Chapter 8
Updates in Vaccine Development Against COVID-19

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Introduction

As the world is passing through COVID-19 pandemic and many international organizations are joining hands to lead the response against the virus, the efforts to find a safe and effective vaccine are intensifying. Currently, no approved vaccines exist to prevent infection with SARS-CoV-2. Therefore, finding a safe and effective vaccine to prevent infection with SARS-CoV-2 is an urgent public health priority. Vaccines are very effective in developing immunity in the body against bacteria or viruses or any other foreign proteins against which they are directed. Therefore, when these foreign organisms later infect human body, it recognizes it and can efficiently neutralize it. Every year, vaccines save many million lives. Vaccines are available to protect against more than 20 deadly diseases, and the ones available against influenza, diphtheria, pertussis, tetanus, and measles are saving millions of

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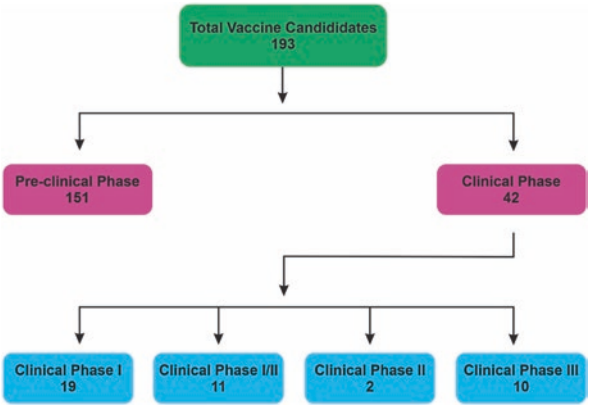
life every year. The efforts are being made at unprecedented pace to make a vaccine that could prevent the infection of SARS-COV2.



Sinovac Biotech, China

An inactivated virus vaccine manufactured by Sinovac Biotech, a Chinese biotechnology and pharmaceutical company, is being investigated in humans. The vaccine is called CoronaVac. A randomized clinical trial sponsored by the Butantan Institute is currently underway. The official title of the trial is, "Double-Blind, Randomized, Placebo-Controlled Phase III Clinical Trial to Evaluate Efficacy and Safety in Healthcare Professionals of the Adsorbed COVID-19 (Inactivated) Vaccine Manufactured by Sinovac." The study was started on July 21, 2020, and was expected to be complete by September 21, 2020 [1]. However, the trial is still recruiting and now expected to be complete by October or November 2020. CoronaVac is one of four vaccines, developed by Chinese companies, in various clinical trials.

In this clinical trial, which is a Phase III trial, CoronaVac is being assessed for its efficacy and safety. CoronaVac is an adsorbed COVID-19 (inactivated) vaccine. The primary purpose of this trial is the prevention of recruited population from COVIC-19 infection. This trial is estimated to recruit about 8870 participants. In this trial, equal number of patients will be recruited to test and control arms. Patients in the test group will receive the CoronaVac vaccine, while patients recruited in the control arm will be given placebo. The dosing protocol involves administering two doses of CoronaVac through intramuscular route, 14 days apart. Efficacy of the vaccine will be measured by detecting symptomatic COVID-19 cases in the second week after administration of the vaccine. Patients will be divided into two categories for evaluation safety of the vaccine. Adverse effects will be measured separately in the two groups, adults (18–59 years) and elderly (60 years and above). Follow-up period will be 1 year. The trial intends to detect adverse effects whose frequency is

1 in 1000 or higher for adult group and 1 in 500 in elderly patients' group. After reaching a target number of 150 patients, an interim preliminary analysis will be carried out to find out the efficacy of the vaccine.

The Chinese company which has manufactured this vaccine announces that CoronaVac will be available to be distributed throughout the world by early 2021. The company is also interested in distributing CoronaVac in the USA, for which they will require to apply to US Food and Drug Administration (FDA). The company has recently shown its intention to apply to the US FDA, once Phase III clinical trials of the vaccine are complete. The CEO of the company, Mr. Yin Weidong, is confident that they will succeed in getting the approval from the US FDA. According to him, the company was China-centric initially, but then it modified its strategy significantly in June and July 2020 and started focusing on other parts of the world as well. Now the company intends to distribute its vaccine to EU, Australia, South America, and the USA, among others. The CEO of Sinovac is confident that the quality of their product and clinical data would be sufficient to clear regulatory and safety hurdles in these countries which have historically blocked Chinese vaccines. The company is convinced that all this is to change.

1. *Wuhan Institute of Biological Products/Sinopharm, China*

   Wuhan Institute of Biological Products Co., LTD, and Sinopharm are the manufacture of this vaccine, called Vero cells. This vaccine is being tested in a Phase III trial. It is a vaccine made from inactivated novel coronavirus (nCoV). The official title of the clinical trial is, "Randomized, Double Blind, Parallel Placebo Controlled, Phase III Clinical Trial to Evaluate the Safety and Protective Efficacy of Inactivated SARS-CoV-2 Vaccine in Healthy Population Aged 18 Years and Above." This trial is being conducted in the United Arab Emirates and is approved by the Abu Dhabi Health COVID-19 Research Ethics Committee [2].

   The trial intends to establish safety and efficacy of the vaccine under investigation by evaluating it in healthy participants. This is placebo-controlled clinical trial in which one group of participants will receive investigational vaccine and the other group will receive placebo, serving as a control arm. Two doses of the vaccine or placebo will be administered. There will be 21 days interval between the first and the second dose. The estimated number of participants in each group is 5000. The primary outcome of the trial is to test the protective ability of this vaccine against COVID-19 infection at least 14 days after vaccination.

   Secondary outcomes of the trial include evaluation of preventive potential of two doses of vaccine against pneumonia and death caused by SARS-COV-2 after 14 days of the last dose; incidence of adverse effects inside 30 minutes of the vaccination and then between 0–7, 8–21, and 28 days after vaccination; incidence of severe adverse effects after 12 months of administration of the last vaccine dose; and measuring COVID-19 antibody levels in vaccinated individuals after complete vaccination.

   China is moving fast in the global completion to develop an effective vaccine to combat SARS-COV-2. It was recently announced that several Chinese citizens have already received this vaccine although the phase III clinical trial is still

underway. These individuals were vaccinated under the government-authorized, emergency use program. The provision of such an emergency use of vaccine is available in Chinese government regulations, although their scope and timing are restricted to a health emergency. It was also announced by the Chinese government officials that high-risk individuals will be given priority, implying frontline healthcare workers and elderly would be the first groups to receive the experimental vaccine.

2. *CanSino Biological Inc./Beijing Institute of Biotechnology, China*

   CanSino Biological Inc. and its collaborator Beijing Institute of Biotechnology are sponsoring a vaccine candidate, Ad5-nCoV, which is in Phase III clinical trial to assess its safety, efficacy, and immunogenicity. Ad5-nCoV vaccine is manufactured by CanSino Biological Inc. and its collaborator Beijing Institute of Biotechnology to be tested in health adults aged 18 years old and above. The official title of the trial is, "A Global Multicenter, Randomized, Double-blind, Placebo-Controlled, Adaptive Designed Phase III Clinical Trial to Evaluate the Efficacy, Safety and Immunogenicity of Ad5-nCoV in Adults 18 Years of Age and Older." The actual starting date of the trial is September 15, 2020, and estimated completion date is January 30, 2022. The study is aimed at enrolling an estimated 40,000 participants, of which 20,000 will be in experimental group and remaining 20,000 in the placebo arm of the study. Ad5-nCoV is a single dose vaccine and given through intramuscular route of administration [3, 4]. The Phase III trial recruiting locations include Shaukat Khanum Memorial Cancer Hospital and Research Center, Lahore, and Shifa International Hospital, Islamabad.

   The efficacy of Ad5-nCoV is determined by measuring its ability to prevent COVID-19 disease. Therefore, the primary outcome measures of the phase III trial include prevention of COVID-19 cases from day 28 to 12 months postvaccination. Timeframe for evaluating severe adverse event is 12 months. Secondary outcome measures include incidence of severe COVID-19 cases from day 14 to 12 months postvaccination. The trial will also evaluate the efficacy of Ad5-nCoV in preventing severe COVID-19 caused by SARS-CoV-2 infection. Incidence of solicited adverse reaction within day 0 to day 7 postvaccination will also be measured as well as the incidence of unsolicited adverse reaction with in day 0 to day 28 postvaccination. After 28 days of postvaccination, immunogenicity of S-RBD IgG antibody through ELISA method will be determined. The seroconversion rate of S-RBD IgG antibody after vaccination and cell-mediated immune response profile from day 28 postvaccination will be measured as secondary outcomes.

3. *University of Oxford/AstraZeneca, UK*

   AZD1222 candidate vaccine was co-invented by the University of Oxford and AstraZeneca. It is being manufactured by AstraZeneca for using in clinical trials. AZD1222 is a nonreplicating viral vector vaccine. The official title of the currently undergoing advanced clinical trial is, "A Phase III Randomized, Double-Blind, and Placebo-Controlled Multicenter Study in Adults to Determine the

Safety, Efficacy, and Immunogenicity of AZD1222, a Nonreplicating ChAdOx1 Vector Vaccine, for the Prevention of COVID-19" [5–8].

This clinical trial started in August 2020, and its estimated primary completion date is December 2, 2020. The trail is estimated to enroll approximately 30,000 participants. The eligibility criteria for inclusion in the trial demand for individuals older than 18 year of age, both male and female. The study objective is to assess the protective efficacy of inactivated SARS-CoV-2 vaccine (Vero cell) after complete course of immunization in preventing disease caused by SARS-CoV-2 in healthy subjects of 18 years and above. The vaccine consists of a single dose given intramuscular route. The primary outcome of the trial is to test the protecting ability of this vaccine against COVID-19 infection at least 14 days after vaccination. Secondary outcomes include measuring growth rate and antibody level (GMT, GMI) of serum antibody against COVID-19 during 12 months from first to last vaccination schedule.

4. *Janssen Pharmaceutica, USA*

Janssen Vaccines & Prevention BV is sponsoring the Phase III clinical trial of adenovirus serotype 26 vector-based vaccine (Ad26.COV2.S). It is a nonreplicating viral vector vaccine (which uses live viruses to carry DNA into human cells), also known as JNJ-78436735. This viral vector vaccine is being assessed for its efficacy in the prevention of molecularly confirmed moderate to severe/critical coronavirus infection. The study is officially named as "A Randomized, Double-blind, Placebo-Controlled Phase 3 Study to Assess the Efficacy and Safety of Ad26.COV2.S for the Prevention of SARS-CoV-2-Mediated COVID-19 in Adults Aged 18 Years and Older." The trial was initiated on September 7, 2020, and is expected to complete by March 10, 2023, with an approximated enrollment of 60,000 participants [9].

This interventional study will compare the efficacy of *Ad26.COV2.S* to a placebo, in preventing molecularly confirmed moderate to severe/critical COVID-19, among adult participants, with or without stable comorbidities which are related to the progression of coronavirus infection. The participants in the experimental arm will receive a single intramuscular (IM) injection of *Ad26.COV2.S* at a dose level of 5*10^10 virus particles (vp) on day 1, whereas participants in the control arm will receive an IM injection of placebo on day 1.

Primary endpoint measures include the number of participants with the first incidence of molecularly confirmed moderate to severe coronavirus infection having seronegative status. The secondary endpoint measures will be including the number of participants with molecularly confirmed coronavirus infection regardless of serostatus, participants requiring medical intervention, and assessment of SARS-CoV-2 viral load by quantitative reverse-transcriptase PCR. Other secondary outcomes consist of finding the number of participants with molecularly confirmed mild infection as per FDA harmonized case definition, burden of disease (BOD) based on symptomatic coronavirus infection, seroconversion between pre- and postvaccination using ELISA, and the number of participants with serious local and systemic adverse events. Secondary endpoint measures will also include assessment of SARS-CoV-2 neutralizing antibody titers by

virus neutralization assay (VNA) and SARS-CoV-2 binding antibodies by ELISA.

Earlier this year, Johnson & Johnson (J&J) and Janssen Pharmaceutical research panel, in collaboration with Beth Israel Deaconess Medical Center, produced and analyzed multiple vaccine candidates using the Janssen AdVac® technology and selected its lead vaccine candidate *Ad26.COV2-S* for the preclusion of coronavirus infection. On June 10, 2020, J&J announced that in Phase I/IIa of clinical trial, the safety, reactogenicity, and immunogenicity of adenovirus serotype 26 (Ad26) vector-based vaccine will be assessed. Data published in Nature on July 30, 2020, reported that the investigational vaccine elicited a robust immune response and successfully averted the subsequent infection and in the preclinical study provided protection in the lungs from the virus in nonhuman primates (NHPs). The study published in Nature on September 3, 2020, reported high-dose intranasal SARS-CoV-2 infection in hamsters caused severe clinical disease, high levels of virus replication, extensive pneumonia, weight loss, and mortality. A single immunization with Ad26.COV2.S protected against SARS-CoV-2-induced pneumonia, weight loss, and mortality.

5. *Moderna/NIAID, USA*

Moderna, Inc., a clinical-stage biotechnology company in the USA, is sponsoring Phase III clinical trial of its mRNA vaccine candidate *mRNA-1273* against COVID-19. The trial will be primarily evaluating the efficacy, safety, and immunogenicity of *mRNA-1273* to prevent coronavirus infection up to 2 years after the second dose of the investigational vaccine. With an estimated enrollment of 30,000 participants, this interventional study is officially named as "A Phase 3, Randomized, Stratified, Observer-Blind, Placebo-Controlled Study to Evaluate the Efficacy, Safety, and Immunogenicity of mRNA-1273 SARS-CoV-2 Vaccine in Adults Aged 18 Years and Older." It was started on July 27, 2020, and is expected to be completed by October 27, 2022. Moderna's vaccine candidate (mRNA-1273) comprises nucleoside-modified messenger RNA (mRNA) which is lipid nanoparticle encapsulated and predetermines the stabilization of SARS-CoV-2 spike (S) glycoprotein in its prefusion conformation. This S glycoprotein is essential for viral entry as it mediates host cell attachment.

The randomized, placebo-controlled trial is being conducted in the USA, testing *mRNA-1273* where participants will be receiving 1 intramuscular (IM) injection of 100 micrograms (ug) *mRNA-1273* on day 1 and on day 29 in the experimental arm and 0.9% sodium chloride (normal saline) injection in the placebo comparator arm [10]. The primary outcome will be the preclusion of symptomatic COVID-19. Key secondary outcomes include the prevention of severe COVID-19 disease (as defined by the need for hospitalization) and prevention of infection by SARS-CoV-2 regardless of symptomology. Based on the number of participants with symptomatic COVID-19, the primary efficacy investigation during Phase III study will be an event-driven analysis. To ensure the ongoing safety monitoring of the participants in the trial, data will be reviewed by an independent Data and Safety Monitoring Board organized by NIAID throughout the study.

In January 2020, Moderna announced the development of this vaccine (named *mRNA-1273*) against coronavirus infection. The Phase I human study of the vaccine candidate began in March 2020, in partnership with the US National Institute of Allergy and Infectious Diseases. On May 25, 2020, Moderna began a Phase IIa clinical trial recruiting 600 adult participants to assess safety and differences in antibody response to two doses of its candidate vaccine, *mRNA-1273*. On July 14, 2020, Moderna published preliminary results of the dose escalation during the Phase I clinical trial of the vaccine, exhibiting a dose-dependent induction of neutralizing antibodies against S1/S2, 15 days postinjection. Reported adverse reactions were mild to moderate, such as fever, fatigue, headache, muscle ache, and pain at the injection site in all dose groups, as well as the association of severity with increased dosage. Comparatively low doses were deemed safe and effective in order to proceed with a Phase III clinical trial utilizing two 100-μg doses administered with 29 days interval. A detailed study plan for the clinical trial was published by Moderna in September 2020. On September 30, CEO Stéphane Bancel said that, if the trial is successful, the vaccine might be available to the public as early as late March or early April 2021.

6. *Novavax, USA*

Novavax, Inc., USA, initiated the Phase III clinical trial of its SARS-CoV-2 recombinant spike protein nanoparticle vaccine (SARS-CoV-2 rS) also known as NVX-CoV2373 in September 2020. This interventional study is officially named as "A Phase 3, Randomized, Observer-Blinded, Placebo-Controlled Trial to Evaluate the Efficacy and Safety of a SARS-CoV-2 Recombinant Spike Protein Nanoparticle Vaccine (SARS-CoV-2 rS) with Matrix-M1™ Adjuvant in Adult Participants 18–84 Years of Age in the United Kingdom." NVX-CoV2373 consists of Matrix-M1 adjuvant which improves immunogenicity and a recombinant SARS-CoV-2 nanoparticle vaccine, constructed from the SARS-CoV-2 spike glycoprotein, which plays a role in human angiotensin-converting enzyme 2 (hACE2) receptor binding of the virus. In this latest phase of the trial, this vaccine will be assessed for its efficacy, safety, and immunogenicity against coronavirus infection in approximately 10,000 participants, aged 18–84 years [11]. The trial is aimed to register at least 25 percent of participants older than 65 years of age and will also prioritize groups that are most affected by coronavirus infection, including racial and ethnic minorities.

Participants in the experimental arm of the clinical trial will receive two doses of an intramuscular vaccine comprising 5 μg of protein antigen with 50 μg Matrix-M1™ adjuvant, administered with 21 days interval, while participants in the control arm of the trial will receive a placebo. The trial has two primary outcomes, including the first incidence of PCR-confirmed symptomatic coronavirus infection with onset at least 7 days after the second dose in participants who have not been previously infected with SARS-CoV-2 as the first primary outcome and the first incidence of PCR-confirmed symptomatic moderate or severe coronavirus infection with onset at least 7 days after the second dose in participants who have not been previously infected with SARS-CoV-2 as the second primary outcome. The primary efficacy results will be based on the number of participants

with symptomatic or moderate/severe coronavirus infection by an event-driven analysis. After reaching 67% of the desired number of these cases, an interim analysis will be carried out.

This ongoing Phase III trial is based on the Novavax's NVXCoV2373 candidate, engineered from the genetic sequence of SARSCoV2, the virus that causes coronavirus infection. This candidate vaccine was developed by Novavax in January 2020 using its recombinant nanoparticle technology to produce antigen derived from the coronavirus spike (S) protein and also consists of Novavax's patented saponin-based Matrix-M™ adjuvant. It is intended to boost the immune response and stimulate the production of neutralizing antibodies. In May 2020, the first human safety trial of the vaccine was started in Australia. During preclinical trials, NVXCoV2373 demonstrated its critical aspect of efficacy, i.e., to stimulate antibody production that blocks the binding of spike protein to receptors (virus targets). NVXCoV2373 was reported to be well tolerated and elicited robust antibody responses in its Phase I part of its Phase I/II clinical trial. Phase II trials of NVX-CoV2373 which began in South Africa in August and continued in the USA and Australia also evaluated the immunogenicity of the candidate vaccine. Research and development president at Novavax Gregory Glenn expects quick enrollment of phase III clinical trial and hopes to provide the near-term view efficacy data from the study soon. According to him, early data showing promising results are expected to support regulatory submissions for licensure in many countries across the globe including the UK, EU, and USA. The vaccine has a favorable product profile that will allow handling in an unfrozen, liquid formulation that can be stored at 2–8 °C, allowing for distribution using standard vaccine channels. Novavax hopes to manufacture up to 2 billion annualized doses, once all capacity has been brought online by mid-2021.

7. *BioNTech SE and Pfizer Inc. USA*

BioNTech SE in collaboration with Pfizer Inc. has developed a vaccine BNT162b2 which is a nucleoside-modified messenger RNA (modRNA) that expresses the SARS-CoV-2 spike glycoprotein, for strong antiviral effects against SARS-CoV-2 infection. The candidate vaccine is at the investigational stage, and the study is officially named as "A Phase 1/2/3, Placebo-Controlled, Randomized, Observer-Blind, Dose-Finding Study to Evaluate the Safety, Tolerability, Immunogenicity, and Efficacy of SARS-CoV-2 RNA Vaccine Candidates Against COVID-19 in Healthy Individuals" [12]. The study was started on April 29, 2020, and expected to be complete by December 11, 2022. It comprises of two phases: the first identifies the preferred vaccine candidate (by assessing the safety, tolerability, and immunogenicity) and its dosage, and the second will be an expanded cohort to evaluate its efficacy.

After Phase I evaluation of a two-dose schedule (21 days apart) in specified age groups, the candidate vaccine BNT162b2 is being further assessed for safety and efficacy in Phase II/III. The vaccinated participants exhibited an observable quantity of epitopes that are specific to the SARS-CoV-2 spike antigen, recognized in T cell responses. The stimulation of high levels of CD4+ and CD8+ T cell-mediated immunity against the receptor-binding domain (RBD) and the

remainder of the spike glycoprotein was also observed. It was well tolerated with mild to moderate fever in less than 20% of participants in all populations. This data supports the decision of BNT162b2 proceeding for Phase II/III, as a two-dose regimen of 30 μg dose level in approximately 30,000 participants that started in July 2020.

Kathrin U. Jansen, senior vice president and head of vaccine research and development, Pfizer, reported these encouraging results after the Phase I safety and immunogenicity data, and her confidence about the potential of the candidate vaccine *BNT162b2* to prevent many millions of SARS-CoV-2 infection cases was high. Ugur Sahin, M.D., CEO, and cofounder of BioNTech, also reported *BNT162b2* dosing completion of more than 11,000 participants and findings of previous trial exhibiting its safety profile and breadth of T cell responses and the progression toward emerging of a safe and effective vaccine candidate. Anticipating clinical success, Pfizer and BioNTech are on way to seek regulatory review of the vaccine candidate BNT162b2 as early as October 2020, and after regulatory approval they plan to provide approximately 100 million doses by the end of 2020 and approximately 1.3 billion doses by the end of 2021 worldwide.

8. *Beijing Institute of Biological Products/Sinopharm, China*

This vaccine is a joint venture of Beijing Institute of Biological Products Co., Ltd., China National Biotec Group Company Limited, and the Huesped Foundation and also sponsored by the Laboratorio Elea Phoenix S.A. They are investigating an inactivated virus vaccine in a Phase III clinical trial in Argentinian population. An inactivated virus vaccine consists of a virus that is obtained by culture and then inactivating it by chemical methods or by simply heating it. Such a virus retains its antigenic potential and can stimulate human immune system but loses its ability to cause the disease in human body. This vaccine (called Vero cells) is an inactivated SARS-COV-2 vaccine which was obtained by infecting African green monkey kidney cells with SARS-COV-2 strain HB02. These cells were then propagated through culturing and then harvested to be inactivated. After that they were concentrated and purified and an adjuvant (aluminum hydroxide) added to it. Volunteers who are administered this vaccine are expected to produce an immune response against SARS-COV-2. This vaccine has already showed in the phase I/II trials that it can produce high levels of antibodies against SARS-COV-2 and is safe.

The clinical trial to test this vaccine is an interventional study aimed to recruit approximately 3000 volunteers in a randomized control trial in which the interventional model is parallel assignment of candidate vaccine and placebo to two separate groups of volunteers. It is a double-blinded study in which both the participant and the physician will be unaware of whether they are in vaccine or placebo group. The official title of the study is "A Randomized, Double Blind, Placebo Parallel-Controlled Phase III Clinical Trial to Evaluate the Efficacy, Immunogenicity and Safety of the Inactivated SARS-COV-2 Vaccine (Vero Cell) in Argentine Healthy Population Aged Between 18 and 85 Years" [13]. The study

had started recruiting volunteers on September 16, 2020, and is expected to be complete by December 2021.

9. *Gamaleya Research Institute, Russia*

The Gamaleya Research Institute of Epidemiology and Microbiology, Health Ministry of the Russian Federation, is sponsoring this vaccine called Gam-COVID-Vac in collaboration with the government of the city of Moscow and a contact research organization, Crocus Medical BV. This vaccine is currently being investigated for its immunogenicity, safety, and efficacy in a randomized controlled, Phase III trial in which both the physician and the study participants would not know whether a participant is receiving a placebo or test vaccine. The official title of the study is "A Clinical Trial of Efficacy, Safety and Immunogenicity of Combined Vector Vaccine Gam-COVID-Vac in SARS-COV-2 Infection Prophylactic Treatment in Republic of Belarus" [14, 15].

In this study, for every participant in the placebo group, three participants will be included in the vaccine group. This means a randomization of 3 to 1 in which the reference or placebo group will contain about 10, 000 participants and the study group receiving the Gam-COVID-Vac combined vector vaccine against the SARS-CoV-2-induced coronavirus infection will have 30,000 participants. All participants will be above 18 years of age, and the total volunteers intended to be recruited for the study is 40,000. However, study participants will be further divided into five age groups: 18–30, 31–40, 41–50, 51–60, and 60+ years.

Each study participant will have one screening visit and five on-site visits to study physicians during a period of 180 ± 14 days period after the first dose of the placebo/vaccine. The participants will be administered placebo/vaccine intramuscularly during vaccination visits 1 and 2 which will be day 0 and day 21 ± 2, respectively. Participants will be asked to visit on days 28 ± 2, 42 ± 2, and 180 ± 14 for subsequent visits 3, 4, and 5, respectively. During these visits, participants' condition and well-being will be examined and recorded. Adverse effects, if any, will also be recorded. If physical visits were not possible due to unavoidable reasons, observations will be made through telemedicine consultation. Additional telemedicine consultation will be provided to all participants throughout the trial period.

In a recent press release, the head of the Gamaleya Research Institute of Epidemiology and Microbiology, Alexander Gintsburg, said that none of approximately 2000 volunteers inoculated so far with both portions of Russia's coronavirus vaccine (Gam-COVID-Vac) have contracted the disease. More data will come as more participants are recruited to the clinical trial. However, there has been global concern after Russia pushed ahead with mass vaccinations alongside randomized Phase III clinical trials of the vaccine. Some scientists have also criticized this move and insisted on prioritizing safety and efficacy of the vaccine as evidenced by the solid science rather than national prestige. However, Mr. Ginstburg defended the approach and contended that it is a war-like situation where people are dying every day like during a war and that they are not cutting corners as suggested by some media comp. He said their fast-paced approach seems alien but it is based on solid science.

Conclusions

It takes long years to develop a vaccine. The reasons it takes so long are myriad, but the first step is to investigate its safety and efficacy in animals. It takes about 6 months of strictly following animal care and handling guidelines and stringent laboratory protocols to complete preclinical studies. Once its safety and efficacy are established in animals, then the vaccine is investigated further in human clinical trials. The vaccine is required to be made at industrial scale for large-scale clinical trials. Although Phases I and II are relatively smaller, Phase III are much larger human trials often requiring tens of thousands of participants in each investigative group of the study. Safety of the vaccine is evaluated in Phase I trials, while efficacy is first established in Phase II trials. The safety and efficacy are evaluated on much larger scale in Phase III clinical trials, and it is the result of this phase which usually convinces the regulatory authority to approve or disapprove the vaccine. Although this entire process may be fast-tracked owing to the severity of the COVID-19 pandemic, safety and efficacy must not be compromised at any stage. Even after regulations are tweaked to fast-track the vaccine approval, it will be still unrealistic to expect a safe and effective vaccine within 6 months after the start of clinical trials. Additional challenges may be faced when a vaccine is approved for general use, especially for mass-producing it to meet the global demand. This would be more likely if scaling up the production involves new technologies that have not been tested previously.

Our experience with coronavirus vaccines has taught us that a safe and effective vaccine against SAR-SCOV-2 would be extremely challenging to develop. Some of the vaccines which have shown to enhance survival and decrease mortality in animals could not prevent infections in humans. Others may cause major complications such as lung damage. Therefore, thorough and long-term safety studies are necessary. Another challenge would be to ensure long-term protection against the virus. Establishing long-term immunity against the virus is relevant to COVID-19 as a significant fraction of the infected individuals are reinfected, albeit with milder symptoms. Therefore, immunity offered by the vaccine should last for many months and preferably for years. Finally, the vaccine should be effective in elderly population who are at increased risk of COVID-19 infection and whose immune system usually responds less well to vaccines than the younger population. We should ensure that the ideal vaccine must provide protection to this most vulnerable section of our population.

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