COVID 19:
Vaccine status January 21; 2021

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Vaccine	Clinical Trials	Results	Regulatory Status

BNT-162b2 (2 injections)	**Phase 3 trial ongoing in individuals 16 y and older** **In mid-October 2020, company allowed by FDA to expand phase 3 trial to adolescents 12 y and older.**	**Primary efficacy analysis:** · **95% effective against clinically evident COVID-19 infection 28 d after 1st dose across all subgroups** [2] · **Well tolerated across all populations** [2] · **170 confirmed cases (placebo group, 162; vaccine group, 8) 10 severe cases after 1st dose (placebo group, 9; vaccine group, 1)** [2] · **Efficacy consistent across age, sex, race, and ethnicity** [2] · **Not evaluated for asymptomatic infection/ carriage** [2] · **Effective against spike N501Y substitution in UK and South Africa variants** [10]	**First approved in United Kingdom on December 2, 2020** **Approved in early December 2020 by Bahrain and Canada** **Emergency use authorized by FDA on December 11, 2020**

mRNA-1273 (2 injections)	US phase 3 trial (COVE) ongoing Phase 2/3 trial began in adolescents 12-17 y in December 2020	Primary efficacy analysis: · Efficacy rate 94.1% · 196 confirmed cases (placebo group, 185; vaccine group, 11) · Only severe illness (30 cases) was in placebo group, including 1 death [11] · 90 d after 2nd dose (30 participants): high levels of binding and neutralizing antibodies that fell but remained elevated · Well tolerated [12]	Emergency use authorized by FDA on December 18, 2020.

AZA-1222 (2 injections)	**Phase 3 trials resumed on October 23, 2020 after being paused globally on September 6.**	· **Participant in United Kingdom diagnosed with transverse myelitis, triggering temporary hold on trial.** **Interim analysis of phase 3 clinical trial in United Kingdom, Brazil, and South Africa:** · **Efficacy 90%, depending on dosage; average efficacy of 70.4% in combined analysis of 2 dosing regimens.** · **131 COVID-19 cases: from 21 d after 1st dose, 10 hospitalizations, all in placebo group (2 classified as severe; 1 death)**	**Approved in United Kingdom December 29, 2020.** **Phase 3 in United States.**

Ad26.COV2.S (1 injection)	**Phase 3 trial (ENSEMBLE) fully enrolled December, 2020 (~45,000 participants)** **Second phase 3 trial (EMSEMBLE 2) announced November 15, 2020, to study effects of 2 doses**	· **Phase 1/2a study (N = 805): Antibodies to SARS-CoV-2 observed after a single injection** · **Neutralizing antibodies against SARS-CoV-2 were detected at day 29 in 90% or more of all participants, regardless of vaccine dose or age group, and reached 100% by day 57; strong T-cell responses and a T_H1 response were also noted** [13]	**Rolling biologics license application submitted in Canada and Europe on December 1, 2020.**

NVX-CoV2373	**Phase 3 trial in United Kingdom concluded enrollment at end of November 2020.** **US and Mexico phase 3 trial began December 2020.**	**Phase 1 data showed the adjuvanted vaccine induced neutralization titers in healthy volunteers that exceeded responses in convalescent serum from mostly symptomatic patients with COVID-19.** [14]	**Phase 3**

BNT-162b2

Overview

- Genetic-code vaccine
- Storage and shipping requirements: Frozen; ultra-cold storage of -70ºC
- Requires reconstitution
- Once thawed, stable while refrigerated for up to 5 days
- Room temperature stability: 2 hours
- Dose: 2 intramuscular injections in deltoid muscle 21 days apart

BNT-152b2 (Pfizer) is a nucleoside-modified messenger RNA (modRNA) vaccine that encodes an optimized SARS-CoV-2 receptor-binding domain (RBD) antigen.

The ongoing multinational phase 3 trial included 43,548 participants 16 years and older who were randomly assigned to receive vaccine or placebo by injection; 43,448 participants received vaccine or placebo (vaccine group, 21,720; placebo group, 21,728). Approximately 42% of global participants and 30% of US participants were of racially and ethnically diverse backgrounds, and 41% of global and 45% of US participants were 56-85 years of age.

Vaccine efficacy was 95%, and no serious safety concerns were observed. The only grade 3 adverse event with a frequency of greater than 2% was fatigue at 3.8%; headache occurred in 2% of participants. Short-term mild-

to-moderate pain at the injection site was the most commonly reported reaction, and severe pain occurred in less than 1% of participants across all age groups. [9]

mRNA-1273

Overview

- Genetic-code vaccine
- Dose: 2 injections 28days apart
- No dilution required
- Shipping and long-term storage: Frozen (-20°C) for 6 months
- After thawing: Standard refrigerator temperatures (2-8°C) for 30 days
- Room temperature: Up to 12 hours

The mRNA-1273 vaccine (Moderna) encodes the S-2P antigen. The US phase 3 trial (COVE) launched on July 27, 2020. The trial was conducted in cooperation with the National Institute of Allergy and Infectious Diseases and included more than 30,000 participants who received 2 100-µg doses or matched placebo on days 1 and 29. The primary efficacy analysis was released November 30, 2020.

The COVE study (n = 30,420) included Americans 65 years and older (24.8%), younger individuals with high-risk chronic diseases (16.7%), individuals who identify as Hispanic or Latinx (20.5%), and individuals who identify as Black or African American (10.4%). [11]

Immunogenicity data at 90 days after the second vaccination was evaluated in 34 participants in the phase 3 trial. [12] A phase 2/3 trial in adolescents 12-17 years begun in December 2020 is expected to enroll 3,000 participants.

AZD-1222

Overview

- Viral vector vaccine
- Phase 3 trial was temporarily put on hold globally on September 6, 2020 after a study participant in the United Kingdom was diagnosed with transverse myelitis. After FDA review in the United States, [15] phase 3 trials resumed there on October 23, 2020.
- Storage: Refrigeration
- Dose: 2 injections 28-days apart

AZD-1222 (ChAdOx1 nCoV-19; AstraZeneca) is a replication-deficient chimpanzee adenoviral vector vaccine containing the surface glycoprotein antigen (spike protein) gene. This vaccine primes the immune system by eliciting antibodies to attack the SARS-CoV-2 virus if it later infects the

body. Owing to the testing of a different coronavirus vaccine last year, development for AZD-1222 was faster than that of other viral vector vaccines.

Results of an interim analysis of the phase 3 clinical trial in the United Kingdom, Brazil, and South Africa are as follows:

One dosing regimen (n = 2741) showed vaccine efficacy of 90% when given as a half dose, followed by a full dose at least 1 month later. Another dosing regimen (n = 8895) showed 62% efficacy when given as 2 full doses at least 1 month apart. The combined analysis from both dosing regimens (N = 11,636) resulted in an average efficacy of 70.4%. All results were statistically significant ($p < .0001$). [16] The phase 3 efficacy trial in the United States is ongoing. Concerns about the clinical trial implementation and data analysis have emerged because the half-dose regimen was not in the approved study design. [17, 18] These concerns will be addressed by regulatory agencies and await publication of the trial data.

Ad26.COV2.S

Overview

- Viral vector vaccine
- Shipping and long-term storage: Frozen (-20ºC) for up to 2 years
- After thawing: Standard refrigerator temperatures (2-8ºC) for up to 3 months
- Dose: 1 injection

The phase 3 trial (ENSEMBLE) for adenovirus serotype 26 (Ad26) recombinant vector-based vaccine (JNJ-78436735; Johnson & Johnson) was launched in September 2020 in the United States, South Africa, and South America. In December 2020, the trial was fully enrolled with approximately 45,000 participants. Interim results for the phase 1/2a trial describing neutralizing antibody titers of more than 90% at day 29 and 100% at day 57 were published in January 2021. [13]

The vaccine uses Janssen's AdVac technology, which enhances vaccine stability (ie, 2 years at -20ºC and at least 3 months at 2-8ºC). This makes the vaccine candidate compatible with standard vaccine distribution channels and new infrastructure would not be required for distribution to people who need it. [19] A second phase 3 trial (EMSEMBLE 2) to observe effects of 2 doses of the vaccine in up to 30,000 participants worldwide was announced on November 15, 2020.

NVX-CoV2373

Overview

- Subunit vaccine
- Dose: 2 injections, 21 days apart

NVX-CoV2373 (Novavax) is engineered using recombinant nanoparticle technology from SARS-CoV-2 genetic sequence to generate an antigen derived from the coronavirus spike protein. This is combined with an adjuvant (Matrix-M). Results of preclinical studies showed that it binds efficiently with human receptors targeted by the virus.

Phase 1/2 trials were initiated in May 2020. Phase 1 data in healthy adults showed that the adjuvanted vaccine induced neutralization titers that exceeded responses in convalescent serum from mostly symptomatic patients with COVID-19. [14]

The phase 3 trial in the United Kingdom has completed enrollment of 15,000 participants, including more than 25% who were older than 65 years. Researchers conducting the US and Mexico phase 3 trial, which started in December 2020, plan to enroll up to 30,000 participants.

How many vaccines are under development for coronavirus disease 2019 (COVID-19)?

Answer

The genetic sequence of SARS-CoV-2 was published on January 11, 2020, and the rapid emergence of research and collaboration among scientists and biopharmaceutical manufacturers followed. Various methods are used for vaccine discovery and manufacturing. As of late November 2020, The New York Times Coronavirus Vaccine Tracker https://www.nytimes.com/interactive/2020/science/coronavirus-vaccine-tracker.html

listed 55 vaccines in human trials, and at least 87 preclinical vaccines were under investigation in animals. [1] A number of antiviral medications and immunotherapies are also under investigation for COVID-19.