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A Review on the Advancements in COVID-19 Treatments and Vaccines Development

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Abstract *The outbreak of the COVID-19 pandemic that is caused by novel SARS-CoV-2 has taken the life of millions of people around the globe and has put a challenge on the whole world for identifying and developing the best possible therapies for preventing and treating this deadly infection. Clinical study and health policy and clinical interventions are required for advancements in the effective and safe treatment and prevention of COVID-19 disease. Many drugs have been tested in clinical trials for their effectiveness and safety against COVID-19. Among them, some have shown promising effects like remdesivir, the only COVID-19 drug approved by FDA till now, dexamethasone, monoclonal antibodies, etc. Biological agents have also been shown to be effective against the virus, such as tocilizumab, convalescent plasma, and interferon. The most effective medical intervention for COVID-19 is a vaccination which is currently in a development phase at a rapid pace. However, two vaccines have been authorized by the FDA and a number of vaccines are in their final clinical phase. This paper will analyze all the current advancements within the treatment against the COVID-19*

Key Words: COVID-19, SARS-CoV-2, Treatment, Vaccines, Patients, Clinical

Introduction

In December 2019, the iCOVID-19 pandemic bring about by the new SRAS-CoV-2 has become a worldwide threat. It is spreading at a rapid pace and till now it has affected 218 countries and territories around the globe. By December 21, 2020, the total number of world wild coronavirus cases are 77,267,863 and it has taken the lives of 1,701,670 people with the USA on the top of the list with 18,267,579 cases and 324,869 total deaths (Worldometer, 2020). The Coronavirus infection can be asymptomatic or may be symptomatic with symptoms including infection of upper respiratory tract and lethal sepsis. Researchers have been looking for new therapies for COVID-19 and the production of safe and efficient vaccines since the outbreak. Various available drugs have been tested pre-clinically and clinically to treat COVID-19. Some of the treatments have proven to be effective against coronavirus and are authorized by the FDA for emergency use while some are still being tested for their effectiveness and safety in clinical trials. The very first FDA approved therapy for COVID-19 is an antiviral medicine Remdesivir that was approved on the 22nd October 2020 by the FDA. Other than that Dexamethasone, a corticosteroid drug authorized in the UK, Convalescent plasma therapy and Monoclonal antibodies Bamlanivimab and Casirivimab and imdevimab are also authorized by FDA.

The most effective solution to this global threat is vaccination against coronavirus. The vaccine development usually takes 10-15 years but in the current scenario rapid vaccine development is the need of the day for preventing this disease. The most common objective in vaccine development is safety and effectiveness. Many COVID-19 vaccines are in development phase because it is not yet confirmed that which will be the most effective and safest ones. The worldwide effort to create an efficient and safe vaccine for COVID-19 is beginning to succeed, as now there are a handful of vaccines around the world that have been authorized and are being used in various

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countries including the USA, China and Russia. Only two COVID-19 vaccines BNT162b2 by Pfizer and BioNTech with reported effectiveness of 95% and mRNA-1273 by Moderna with 94.1% effectiveness data have been yet approved by the FDA. More than 100 candidates for vaccines are currently i n the clinical development process.

Possible Treatments for COVID-19

The use of following drugs to treat COVID-19 is recommended by the National Health Commission & Traditional Chinese Medicine State Administration: anti-virals, e.g. remdesivir, lopinavir and ritonavir, interferon, arbidol, chloroquine, corticosteroids, monoclonal antibodies, convalescent plasma, antibiotics, and steroidal therapies. Tocilizumab is also being used in the case of lung lesions and elevated levels of IL-6. Glucocorticoids are used for three to five days in patients with critical condition. Traditional Chinese Medicines are also being used as indicated in the guidelines. Natural compounds also have a potential against coronavirus, as in-silico experiments have shown that Chinese herbal treatments may include ianti-SARS-CoV-2 substances for viral respiratory infection therapy. (Zhang, Wu, Zhang, Deng & Peng, 2020). The Neutraceuticals may also help in preventing and controlling coronavirus by increasing the production of type 1 interferone by either amplifying TLR7 or MAVS (McCarty & DiNicolantonio, 2020). Other than these drugs, oxygen therapy is also being given to patients and mechanical ventilation is initiated for those patients with more severe condition.

Supportive Care and Respiratory Support

Oxygen treatment is the first step in the event of breathing impairment triggered by COVID-19. More than 75% of COVID-19 admitted patients need oxygen treatment and mechanical ventilation for those who are in more critical condition than other patients. A non-invasive or invasive mechanical ventilation (NIV or IMV) is required in the event of respiratory failure. Oxygen Therapy was given to 41.3% and 6.1% required mechanical ventilation in a recent clinical study on 1099 COVID-19 patients. (Guan et al, 2020). Oxygen heated high-flow nasal canula may be delivered to those patients who don't respond to oxygen therapy (Alhazzani et al, 2020). Lung-protective ventilation with 4-8 mL/kg tidal volumes and less than 30 mg Hg plateau pressure is suggested for patients who require invasive mechanical volumes (Alhazzani et al, 2020).

Targeting the Virus

The groups of drugs being tested and developed for the treatment and control of COVID-19 are as follows: antivirals (e.g., remdesivir, favipiravir), anti-inflammatory drugs (dexamethasone, methylprednisolone), anti-malarial drugs (e.g., Chloroquine and hydroxychloroquine), HIV-1 protease inhibitors (e.g., Lopinavir/ritonavir), antibiotics (e.g., Azithromycin), antibodies (e.g., convalescent plasma, immunoglobulins), anticoagulants (e.g., heparin), monoclonal antibodies (e.g., tocilizumab, anakinra,), and antifibrotics (e.g., tyrosine kinase inhibitors). These different treatments have different efficacies depending on at which stage of illness, it is given and in different manifestations of the disease. In the early stages, viral inhibition is the most effective treatment. Immunomodulatory agents are used for preventing the further progression of disease in hospitalized patients and anticoagulants prevent thromboembolic complications. More preclinical and clinical trials should validate the potency and protection profile of all of these drug applicants against COVID-19.

Commonly Used COVID-19 Drugs and Emergency Use Authorized Therapies (EUA)

The FDA issues Emergency Use Authorization to ensure the availability of new medications and health devices for patients during any public health emergency including COVID-19. If no alternative exists, EUA encourages new treatment for patients, but it doesn't mean that the drug has been approved by the FDA.

Remdesivir (The FDA Approved Drug for COVID-19)

Remdesivir is an antiviral medicinal product that is given in hospitals as an intravenous (IV) infusion. Remdesivir inhibits viral replication by preventing RNA transcription via connection to the RNA polymerase. Remdesivir shows in vitro activity against SARS-CoV-2. In a COVID-19 report of rhesus macaque, the treatment with remdesivir began shortly after inoculation; in comparison to the animals in control group, the animals treated with remdesivir had less viral load in their lungs and therefore less pulmonary damage. (Williamson et al., 2020).

Some clinical studies were performed for the safety and efficacy evaluation of remdesivir against

coronavirus. Remdesivir provided outstanding care and treatment outcomes for the first patient iCOVID-19 in the US (Holshue et al, 2020). On 22 October, 2020, remdesivir was approved by the FDAiCOVID-19 patients 12 years of age and older who needed to be hospitalized. The basis of this approval were three positive study results.

On 19 November 2020, the FDA also authorized a combination of remdesivir and JAK inhibitor, baricitizinib, for treating hospitalized patients aged 2 years and older and require oxygen and intrusion mechanical ventilation (Commissioner, 2020).

Clinical Data

A randomized, double-blind, placebo-controlled clinical study was performed in 1063 hospitalized COVID-19 patients and with involvement of lower respiratory tract. The result revealed that patients who were randomly treated with IV remdesivir had a lower recovery period of 11 days than the patients in the placebo groups who were recovered in 15 days (Beigel et al, 2020). In the second study, an additional randomized open-label study of 397 COVID-19 patients was carried out, but they did not need mechanical ventilation and the findings indicated that there was no change in 5 days of remdesivir treatment to 10 days of treatment on day 14 based on their clinical status(Goldman et al, 2020).

In the third study, hospitalized patients with mild COVID-19 who received remdesivir for 5 days improved faster than those who did not receive the drug. Compared to those who did not receive remdesivir, the clinical condition of those patients who undergo remdesivir treatment for ten days did not vary.

Dexamethasone

Dexamethasone belongs to the class of corticosteroids. It is being used for treating rheumatoid arthritis, allergic reactions, asthma and various autoimmune conditions. Dexamethasone is currently also being used for treating COVID-19 patients. Dexamethasone was authorized by UK to lower the death risk in COVID-19 patients who are hospitalized.

Clinical Data

The United Kingdom has performed a randomized Medical study RECOVERY to approximate the efficacy of dexamethasone in COVID-19 patients, in which 2104 COVID-19 patients were given 6 mg dexamethasone randomly daily for 10 days and 4321 received daily treatment and findings demonstrated a reduction in all mortality rate by 28 days (21.6% vs. 24.6%; the age-based ratio of 0.83; P<.001) (Horby et al, 2020).Based upon the evidence, the use of dexamethasone for iCOVID-19 patients under respiratory support was suggested by four United States chief medical officers on 16 June 2020. A more successful COVID-19 medication, methylprednisolone decreases Hospital mortality rates. In 201 COVID-19 and ARDS patients in Wuhan, China, retrospectively, longitudinal research suggests that methylprednisolone decrease the mortality risk for COVID-19 patients (relative risk, 0.38 (95% CI, 0.20-0.72)) (Wu et al, 2020).

Convalescent Plasma Therapy

Patients recovered from COVID-19, their plasma with a strong neutralizing antibody titre is a potential treatment of COVID-19 which does not have significant side effects. The antibodies found in convalescent plasma fight the virus. The safety and efficacy of convalescent plasma therapy should be checked in patients of COVID-19. The convalescent plasma therapy is most commonly used as prophylaxis in high-risk individuals, health care providers, and in those individuals that are vulnerable with any underlying medical conditions. Convalescent plasma received EUA for hospitalized patients from FDA on August 23, 2020.

Clinical Data

A recent study in five critical patients of COVID-19 and ARDS in Third People's Hospital in Shenzhen, China who undergo convalescent plasma therapy from five recovered patients of COVID-19, 10-22 days after admission has shown an advancement in all patients' clinical condition and perceived it as a combination of improving their fever, partial oxygen pressure, serum antibody titer, virus count and ARDS (Shen et al, 2020). However, there is no statistical discrepancy between patients undergoing plasma treatment and regular treatment alone within 28 days from a randomized, multi-center, and Open-label, medical study in China with 103 critical COVID-19 patients (51.9 percent vs 43.1 percent) (Li et al, 2020).

Monoclonal Antibodies

MABs are produced in the laboratory. The body takes weeks to grow its antibodies, so it is possible to

combat infections easily by using monoclonal antibodies. Monoclonal antibodies aimed at avoiding organ damage by targeting the inflammatory reaction after SRS-CoV-2 infection, including interleukin 1, interferon-gamma, interleukin 6, and complement factor 5a (Sanders, Monogue, Jodlowski & Cutrell, 2020). The adverse effects of convalescent plasma can be mitigated by complex monoclonal antibodies. The neutralizing SARS-CoV-2 monoclonal antibodies can be medicinal and prophylactic and can aid in the designing and development of vaccines (Marston, Paules, & Fauci, 2020).

Monoclonal antibodies neutralizing coronavirus specifically attacks glycoproteins from the surface that enable the virus to invade hosts. The glycoprotein is also the target of all other monoclonal antibodies. The association of the viral spike protein and ACE2 receptor in various cell types triggers the viral infection, but monoclonal antibodies block this occurrence.

Regeneron and Eli Lilly are being developing two monoclonal antibodies, known as Bamlanivimab (LY-CoV555) and Casirivimab & Imdevimab REGN-COV2, both of which have been approved for emergency therapy by FDA in November, 2020.

Bamlanivimab (LY-CoV555)

Food and Drug Administration granted EUA to Bamlanivimab for usage among adults and pediatrics people 12 years of age and older, not less than 40 kg of weight and at a significant risk for further development of illness or hospitalization (Commissioner, 2020). By functioning against iSARS-CoV-2 s protein spike, the virus is stopped from penetrating and destroying human cells by Bamlanivimab.

Clinical Data

A placebo-controlled process, double-blind, phase 2 randomized testing of newly diagnosed Ambulatory patients with medium COVID-19 condition was used for the FDA's results. Bamlanivimab has not been authorized for hospitalized patients or other patients needing oxygen therapy (Commissioner, 2020). In this study 452 patients had a random IV infusion of LY-CoV555 at either of 3 doses of 2800 mg, 700 mg, 7000 mg or placebo (Chen et al, 2020). According to FDA announcement, 700 mg of bamlanivimab was administered to 101 participants of the trial, 2800 mg was given to 107 patients, 101 received 7000 mg, and a placebo was given to 156 participants within 3 days of fist COVID-19 test. In COVID-19 patients who were at higher risk, 28 days after treatment, Bamlanivimab reportedly decreased their hospital admittance and emergency department visits in comparison with placebo (3 percent vs 10 percent) (Commissioner, 2020).The EUA was released following the declaration by Eli Lilly in October, about the ineffectiveness of bamlanivimab in hospitalized patients from Covid-19. A week ago, 326 trials of drugs were discontinued for safety grounds for mild to serious covid-19 patients (Active-3 trial). (Dyer, 2020).

Casirivimab and Imdevimab (REGN-COV2)

The FDA issued EUA on 21 November 2020 for treating adults and pediatrics patients aged 12 years and older with monoclonal antibodies casirivimab and imdevimab, measuring 40 kilograms at least in moderately severe conditions and at greater risk for further disease progression (Commissioner, 2020).

These both monoclonal antibodies should be given together by IV infusion. The use for hospitalized patients under oxygen therapy are not approved for Casirivimab and imdevimab (Commissioner, 2020).

Clinical Data

In 4 late-stage clinical trials, REGN-COV2 is being evaluated. The efficacy of casirivimab and imdevimab is currently being tested for the reduction of the viral load in two-phase 2/3 trials, relative to placebo, in hospitalized and non-hospitalized adult patients of COVID-19. This FDA approval was focused on a randomized, double-blind clinical trial with placebo-control, which involved 799 adult cases not in the hospital with COVID-19 (Commissioner, 2020). 266 of these patients received 1200 mg each, a cocktail of these two MABs casirivimab and imdevimab, 267 patients received 4000 mg, each of a cocktail of casirivimab and imdevimab intravenously and 266 were placed in placebo group, three days after testing positive with COVID-19.On day 7 there was a greater reduction in viral load in patients who received a cocktail of casirivimab and imdevimab as compared to the placebo group. The hospitalization and the emergency room visits of COVID-19 patients at great risk relative to placebo patients is both decreased by Casirivimab and Imdevimab (3 percent vs 9 percent). However, its safety and effectiveness must be constantly tested.

Other Potential Agents for Treating COVID-19

Chloroquine and Hydroxychloroquine

Chloroquine and hydroxychloroquine comprise the class of antimalarial. Chloroquine shows effectiveness against in vitro SARS-CoV-2 and can contribute to immunomodulation (Gao, Tian & Yang, 2020). More than 100 patients of COVID-19 proved that chloroquine is better than control treatment, which avoids exacerbation of the pneumonia, increases pulmonary imaging studies, encourages conversations with the virus negative and decreases disease progression. (Gao, Tian & Yang, 2020).

Hydroxychloroquine also demonstrated effectiveness against the iSARS-CoV-2i virus in an in vitro analysis. Results of a non-randomized clinical trial of 36 patients of COVID-19 demonstrated a remarkable depletion in the load of virus in patients who received hydroxychloroquine relative to control patients, and after third post-inclusion day there was a substantial difference between patients who received hydroxychloroquine and patients of control group (Gautret et al, 2020)

New randomized clinical trials found little advantage of Chloroquine and hydroxychloroquine in reducing viral load, reducing death rate, or other effects in hospitalized patients of COVID-19 in comparison to routine care (Tang et al, 2020). Also, the FDA has withdrawn its EUA to administer these medications and stated that they are not effective in treating and preventing COVID-19 as it was reported that Chloroquine and hydroxychloroquine have severe heart-related adverse effects.

Azithromycin

Azithromycin belongs to the class of macrolide antibiotics. A clinical evaluation was done on 36 COVID-19 patients, 26 of them were placed in the group of hydroxychloroquine and ten in the control group. In order to eliminate secondary bacterial infections, 6 out of 26 hydroxychloroquine treated patients received Azithromycin. Patients who received both hydroxychloroquine and azithromycin recovered from the illness on the 6th day, compared with just 57.1% of the patients who were treated alone with hydroxychloroquine. (Gautret et al, 2020) This has shown the effectiveness of the combination of azithromycin and hydroxychloroquine.

Tocilizumab

Tocilizumab is a MAB, it inhibits the IL-6 inflammatory cytokine that causes reduced oxygen dissemination in the lungs. Tocilizumab is also a possible therapy for severe COVID-19. An improvement in intake of oxygen, pulmonary opacification, fever, C-reactive protein levels, and blood lymphocyte levels was seen in a clinical study conducted in China with 21 patients of COVID-19 who received tocilizumab. After 13.5 days 19 of the 21 (90.5 percent) patients were discharged from hospital showing the effectiveness of treatment with tocilizumab but further study into its effectiveness and safety is required. (Xu et al, 2020)

Interferons

IFN- α is belongs to the class of antivirals, used to treat multiple viral infections such as hepatitis, and IFN-ß is a protein produced by the body that combines the body's antiviral function. IFN-α and IFN-ß both have in vitro antiviral activity against coronavirus with IFN-ß more effective against the virus.

SARS-CoV-2 demonstrated substantial depletion of viral replication in a study conducted in-vitro after recombinant type-I IFN-α therapy. (Lokugamage et al, 2020) IFN- α is a potential treatment of COVID 19 is also advised by the Guidelines of the National Committee for Health and the State Government of Traditional Chinese Medicine. However, subsequent clinical trials are critical to check interferons safety and effectiveness for COVID-19.

Development of Vaccines

Vaccines are innocuous composition of pathogens that stimulate immune reactions in the body by creating a wide range of B and T cells. Several scientists and researchers have collaborated to develop the COVID-19 vaccine. Most vaccine applicants have used the S-protein of iSARS-CoV-2 virus. (Dhama et al, 2020) Approximately 7% of vaccines in pre-clinical studies are effective based on experience and candidates who have completed clinical trials have a 20% chance of success. (THE LATEST ON THE COVID-19 GLOBA SIYUATION & VACCINE DEVELOPMENT, 2020) In North American 36 (46%) vaccine developers are approved for success and conducted a significant part of the vaccine-enhancement process, in comparison to 14 (18%) in China, 14 (18%) in Asia (except China) and Australia and 14 (18%) in Europe. (Thanh Le et al, 2020). COVID-19 developing vaccines are produced with either live attenuated viruses, protein subunit, inactivated viruses, VLPs, replicating and non-replicating viral vectors, nanoparticles, RNA, DNA etc. with each having distinct merits and demerits (Wang, Shang, Jiang & Du, 2020). By the most recent update by the

World Health and Safety Organization (WHO) on 16 December 2020, 56 vaccine applicants are currently in the clinical stage and 166 are in ore-clinical stage (table 1) ("Draft Landscape of COVID-19 candidate vaccines", 2020).

Table 1. Number and Percentage of COVID-19 Vaccine Candidates in Clinical and Preclinical phase

S.No	Candidate vaccines in clinical phase	No. and %		S.No	Candidate vaccines in pre-clinical phase	No. and %	
1	Protein subunit	17	30%	1	Protein subunit	60	36%
2	Viral Vector (non-replicating)	9	16%	2	RNA	22	13%
3	DNA	7	13%	3	Viral Vector (non-replicating)	19	11%
4	Inactivated Virus	7	13%	4	Viral Vector (replicating)	18	11%
5	RNA	7	13%	5	DNA	16	10%
6	Viral Vector (replicating)	3	5%	6	Virus Like Particle	16	10%
7	Virus Like Particle	2	4%	7	Inactivated Virus	10	6%
8	VVr + Antigen Presenting Cell	2	4%	8	Live Attenuated Virus	2	1%
9	Live Attenuated Virus	1	2%	9	Live Attenuated Bacterial Vector	2	1%
10	VVnr + Antigen Presenting Cell	1	2%	10	Bacterial Vector (replicating)	1	1%

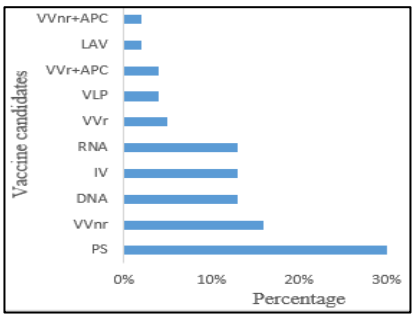

Figure 1: Bar graph showing the percentages of vaccine candidates in clinical phase.

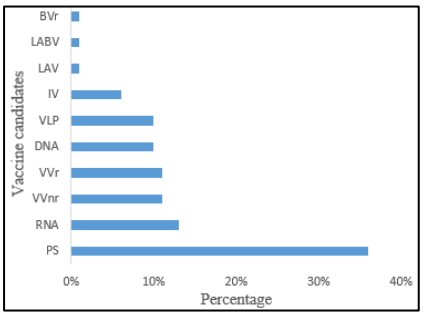

Figure 2: Bar graph showing the percentages of vaccine candidates in preclinical phase.

As of 18 December 2020, researchers tested 63 vaccines in human clinical studies and 18 reached the final stage and pre-clinically tested at least 85 in candidates of vaccine. (Corum & Zimmer, 2020) Safety and dosage of 43 vaccines are evaluated in phase 1, 20 vaccines have been tested for safety in stage 2, 18 are in wide-ranging phase 3 trials, 6 candidates are approved for early or reduced use, 2 full use vaccines have been approved and 1 vaccine has been discontinued after trials (figure 3)

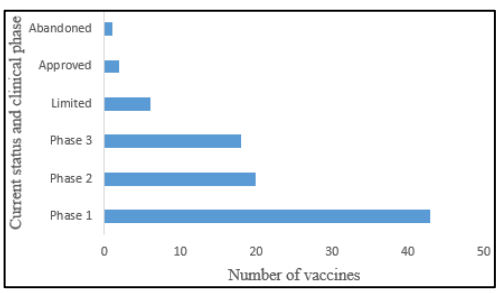

Figure 3: Bar graph showing the number of vaccines in clinical phases, limited, approved and abandoned

FDA Approved Vaccines for COVID-19

Pfizer and BioNTech Vaccine (BNT162b2)

First ever emergency use authorization of vaccine to combat COVID-19 in patients aged 16 years or older was issued by the FDA to Pfizer and BioNTech vaccine on 11 December 2020. (Commissioner, 2020). This EUA permits the delivery of Pfizer and BioNTech vaccine in the USA. Currently it is Approved/authorized in the United Kingdom, Bahrain, Canada, Mexico, United States, Singapore, Oman, Kuwait and Saudi Arabia.

Pfizer and BioNTech sent their BNTI62b2 vaccine candidate to the FDA for emergency use authorization in November 2020, after a phase III clinical vaccine trial. Pfizer and BioNTech vaccine is a nucleoside altered mRNA vaccine. It encodes the mutant version of the SARS-CoV-2 full-spike virus protein and induces immune reaction against the virus. The mRNA vaccine, BNT162b2, has been observed in a phase III trial to be up to 95 percent effective 28 days after the initial injection. (Mahase, 2020b) 170 confirmed cases of COVID-19 were analyzed and 162 were in the placebo category in this clinical study. Nine out of ten critical cases were placed in the placebo group.

Safety Data

The Phase 3 experiment started on July 27, 2020 with 43661 participants. Approximately 42% of the participants worldwide and 30% of the participants from USA had "racial and ethnic categories" while 41% global participants and 45% participants from US were 56-85 years of age (Mahase, 2020c). Pfizer found that the effectiveness was consistent across the population of the race, gender, age and different ethnic groups, while people aged 65 years and older experienced 94 percent efficacy. No research findings have yet been released by Pfizer.

A requested safety results from the randomized sub-set of some 8000 patients aged 18 and older and another safety data that was not requested from some 38000 participants of the study, who were traced for an average of two months following the second dose, was also made accessible to the review committee (Mahase, 2020c).The data review committee for the vaccine found no major safety concerns. The data examination, however, did not assess the safety and immune reaction after two weeks succeeding the second dose. (Mulligan et al, 2020)

The United Kingdom has reached an agreement for 40 million doses of BNT162b2 vaccine that will be adequate to vaccinate about 20 million people and its supply will be surprising in 2020 and 2021. The vaccine will be first administered to the home care residents and workers and after that to the health care workers and people more than 80 years of age.

Modern Vaccine (mRNA-1273)

The FDA provide EUA to the second vaccine against COVID-19 on December 18, 2020. (Commissioner, 2020). This EUA allows the vaccine to be distributed all over USA for individuals of 18 years or older. Moderna vaccine is m-RNA based vaccine known as m-RNA-1273. The body will generate various spike protein copies when the vaccination is taken, as directed by the small piece of SARS-CoV-2 mRNA in the vaccine. The spike protein produced by the body does not induce disease and generate an immune reaction to oppose SARS-CoV-2. It is known to be reasonably safe since it is neither composed of the inactivated virus nor the live virus's subunits (Tu et al, 2020).

Safety Data

Two doses of the Moderna vaccine are given to generate immunity against the virus. The second dose is given one month after receipt of the first dose. The safety evidence available in support of the EUA includes the study of 30,351 individuals participating in a continued randomized placebo evaluation performed in the United States. (Commissioner, 2020). 15,185 were in the vaccination group and 15,166 were in the placebo group where a saline placebo was taken and they received a second dose after an average of two months. Exhaustion, discomfort at the injection site, muscle suffering, headache, knee pain, chills, injection swollen lymph nodes, nausea, vomiting, and fever have been the most frequently recorded side effects. Following the second dose, the majority of such side effects were identified as after the first dose.

Effectiveness Data

An overview of 28,207 participants in the continuing randomized, placebo-controlled trial who had no signs of SARS-CoV-2 infection before to the first dose of the vaccine provides efficacy statistics to hold up the EUA. (Commissioner, 2020). The vaccination group comprises 14,134 of these participants and the placebo group 14,073. There were 11 COVID-19 patients in vaccination group and 18 COVID-19 cases in placebo and the effectiveness of vaccine was 94.1 percent to prevent the disease. The Data is not enough

to demonstrate how long this vaccine protects against COVID-19 and stops the virus from being spread from person to person.

After an interim review of its Phase III study that showed 94.5% effectiveness of the vaccine, the UK obtained 5 million dosage of the covid-19 mRNA-1273 vaccine from Moderna, a Biotech Firm of USA (Mahase, 2020a)

Other Authorized/ Approved Vaccines

According to latest update posted by Regulatory Affairs Professionals Society (RAPS) on 21 December 2020, CoronaVac, Sputnik V, BBIBP-CoV, EpiVacCorona and a Sinopharm-Wuhan's inactivated vaccine have been approved by China, Russia, UAE and Bahrain.

Table 2. Leading Vaccines in Phase 3 of Clinical Trials

Vaccine	Developer	Type	Phase	Authorization/Approval
BNT162b2	Pfizer - BioNTech	mRNA	2/3	Authorized by the FDA for emergency situation use in U.S. and other countries. Approved in Canada, UK, Bahrain, Mexico, Singapore, Oman, Saudi Arabia, Kuwait
mRNA-1273	Moderna	mRNA	3	Authorized by the FDA for emergency use in U.S
CoronaVac	SinoVac	IV	3	Restricted use in China
BBIBP-CorV	Sinopharm-Beijing	IV	3	U.A.E., Bahrain, Approved In China, limited use
No name announced	Sinopharm-Wuhan	IV	3	In China, limited use, U.A.E.
EpiVacCorona	Institute Vector	Protein	3	In Russia, early use
NVX-CoV2373	Novavax	Protein	3	--------
Sputnik V	Gamaleya	Adenovirus	3	In Russia, early use
Ad5-nCoV	CanSino	Adenovirus	3	In China, limited use
JNJ-78436735	Johnson & Johnson	Adenovirus	3	---------
AZD1222	Sweden Oxford-AstraZeneca	Adenovirus	2/3	---------

CoronaVac

It is an inactivated vaccine (formalin with alum adjuvant) developed by china based biotechnology company Sinovac biotech. CoronaVac is approved by china as a part of their emergency use program for those individuals who are at high risk including health care workers and essential personnel.

A phase 3 clinical trial with Instituto Butantan in Brazil, Indonesia and Turkey and a trial consisting of 9000 patients in healthcare industry is undergoing. A phase ½ trial with 743 healthy volunteers and a phase 1 clinical trial with 143 individuals and a phase 2 clinical trial with 600 individuals was also started by Sinovac. The vaccine was 91.4% effective based on the results of interim trial of 22,714 participants, but these results have not been reviewed yet

Sputnik V

Sputinik V is a viral vector vaccine (non-replicating).

The vaccine is being tested in phase 3 trial in Russia and internationally by the Gameleya Research Institute in Russia and the Health Ministry of Russian Federation. Russia approved this vaccine as their first COVID-19 vaccine.

The results of a continuing phase 3 trial of 40,000 individuals in Russia is yet to be published. Other than Russia the vaccine is also being evaluated in UAE and Belarus.

BBIBP-CorV

BBIBP-CorV is an inactivated viral vaccine being developed by Sinopharm China. BBIBP-CorV is approved by china as a part of their emergency use program for those individuals who are at high risk including health care workers and essential personnel. The vaccine is also authorized for use in UAE and Bahrain.

The vaccine is presently being evaluated in China in a phase 2 and phase 3 trial, and also in Argentina in a phase 3 trial. The results of the late phase trial have not yet been issued.

EpiVacCorona

EpiVacCorona is a peptide vaccine that is developed by the Vector Institute. The phase 3 trials of the vaccine have not yet been started which were to begin in November or December, but Russia has given regulatory approval to the vaccine.

An inactivated virus vaccine against COVID-19 is being developed by Wuhan institute of Virology and Sinopharm whose name is not yet announced. This inactivated vaccine is approved by china as a part of their emergency use program for those individuals who are at high risk including health care workers and essential personnel. The data of phase 3 trial for this vaccine is not yet been published.

Conclusion

COVID-19 pandemic had caused a global health emergency with currently 218 countries and territories have been affected with about 21 million people and death toll of about 1.7 millions. The effectiveness and safety of different drugs are rapidly evaluated and new COVID-19 treatments and vaccines are being developed. So far, the only approved COVID-19 treatment drug is Remdesivir. The only two FDA authorized vaccines against COVID-19 are BNT162b2 and mRNA-1273. However, the effective treatment and prevention of COVID-19 requires further research and clinical investigation as various new aspects of the disease are exploring and many infection, transmission and treatment aspects remain unclear.

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