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Review Article

Immunization Priority of COVID-19 Vaccine in India

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ABSTRACT

The development of COVID-19 vaccine is of paramount importance to provide panacea to people the world over. Pharmaceutical and biotechnology companies globally are in the race to develop the lifesaving preventive vaccine. Moderna, an American pharmaceutical firm has commenced human trials. Scientists at Oxford University have started human trials in approximately 10,400 healthy adult volunteers. In India over 30 groups are involved with vaccine development, with 6 pharmaceutical and biotechnology companies. Serum Institute of India, Pune has a collaboration with Oxford University, UK, for mass production of the vaccine. The vaccine is likely to cost INR 1000/ per dose. The guidelines for priority for vaccination in India is under development by Ministry of Health, Government of India. It is recommended that the first priority should be given to frontline health workers, like doctors, nurses and paramedical personnel. second priority be given to police force and essential workers like cleaning staff, electricians, plumbers and other workers. Every current vaccine strategy has distinct advantages and disadvantages. Therefore, it is paramount that multiple strategies be advanced quickly and then evaluated for safety and efficacy.

Keywords: COVID-19 Vaccine, Prioritization, First Priority, Healthcare Professionals.

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INTRODUCTION

In December 2019, a novel coronavirus pneumonia emerged in Wuhan, China, linked initially to animal-to-human trans-mission in local wet markets. Subsequently, human-to-human transmission of the virus commenced, resulting in widespread respiratory illness in Wuhan and other urban areas of Hubei Province, China. The coronavirus then spread across China and at least 20 other nations.[1] On February 11, the World Health Organization named the virus SARS-CoV-2 and the syndrome was named COVID-19, or coronavirus disease 2019.[2] Although not as lethal as the severe acute respiratory syndrome (SARS) outbreak in 2003, COVID-19 is still characterized by severe respiratory illness and significant mortal-ity, especially among individuals over the age of 60 years and in those with underlying chronic conditions such as diabetes and hypertension.[1] Moreover, SARS-CoV-2 is highly transmissible with an estimated reproductive number (R_0) of 2.2, i.e., one infected individual is estimated to transmit the virus to 2.2 other individuals, and a mean incubation period of 5.8 days.[1]

The finding that SARS-CoV-2 is transmitted from infect-ed individuals without symptoms[3], together with its ability to cause pandemic disease within a period of weeks, suggests that control of this viral infection will be challenging without the prospect of a vaccine. Here we provide a brief overview of some of the major candidates and the challenges of implementing vaccine strategies. Since much of the information about these vaccines has not yet entered the peer-reviewed literature, for this brief overview, we rely significantly on the information made publicly available on websites and other documents.

COVID-19 AND TARGET PRODUCT PROFILE

Like the SARS coronavirus, SARS-CoV-2 is believed to have originated from bats before infecting one or more mammal species sold in Wuhan animal markets. One of the major hurdles in the early development of SARS coronavirus vaccines has been the finding of undesired immunopotentiation in the form of eosinophilic

infiltration or increased infectivity, which is noted to occur following challenge infections after immunizations with whole virus vaccines or even complete spike protein vaccines.[4] The basis of this finding is still under investigation, but it was not considered surprising given that this phenomenon also occurred with whole virus respiratory syncytial virus (RSV) vaccines.[4] Therefore, any vaccine target product profile (TPP) must give full safety considerations to avoid the immunopotentiation.

Another key element of a SARS-CoV or SARS-CoV-2 vaccine TPP is the intended target population. Currently, those at the highest risk of acquiring COVID-19 or suffering significant health deterioration are frontline healthcare workers, individuals over the age of 60 years, or those with underlying diabetes and hypertension.[5] Therefore, such populations might be prioritized for vaccine clinical trials or licensure.

The structure of a coronavirus particle is depicted on the left, with the different viral proteins indicated. The S protein is the major target for vaccine development. The spike structure shown is based on the trimeric SARS-CoV-1 spike (PDB: 5XL3). One trimer is shown in dark blue, and the receptor binding domain, a main target of neutralizing antibodies, is highlighted in purple. The other two trimers are shown in light blue. SARS-CoV-2 vaccine candidates based on different vaccine platforms have been developed, and for some of them, pre-clinical experiments have been initiated.

For one mRNA-based candidate, a clinical trial recently started to enroll volunteers shortly (ClinicalTrials.gov: NCT04283461). However, many additional steps are needed before these vaccines can be used in the population, and this process might take months, if not years.

Table 1. Vaccine Candidates in Development against SARS-CoV-2

Vaccine Type	Platform	Protein Target	Stage	Clinical Trial Designation	Company or Institution	Vaccine Name	Status
mRNA	Lipid-encapsulated mRNA	S	Phase 1	NCT04283461 (45 subjects)	Moderna	mRNA-1273	Recruiting
DNA	DNA plasmid	S	Phase 1	NCT04336410 (40 subjects)	Inovio Pharmaceuticals	INO-4800	Recruiting
Human adenovirus (Ad5)	Viral-vectored	S	Phase 1	NCT04313127 (108 subjects)	CanSino Biologics	Ad5-nCoV	Active
Chimpanzee adenovirus	Viral-vectored	S	Phase 1/2	NCT04324606 (510 subjects)	University of Oxford	ChAdOx1 nCoV-19	Planned (4/20)
Spike protein	Bacterially produced soluble protein (oral)	S	Phase 1	NCT04334980 (84 subjects)	Symvivo Corporation	bacTRL-Spike	Planned (4/30)
BCG vaccine	Immune stimulatory	None	Phase 3	NCT04327206 (4170 subjects) NCT04328441 (1000 subjects)	Murdoch Childrens Research Institute University Medical Center, Netherlands	BCG vaccine	Recruiting

Information adapted from https://ClinicalTrials.gov.

Table 1: Vaccine Candidates in Development against SARS-CoV-2

THE STRATEGIES

Shown in Table 1 is a summary of the major COVID-19 vaccines under development. This list is not exhaustive but instead reflects some of the major vaccines highlighted in company materials or publicly available documents, including biocentury.com.[7]

Whole Virus Vaccines Live-attenuated or inactive whole virus vaccines represent a classic strategy for viral vaccinations. According to an industry newsletter, Johnson & Johnson is one of the few multinational companies embarking on COVID-19 vaccines[8]; similar to their Ebola vaccine platform, they are employing Janssen's AdVac® adenoviral vector and manufacturing in their PER.C6® cell line technology.[8,9] In addition, researchers at the University of Hong Kong have developed a live influenza vaccine that expresses SARS-CoV-2 proteins.[10] Finally, Codagenix has developed a "codon deoptimization" technology to attenuate viruses[11] and is exploring SARS-CoV-2 vaccine strategies. A major advantage of whole virus vaccines is their inherent immunogenicity and ability to stimulate toll-like receptors (TLRs) including TLR 3, TLR 7/8, and TLR 9. However, live virus vaccines often require extensive additional testing to confirm their safety. This is especially an issue for coronavirus vaccines, given the findings of increased infectivity following immunization with live or killed whole virus SARS coronavirus vaccines.[4]

Subunit Vaccines Subunit vaccines for both SARS coronaviruses rely on eliciting an immune response against the S-spike protein to prevent its docking with the host ACE2 receptor.[4] Already, under funding from the Coalition for Epidemic Preparedness (CEPI), the University of Queensland is synthesizing viral surface proteins, to present them more easily to the immune system. Moreover, Novavax has developed and produced immunogenic virus-like nano-particles based on recombinant expression of the S-protein[12] while Clover Biopharmaceuticals is developing a subunit vaccine consisted of a trimerized SARS-CoV-2 S-protein using their patented Trimer-Tag® technology[14], although some full-length S-proteins for SARS also elicit increased infectivity and eosinophilic infiltration. Accordingly, a consortium led by Texas Children's Hospital Center for Vaccine Development at Baylor College of Medicine (including University of Texas Medical Branch

and New York Blood Center) has developed and tested a subunit vaccine comprised of only the receptor-binding domain (RBD) of the SARS-CoV S-protein.[4,13,14] When formulated on alum, the SARS-CoV RBD vaccine elicits high levels of protective immunity on the homologous virus challenge.

An advantage of the RBD-based vaccine is its ability to minimize host immunopotentiation.[4] Initial findings that the SARS-CoV-2 and SARS-CoV-2 RBDs exhibit more than 80% amino acid similarity and bind to the same ACE2 receptor offer an opportunity to develop either protein as a subunit vaccine as shown in Fig 1.

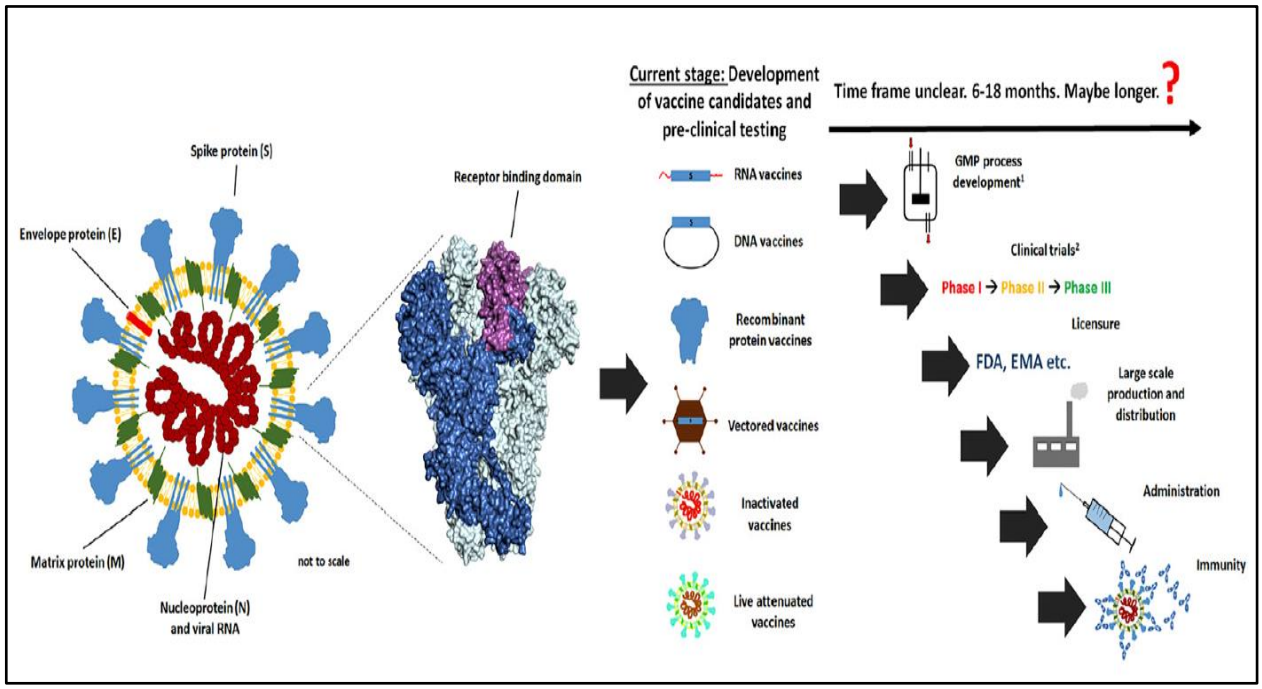

Figure 1. Overview of Potential SARS-CoV-2 Vaccine Platforms [15]

Nucleic Acid Vaccines Several major biotechs have advanced nucleic acid vaccine platforms for COVID-19. For example, Inovio Pharmaceuticals is developing a DNA vaccine, while others, such as Moderna Therapeutics and Curevac, are exploring RNA vaccine platforms. The concept of immunizing with DNA began with promising results in mice in 1993 showing protective immunity against influenza, but for de-cades, these findings have not translated to similar findings in humans. More recently, new modifications and formulations have improved nucleic acid performance in humans, with an expectation that this approach might eventually lead to the first licensed human nucleic acid vaccine.

CONCLUSION

A race is on to develop COVID-19 vaccine globally. Moderna, an American biotechnology firm has started human trials in 45 healthy adult volunteers. Scientists in Oxford University have enrolled approximately 10, 500 healthy adult volunteers for human trials. In India, over 30 groups are involved in development of the COVID-19 vaccine along with collaboration with global firms. Six pharmaceutical and biotechnology firms are working on the development of the vaccine. Serum Institute of India, Pune has tied up with Oxford University, UK for mass production of the vaccine. The approximate cost given by Serum Institute of India is approx. INR 1000 per dose. It is recommended that the first priority should be given to frontline health workers, like doctors, nurses and paramedical personnel. second priority be given to police force and essential workers like cleaning staff, electricians, plumbers and other workers. Every current vaccine strategy has distinct advantages and disadvantages.

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