Letter

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Latest updates on COVID-19 vaccines

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SUMMARY The ongoing outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has raised a grave concern and a severe global health burden. Since no effective drugs have been approved for satisfactory prevention and treatment, the development of COVID-19 vaccines has attracted global attention. To date, a large number of COVID-19 vaccines are being rapidly developed worldwide, with thirteen candidates in Phase 3 trials, 52 tested in clinical trials, and 162 in preclinical evaluation. Here, we summarize the latest progress of all 13 COVID-19 vaccines in Phase 3 trails. Furthermore, some vaccines have received approval or emergency use approvals. We focus on the potential issues related to vaccination including vaccine acceptance, vaccine promotion, and vaccine distribution.

Keywords COVID-19, SARS-CoV-2, vaccine acceptance, vaccine promotion, vaccine distribution

The pandemic of Coronavirus Disease 2019 (COVID-19) has raised a severe global threat. The causative pathogen novel SARS-CoV-2 (previously called 2019-nCoV) was first identified in Wuhan, China in early December 2019 and has been recently named as the Coronavirus Disease-2019 (COVID-19) by the World Health Organization (*1,2*). As of 17 December 2020, more than 74,087,090 cases of COVID-19 have been confirmed in over 200 countries and 6 continents, resulting in approximately 1,646,687 deaths (*3*). Since no effective vaccine existed, the development of a safe and effective COVID-19 vaccine, urgent for disease control, has attracted global attention.

Most recently, thirteen COVID-19 vaccines are being evaluated in Phase 3 clinical trials (Table1). Pfizer/BioNTech first confirmed that the mRNA vaccine (BNT162b2) is 95% effective against COVID-19 within 28 days after the first dose (*4*). Thereafter, the vaccine was authorized for Emergency Use Authorization (EUA) by the FDA, and approved for emergency use in early December in the UK, Canada, and the US, respectively (*5*). Another COVID-19 mRNA vaccine (mRNA-1273) was demonstrated to be 94.5% effective against COVID-19 in Phase 3 clinical trial (*6*). The Food and Drug Administration (FDA) endorsed mRNA-1273 as safe and efficacious on 15 December 2020 (*7*).

Four Adenovirus vaccines are in Phase 3 clinical trials. They are AZD1222 from AstraZeneca/Oxford, Ad26.COV2.S from Johnson & Johnson/Janssen, Ad5-nCoV from CanSino Biologics, and Gam-COVID-Vac from Gamaleya Research Institute. In their press release, AstraZeneca/Oxford reported a 70% reduction of COVID-19 infection in Phase 3 trial of AZD1222, and plan to apply for Emergency Use Authorization (EUA) with the World Health Organization in the coming week (*8-10*). The Ad5-nCoV received Military Specially-needed Drug Approval for use in the Chinese military on June 25, 2020 (*10,11*).

Of note, three companies chose the typical vaccine platform. They are inactivated vaccines, including BBIBP-CorV from the Beijing Institute of Biological Products/Sinopharm, CoronaVac from the Wuhan Institute of Biological Products/Sinopharm, and BBV152 from Bharat Biotech in India. The two vaccines from China, BBIBP-CorV and CoronaVac, submitted for a marketing application to the State Food and Drug Administration at the end of December, 2020 (*10,11*). Two protein subunit vaccines from Novavax and Anhui Zhifei Longcom Biopharmaceutical are in Phase 3 trails now. The Phase 3 trial of NVX-Cov2373 begins with 10,000 participants in both the UK and the U.S in October. The Phase 3 trial of ChiCTR2000040153 begins with 29,000 participants in July, 2020 (*10,11*).

Indeed, the main problem of vaccine development has changed to vaccine acceptance, promotion, and distribution following development of COVID-19 vaccines. It should be another global public-health challenge after ensuring the vaccines safety, efficacy, and durability. Once approved, an equitable plan for vaccine allocation according to demographic structure and underlying recipient conditions is needed (*11*).

Table 1. The thirteen COVID-19 vaccines are being evaluated in Phase 3 clinical trials

Developer	Platform	Type	Partici-pants for Phase III	Storage demands	Approval	Schedule for vaccina-tion	*Ref*
Pfizer/BioNTech BNT162, Tozinameran	RNA	3 LNP-mRNAs	44,000	–70ºC	UK, CAN, USA	Submitted for regula-tory review (02/11) Approve for EUA in UK, CAN, USA (2/12, 9/12, 11/12) 50 million does (at the end of 2020) 130 million (2021)	(*4,5*)
Moderna mRNA-1273	RNA	LNP-encapsulated mRNA	30,000	2–8ºC	unknown	Submitted for regula-tory review (30/11)	(*6,7*)
AstraZeneca/Oxford AZD1222	Non-Replicating Viral Vec-tor	ChA-dOx1-S	65,000	2–8ºC	unknown		(*8,9*)
Johnson & Johnson Ad26.COV2. S	Non-Replicating Viral Vec-tor	Adenovirus Type 26 vector	60,000	2–8ºC	unknown		(*10*)
Novavax NVX-CoV2373	Protein Subunit	Full length recombi-nant SARS CoV-2 glycopro-tein nano-particle vaccine adjuvanted with Matrix M	45,000	2–8ºC	unknown		(*10*)
Sinovac CoronaVac	Inactivated	Inactivated	26,000	2–8ºC	unknown		(*10*)
Wuhan Institute of Bio-logical Products/Sinopharm	Inactivated	Inactivated	15,000	2–8ºC	unknown		(*10*)
Sinopharm Inactivated virus, BBIBP-CorV	Inactivated	Inactivated	50,000	2–8ºC	unknown		(*10*)
Bharat Biotech BBV152	Inactivated	Whole-Virion Inacti-vated	25,000	2–8ºC	unknown	Military Special-ly-needed Drug Ap-proval for emergency use in the Chinese military (25/06)	(*10*)
CanSino Biologics Ad5-nCoV	Non-Replicating Viral Vec-tor	Adenovirus Type 5 Vector	40,000	2–8ºC	unknown		(*10*)
Gamaleya Research In-stitute Gam-COVID-Vac (Sput-nik V)	Non-Replicating Viral Vec-tor	Adeno-based (rAd26-S+rAd5-S)	40,000	–18ºC	unknown		(*10*)
Anhui Zhifei Longcom Biopharmaceuti-cal/Institute of Microbiology, Chinese Academy of Sciences	Protein Subunit	Adjuvanted recombi-nant protein (RBD-Dimer) ex-pressed in CHO cell	29,000	2–8ºC	unknown		(*10*)
Medicago Inc.	VLP	Plant-derived VLP adjuvanted with AS03	20,000	unknown	unknown		(*10*)

Moreover, a well-prepared logistical distribution model, including storage and delivery, is necessary.

Due to the drastic public health interventions taken by China to control COVID-19, only 19 cases were found on December 18, 2020. Hence, only 12.2% of respondents perceived of COVID-19 as a very high risk, which might be problematic for acceptance of COVID-19 vaccination in China (*12*). However, Wang *et al*. reported a high acceptance of COVID-19 vaccination in China (*12*). About ninety-one percent of the participants intend to receive COVID-19 vaccination, with the majority of them accepting both immunization schedules (routine or emergency immunization) and types (domestic or imported) of vaccines (*11*). Contrarily, in countries where COVID-19 is endemic, such as the United States, the willingness to vaccinate against it has dropped from 71% in April to 53.6% in October. It's reported that the proportion of COVID-19 vaccination hesitant and unwilling participants has increased from 10.5% to 14.4%, and 18.5% to 32% respectively. Undecided/ unwilling attitude toward vaccination is closely related to non-degree, black, aged 65+, high income groups, and those with concerns about potential side effects (*13*).

Promotion strategies according to different vaccination acceptance levels, should be taken for a national COVID-19 vaccine promotion program. Five COVID-19 promotion strategies were described by Kevin G et al. These strategies include making vaccines free, making access to valued settings conditional after vaccination, using public endorsements, providing priority access to those who first sign up, and transforming individual vaccination decisions into a public act (*14*).

Almost all vaccine candidates mentioned above require cool storage with different demands. The distribution chains need cooperation from both government and business for cold storage and global transport. Pfizer's shot needs to be stored at around minus 70ºC, Gam-COVID-Vac (Sputnik V) demands a minus 18ºC storage temperature, and the others need to be stored at 2-8ºC. Despite the rapid development and production of vaccines, the distribution of vaccines is still an immense task, especially among socioeconomically deprived groups, rural populations, and un-developed countries. The distribution of vaccines between these regions requires the cooperation and cross-talk of multiple governments and political circles. These regions should be assisted with efficient logistics services.

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