EURORDIS
RARE DISEASES EUROPE

Monthly update

Research & development of vaccines to prevent SARS-coV2 infection

Updated September 2020

Disclaimer

No vaccine against COVID-19 is approved. This document does not provide guidance on what vaccine or medicines to take. Please avoid self-prescription and always refer to your doctor before making any treatment decision.

This document provides a selection of updates on the research and development of vaccines for the current coronavirus infection. Those highlights are for the information of patient organisations/ groups, advocates and people living with a rare disease. EURORDIS takes reasonable steps to verify the accuracy of the information presented. This document does not constitute, and shall not be deemed or construed as, any approval or endorsement by EURORDIS of such product or entity.

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A 'must-read' introduction

This document provides a selection of updates on the research and development of vaccines to prevent SARS-coV2 infection that causes COVID-19. Those highlights are for the information of patient organisations/ groups, advocates and people living with a rare disease. EURORDIS takes reasonable steps to verify the accuracy of the information presented. This document does not constitute, and shall not be deemed or construed as, any approval or endorsement by EURORDIS of such product or entity.

This document does not provide guidance on what vaccines to take. Please avoid self-prescription and always refer to your doctor before making any treatment decision.

EURORDIS has a role in disseminating up-to-date information that could be useful for people living with a rare disease, who are exposed to the SARS-coV2 virus infection. Some rare diseases constitute an aggravated risk when infected by C-19. Some products being studied for C-19 are already approved or used off-label for some rare diseases, with potential information confusion and shortages risks. In other rare diseases, some products being studied for C-19 may have medicinal products interactions with medicines used in the care of these diseases. All good reasons to inform patient advocates with curated though raw information material to empower their respective actions. EURORDIS's Task Force on Drug Information, Transparency and Access (DITA) was tasked to prepare and regularly update this document. This task force is composed of EURORDIS volunteers and staff.

This document is an editorial selection and highlights the most recent developments for products being currently tested in phase III clinical trials, measuring their efficacy and toxicity. It is by no mean an exhaustive list of all therapeutic research. To avoid repeating the same situation than for the last Ebola outbreak, where the evaluation of potential treatments could not be completed (not enough participants as the trials were started too late), clinical trials against COVID-19 were authorised very soon after the epidemic started. The priority is to enrol participants in authorised trials.

For any questions or clarification, please contact François Houÿez: francois.houyez@eurordis.org

Resources

- EUnetHTA Covid-19 Rolling Collaborative Reviews https://eunethta.eu/rcr01-rcrxx/
- Horizon scanning for treatments and vaccines by the Austrian HTA institute GÖG https://eprints.aihta.at/1234/
- World Health Organization: https://www.who.int/blueprint/priority-diseases/key-action/Table_of_therapeutics_Appendix_17022020.pdf?ua=1
  All trials for COVID-19: https://www.who.int/docs/default-source/coronaviruse/covid-19-trials.xls?sfvrsn=a8be2a0a_6&ua=1
- The NIH register of clinical trials includes 210 clinicals trials to treat COVID 19 (as of 30 March 2020). You can consult here: https://clinicaltrials.gov

And also

- A review of the most advanced research was published here in March 2020:

  Research and Development on Therapeutic Agents and Vaccines for COVID-19 and Related Human Coronavirus Diseases. Cynthia Liu et al. ACS Cent. Sci., 315-331. Published 12/03/2020
  https://pubs.acs.org/doi/10.1021/acscentsci.0c00272

- Other information (infography): https://www.visualcapitalist.com/every-vaccine-treatment-covid-19-so-far
- Video on the pathophysiology of the virus, the dynamic of the pandemic and how to fight it

  https://youtu.be/BtN-goy9VOY

Vaccines in development

This document is a summary of information on vaccines in development to prevent the SARs-coV2 infection, intended for people living with a rare disease. Sources include the European Medicines Agency and EUnetHTA, the European Network of HTA Agencies that publishes rolling collaborative reviews and horizon scanning reports.

Of all vaccines in development to prevent the infection, the EURORDIS's Drug Information, Transparency and Access Task Force decided the following selection for its own review:

1. The most advanced vaccine candidates: products in clinical development already, with emphasis on products in phase II, phase II/III and/or phase III.
2. Products with specific issues on efficacy or safety for some groups of rare diseases

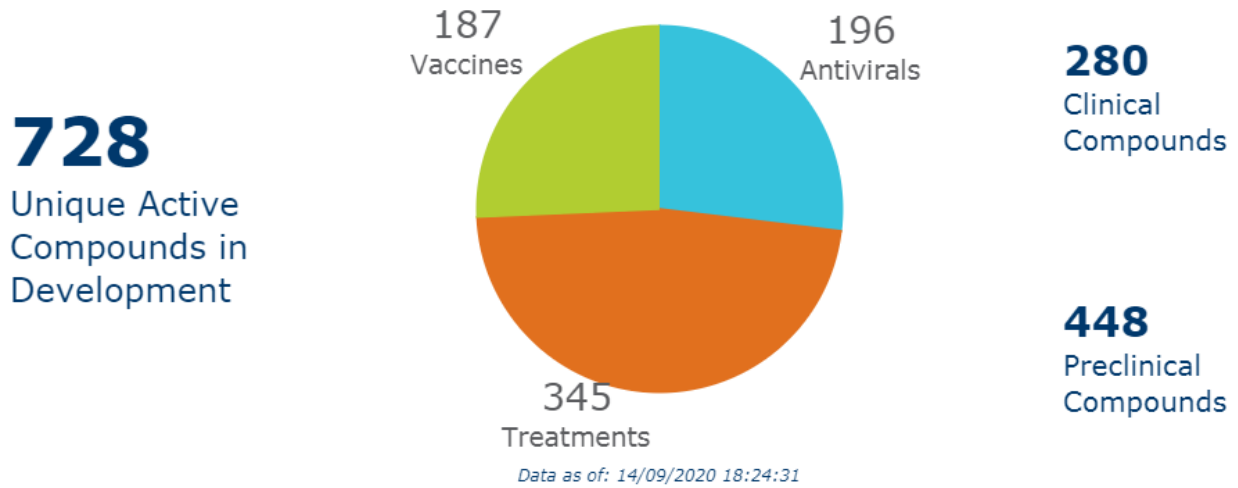

Figure 1: https://www.bio.org

Latest news

AztraZeneca vaccine trial RESTARTED

On 8 September 2020, the British-Swedish pharmaceutical company confirmed that one of the volunteers in a UK trial of the vaccine had developed an unexplained illness due to possible adverse reaction in one participant.[1]

This is the second time AztraZeneca had to suspend their vaccine trials: there was a brief trial pause in July while a safety review took place after one volunteer was confirmed to have an undiagnosed case of multiple sclerosis, which the independent panel concluded was unrelated to the vaccine.

On September 12th, the U.K. Medicines Health Regulatory Authority recommended that the study resume after an independent review of the safety data triggered a pause on Sept. 6, Oxford said in a statement. It declined to disclose details about the volunteer's illness.

No announcement was made on the status of trials outside the U.K. Trials were underway in the U.S., Brazil, South Africa and India before being paused after the safety review.

Oxford said some 18,000 people have received "study vaccines" as part of the trials. The trial started just as rates of infection in the U.K. began dropping in May, making it harder to demonstrate whether the vaccine works.

Response from 9 companies to US President for the development of a vaccine

"We, the undersigned biopharmaceutical companies, want to make clear our on-going commitment to developing and testing potential vaccines for COVID-19 in accordance with high ethical standards and sound scientific principles". The industry promise to stick to scientific principles and keep politics out of the approval process comes after President Donald Trump emphasized that a vaccine would likely be ready for public use before the Nov. 3 election. [2]

All nine companies are individually or jointly developing a candidate COVID-19 vaccine supported at least in part with federal dollars, which so far amounts to more than $10 billion (AstraZeneca, Johnson & Johnson, Moderna Inc., Novavax Inc., Merck, Sanofi and GlaxoSmithKline, and Pfizer Inc., BioNTech).

[1] ABC News Australia https://www.abc.net.au/news/2020-09-10/astrazeneca-oxford-covid-19-vaccine-trial-no-final-diagnosis/12648248

[2] Karen Weintraub and Elizabeth Weise USA TODAY. Sep 8, 2020 https://eu.usatoday.com/story/news/health/2020/09/08/covid-19-vaccine-developers-letter-politics-science/5741193002/

Vaccine platforms

Platform		Description	Examples
Inactivated		Whole virus, killed (heated or chemically). It cannot cause illness. In general, inactivated viruses do not provide as strong immune response as an attenuated virus vaccine, so repetition of doses needed	Polio virus influenza
Live attenuated		Live attenuated vaccines are made up of whole viruses that have been weakened in a lab (usually through culturing). In general, stronger immune response than inactivated vaccines	Tuberculosis Varicella MMR (Measles, mumps, rubella) Influenza
Subunit		Fragment or portion of the virus introduced into the body. This fragment is enough to be recognised by the immune response and stimulate immunity	Pertussis HPV Hep. B
Viral vector		Viral vector vaccines insert a gene for a viral protein into another, harmless virus (replicating or non-replicating). This harmless virus then delivers the viral protein to the vaccine recipient, which triggers an immune response.	Ebola Veterinary vaccines Recombinant influenza vaccine
mRNA		Work by introducing an mRNA sequence (the molecule that tells cells what to build) coded for a disease specific antigen. Once this antigen is reproduced within the body, it is recognised and triggers an immune response.	None
DNA		Work by inserting synthetic DNA of viral gene(s) into small DNA molecules called plasmids. Cells take in the DNA plasmids and follow their instructions to build viral proteins, which are recognised by the immune system, and prepare it to respond to disease exposure.	None

Updated September 2020

Vaccines

Vaccine pipeline

WHO is tracking 34 candidates in various stages of development. Here are information on the most advanced candidates (phase I-2, phase 2-3 or phase 3) with their estimated completion date (interim analysis will be performed before the end-date).

Company	Vaccine	Platform	Phase	Completion date*	Country	Reference
Moderna	mRNA-1273	RNA	Phase 3	October 2022	USA	NCT04470427
CansinoBio	Ad5-nCov	Non-replicating viral vector	Phase 2		China	
Inovio	Ino-4800	Synthesised DNA plasmid vaccine	Phase 1		China, South Korea	
Novavax		VLP recombinant nano-protein	Phase 1-2		Australia, USA	NCT04368988
GSK/Dynavax		molecular clamp	Phase 1		Australia	
CureVac	CVnCoV	mRNA-based vaccine	Phase 1		Belgium, Germany	
BioNtech/Pfizer	BNT-162	mRNA based vaccine	Phase 2-3	November 2022	USA, Germany	NCT04368728
Sinovac	CoronaVac	Inactivated virus	Phase 3	October 2021	China, Brazil	NCT04456595
GSK / Sanofi		Recombinant protein, adjuvant	Phase 1-2		USA	
AztraZeneca	ChadOx1nCov-19	Non-replicating viral vector	Phase 3	August 2021	GBR	NCT04400838
Shenzen Inst.	LV-SMENP-Dc	Lentivirus	Phase 1-2		China	
Research	BCG vaccine	Live attenuated	Phase 2-3	April 2021	Netherlands	NCT04328441
Murdoch CRI	BCG vaccine	Live attenuated	Phase 2-3	June 2021 or March 2022	Australia	NCT04327206
Sinopharm	Vero-Cell	Inactivated virus	Phase 3	July 2021	China	ChiCTR2000034780
Gamaleya	Gam-COVID-Vac	viral two-vector vaccine (sputnik v)	Phase 1-2		Russia	

Moderna - National Institute of Allergy and Infectious Diseases

Developer

ModernaTX, Inc. in collaboration with NIAID and sponsored by NIAID/ Coalition for Epidemic Preparedness Innovations (CEPI).

Description

The mRNA-1273 vaccine candidate developed by ModernaTX, Inc. in collaboration with NIAID is an encapsulated mRNA-based vaccine (mRNA-1273). It is intended for the prevention of infection through a protein of SARS-CoV-2 that is the key into the human cell. An mRNA-based virus has not been approved for use in humans yet. It is a synthetic RNA strand designed to elicit an immune-response to produce antibodies against SARS-coV2.

To learn more on mRNA vaccines and how they were discovered, an informative video by the NIH Vaccine Research Centre here: https://www.youtube.com/watch?v=uXcA-mByGfw&feature=youtu.be

Development phase

Currently, there is a phase 1 trial with 45 healthy participants (NCT04283461). It takes place in three centres in the US where the participants are split to 3 groups where they receive two injections of low, medium or high doses of mRNA-1273.

Results: After the second vaccination, serum neutralising activity was detected by two methods in all participants evaluated, with values generally similar to those in the upper half of the distribution of a panel of control convalescent serum specimens.

Moderna finalised the phase 3 protocol based on feedback from the U.S. Food and Drug Administration (FDA). The trial is currently ongoing (NCT04470427):

- Design: randomised to 1:1 placebo-controlled trial
- Enrolment: approximately 30,000 participants enrolled in the U.S
- Dose: the 100 µg dose level was chosen as the optimal dose level, based on the results of the Phase 1 study. As of 17 August 2020, a preliminary report with the results from the above-mentioned phase 1 study was published.[3]

[3] Jackson L., Anderson E., Rouphael N., Roberts P., Makhene M., Coler R., et al. An mRNA Vaccine against SARS-CoV-2 — Preliminary Report. New England Journal of Medicine. 2020. DOI: 10.1056/NEJMoa2022483.

- Interim analysis: possibly after the first 10,000 participants are recruited, depending on the occurrence of events (infections), not before mid-November 2020

CansinoBio

Developer

CanSino Biologics Inc. and the Beijing Institute of Biotechnology

Description

The AD5-nCoV vaccine candidate is a replication-defective adenovirus type 5 (viral vector) that expresses SARS-CoV-2 spike proteins (antigens). The platform (non-replicating viral vector) of AD5-nCoV was originally used for an Ebola vaccine (time to market minus 3 years).

Development phase

The first clinical phase 1 trial (ChiCTR2000030906/ NCT04313127) with 108 healthy adults is a single-centre dose-escalation study to test both the safety and tolerability of AD5-nCoV injections in three intervention groups using different dosages (low, medium and high). Specific T-cell response peaked at day 14 post-vaccination. (See results)[4]

As of 17 August, 2020 the results from the a phase 2 RCT were published:[5]

Both doses of the vaccine induced significant neutralising antibody responses to live SARS-CoV-2.

Severe adverse reactions were reported by 24 (9%) participants in the 1×10^{11} viral particles dose group and one (1%) participant in the 5×10^{10} viral particles dose group. No serious adverse reactions were documented. Authors concluded that the Ad5-vectored COVID-19 vaccine at 5×10^{10} viral particles is safe, and induced significant immune responses in the majority of recipients after a single immunisation.

[4] Zhu F et al. Safety, tolerability, and immunogenicity of a recombinant adenovirus type-5 vectored COVID-19 vaccine: a dose-escalation, open-label, non-randomised, first-in-human trial. The Lancet. 2020;395(10240):1845-1854. DOI: 10.1016/S0140-6736(20)31208-3.

[5] Zhu F. et al. Immunogenicity and safety of a recombinant adenovirus type-5-vectored COVID-19 vaccine in healthy adults aged 18 years or older: a randomised, double-blind, placebo-controlled, phase 2 trial. The Lancet. 2020;396(10249):479-488. DOI: 10.1016/S0140-6736(20)31605-6.

Inovio Ino-4800

Developer

Inovio Pharmaceuticals Inc.

Description

Ino-4800 is a DNA plasmid vaccine based on a DNA platform. The DNA is hereby synthesised in a laboratory, hence, no actual virus samples are required.

The company's DNA platform was previously utilised for a MERS-CoV vaccine (INO-4700) tested in a phase I trial.

Development phase

A phase 1 clinical trial started in April 2020. The results are aimed to be presented and published later (April 2021).

The phase 1, non-randomised, open-label, sequential assignment clinical trial (NCT04336410) in 40 healthy adult volunteers aims to evaluate the safety, tolerability and immunological profile of INO-4800 administered by intradermal (ID) injection followed by electroporation (EP) using CELLECTRA® 2000 device.

Phase 1/2 trial (NCT04447781) aims to evaluate the safety, tolerability and immunological profile of INO-4800 administered by intradermal (ID) injection followed by electroporation (EP) using the CELLECTRA® 2000 device in 160 healthy adults aged 19 to 64 years in Republic of K

To date, no completed studies in humans are available for the INO-4800 vaccine candidate.

Novavax

Developer

Novavax and co-sponsored by Coalition for Epidemic Preparedness Innovations (CEPI)

Description

Recombinant protein nanoparticle technology platform that is to generate antigens derived from the coronavirus spike (S) protein. Novavax also expects to utilise its proprietary Matrix-M™ adjuvant in order to enhance immune responses.

Development phase

Novavax initiated a Phase 1/2 clinical trial in May/June 2020. Novavax has previous experience with both MERS and SARS.

The phase 1/2, randomised, placebo-controlled, triple-blind, parallel assignment clinical trial (NCT04368988) in 131 healthy adults aims to evaluate the immunogenicity and safety of SARS-CoV-2 rS nanoparticle vaccine with or without Matrix-M adjuvant in healthy participants ≥ 18 to 59 years of age.

An interim analysis of Part 1 safety and immunogenicity data will be performed prior to an optional expansion to Part 2.

To date, no completed studies in humans are available for Novavax COVID-19 vaccine.

GSK / Dynavax

Developer

Dynavax, Glaxo Smith Kline and the University of Queensland.

Description

The potential vaccine uses a molecular clamp stabilised Spike proteins. The so-called 'molecular clamp' technology is intended to prevent infection by synthesising surface proteins and „clamping" them into shape. In so doing, the immune system may induce a response, by recognising them as the correct antigen on the surface of the virus, more easily.

Initially, this technology was designed to be a platform for generating vaccines against different viruses such as influenza, Ebola, and the MERS coronavirus.

Development phase

A Phase 1 randomised, double blind, placebo-controlled, dosage-escalation trial started on July 13, 2020 (ACTRN12620000674932/NCT04495933). The estimated study completion date is September 2021.

To date, no completed studies in humans are available for the candidate vaccine.

CureVax

Description

A protamine-complexed mRNA-based vaccine expressing undisclosed SARS-CoV-2 protein(s). This means that CureVac's technology uses mRNA as a data carrier in order to train the human body to produce ideal levels of proteins. Thereby the immune system is stimulated and can respond to antigens

Development phase

Phase 1 (NCT04449276) study aims to evaluate the safety and reacto-genicity profile after 1 and 2 dose administrations of CVnCoV at different dose levels.

AztraZeneca vaccine RESTARTED

On 8 September 2020, the British-Swedish pharmaceutical company confirmed that one of the volunteers in a UK trial of the vaccine had developed an unexplained illness due to possible adverse reaction in one participant.[6]

All trials of this vaccine, which have so far included at least 17,000 people across the UK, Brazil and South Africa, have been halted.

This is the second time: there was a brief trial pause in July while a safety review took place after one volunteer was confirmed to have an undiagnosed case of multiple sclerosis, which the independent panel concluded was unrelated to the vaccine.

On September 12th, the U.K. Medicines Health Regulatory Authority recommended that the study resume after an independent review of the safety data triggered a pause on Sept. 6, Oxford said in a statement. It declined to disclose details about the volunteer's illness.

No announcement was made on the status of trials outside the U.K. Trials were underway in the U.S., Brazil, South Africa and India before being paused after the safety review.

Oxford said some 18,000 people have received "study vaccines" as part of the trials. The trial started just as rates of infection in the U.K. began dropping in May, making it harder to demonstrate whether the vaccine works.

Developer

The ChAdOx1 nCoV-19 (AZD1222) is developed by AstraZeneca, licensed from Oxford University) vaccine candidate developed by the Jenner Institute at Oxford University.

Description

It is based on a non-replicating viral vector. A chimpanzee adenovirus platform is hereby used. This platform was previously utilised in clinical phase I trials for a vaccine against MERS.

The vaccine candidate uses a genetically modified safe adenovirus that may cause a cold-like illness. The intended prevention is through the modified adenovirus producing Spike proteins, eventually leading to the formation of antibodies to the coronavirus's Spike proteins.

[6] ABC News Australia https://www.abc.net.au/news/2020-09-10/astrazeneca-oxford-covid-19-vaccine-trial-no-final-diagnosis/12648248

Development phase

Currently, the first clinical phase 1/2 trial in 510 healthy adults is ongoing (ISRCTN 15281137).

Primary endpoints are measured within six months and an optional follow-up visit is offered at day 364. The study is estimated to be completed in May 2021.

In parallel, a Phase 2b/3 study (EUdraCT 2020-001228-32/NCT04400838) is ongoing, to determine the efficacy, safety and immunogenicity of ChAdOx1 nCoV-19. The primary endpoint is virologically confirmed (PCR positive) symptomatic COVID-19 infection.

A Phase 3 RCT (ISRCTN89951424) started in Brazil and South Africa, with another country in Africa set to follow, as well as a trial in the US. Participants are randomly allocated to receive the investigational vaccine or a well-established meningitis vaccine The study is estimated to be completed in July 2021.

Completion: August 20201. Interim analysis before, but completion needed for statistical power to analyse all 11 subgroups.

Exclusion criteria

Many rare conditions are not compatible with the inclusion in this trial (it is a phase 2b/3, with intense toxicity monitoring).

Results

As of 17 August, 2020, a preliminary report with the results from the phase 1/2 single-blind, RCT (ISRCTN 15281137/NCT04324606/EudraCT 2020-001072-15) was published. 1,077 participants were enrolled and assigned to receive either ChAdOx1 nCoV-19 (n=543) or MenACWY (n=534), ten of whom were enrolled in the non-randomised ChAdOx1 nCoV-19 prime-boost group.

There were no serious adverse events.

In the ChAdOx1 nCoV-19 group, spike-specific T-cell responses peaked on day 14. Anti-spike IgG responses rose by day 28 and were boosted following a second dose.

Authors concluded that ChAdOx1 nCoV-19 showed an acceptable safety profile, and homologous boosting increased antibody responses and together with the induction of both humoral and cellular immune responses, support largescale evaluation of this candidate vaccine in an ongoing phase 3 programme.[7]

[7] Folegatti P. et al. Safety and immunogenicity of the ChAdOx1 nCoV-19 vaccine against SARS-CoV-2: a preliminary report of a phase 1/2, single-blind, randomised controlled trial. The Lancet. 2020;396(10249):467-478. DOI: 10.1016/S0140-6736(20)31604-4.

BioNTech

Developer

Developed by BioNTech in collaboration with Fosun Pharma and Pfizer

Description

mRNA platform-based vaccine expressing codon-optimized undisclosed SARS-CoV-2 protein(s)

Development phase

BNT-162 entered clinical testing by the end of April 2020 and R&D is supposed to be carried out both in the US and in Germany. This is a phase 1/2, randomised, placebo-controlled, triple-blind, dose-finding, and vaccine candidate-selection study in healthy adults (NCT04368728/EudraCT 2020-001038-36).

Phase 2/3 RCT has started also (NCT04368728/EudraCT 2020-002641-42) with aim to describe the safety, tolerability, immunogenicity and efficacy of BNT-162. The estimated number of participants is 29481, and completion study date November 2022.

To date, no completed studies in humans are available for the BNT-162 vaccine.

SinoVac

Developer

The private Chinese biopharmaceutical company Sinovac Biotech Ltd.

Description

CoronaVac, an inactivated COVID-19 vaccine candidate.

Development phase

The phase 1 and 2 trials started on April 16, 2020 in Jiangsu Province, China.

According to Sinovac announcement, preliminary phase I/II results showed that there was no serious adverse event after vaccinating a total of 743 volunteers. 90% seroconversion was observed in the phase II clinical trial 14 days after completion of a two-dose vaccination at day 0 and day 14

A Phase II study on elderly adults is being conducted which will be followed by child and adolescent groups. The phase II trial is expected to be completed at the end of 2020.

Sinovac registered a new Phase 3 RCT (NCT04456595), aiming at assessing efficacy and safety of the Adsorbed COVID-19 (inactivated) vaccine in health care professionals in Brazil. Estimated number of participants is 8,870.

Interim preliminary efficacy analysis can be triggered by reaching the target number of 150 cases. The study is estimated to be completed in October 2021.

China National Pharmaceutical Group Corporation (SINOPHARM)

Developer

Sinopharm is a state-owned Chinese company

Description

Vero-Cell is a β-propiolactone–inactivated whole-virus vaccine against COVID-19.

Development phase

A phase 3 double-blind, placebo controlled RCT has been initiated (ChiCTR2000034780), to evaluate the protective efficacy of inactivated SARS-CoV-2 Vaccine (Vero Cell) after full course of immunisation in healthy subjects aged 18 years old and above. The study is estimated to be completed in July 2021.

Sanofi-GSK

Developer

Sanofi developers a recombinant protein (technology already use for a flu vaccine) while GSK provides an adjuvant.

Development phase

A phase 1-2 randomised, double-blinded, placebo controlled trial is in progress with 440 participants (NCT04537208), recruiting in the USA only.

A phase 3 trial could be submitted end 2020.

BCG Vaccine

Developer

Two research groups, one in the Netherlands, and one in Australia.

Description

Live attenuated virus: repurposing thee BCG vaccine, originally for tuberculosis, to fight SARS-CoV2 in healthcare workers at high risk.

Development phase

RCTs in Netherlands (BCG-CORONA phase 3 trial, NCT04328441) and Australia (BRACE phase 3 trial, NCT04327206) aim to assess whether BCG-Danish reduces the incidence and severity of COVID-19 in health-care workers, and the effect this has on days off work.

1,000 healthcare professionals to be enrolled in 8 hospitals to receive the vaccine or placebo.

Sputnik V Vaccine (Russia)

This Russian COVID-19 vaccine Sputnik V is the first in the world with a national authorisation for human use. It was approved for public use even ahead of its Phase III trial. No trial data are published.

Developer

Gamaleya Research Institute of Epidemiology and Microbiology,

Description

Gam-COVID-Vac is a viral two-vector vaccine based on the human adenovirus, a common cold virus, fused with the spike protein of SARS-CoV-2 to stimulate an immune response.

Development phase

Sputnik V is approved for distribution in Russia, despite having been tested only in a small number of people in early-stage clinical trials that lasted two months, normally a process requiring a year or more of clinical assessment for proof of vaccine safety and efficacy against viral disease.[8]

In fact, no phase 3 trial has started as of September 2020.

[8] "Safety and immunogenicity of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine in two formulations: two open, non-randomised phase 1/2 studies from Russia". The Lancet: 1–11. 4 September 2020. doi:10.1016/S0140-6736(20)31866-3.

Initiatives of interest

Vaccine trials and initiatives

COVID-19 Prevention Trial Network (COVPN)

NIAID established a new clinical trials network - The COVID-19 Prevention Trials Network (COVPN), that aims to enroll thousands of volunteers in large-scale clinical trials testing a variety of investigational vaccines and monoclonal antibodies intended to protect people from COVID-19.

The first Phase 3 clinical trial that the COVPN is expected to conduct with the investigational mRNA-1273 vaccine, developed by NIAID scientists and their collaborators at Moderna, Inc., based in Cambridge, Massachusetts.[9]

ACCESS (vACcine Covid-19 monitoring ReadinESS)

Utrecht scientists (in close collaboration with RIVM, Netherlands Pharmacovigilance centre LAREB and the PHARMO Institute in the Netherlands) are leading an European project with the aim to create an infrastructure and to prepare European organisations to collaboratively evaluate the benefits, coverage and risks of the novel COVID-19 vaccines in their post-licensure phase. The project is funded by the European Medicines Agency (EMA).[10]

COVAX

The COVAX initiative consists in purchasing distributing fairly two billion vaccine doses in 2021. It emerged from the World Health Organization (WHO), the Coalition for Epidemic Preparedness Innovations (CEPI) and from GAVI, the Vaccine Alliance.

[9] https://www.nih.gov/news-events/news-releases/nih-launches-clinical-trials-network-test-covid-19-vaccines-other-prevention-tools
[10] https://www.uu.nl/en/news/monitoring-the-benefits-and-safety-of-the-new-corona-vaccines

NIAID Vaccine Research Centre

Almost of developments of SARS-coV2 vaccines derive from research for an HIV vaccine.[11]

[11] Barney Graham, Deputy Director, Vaccine Research Centre

Cheat Sheet: **COVID-19 vaccine pipeline**

AVAC
25 Years and Counting

Primary sponsor(s)	Description	Platform	Funders	Status	Considerations	Read more
U. of Oxford AstraZeneca	AZD1222 *Chimpanzee Adeno vector expressing SARS-CoV-2 spike protein.*	Viral vector	USG ($1.2B) CEPI/GAVI ($750M) IT, FR, DE and NL ($843M) *Warp Speed* Finalist* *COVAX** Portfolio*	Ph. I/II ongoing: 1090 vols/UK Ph. II/III ongoing: • 10,260 vols/UK, • 2000/Brazil, RSA Ph3 expected: 30K vols/US (Aug. 2020) *Efficacy data expected Sept. 2020.*	Immunogenicity: Preliminary Ph. I/II data showed both antibody and T-cell responses. Manufacturing/delivery: Adeno vector vaccines could conceivably be manufactured quickly and at scale (capacity to produce 2B doses has already been secured). Platform history: No Adeno vector vaccines currently licensed for use in humans.	*Science*
Moderna	mRNA-1273 *Synthetic messenger RNA that encodes for SARS-CoV-2 spike protein.*	mRNA	USG ($955M) CEPI/GAVI (Undisclosed) *Warp Speed Finalist* *COVAX Portfolio*	Ph. I ongoing: • 155 vols/US • Preliminary data Ph. II ongoing: 600 vols/US Ph. III ongoing: 30,000 vols/US *Efficacy data expected Nov. 2020.*	Immunogenicity: Ph. I data showed after two doses volunteers had more neutralizing antibodies than most individuals who have recovered from COVID. Manufacturing/delivery: mRNA vaccines are relatively easy to scale and manufacture (potential for 1B doses by 2022); likely to require two doses, but a third may be necessary. Platform history: No licensed mRNA vaccines.	Moderna Statement
Inovio	INO-4800 *DNA plasmid vaccine with electroporation.*	DNA	CEPI ($17.2M) BMGF ($5M) USG ($71M) *COVAX Portfolio*	Ph. I ongoing: 40 vols/US Ph. II/III ongoing: 160 vols/S Korea Ph. II/III trial planned: Q2/3 2020	Immunogenicity: Preliminary Ph. I data shows antibody and cellular immune responses. Manufacturing/delivery: INO-4800 is stable at room temperature for more than a year and is not required to be frozen in transport or storage. Platform history: No licensed DNA vaccines for use in humans.	Inovio Ph. 1 Statement
Novavax	NVX-COV2373 *Full-length recombinant SARS-CoV-2 glycoprotein nanopartical vaccine adjuvanted with Matrix M.*	Protein Subunit	CEPI ($388M) USG ($1.6B) *Warp Speed Finalist* *COVAX Portfolio*	Ph. I ongoing: 130 vols/Australia Ph. II ongoing: 2900 vols/ RSA Ph. III planned: 30,000 vols/US+ (Oct. 2020)	Immunogenicity: Ph. I data showed both antibody and T-cell responses. Manufacturing/delivery: GMP production initiated with capacity for large-scale manufacturing (est. 1B doses by end of 2021). Platform history: The same nanoparticle platform succeeded in a Ph. III trial for NanoFlu, an influenza vaccine for older adults.	Novavax statement
J&J	Ad26.SARS-CoV-2 *Ad26 vector expressing SARS-CoV-2 spike protein.*	Viral vector	J&J investment (~$500M) USG ($456M) *Warp Speed Finalist*	Ph. I/IIa ongoing: 1045 vols/US and Belgium Ph. III planned: 30K vols/US+ (Sept 2020)	Immunogenicity: Preclinical data shows that protected monkeys after one dose; the potential for preexisting immunity against Ad 26. Manufacturing/delivery: TBC. Platform history: Utilizes the same technology used to make its Ebola vaccine, which was granted European regulatory approval in May 2020.	*Nature*
Merck / IAVI	*VSV vector expressing SARS-CoV-2 spike protein.*	Viral vector	USG ($38M)	Preclincial	Immunogenicity: TBC, though replicating viral vectors potentially lead to robust immune responses triggered by a single dose. Manufacturing/delivery: TBC. Platform history: Use of an established vaccine technology (Ebola) could speed development.	IAVI Statement
Pfizer / BioNTech	BNT162b2 *mRNA that encodes for SARS-CoV-2 spike protein.*	mRNA (x4)	Pfizer ($500M) USG ($1.9M) *Warp Speed Finalist*	Ph. I/II ongoing: 200 vols/Germany Ph. II/III ongoing: 30K vols/US, Brazil, Argentina, Germany (120 sites)	Immunogenicity: Ph. I/II data shows both neutralizing antibody and T-cell responses. Manufacturing/delivery: mRNA vaccines are relatively easy to scale and manufacture. Platform history: No licensed mRNA vaccines.	*New York Times*
Imperial College	*Synthetic self-amplifying RNA producing SARS-CoV-2 spike protein.*	Self-amplifying RNA	UK ($50.7M) Philanthropies ($6.2M)	Ph. I/II ongoing: 300 vols/UK Ph. III planned: 6000/UK	Immunogenicity: TBC. Manufacturing/delivery: Imperial College created a special-purpose company to sell the vaccine (VacEquity) at lowest possible cost in UK and LMICs. Platform history: No licensed self-amplifying RNA vaccines.	*New York Times*
CureVac	CVnCoV *mRNA vaccine that encodes for the spike protein formulated with lipid nanoparticles.*	mRNA	CEPI ($8.3M) EC ($86.2M) DE ($335M) USG. (Undisclosed) *COVAX Portfolio*	Ph. I ongoing: 168/Germany, Belgium	Immunogenicity: TBC. Manufacturing/delivery: mRNA vaccines are relatively easy to scale and manufacture. Platform history: No licensed mRNA vaccines.	CureVac statement

Primary sponsor(s)	Description	Platform	Funders	Status	Considerations	Read more
CanSino Biologics	Ad5-nCoV *Ad5 vector expressing SARS-CoV-2 spike glycoprotein.*	Viral vector	No funding disclosed.	Ph. I complete: 108 vols/China (published) Ph. II ongoing: • 508 vols/China • 696 vols/Canada	Immunogenicity: Ph. I participants developed binding antibodies, neutralizing antibodies and T-cell responses; potential for pre-existing immunity against Ad5. Manufacturing/delivery: TBC. Platform history: Received Chinese military approval as a "specially needed drug".	*Lancet* *FiercePharma*
Clover BioPharma / GSK	SCB-2019 *A trimeric subunit spike protein developed by China-based Clover, delivered alongside an adjuvant.*	Subunit	CEPI ($3.5M)	Ph. I ongoing: 150 vols/Australia Ph. II/III planned.	Immunogenicity: In preclinical studies, adjuvanted SCB-2019 induced neutralising antibodies in animals. Manufacturing/delivery: The adjuvant system is designed to boost the immune response and allow less to be used per dose, potentially allowing more doses to be supplied. GSK will manufacture 1B doses of its adjuvant system in 2021. Platform history: TBC.	Press release
Sanofi / GSK	*DNA from the surface protein of the SARS-CoV-2 virus is inserted into insect cells, which express antigen that is then purified and combined with GSK's pandemic AS03 adjuvant.*	Subunit	USG ($2.1B) *Warp Speed Finalist*	Ph. I/II planned: Sept. 2020 Ph. III planned: 30K vols/ US+ (Dec. 2020)	Immunogenicity: TBC Manufacturing/delivery: The adjuvant system is designed to boost the immune response and allow less to be used per dose, potentially allowing more doses to be supplied. GSK will manufacture 1B doses of its adjuvant system in 2021. Platform history: Same platform as vaccine candidates for Influenza, SARS-CoV (FDA approved vaccine).	Sanofi Statement

The COVID-19 vaccine pipeline 'Cheat Sheet' reflects front-runner candidates along with products with significant investments from the USG, CEPI and the ACT-A COVAX pillar.

Refresher on vaccine platforms

Platform	About	Licensed products	Learn more
Inactivated	Inactivated vaccines consist of the whole virus, which has been killed with heat or chemicals so that it can't cause illness. In general, inactivated virus vaccines do not provide as strong of an immune response as live attenuated vaccines, so additional doses may be needed.	Polio	*Inactivated viral vaccines*
Live attenuated	Live attenuated vaccines are made up of whole viruses that have been weakened in a lab (usually through culturing). They tend to elicit a stronger immune response than inactivated vaccines.	MMR Varicella TB	*Live attenuaed vaccines- historical successes and current challenges*
Subunit	Subunit vaccines introduce a fragment or portion of the virus into the body. This fragment is enough to be recognized by the immune response and stimulate immunity.	Pertussis HPV Hep. B	*Subunit Vaccines*
Viral vector	Viral vector vaccines insert a gene for a viral protein into another, harmless virus (replicating or non-replicating). This harmless virus then delivers the viral protein to the vaccine recipient, which triggers an immune response.	Ebola Veterinary vaccines	*What are viral vector vaccines?*
mRNA	RNA vaccines work by introducing an mRNA sequence (the molecule that tells cells what to build) coded for a disease-specific antigen. Once this antigen is reproduced within the body, it is recognized and triggers an immune response.	None	*An introduction to RNA vaccines*
DNA	DNA-based vaccines work by inserting synthetic DNA of viral gene(s) into small DNA molecules called plasmids. Cells take in the DNA plasmids and follow their instructions to build viral proteins, which are recognized by the immune system, and prepare it to respond to disease exposure.	None	*WHO: About DNA vaccines*

*Operation Warp Speed: US government body responsible for strategic approach, coordination and resource allocation for COVID-19 vaccines
**COVAX: The vaccine pillar of ACT-A, the global collaboration to accelerate development, production and equitable access to new diagnostics, therapeutics and vaccines. COVAX is led by GAVI, CEPI and WHO.

About AVAC. AVAC is a non-profit organization that uses education, policy analysis, advocacy and a network of global collaborations to accelerate the ethical development and global delivery of new HIV prevention options as part of a comprehensive response to the pandemic. For more information, visit ***www.avac.org***