Latest updates on COVID-19 vaccines

Qian Li, Hongzhou Lu*

Department of Infectious Diseases, Shanghai Public Health Clinical Center, Shanghai, China.

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 trials. 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                                      | Participants for Phase III | Storage demands | Approval | Schedule for vaccination | Ref |
|-------------------------------|---------------------------|-------------------------------------------|----------------------------|-----------------|----------|--------------------------|-----|
| Pfizer/BioNTech               | RNA                       | 3 LNP-mRNAs                               | 44,000                     | -70°C           | UK, CAN, USA | Submitted for regulatory review (02/11) | (4,5) |
| BNT162, Tornameran            |                           |                                           |                            |                 |          | Approve for EUA in UK, CAN, USA (2/12, 9/12, 11/12) |     |
|                               |                           |                                           |                            |                 |          | 50 million does (at the end of 2020) |     |
|                               |                           |                                           |                            |                 |          | 130 million (2021) |     |
| Moderna mRNA-1273             | RNA                       | LNP-encapsulated mRNA                     | 30,000                     | 2-8°C           | unknown  | Submitted for regulatory review (30/11) | (6,7) |
| AstraZeneca/Oxford AZD1222    | Non-Replicating Viral Vec-tor | ChAd-dOx1-S                               | 65,000                     | 2-8°C           | unknown  |                          | (8,9) |
| Johnson & Johnson Ad26.COV2. S | Non-Replicating Viral Vec-tor | Adenovirus Type 26 vector             | 60,000                     | 2-8°C           | unknown  |                          | (10) |
| Novavax NVX-CoV2373           | Protein Subunit           | Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M | 45,000 | 2-8°C | unknown |                          | (10) |
| Sinovac CoronaVac             | Inactivated               | Inactivated                               | 26,000                     | 2-8°C           | unknown  |                          | (10) |
| Wuhan Institute of Biological Products/Sinopharm | Inactivated | Inactivated                               | 15,000                     | 2-8°C           | unknown  |                          | (10) |
| Sinopharm Inactivated virus, BBIBP-CorV | Inactivated | Inactivated                               | 50,000                     | 2-8°C           | unknown  |                          | (10) |
| Bharat Biotech BBV152         | Inactivated               | Whole-Virion Inactivated                  | 25,000                     | 2-8°C           | unknown  | Military Special-ly-needed Drug Approval 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                     | 2-8°C           | unknown  |                          | (10) |
| Gamaleya Research Institute Gam-COVID-Vac (Sput-nik V) | Non-Replicating Viral Vec-tor | Adeno-based (rAd26-S+rAd5-S)             | 40,000                     | -18°C           | unknown  |                          | (10) |
| Anhui Zhifei Longcom Biopharmaceutical Institute of Microbiology, Chinese Academy of Sciences | Protein Subunit | Adjuvanted recombinant protein (RBD-Dimer) expressed in CHO cell | 29,000 | 2-8°C | 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.

**Funding:** This work was supported by the foundation of Shanghai key Infectious Disease Project (shslczdzk01102).

**Conflict of Interest:** The authors have no conflicts of interest to disclose.

**References**

1. World Health Organization. Clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected: interim guidance, 28 January 2020. World Health Organization [https://www.who.int/iris/handle/10665/330893] (accessed December 10, 2020).
2. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020; 395:497-506.
3. World Health Organization. Coronavirus disease (COVID-19) situation reports. [https://www.who.int/emergencies/diseases/novel-coronavirus-2019/situation-reports] (accessed December 10, 2020).
4. Pfizer Press Release. Pfizer and Biotech announce vaccine candidate against Covid-19 achieved success in first interim analysis from phase 3 study. [https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-bioNTech-announce-vaccine-candidate-against-covid-19](https://www.pfizer.com/news/press-release/press-release-detail/pfizer-and-bioNTech-announce-vaccine-candidate-against-covid-19) (accessed December 11, 2020).
5. Pfizer Press Release. Our COVID-19 vaccine study—what's next? [https://www.pfizer.com/news/hot-topics/our-covid-19-vaccine-study-what-s-next](https://www.pfizer.com/news/hot-topics/our-covid-19-vaccine-study-what-s-next) (accessed December 11, 2020).
6. Moderna Press Release. Moderna's COVID-19 vaccine candidate meets its primary efficacy endpoint in the first interim analysis of the phase 3 COVE study. [https://ir.modernatx.com/news-releases/news-release-details/modernas-covid-19-vaccine-candidate-meets-its-primary-efficacy](https://ir.modernatx.com/news-releases/news-release-details/modernas-covid-19-vaccine-candidate-meets-its-primary-efficacy) (accessed December 10, 2020).
7. Moderna Press Release. Moderna announces primary efficacy analysis in phase 3 COVE study for its COVID-19 vaccine candidate and filing today with U.S. FDA for emergency use authorization. [https://ir.modernatx.com/news-releases/news-release-details/moderna-announces-primary-efficacy-analysis-phase-3-cove-study](https://ir.modernatx.com/news-releases/news-release-details/moderna-announces-primary-efficacy-analysis-phase-3-cove-study) (accessed December 10, 2020).
8. AstraZeneca Press Release. AZD1222 vaccine met primary efficacy endpoint in preventing COVID-19. [https://www.astrazeneca.us/media-centre/press-releases/2020/azd1222hr.html](https://www.astrazeneca.us/media-centre/press-releases/2020/azd1222hr.html) (accessed December 11, 2020).
9. Voysey M, Clemens SAC, Madhi SA, et al. Safety and efficacy of the ChAdOx1 nCoV-19 vaccine (AZD1222) against SARS-CoV-2: an interim analysis of four randomised controlled trials in Brazil, South Africa, and the UK. Lancet. 2020; S0140-6736(20)32661-1.
10. World Health Organization. Draft landscape of COVID-19 candidate vaccines [https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines](https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines) (accessed December 11, 2020).
11. Wang W, Wu Q, Yang J, Dong K, Chen X, Bai X, Chen X, Chen Z, Viboud C, Ajelli M, Yu H. Global, regional, and national estimates of target population sizes for covid-19 vaccination: descriptive study. BMJ. 2020; 371:m4704.
12. Wang J, Jing R, Lai X, Zhang H, Lyu Y, Knoll MD, Fang H. Acceptance of COVID-19 Vaccination during the COVID-19 Pandemic in China. Vaccines (Basel). 2020; 8:482.
13. Michael D, Eric R. Willingness to vaccinate against COVID-19 in the US: Longitudinal evidence from a nationally representative sample of adults from April-October 2020. medRxiv. 2020; [https://www.medrxiv.org/content/10.1101/2020.11.27.20239970v1](https://www.medrxiv.org/content/10.1101/2020.11.27.20239970v1) (accessed December 11, 2020).
14. Kevin G, George L, Alison M. Behaviorally informed strategies for a national COVID-19 vaccine promotion program. JAMA. 2020; doi: 10.1001/jama.2020.24036.

Received December 18, 2020; Revised December 23, 2020; Accepted December 24, 2020.

*Address correspondence to:
Hongzhou Lu, Department of Infectious Diseases, Shanghai Public Health Clinical Center, 2901 Caolang Road, Shanghai 201508, China.
E-mail: luhongzhou@fudan.edu.cn

Released online in J-STAGE as advance publication December 25, 2020.