary, UAE, Serbia
mRNA-1273	mRNA-based vaccine	Moderna, BARDA, NIAID	USA	Canada, Israel, Saudi Arabia, Switzerland, United Kingdom, United States, EU, Faroe Islands, Greenland, Iceland, Norway
Comirnaty (BNT162b2)	mRNA-based vaccine	Pfizer, BioNTech; Fosun Pharma	Multinational	United Kingdom, Bahrain, Canada, Mexico, USA, Singapore, Costa Rica,

				Ecuador, Jordan, Panama, Chile, Oman, Saudi Arabia, Argentina, Switzerland, Kuwait, EU, Philippines, Pakistan, Colombia, Iraq, Israel, Qatar, Singapore, United Arab Emirates, Faroe Islands, Greenland, Iceland, Malaysia, Norway, Serbia
Janssen	recombinant, replication-incompetent adenovirus serotype 26 (Ad26) vector vaccine,	Janssen Biotech Inc., a Janssen Pharmaceutical Company of Johnson & Johnson	Australia	Andorra, Bahrain, Bangladesh, Botswana, Brazil, Brunei, Canada, Chile, Colombia, Ghana, Guinea, Honduras, Jordan, Kuwait, Libya, Malaysia, Maldives, Marshall Islands, Mexico, Micronesia, Moldova, Morocco, New Zealand, Nigeria, Palau, Philippines, Saudi Arabia, South Africa, South Korea, Taiwan, Thailand, Tunisia, Ukraine, United Kingdom, United States.

On December 2, 2020, United Kingdom (UK) became the first country to approve the COVID-19 vaccine, BNT162, developed by Pfizer and BioNTech via Emergency Use Authorization (EUA). WHO approved BNT162 for emergency use on December 31, 2020 to allow for easier global manufacturing and distribution. Similar EUA processes were adapted by several countries including, United States, Canada, Russia, China, and India to approve different COVID-19 vaccine candidates (CVCs) and the list is growing.[1]

- **BNT162 vaccine by Pfizer and BioNTech**

On December 2, 2020, UK became the first country to approve COVID-19 vaccine BNT162 developed by Pfizer and BioNTech via EUA. On December 11, 2020 US FDA issued first EUA for BNT162 have demonstrated 95% efficacy in preventing disease in phase III clinical trial results. Later Canada and Mexico also approved BNT162 via respective EUA pathways. On December 31, 2020, WHO approved first vaccine candidate, BNT162, for emergency use thereby making it easier to manufacture and distribute this vaccine globally.[1]

Mechanism of action

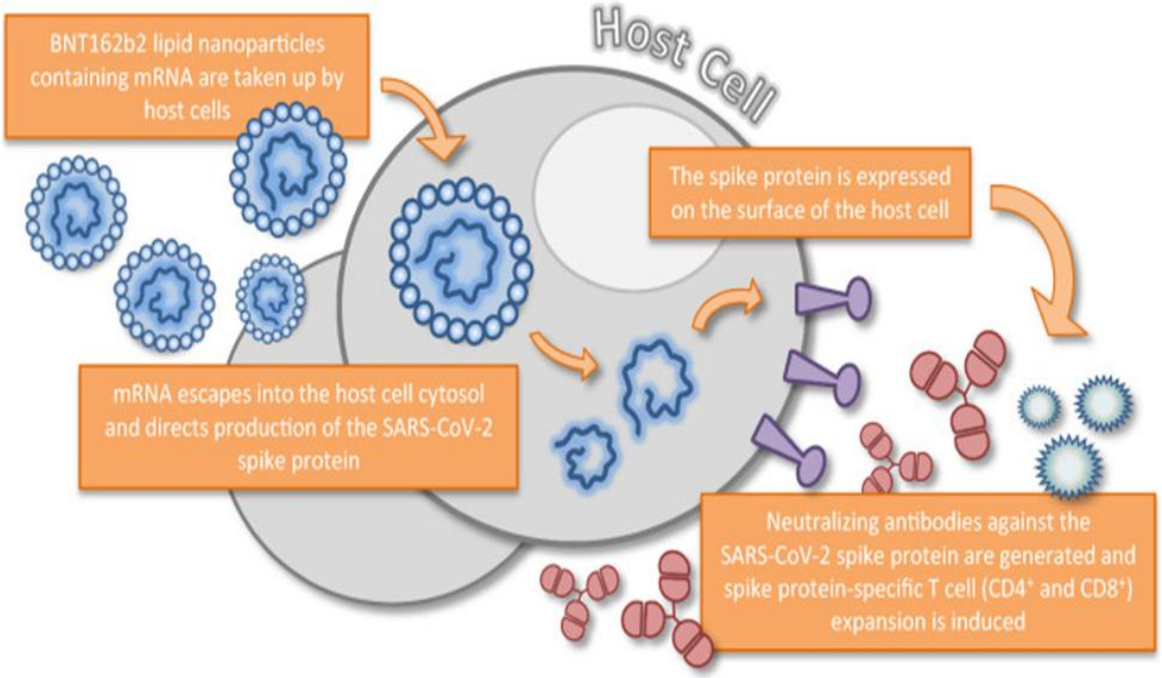

Fig. 2: Mechanism of action of BNT162 vaccine by Pfizer and BioNTech.[5]

BNT162b2 is comprised of nucleoside-modified mRNA formulated in lipid nanoparticles. The mRNA encodes the membrane-anchored, full-length SARS-CoV-19 spike protein and contains mutations which stabilize the spike protein in an antigenically preferred, prefusion conformation. The lipid nanoparticles protect the non-replicating RNA from degradation and allow it to be delivered into host cells after intramuscular injection. Once inside host cells, the mRNA is translated into SARS-CoV-2 spike protein, which is expressed on the surface of the host cells. The transient expression of this spike antigen induces neutralizing antibody and cellular immune responses against it, which may confer protection against COVID-19.[5]

Administration

BNT162b2 is available in a multiuse vial which requires cold storage (posing a logistical challenge for the distribution of the vaccine) and must be thawed and diluted before use. Each vial contains six 30 µg doses after dilution. BNT162b2 is administered intramuscularly (ideally into the deltoid muscle) as a course of two 30 µg doses, with a recommended dose interval of 21 days. Full protection against COVID-19 may not be achieved until 7 days after administration of the second dose. As is the case with other vaccines, BNT162b2 may not protect every recipient.[5]

Vaccine adverse event

The most common local reaction was pain at the injection site, with 66%-83% of recipients, depending on the age, reporting the reaction and only 8%-14% of placebo recipients developing the symptom. Systemic reactions such as headache, fatigue, and fever were also observed, predominantly in the younger population, with headache and fatigue being reported by more than 52%-59% of vaccine recipients, and fever was reported by 11%-16% of recipients. Some of the recipients also reported severe adverse events between the first dose and the second dose that was given after one month. One of them developed pancreatitis, and none of the placebo recipients had such an event.[6]

Due to limited data, the use of BNT162b2 during pregnancy should only be considered if the potential benefits are deemed to outweigh any potential risks for the mother and foetus. It is unknown whether BNT162b2 is present in human breast milk.

Storage

This vaccine requires ultra-low temperature freezer for storage up to 6 months. Temperature-controlled thermal shippers utilizing dry ice to maintain recommended temperature conditions of -70°C±10°C for up to 10 days will be needed for transportation. Each thermal shipper should have a reusable GPS temperature monitoring device.[7]

- **mRNA-1273 vaccine by moderna**

Moderna's mRNA-1273 becomes the second CVC to be approved by FDA under EUA.[1] mRNA-1273 is created by Moderna Inc in collaboration with National Institute of Allergy and Infectious Diseases (NIAID) and Coalition for Epidemic Preparedness Innovations (CEPI).[24]

Mechanism of action

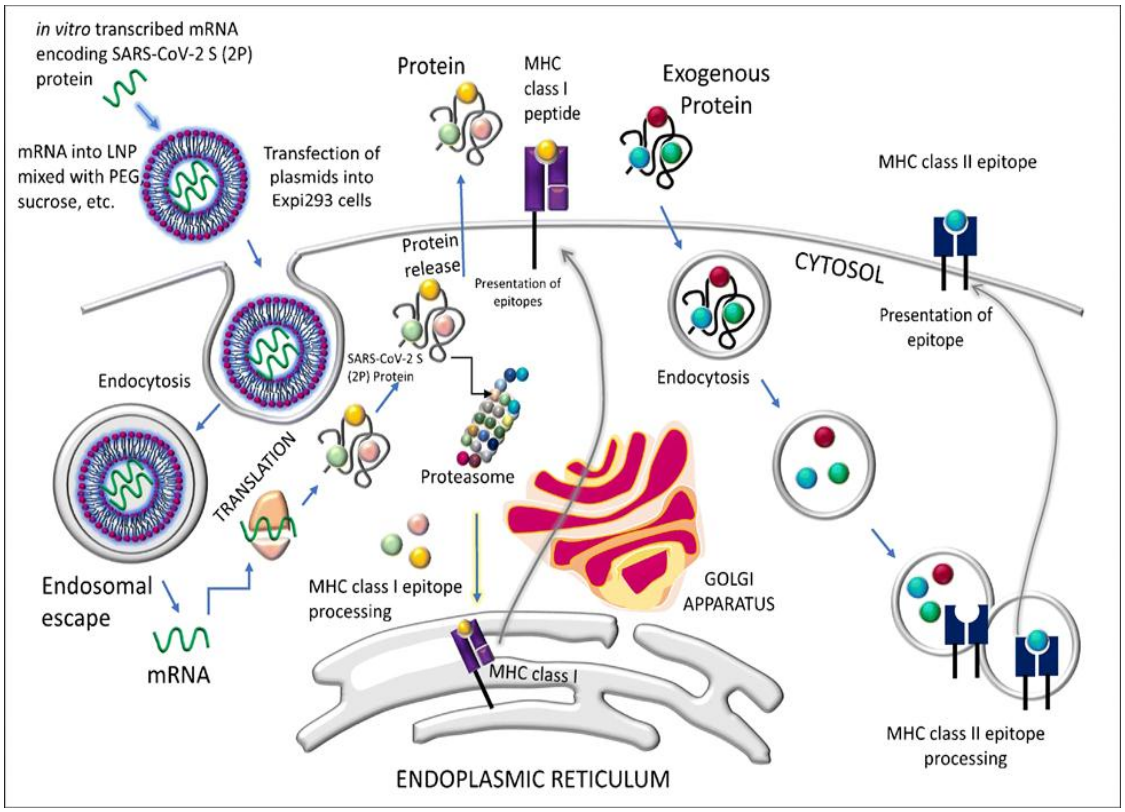

Fig. 3: A model showing the scheme of the mechanisms of action of the mRNA-1273 vaccine (adapted from the description reported by Corbett et al.)[8]

Briefly, following transfection and endocytosis, the mRNA is translated within the host to make SARS-CoV-2 S protein, which is released and also undergoes the MHC class I processing for the antigenic presentation on the host cell surface. The exogenous protein undergoes endocytosis followed by processing by MHC class II.

The chemistry of the mRNA-1273 (Moderna TX, Inc.) vaccine is based on the contentment of

1. The nucleoside-modified messenger RNA (modRNA), i.e., the mRNA (as stated earlier) as the active ingredient that encodes the viral spike glycoprotein (S) of SARS-CoV-2 (i.e., RNA serves as the template to generate the specific protein that triggers the host immune response against the virus).
2. Lipid nanoparticles (LNPs) with complexed polyethylene glycol (PEG), phosphocholine, and cholesterol (this is to be noted here that BioNTech-Pfizer and Moderna encapsulate their mRNA vaccines within LNPs which aids in the delivery of the RNA and protects the RNA from degradation).

3. Salts including potassium chloride and sodium chloride, and monobasic potassium phosphate and the dibasic sodium phosphate dihydrate which serve as the buffer.
4. Sucrose, which acts as the cryoprotectant assuring that the lipid does not get too much sticky at the extremely cold temperature during storage.
5. The development procedure of the mRNA-1273 vaccine has been very well described by Corbett et al. Briefly, a DNA fragment consisting of the immunogen open reading frame (ORF) flanked by 5′ untranslated region (5′ UTR) and the 3′ UTR is used as a template on which the T7 RNA polymerase mediates transcription to generate the mRNA encoding SARS-CoV-2 S (2P) protein, followed by the enzymatic addition of the cap structure and the subsequent purification of the mRNA. For encapsulation of the preclinical mRNA into the LNPs, the modified ethanol-drop nanoprecipitation process is applied whereby PEGs are mixed with the mRNA (maintaining pH at 5.0 in the acetate buffer), neutralized, and finally, sucrose is added as a cryoprotectant as stated above, and the final solution is filter sterilized. Prior to use, vials filled with the formulated LNP are stored in –70 °C, and before the in vivo application, the product is assessed for a range of variables as described recently.[8]

Administration

The recommended schedule is two doses (100 µg, 0.5 ml each) given intramuscularly into the deltoid muscle. An interval of 28 days between doses is recommended. If the second dose is inadvertently administered less than 28 days after the first, the dose does not need to be repeated. If administration of the second dose is inadvertently delayed it should be given as soon as possible thereafter, according to the manufacturer's instructions. It is currently recommended that individuals receive no more than two doses in total. Intended use in Persons aged 18 years and above.[10]

Adverse events

some adverse effects of the vaccination in the trial stage have been noticed as the onset of fatigue, headache, muscle and joint pains, chills, fever, and, in some cases of the participants, the lymphadenopathy.[8]

"COVID arm" is an uncommon adverse effect that can present as a localized, transient erythematous rash several days following the first dose of the Moderna COVID-19 vaccine.[9] Although most cases resolve spontaneously, topical steroids and oral histamines have proven to be successful in clearing the rash and controlling symptoms.[9]

- **AZD1222 by Astra Zeneca and University of oxford**

On December 30, 2020, UK and on January 2, 2021, India approved AZD1222 COVID-19 vaccine developed by AstraZeneca and the Oxford Vaccine Group at the University of Oxford. It was previously called as ChAdOx1, a chimpanzee adenovirus vaccine. This group has previously developed a MERS vaccine. In India, this vaccine is jointly developed by Serum Institute of India and AstraZeneca and is branded as Covishield. Oxford University and AstraZeneca, a pharmaceutical company both are engage in developing Covishield vaccine. Its Indian partner "Serum institute" Pune, is enduring for production of viral vector vaccine as brand name AZD1222. This contains weakened, genetically modified, non-replicating strains of SARS-CoV-2 and adenovirus (causative of common cold). From the interim analysis, AZD1222 is found 70.4% efficacious against prevention of COVID-19 with no prominent adverse effects.[12]

Mechanism of action

AZD1222 vaccine is a monovalent vaccine composed of a single recombinant, replication-deficient chimpanzee adenovirus vector encoding the S glycoprotein of SARS-CoV-2 (ChAdOx1-S (recombinant). The SARS-CoV-2 S immunogen in the vaccine is expressed in the trimeric prefusion conformation. The coding sequence has not been modified, in order to stabilize the expressed S-protein in the prefusion conformation. Adenoviruses are non-encapsulated, icosahedral particles (virions), and contain a single copy of the double-stranded DNA genome. The expression cassette for the SARS-CoV-2 spike protein fused to the tissue plasminogen activator leader sequence uses a modified human cytomegalovirus promoter and a bovine growth hormone polyadenylation sequence.[11]

Composition

One dose (0.5ml) contains 5 x 1010 ChAdOx1-S (recombinant) viral particles. The vaccine is produced in genetically modified human embryonic kidney (HEK) 293 cells. In addition to ChAdOx1-S (recombinant), this product also contains the excipients L-histidine, L-histidine hydrochloride monohydrate, magnesium chloride hexahydrate, polysorbate 80, ethanol, sucrose, sodium chloride, disodium edetate dihydrate and water for injection. None of the excipients are of animal or human origin. The excipients are well established for pharmaceutical products.[11]

Administration

The vaccination course consists of two doses (each 0.5 ml) and should be administered within 4–6 weeks apart.[12]

Adverse events

Very common (≥10% of subjects): headache, nausea, myalgia, arthralgia, injection site tenderness, injection site pain, injection site warmth, injection site pruritus, fatigue, malaise, feverishness, chills.

Common (1–10% of subjects): injection site swelling, injection site erythema, fever ≥ 38 °C.[11]

Storage

A shelf-life of 6 months is proposed. Chemical and physical in-use stability from the time of vial opening (first needle puncture) to administration is up to 48 hours in a refrigerator (2–8 ºC). Within this period, the product may be kept and used at temperatures up to 30 ºC for a single period of up to 6 hours, after which it must be discarded. It should not be returned to the refrigerator.[11]

- **CoronaVac by Sinovac**

CoronaVac (formerly PiCoVacc) is approved by China through EUA. CoronaVac is a formalin-inactivated and alum adjuvanted vaccine candidate developed by Sinovac Biotech, China. Results from preclinical studies showed partial or complete protection in non-human primates exposed to SARS-CoV-2.[1]

Mechanism of action

The Chinese company Sinovac produced a coronavirus vaccine called CoronaVac. They used the Inactivated viruses, technique that have been used for over a century against several diseases. After being injected in the body, the inactivated viruses are engulfed by immune cells called antigen presenting cells. The latter degrade the inactivated virus and display some of its protein on the surface of the cell. B cells and Helper T cells identify the spike proteins. The immune cells get activated and proliferate antibodies against the antigen.[13]

Administration

The recommended schedule is two doses given intramuscularly. An interval of 14 days between doses is recommended.[13]

Adverse event

Side effects, which was found to be 62.5%. Injection site pain (41.5%) was the most common local SE, while fatigue (23.6%), headache (18.7%), muscle pain (11.2%) and joint pain (5.9%) were the common systemic SEs. Female healthcare workers (67.9%) were significantly more affected by both local and systemic SEs compared to their male counterparts (51.4%). Younger age, previous infection, and compromised health status (chronic illnesses and regular medicines uptake) can be associated with an increased risk of CoronaVac SEs. Most SEs are rather minor reactions that persist in most cases for one to three days.[14]

Storage

Sinovac can be stored in standard refrigerators at 2-80˚C.

- **Sputnik V by the gamaleya research institute, russia**

Russia has approved first CVC as Sputnik V (previously as Gam-COVID-Vac). The Gamaleya Research Institute in Russia and Health Ministry of the Russian Federation are assessing their non-replicating viral vector vaccine, Sputnik V, in a Phase 3 trial. On August 11, 2020, Russia approved the "Sputnik V" anti-SARS-CoV-2 vaccine developed by Moscow's Gamaleya Institute.[1]

Mechanism of action

Sputnik V vaccine is first registered inoculating candidate against COVID-19. This vaccine is different from conventional as they do not contain antigen rather induce body's cells to produce the same. There is a modified virus vector that gets activated after interacting with spike proteins of SARS-CoV-2 and delivers genetic codes for antigen. Virus vector lacks genes responsible for reproduction and making its copies in body cells. It is used to deliver genetic material from another virus that is targeted for vaccination. A genetic code of S protein from SARS-CoV-2 virus is inserted into two different viral vectors that develop immunity against delivered S proteins after prime and boost immunization. Gamaleya center of Russia used unique and novel technology using two adenovirus vectors (Ad 26 and Ad 5) that boosts immunity after 21 days. In the first dose, Ad26 is given and, the second dose of Ad5 is administered after 21 days. This strategy has an advantage as, after the first dose, antibodies are produced against the Ad26 serotype. The second dose is of Ad5 serotype; therefore, the body is stimulated to produce an enhanced immune response.[3]

Administration

The recommended schedule is two doses given intramuscularly. An interval of 21 days between doses is recommended.

Adverse event

The vaccine was generally safe, and the most common adverse reactions were injection site pain and fever.[18]

Storage

vaccine needs to be stored at -18°C, freezer temperature, and another uses dried (lyophilised) material that can be stored at 2 to 8°C in a range of standard refrigerators, which would aid transport and distribution.[15]

- **BBIBP-CorV by Sinopharm and Beijing institute of biological products, China**

BBIBP-CorV is inactivated CVC developed by Sinopharm in association with Beijing Institute of Biological Products, China. Firstly China and later on United Arab Emirates (UAE) approved the vaccine through EUA.[1]

Mechanism of action

BBIBP-CorV vaccine contains a SARS-CoV-2 strain inactivated inside Vero Cells. Investigation shows this vaccine induces neutralizing antibodies in several mammalian species while also showing protective efficacy with SARS-CoV-2 challenge in rhesus macaques. As of August 2020, this vaccine is being tested for prophylaxis against COVID-19 in human clinical trials. In preclinical studies, BBIBP-CorV produced a better immune response in guinea pigs, mice, rats, rabbits, and non-human primates to protect against SARS-CoV-2.[16] In the phase I and II trials, BBIBP-CorV was safe and well-tolerated at all three doses (2 μg, 4 μg, or 8 μg) on days 0 and 28. A robust immune response was observed in 100% of vaccine recipients. The phase III trial of BBIBP-CorV is ongoing in Abu Dhabi, UAE.[17,19]

Administration

The results showed that the BBIBP-CorV vaccine was safe and well tolerated in all groups, that neutralizing antibodies were produced in all subjects 42 days after prime inoculation, and that the strongest neutralization GMT occurred at a dose of 4 μg with the 0/21 or 0/28 day inoculation schedule.[18]

Storage

BIBP-CorV could be transported and stored at normal refrigerated temperatures.

- **COVID-19 vaccine by Sinopharm and The wuhan institute of virology, China**

China approved this vaccine via EUA. Sinopharm and Wuhan Institute of Virology under the Chinese Academy of Sciences have developed an inactivated CVC.[1]

Mechanism of action

New Crown COVID-19 has been developed by Wuhan Institute of Biological Products and Sinopharm as an inactivated whole-virus, alum-adjuvant vaccine. The whole virus cultivated in vitro and infected cells was further inactivated using β-propiolactone and adsorbed to 0.5 mg alum. The phase 1 clinical trial was carried out using three doses (10 μg, 5 μg, and 2.5 μg) of antigen. The results revealed that the vaccine has better safety profiles and strong neutralizing antibody response in all three doses. There were no severe side effects. Phase II clinical trials were undertaken using a 5 μg antigen, and the results displayed New Crown COVID-19 vaccine can effectively generate antibody titer with fewer side effects. A booster dose is essential to produce enough immune response, with (21 days and 28 days) interval between the first doses. The booster dose triggers a better antibody titer as compared to the 14-day intervals. Generally, the New Crown COVID-19 vaccine candidate displayed acceptable safety and a better immunogenic profile, supporting its assessment in the ongoing phase III trials. A phase III (ChiCTR2000034780) clinical trial began in July 2020 and planned to enroll 21,000 participants. Phase III (ChiCTR2000034780) clinical trials are currently taking place in the United Arab Emirates. Sinopharm gave these candidate vaccines to thousands of people under emergency use conditions approved by the Chinese Government.[19]

Adverse events

The most common adverse reaction was injection site pain, followed by fever.[18]

- **Epi vac corona by federal budgetary research institution state research center of Virology and Biotechnology, Russia**

Russia also granted regulatory approval to EpiVacCorona, a peptide vaccine candidate for COVID-19, developed by Federal Budgetary Research Institution State Research Center of Virology and Biotechnology. The unique feature of EpiVacCorona is that it contains the

fragment of synthetic peptide antigen of the virus. According to consumer health watchdog, EpiVacCorona has proved to be 100% effective in early-stage trials.[1]

Mechanism of action

EpiVacCorona, a peptide vaccine is developed by Russian Institute "CanSino Biologics, Vector State Research Center of Virology and Biotechnlogy." The system contains fragments extracted from virus and synthetic peptides that form active antigens in body. EpiVacCorona vaccine stimulates body to produce immunogenic responses by releasing antibodies into host's blood and lymph. The vaccine does not persuade reactogenic responses and is considered for high safety. EpiVacCorona vaccine provokes an immunogenic response against SARS-CoV-2 and maintains future immunity. Russian authorities' claim its effectiveness and prepare for mass immunization in 2021. At present, the vaccine appears in phase 3 including clinical trials (NCT04527575) on adults and pregnant ones as it does not exhibited embryotoxic activity.[3]

Administration

The vaccine delivered via intramuscular route and aluminium hydroxide serves as an immunological adjuvant.

Adverse event

The most common adverse reactions were mild pain and redness at the injection site or mild fatigue.

- **COVAXIN by Bharat Biotech and National institute of Virology, India**

COVAXIN, which is an indigenous COVID-19 vaccine to fight against corona virus, has been developed by Bharat Biotech in collaboration with Indian Council of Medical Research (ICMR) and National Institute of Virology (NIV). Whole Virion Inactivated Vero Cell derived platform technology was used to developed the vaccine. The Vero cell manufacturing platform has an excellent safety record of more than 300 million doses. The inactivated vaccines cannot possibly replicate and are thus cannot likely revert and cause pathological effects. They are manufactured using dead virus, incapable of infecting people but still able to instruct the immune system to mount a defensive reaction against an infection. On January 2, 2021, India approved an inactivated vaccine called Covaxin, developed by Bharat Biotech and India's National Institute of Virology.[20]

Mechanism of action

The vaccine is similar to CoronaVac (the Chinese vaccine developed by Sinovac) in that it uses a complete infective SARS-CoV-2 viral particle consisting of RNA surrounded by a protein shell, but modified so that it cannot replicate.[21] After being injected in the body, the inactivated viruses are engulfed by immune cells called antigen presenting cells. The latter degrade the inactivated virus and display some of its protein on the surface of the cell. B cells and Helper T cells identify the spike proteins. The immune cells get activated and proliferate antibodies against the antigen.[13]

Composition

COVAXIN is an inactivated vaccine obtained from the SARS-CoV-2 strain. The vaccine is used along with immune stimulants, commonly known as vaccine adjuvants (Alhydroxiquim-II), to improve immune response and longer-lasting immunity. The vaccine candidate is produced through the formulation of the inactivated virus with Kansas-based ViroVax's Alhydroxiquim-II adjuvant. COVAXIN mainly contains 6µg of whole-virion inactivated SARS-CoV-2 antigen (Strain: NIV2020-770), and the other inactive components such as 250µg aluminium hydroxide gel, 15µg TLR 7/8 agonist (imidazoquinolinone), 2.5mg TM 2-phenoxyethanol, and phosphate buffer saline up to 0.5ml. The vaccine requires no sub-zero storage and reconstitution requirement and available for use in multi-dose vials, stable at 2-6°C.[20]

Administration

Covaxin comes as a two-dose regimen, recommended to be taken intramuscularly 28 days apart.[21]

Adverse event

Bharat Biotech also listed the risks/side effects of Covaxin. These include: "Injection site pain, site swelling, site redness, site itching, stiffness in the upper arm, weakness in injection arm, body ache, headache, fever, malaise, weakness, rashes, nausea, vomiting".[20]

Caution for vaccination

Persons should not get the Covaxin if he or she Have any history of allergies, Have fever, Have a bleeding disorder or are on a blood thinner, Are immune-compromised or are on a medicine that affects your immune system, Are pregnant/breastfeeding, Have received

another COVID-19 vaccine, Any other serious health-related issues, as determined by the vaccinator/officer supervising vaccination.

Storage

It is a vaccine with no sub-zero storage, no reconstitution requirement, and ready to use liquid presentation in multi-dose vials, stable at 2-8 °C.[20]

- **Janssen COVID-19 Vaccine**

Janssen Biotech Inc., a Janssen Pharmaceutical Company of Johnson & Johnson developed a vaccine. The Janssen COVID-19 vaccine is a recombinant, replication-incompetent adenovirus serotype 26 (Ad26) vector vaccine, encoding the stabilized prefusion spike glycoprotein of SARS-CoV-2, the virus that causes COVID-19.[22] On February 28, 2021, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for use of the Janssen COVID-19 vaccine in persons aged ≥18 years for the prevention of COVID-19. This vaccine is the third COVID-19 vaccine authorized under an EUA for the prevention of COVID-19 in the United States.[22]

Mechanism of action

Janssen vaccine, viral-vector based vaccines, use a double-stranded DNA. The viral vector is a modified adenovirus that is stripped of any disease-causing genes to become a harmless virus. Moreover, the researchers added the coronavirus spike protein gene to the viral vector which acts now as a delivery system, providing a mean to enter the cell and introduce the code of the targeted antigen. Once inside the cell, the modified virus enters to the nucleus, where the spike protein gene is copied into mRNA and then translated outside the nucleus to proteins. Consequently, the spike proteins migrate to the surface of the cells and trigger an immune response. B cells helper T cells as well as cytotoxic T cells are activated. To note, the adenovirus itself activate the immune system by turning on the cell's alarm system. By initiating this alarm, these vaccines trigger the immune system to act more powerfully to the spike proteins.[13]

Administration

Vaccination with the Janssen COVID-19 vaccine consists of a single dose (5×10^{10} virus particles per 0.5-mL dose) administered intramuscularly.[22]

Adverse event

The most commonly reported side effects were pain at the injection site, headache, fatigue, muscle aches and nausea. Most of these side effects occurred within 1-2 days following vaccination and were mild to moderate in severity and lasted 1-2 days.[23]

Storage

The Janssen COVID-19 vaccine is feasible to implement, requiring only a single dose and refrigerator temperatures (36°F–46°F [2°C–8°C]) for transportation and storage.[22]

CONCLUSION

The review outlines the real knowledge regarding covid 19 vaccines authorized by EUA. The review concentrates on the kind of vaccine, administration route, effective dosing, observed side effects and storage conditions of various covid 19 vaccine candidates approved for use by various nations like America, China, Russia, Australia, and India. COVID-19 vaccine development has thrown major challenges in vaccine R&D. The world is facing a major health crisis and economic devastation, and one of the definitive solutions is to have an effective and safe vaccine in the shortest possible time. COVID-19 vaccines approved so far are able to elicit immunity with a high degree of efficacy, it is not yet known how durable the immunity will be.

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Abbreviations

- **COVID-19:** coronavirus disease 2019
- **MERS-CoV:** Middle East respiratory syndrome coronavirus
- **SARS-CoV:** severe acute respiratory syndrome-associated coronavirus
- **SARS-CoV-2:** severe acute respiratory syndrome coronavirus 2
- **S protein:** spike protein of SARS-CoV-2
- **RBD:** receptor binding domain
- **VLP:** virus-like particle
- **EUA:** Emergency Use Authorization
- **CVCs:** COVID-19 vaccine candidates

- **HEK:** human embryonic kidney
- **UAE:** United Arab Emirates
- **ICMR:** Indian Council of Medical Research
- **NIV:** National Institute of Virology
- **ACIP:** Advisory Committee on Immunization Practices

REFERENCES

1. Kashte, Shivaji, et al. "COVID-19 vaccines: rapid development, implications, challenges and future prospects." Human Cell, 2021; 1-23.
2. https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines
3. MISRA, SHASHI KIRAN, KAMLA PATHAK, DEVENDER PATHAK, and RAMAKANT YADAV. "CURRENT UPDATES ON COVID-19 VACCINES." Asian Journal of Pharmaceutical and Clinical Research, 2021; 17-23. Feng, Gong, Lanjing Zhang, Ke Wang, Bohao Chen, and Harry Hua-Xiang Xia. "Research, Development and Application of COVID-19 Vaccines: Progress, Challenges, and Prospects." Journal of Exploratory Research in Pharmacology, 2021; 6(2): 31-43.
4. World Health Organization. Background document on the mRNA vaccine BNT162b2 (Pfizer-BioNTech) against COVID-19: background document to the WHO interim recommendations for use of the Pfizer–BioNTech COVID-19 vaccine, BNT162b2, under emergency use listing, 14 January 2021. No. WHO/2019-nCoV/vaccines/SAGE_recommendation/BNT162b2/background/2021.1. World Health Organization, 2021.
5. Parkash, Om, Artem Sharko, Aneeba Farooqi, Grace W. Ying, and Prashant Sura. "Acute Pancreatitis: A Possible Side Effect of COVID-19 Vaccine." Cureus, 2021; 13: 4.
6. World Health Organization. mRNA vaccines against COVID-19: Pfizer-BioNTech COVID-19 vaccine BNT162b2: prepared by the Strategic Advisory Group of Experts (SAGE) on immunization working group on COVID-19 vaccines, 22 December 2020. No. WHO/2019-nCoV/vaccines/SAGE_evaluation/BNT162b2/2020.1. World Health Organization, 2020.
7. Noor, Rashed. "Developmental Status of the Potential Vaccines for the Mitigation of the COVID-19 Pandemic and a Focus on the Effectiveness of the Pfizer-BioNTech and Moderna mRNA Vaccines." Current clinical microbiology reports, 2021; 1-8.
8. Wei, Nancy, Mary Fishman, Debra Wattenberg, Marsha Gordon, and Mark Lebwohl. "“COVID arm”: A reaction to the Moderna vaccine." JAAD case reports, 2021.

9. World Health Organization. (2021). Interim recommendations for use of the Moderna mRNA-1273 vaccine against COVID-19: interim guidance, 2021; 25: 15. (No. WHO/2019-nCoV/vaccines/SAGE_recommendation/mRNA-1273/2021.2). World Health Organization.
10. World Health Organization. Background document on the AZD1222 vaccine against COVID-19 developed by Oxford University and AstraZeneca: background document to the WHO Interim recommendations for use of the AZD1222 (ChAdOx1-S [recombinant]) vaccine against COVID19 developed by Oxford University and AstraZeneca, 1 March 2021. No. WHO/2019-nCoV/vaccines/SAGE_recommendation/AZD1222/background/2021.2. World Health Organization, 2021
11. MISRA, SHASHI KIRAN, KAMLA PATHAK, DEVENDER PATHAK, and RAMAKANT YADAV. "CURRENT UPDATES ON COVID-19 VACCINES." Asian Journal of Pharmaceutical and Clinical Research, 2021; 17-23.
12. Cima Hamieh, M. D., M. D. Mahmoud El Hussein, M. D. Yara Skaff, M. D. Jim Abi Frem, and M. D. Elie Zaghrini. "COVID-19 Vaccines, What do we know so Far? A Narrative Review."
13. Riad, Abanoub, Derya Sağıroğlu, Batuhan Üstün, Andrea Pokorná, Jitka Klugarová, Sameh Attia, and Miloslav Klugar. "Prevalence and risk factors of CoronaVac side effects: an independent cross-sectional study among healthcare workers in Turkey." Journal of Clinical Medicine, 2021; 10(12): 2629.
14. Baraniuk, Chris. "Covid-19: What do we know about Sputnik V and other Russian vaccines?." Bmj, 2021; 372.
15. Wang, Hui, Yuntao Zhang, Baoying Huang, Wei Deng, Yaru Quan, Wenling Wang, Wenbo Xu et al. "Development of an inactivated vaccine candidate, BBIBP-CorV, with potent protection against SARS-CoV-2." Cell, 2020; 182(3): 713-721.
16. Xia, Shengli, Yuntao Zhang, Yanxia Wang, Hui Wang, Yunkai Yang, George Fu Gao, Wenjie Tan et al. "Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBIBP-CorV: a randomised, double-blind, placebo-controlled, phase 1/2 trial." The Lancet Infectious Diseases, 2021; 21(1): 39-51.
17. Li, Dan-Dan, and Qi-Han Li. "SARS-CoV-2: vaccines in the pandemic era." Military Medical Research, 2021; 8(1): 1-15.
18. Belete, Tafere Mulaw. "Review on up-to-date status of candidate vaccines for COVID-19 disease." Infection and drug resistance, 2021; 14: 151.

19. Darbar, Soumendra, Sangita Agarwal, and Srimoyee Saha. "COVID19 Vaccine: COVAXIN®-India's First Indigenous Effective Weapon to Fight against Coronavirus (A Review)."
20. Thiagarajan, Kamala. "What do we know about India's Covaxin vaccine?." Bmj, 2021; 373.
21. Oliver, Sara E., et al. "The advisory committee on immunization practices' interim recommendation for use of Janssen COVID-19 vaccine—United States, February 2021." Morbidity and Mortality Weekly Report, 2021; 70(9): 329.
22. https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/janssen-covid-19-vaccine
23. https://en.wikipedia.org/wiki/List_of_COVID19_vaccine_authorizations#Johnson_&_Johnson
24. Alturki, Sana O., Sawsan O. Alturki, Jennifer Connors, Gina Cusimano, Michele A. Kutzler, Abdullah M. Izmirly, and Elias K. Haddad. "The 2020 pandemic: current SARS-CoV-2 vaccine development." Frontiers in immunology, 2020; 11: 1880.
25. Krammer, Florian. "SARS-CoV-2 vaccines in development." Nature, 2020; 586: 7830, 516-527.
26. Hashan, Mohammad Rashidul, Nicolas Smoll, Catherine King, Hannah Ockenden-Muldoon, Jacina Walker, Andre Wattiaux, Julieanne Graham, Robert Booy, and Gulam Khandaker. "Epidemiology and clinical features of COVID-19 outbreaks in aged care facilities: A systematic review and meta-analysis." EClinicalMedicine, 2021; 100771.
27. Kostoff, Ronald N., Michael B. Briggs, Alan L. Porter, Demetrios A. Spandidos, and Aristidis Tsatsakis. "[Comment] COVID-19 vaccine safety." International journal of molecular medicine, 2020; 46(5): 1599-1602.