DOI: 10.7860/JCDR/2020/13049.13671

Editorial

Immunology and Infectious Diseases Section

COVID-19 Pandemic: Will a Vaccine be Available Soon?

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INTRODUCTION

Coronaviruses (CoV) constitute a large family of viruses, ranging from relatively harmless ones, such as the rhinoviruses causing common cold, to more severe ones, such as the Severe Acute Respiratory Syndrome (SARS) CoV (now known as SARS-CoV-1) and the Middle East Respiratory Syndrome (MERS) CoV. SARS-CoV-1 was first detected in China in 2003, while MERS CoV was first detected in Saudi Arabia in 2012. The current SARS-CoV-2 (until recently known as 2019 novel coronavirus or 2019-nCoV) was first detected in December 2019 in Wuhan, China. The disease that this virus causes has been termed COVID-19 (*Co*rona *Vi*rus *D*isease-2019). SARS-CoV-2 is a new virus that has not been previously detected in humans. Of the two types of CoV (α and β), SARS-CoV-2 belongs to the category of β-coronaviruses [1].

Coronaviruses are zoonotic in nature, meaning that their normal reservoir are animals, but can spill-over and infect humans, causing major outbreaks. For example, SARS-CoV-1 is transmitted by civet cats, while MERS-CoV is transmitted by dromedary or one-humped camels. Bats have been found to be the animal reservoir for the current SARS-CoV-2 [1].

The most common symptoms of SARS-CoV-2 infection include fever, cough, and shortness of breath. More severe symptoms include acute respiratory distress syndrome (ARDS), pneumonia, renal failure and if left untreated, even death [1].

GENESIS AND PROGRESSION OF THE COVID-19 PANDEMIC

The very first cases of 'pneumonia of unknown cause' were reported to the World Health Organisation (WHO) from Wuhan on 31 December 2019. The cases rapidly multiplied and soon transformed into a nationwide outbreak in China, which subsequently spread to other countries. On 30 January 2020, WHO declared the SARS-CoV-2 outbreak as a *'Public Health Emergency of International Concern'*. By 11 March 2020, there were 118,000 cases in 114 countries, with 4,219 deaths. Consequently, on 12 March 2020, Dr. Tedros Adhanom Ghebreyesus, WHO's Director-General declared the outbreak as a pandemic [2, 3]. Originally, China was the worst hit, with the highest number of cases, followed by Italy. However, at the time of writing (7.30 PM- IST; 30 March, 2020), the US occupies the top spot with respect to the total number of cases (142,793 cases), followed by Italy (97,689 cases), Spain (85,195 cases) and China (81,470 cases). Interestingly, the total number of deaths in the US (2,490 deaths) is lower than Italy (10,779 deaths), Spain (7,340 deaths) and China (3,304 deaths), indicating that its pandemic response has been comparatively better than the other three countries. At this same timepoint, the global figures stand at 740,235 cases and 35,035 deaths, while India reports 1,071 cases and 29 deaths [4].

WHO'S RESPONSE TO THE COVID-19 PANDEMIC [5]

In order to tackle the COVID-19 pandemic, WHO has launched the *Strategic Preparedness and Response Plan (SPRP)*, which prioritises public health measures in countries affected by the pandemic. In February, WHO requested the global community to donate USD 675 million for supporting its SPRP initiative during the period February to April 2020. So far (as of 30 March, 2020), the WHO has received USD 622 million from the international community. The SPRP is coordinating international efforts and providing operational support to strengthen the health systems of economically weaker countries, so that they can tackle the COVID-19 pandemic on a war footing. It is also expediting priority research and innovation for developing vaccines in a time bound manner.

The immediate objectives of the plan include the following:

- Stopping human-to-human transmission of the virus.
- Reducing transmission of the virus from animal reservoirs.
- Identifying and isolating cases so that they can be treated as early as possible.
- Communicating real-time information about the outbreak so that timely precautionary measures can be taken.
- Minimising social and economic impact, especially for nations with weaker health systems.

GLOBAL VACCINE DEVELOPMENT EFFORTS: CURRENT STATUS

Vaccine development efforts are being spearheaded by the *Coalition for Epidemic Preparedness Innovations (CEPI)*, headquartered in Oslo, Norway. CEPI is a global partnership that was specifically set-up to develop vaccines in health emergencies such as the present pandemic.

The latest version (26 March, 2020) of *WHO's Draft Landscape of COVID-19 Candidate Vaccines*, clearly shows that there are a total 54 COVID-19 vaccine candidates in the pipeline, of which, two are underdoing Phase I clinical trials and 52 are in pre-clinical development [6]. All these 54 vaccine candidates are of various types and use different vaccine platforms. These vaccine platforms include (i) protein subunit (18 candidates), (ii) DNA (3 candidates), (iii) RNA (8 candidates), (iv) inactivated virus (2 candidates), (v) live-attenuated virus (2 candidates), (vi) replicating viral vector (5 candidates), (vii) non-replicating viral vector (8 candidates), (viii) virus-like particle (VLP: 1 candidate), and (ix) 7 candidates for which the vaccine platform is unknown.

COVID-19 Vaccines Undergoing Phase I Clinical Trials

The two vaccine candidates undergoing Phase I clinical trials are briefly discussed below:

RNA vaccine [7]: This RNA vaccine candidate uses messenger RNA (mRNA) molecules encoding viral sequences that generate the desired immune response following vaccination. This candidate, named as 'mRNA-1273', uses the same platform as multiple other vaccine candidates. mRNA-1273 is a novel lipid nanoparticle (LNP)-encapsulated mRNA-based vaccine that encodes for a full-length, prefusion stabilised spike (S) protein of SARS-CoV-2. This vaccine has been developed by the National Institute of Allergy and Infectious Diseases (NIAID), Maryland, USA. A Phase I, non-randomised, open-label, dose ranging clinical trial is currently being conducted in 45 men and non-pregnant women, aged between 18 and 55 years. Moderna Inc., a biotechnology company based in Cambridge, Massachusetts is manufacturing the mRNA-1273 for the clinical trial. This clinical trial is designed to assess the safety, immunogenicity and reactogenicity of mRNA-1273. The trial started on 3 March, 2020 and is expected to be completed by 1 June, 2021. The trial is being conducted at Kaiser Permanente Washington Health Research Institute, Seattle and is sponsored by NIAID, Maryland, USA.

Non-replicating viral vector vaccine [8]: This vaccine candidate uses an adenovirus type 5 vector for vaccine delivery. The same vaccine platform has been used as for the Ebola vaccine. It is currently undergoing a Phase I non-randomised, single-center, open-label, dose-escalation clinical trial in healthy adults aged between 18 and 60 years. The trial started on 16 March, 2020 and is expected to be completed by 31 December, 2020. This vaccine candidate has been developed by CanSino Biologics Inc., Tianjin and the Institute of Biotechnology, Academy of Military Medical Sciences, Beijing, China. The clinical trial is sponsored by Jiangsu Provincial Center for Disease Control and Prevention, Jiangsu, China.

Other Notable COVID-19 Vaccine Candidates

Besides the above two front-runners, there are a few other vaccine candidates that warrant special mention. These are briefly discussed below:

DNA vaccine [9,10]: This vaccine candidate (INO-4800) has been developed by Inovio Pharmaceuticals and utilises the *DNA Vaccine Platform*. This DNA vaccine uses synthetic viral genes encoding the selected antigen, which is expressed and translated into the respective protein upon delivery of the DNA vaccine construct into a potential vaccinee. The antigen activates the vaccinated person's adaptive immune system, which generates robust antibody (B-cell) and cellular (T-cell) immune responses. This DNA vaccine candidate-originally developed by Advaccine Biotech (Beijing, China)-is being taken forward by Inovio Pharmaceuticals for advanced development and is being supported by a USD 9 million grant from CEPI. This vaccine is expected to soon enter Phase I clinical trials in parallel, both in USA and China.

Protein subunit vaccine [9]: The University of Queensland, Australia is developing a protein subunit vaccine using the novel *Molecular Clamp Vaccine Platform*, which enables rapid and targeted vaccine development against specific viral pathogens. Using this technology, the synthesised viral surface proteins are 'clamped' into shape so that they are easier to recognise by the immune system as the correct antigen. The University of Queensland has received a USD 10.6 million grant from CEPI to develop this transformative new vaccine technology.

Recombinant subunit-trimer vaccine [11]: Clover Biopharmaceuticals (Chengdu, China) is developing a recombinant subunit-trimer (S-Trimer) vaccine against SARS-CoV-2 using its patented *Trimer-Tag© Technology*. This SARS-CoV-2 recombinant protein S-Trimer vaccine will be produced using a rapid mammalian cell culture-based expression system. The highly purified S-Trimer vaccine will be available within the next 6-8 weeks for pre-clinical testing in animal models. Moreover, the company has the capacity to rapidly scale-up the technology to produce large quantities of this SARS-CoV-2 vaccine.

Oral recombinant vaccine [12]: Vaxart Inc., a clinical-stage biotechnology company based in San Francisco, USA is developing an oral recombinant vaccine in tablet form, based on the published genome sequence of SARS-CoV-2. The company will be using its proprietary *VAAST™ Oral Vaccine Platform* to produce this vaccine, which will generate both mucosal and systemic immunity. Importantly, the mucosal immune response will be of particular interest as SARS-CoV-2 enters the body by infecting the mucosal lining of the upper respiratory tract.

The above vaccine candidates use rapid response platform technologies so that they can proceed for clinical testing as soon as possible. The vaccine candidates utilise the same basic backbone for making standard vaccine constructs, which can be adapted for developing vaccines for different pathogens by inserting the respective gene segments encoding specific antigens from these pathogens, which in this case is SARS-CoV-2. Importantly, GlaxoSmithKline (GSK), the leading global vaccine manufacturer, is supporting the vaccine development efforts by providing its proprietary adjuvants for boosting the vaccines.

CHALLENGES REMAIN [13]

The two major challenges that confront vaccine developers is whether a vaccine will be available in time and whether it will be possible to scale-up to produce enough doses of the vaccine.

All the vaccine candidates highlighted in the foregoing discussion use pioneering technologies that are designed to accelerate the development of vaccines in emergency situations, such as the current COVID-19 pandemic. Although research is progressing at breakneck speed, it will take at least 12 to 18 months before a safe and effective vaccine becomes available. Moreover, once a vaccine is developed, quickly mass producing it will still remain a huge hurdle. Companies like Moderna and Inovio are currently capable of manufacturing 100 million and 100,000 doses per year, respectively. The researchers at the University of Queensland indicate that they are capable of producing 200,000 doses within 6 months. Despite these efforts, the number of doses would be far from sufficient to protect the entire global population. Hence, it may just be too little too late!

REFERENCES

[1] Coronavirus. Available at: https://www.who.int/health-topics/coronavirus; Accessed on 08.02.2020.

[2] WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020. Available at: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020; Accessed on 30.03.2020.

[3] WHO announces COVID-19 outbreak a pandemic. Available at: http://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/news/news/2020/3/who-announces-covid-19-outbreak-a-pandemic; Accessed on 30.03.2020.

[4] COVID-19 coronavirus pandemic. Available at: https://www.worldometers.info/coronavirus/; Accessed on 30.03.2020.

[5] WHO Director-General's opening remarks at the media briefing on COVID-19 - 30 March 2020. Available at: https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---30-march-2020; Accessed on 31.03.2020.

[6] WHO Draft Landscape of COVID-19 Candidate Vaccines-26 March 2020. Available at: https://www.who.int/blueprint/priority-diseases/key-action/Novel_Coronavirus_Landscape_nCoV_Mar26.PDF?ua=1; Accessed on 31.03.2020.

[7] Safety and immunogenicity study of 2019-nCoV vaccine (mRNA-1273) for prophylaxis SARS CoV-2 infection. ClinicalTrials.gov, US National Library of Medicine, National Institutes of Health, USA. Available at: https://clinicaltrials.gov/ct2/show/NCT04283461?term=mrna-1273&draw=2&rank=1; Accessed on 01.04.2020.

[8] A phase I clinical trial for recombinant novel coronavirus (2019-COV) vaccine (adenoviral vector). Chinese Clinical Trial Registry (ChiCTR), Chengdu, Sichuan, China. Available at: http://www.chictr.org.cn/showprojen.aspx?proj=51154; Accessed on 01.04.2020.

[9] CEPI to fund three programmes to develop vaccines against the novel coronavirus, nCoV-2019. Available at: https://cepi.net/news_cepi/cepi-to-fund-three-programmes-to-develop-vaccines-against-the-novel-coronavirus-ncov-2019/; Accessed on: 08.02.2020.
[10] Novel coronavirus: major vaccines/drugs in the pipeline. Available at: https://www.clinicaltrialsarena.com/analysis/coronavirus-mers-cov-drugs/; Accessed on: 08.02.2020.
[11] Clover initiates development of recombinant subunit-trimer vaccine for Wuhan coronavirus (2019-nCoV). Available at: http://www.cloverbiopharma.com/index.php?m=content&c=index&a=show&catid=11&id=40; Accessed on 09.02.2020.
[12] Vaxart announces initiation of coronavirus vaccine program. Available at: https://investors.vaxart.com/news-releases/news-release-details/vaxart-announces-initiation-coronavirus-vaccine-program; Accessed on: 09.02.2020.
[13] Scientists are moving at record speed to create new coronavirus vaccines-but they may come too late. Available at: https://www.sciencemag.org/news/2020/01/scientists-are-moving-record-speed-create-new-coronavirus-vaccines-they-may-come-too; Accessed on 08.02.2020.

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PLAGIARISM CHECKING METHODS: [Jain H et al.]
- Plagiarism X-checker: Feb 10, 2020
- Manual Googling: Apr 07, 2020
- iThenticate Software: Apr 09, 2020 (12%)

ETYMOLOGY: Editorial

AUTHOR DECLARATION:
- Financial or Other Competing Interests: None
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Feb 09, 2020**
Date of Peer Review: **Mar 20, 2020**
Date of Acceptance: **Apr 07, 2020**
Date of Publishing: **May 01, 2020**