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Leading Article

Some Key Facts About COVID-19 Vaccine

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Introduction

The world is experiencing an unprecedented health crisis with severe socio-economic consequences due to the COVID-19 pandemic. The disease was declared a pandemic on 11th March 2020 by WHO. Till December 7, it had affected about 69 million people worldwide and taken away about 1.6 million lives.[1] In Bangladesh the first case was detected on 8/03/2020. Between 9th March and 7th December 2020, a total of 485,965 COVID-19 confirmed cases were reported including 6,967 related deaths.[2]

To reduce the tragic loss of life and help get the pandemic under control, along with present interventions like use of face mask, social distancing, hand washing and contact tracing, safe and effective COVID-19 vaccines are also needed. As there is no break-through in the therapeutics, general population are putting lots of hopes on the vaccines coming through, as for every infectious disease prevention is the ultimate goal.

COVID-19 Vaccine

The first novel coronavirus genome sequence was made publicly available on January 10th 2020.[3] The sequence was deposited in the GenBank database (accession number MN908947). Within weeks of its publicity companies around the world jumped into the business of vaccine research and development. In an unprecedented race over 300 vaccine candidates are in the development phases with eleven of them in phase 3 trials till end of November[4] (Table-I) with 4 companies claiming their vaccines to be effective and safe through "press release"[4] (Table-II). Each type of vaccine has different advantages and disadvantages[5] (as shown in Table-III).

Table-I

Types of COVID19 candidate vaccines being in development phase

Platform	Types	
Virus vaccines	Attenuated	Inactivated
Viral vector vaccines	Replicating viral vector	Non-replicating viral vector
Nucleic acid vaccines	DNA vaccines	RNA vaccines
Protein based vaccines	Protein sub-units	Virus-like particles
Total candidate vaccine- 300 plus, 11 in Phase-3, 4 claim effective and through "Press release"		

Table-II

Vaccines for which interim analyses were published through "press releases"

	Pfizer BioNTech	Moderna	Gamaleya	Astra Zeneca
Platform	mRNA	mRNA	ad26-Ad5 prime boost	Chimpanzee adeno-viral vector
Date of press release	Nov 9, 2020	Nov 16, 2020	Nov 11, 2020	Nov 23, 2020
Preliminary point estimate	90% (later 95%)	94.5%	92%	70% (90% in sub group)
Total number of cases	170 (8 in vaccine group)	95 (5 in vaccine group)	20	131
Severity of cases	10 severe cases non in vaccine group	11 severe cases, non in vacine group	no informaiton	None in vaccine group
Phase 3 enrollment	43,661	30,000	Target 40,000 (by time of press release 20000	24,000 (UK, Brazil, South Africa-upto 60,000 worldwide)
Cold chain requirements	Ultra cold chain: -70 degree C	-20 degree C	2-8 degree C	2-8 degree C

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Table-III

Advantages and Disadvantages with different vaccine platform

Platform	Advantages	Disadvantages
DNA vaccines	• Enhances humoral and cellular immune responses. Stable, and can be easily prepared and harvested in large quantities	• The safety and efficacy of vaccines for use in humans remain unknown
RNA vaccines	• Can be rapidly developed and have potential for low-cost manufacture.	• The properties of mRNA may influence its cellular delivery and organ distribution • Whether it is safe or not in humans, this remains unknown & require ultra cold chain
Inactivated vaccines	• Can be easily produced and stably express conformation dependent antigenic epitopes	• The unimportant antigen may skew the immune response & needs the biosafety level 3
Vector vaccines	• Can infect APCs directly, and is physically and genetically stable	• May induce prior immunity to the vector
Sub Unit vaccines	• May protect immunized animals from viral infection.	• May have limited efficacy and make immune responses unbalanced

Much like the virus, the speed of vaccine development has been unprecedented. While a candidate vaccine used to take 10-15 years in usual period, the situation is dramatic with COVID 19. Due to the scale of worldwide morbidity and mortality and crippled state of the world economy, the same vaccine development process is taking 10 months to 1.5 years only[6] (Table-IV). Countries are giving Emergency Use Authorization (EUA) using some specific clinical consideration for such authorization[7] (Table-V).

Table-IV

Accelerated way in development of vaccines during present pandemic of COVID-19

Traditional development:								
Design and exploratory preclinical studies	preclinical, toxicology studies	Investigational new drug application	Clinical trial Phase-1	Phase-2	Phase-3	Biologic license application	Regulatory review by FDA, EMA etc.	Large-scale production and distribution
(years)	2-4 yrs		1-2 yrs	2 yrs	2-3 yrs		1-2 yrs	15 yrs or longer
SARS COVID 2 vaccine development								
Design and exploratory preclinical studies	Process development preclinical, toxicology studies	Investigational new drug application	Clinical trial Phase-1 Phase-2 Phase-3			Biologic license application	Regulatory review by FDA, EMA etc.	
(months) Pre-existing from SARS-CoV and MERS- CoV	(months) Partially pre- existing and parallel development		Overlapping clinical phases			Review on a rolling basis	(1–2 months)	10m to 1.5 yrs

Table-V

Clinical considerations for Emergency Use Authorization (EUA) by FDA

- A favorable benefit/risk determination
- Efficacy with a point estimate of at least 50% vs placebo comparator an appropriately alpha-adjusted confidence interval lower bound >30%
- At least half of subjects followed for both safety and efficacy for at least 2 months following completion of the full vaccination regimen
- Safety data from throughout clinical development (over 3000 Phase-3 vaccine recipients)
- Sufficient cases of severe COVID 19 to assess for signals of enhanced disease

Although some of the vaccine candidates are receiving EUA there remains many unanswered question. So far none of the Phase 3 trials of the COVID-19 vaccines were conducted below the age of 18 years. Neither have any of the trial been conducted amongst pregnant women, though there is some data amongst those volunteers who became pregnant after the first dose. The most important concern is that we do not know how long the protection may remain.[6] Moreover, Antibody-dependent enhancement poses a theoretical obstacle to vaccine development and is being carefully evaluated. The extent to which pre-existing antibodies to SARS-CoV-2 (and potentially to SARS-CoV-1) might contribute to antibody-dependent enhancement and disease severity also remains in question. However, no evidence of antibody-dependent enhancement has been found in animal models or in humans in phase 3 clinical trials.[8] There is another concern with respect to mutations of SARS-CoV-2. Vaccine development could be obstructed if the mutated virus later evades immunity to the spike glycoprotein used to construct the vaccine. All the above scenarios need to be considered even if effective vaccines are found.[8]

Global equity in vaccine availability – ACT Accelerator, COVAX

It is expected that effective and safe vaccine will be available soon but we also need to think about its distribution! Some of the candidate vaccines require -70^{0}C storage which is available in a handful of countries. The cost could be another limiting factor. The high-tech production technology could prevent tech-transfer posing the possibility of inequity in availability of the benefit for the common people.

Luckily there are some movements in this respect. On April 24, 2020 Access to COVID-19 Tools (ACT) Accelerator was launched under the leadership of WHO. The ACT Accelerator brings together governments, scientists, businesses, civil society, philanthropists and global health organizations (with reputed organization like Bill & Melinda Gates Foundation, CEPI, FIND, Gavi, the Global Fund, Unitaid, Wellcome, WHO and the World Bank). The idea is to develop a global collaboration/partnership to accelerate development, production and equitable access to COVID-19 diagnostics, therapeutics and vaccines. The vaccine partnership, COVID-19 Vaccine Global Access (COVAX), aims to accelerate the development and manufacture of COVID-19 vaccines, and to guarantee fair and equitable access for every country in the world. The COVAX offers enough vaccines for at least 20% of the total population of the participating countries by end of 2021, secure a diverse and actively managed basket of vaccines, delivering the vaccines as soon as it will be available, thus ending the acute phase of the pandemic and helping in rebuilding the economies.[9,10] The price will be negotiated with the likelihood of participating low income and low to medium income countries getting it free or at negotiated price.

Country preparedness

Bangladesh has joined the COVAX and is expected to get vaccine for 20 % of its population. It will start coming as soon as the vaccines are authorized by WHO or relevant authorities. But before that countries needs to prepare the National Vaccine Deployment Plan (NVDP)[11-13] as per guidelines developed by SAGE, WHO, that includes among others storage, logistics, country authorization, prioritizing the population group, how to deliver and pharmaco vigilance plan. Bangladesh has already developed the NVDP as per those guidelines given.

Conclusion

Vaccine should not be considered as the only tool for the control of the COVID-19 pandemic. Public health measures like the use of facemask, hand washing, social distancing, and avoiding of unnecessary crowd are easy and affordable measures with minimum cost and needs to be implemented strictly.

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