INSELGRUPPE

COVID-19 Impfungen – von Sputnik ad Astra

Cornelia Staehelin, 1. Februar 2021

Vaccine Platforms SARS-CoV-2

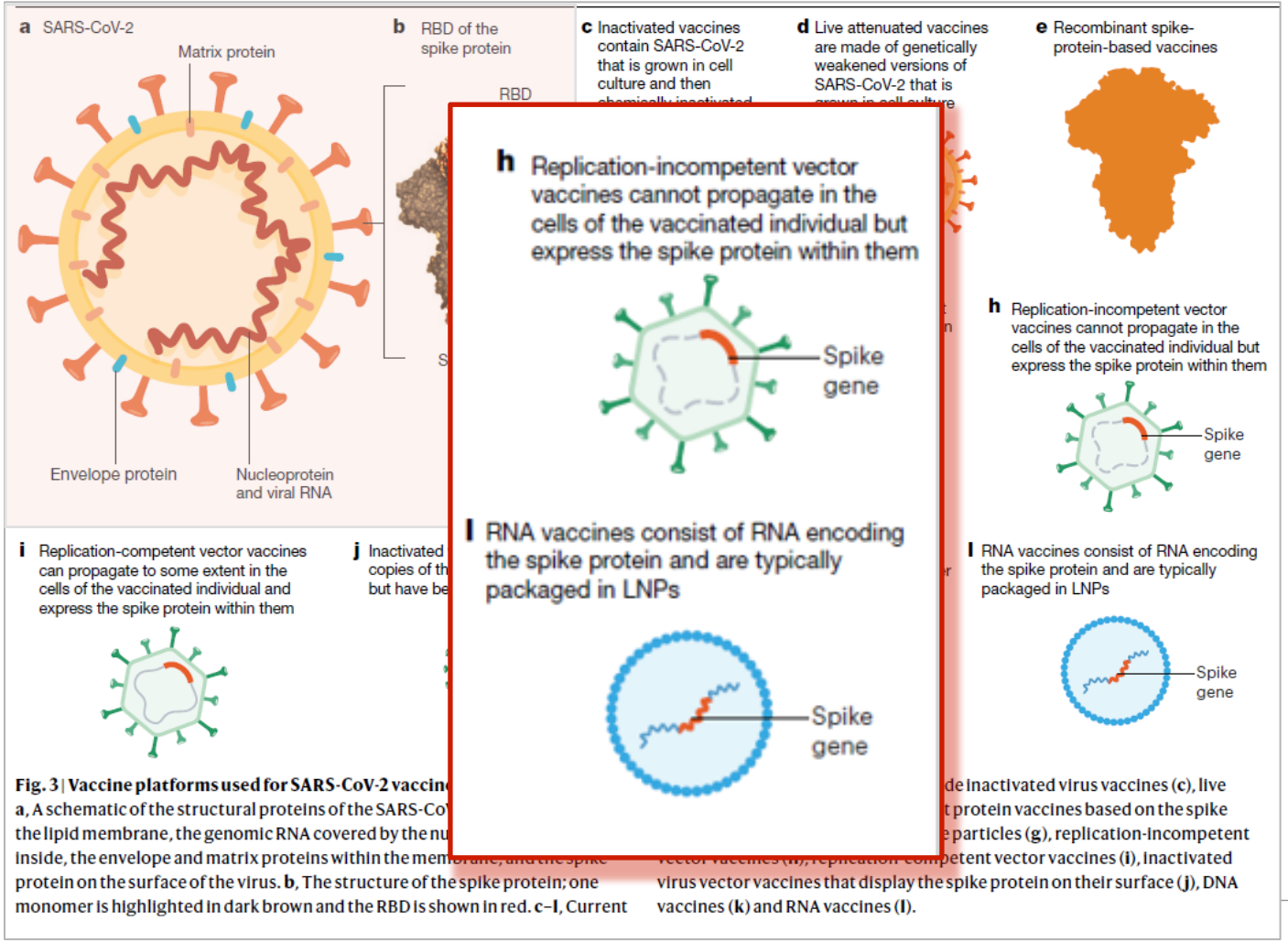


Fig. 3 | Vaccine platforms used for SARS-CoV-2 vaccin …de inactivated virus vaccines (**c**), live **a**, A schematic of the structural proteins of the SARS-Co… …t protein vaccines based on the spike the lipid membrane, the genomic RNA covered by the nu… …e particles (**g**), replication-incompetent inside, the envelope and matrix proteins within the mem…, and the spike …petent vector vaccines (**i**), inactivated protein on the surface of the virus. **b**, The structure of the spike protein; one virus vector vaccines that display the spike protein on their surface (**j**), DNA monomer is highlighted in dark brown and the RBD is shown in red. **c**–**l**, Current vaccines (**k**) and RNA vaccines (**l**).

- RBD – receptor binding domain
- VLP – virus-like particles
- LNP – lipid nanoparticles

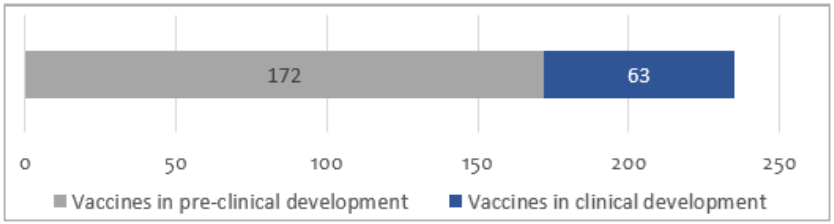
Kramer; Nature Review 2020

World Health Organization

R&DBlueprint
Powering research to prevent epidemics

COVID-19 - Landscape of novel coronavirus candidate vaccine development worldwide

Dienstag, 5. Januar 2021



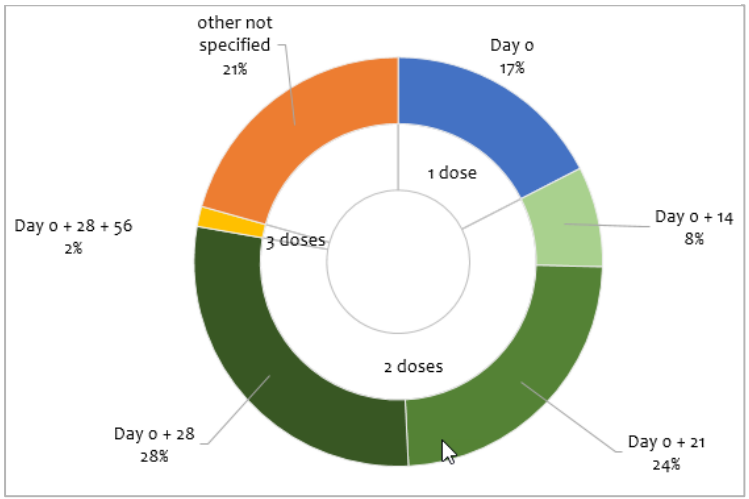
Candidates in clinical phase

Filter: All

Select phase of development (default is all)

Platform		Candidate vaccines (no. and %)	
PS	Protein subunit	19	30%
VVnr	Viral Vector (non-replicating)	10	16%
DNA	DNA	8	13%
IV	Inactivated Virus	9	14%
RNA	RNA	7	11%
VVr	Viral Vector (replicating)	4	6%
VLP	Virus Like Particle	2	3%
VVr + APC	VVr + Antigen Presenting Cell	2	3%
LAV	Live Attenuated Virus	1	2%
VVnr + APC	VVnr + Antigen Presenting Cell	1	2%
		63	

Dosage, schedule and route of admistration of candidates in clinical phase



Dosage & schedule		Candidate vaccines (no. and %)	
Route of admininstration			
Oral		**3**	**5%**
Injectable		**52**	**83%**
SC	Sub cutaneous	2	3%
ID	Intra dermal	3	5%
IM	Intra muscular	47	75%
TBD / No Data (ND)		**8**	**13%**

https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

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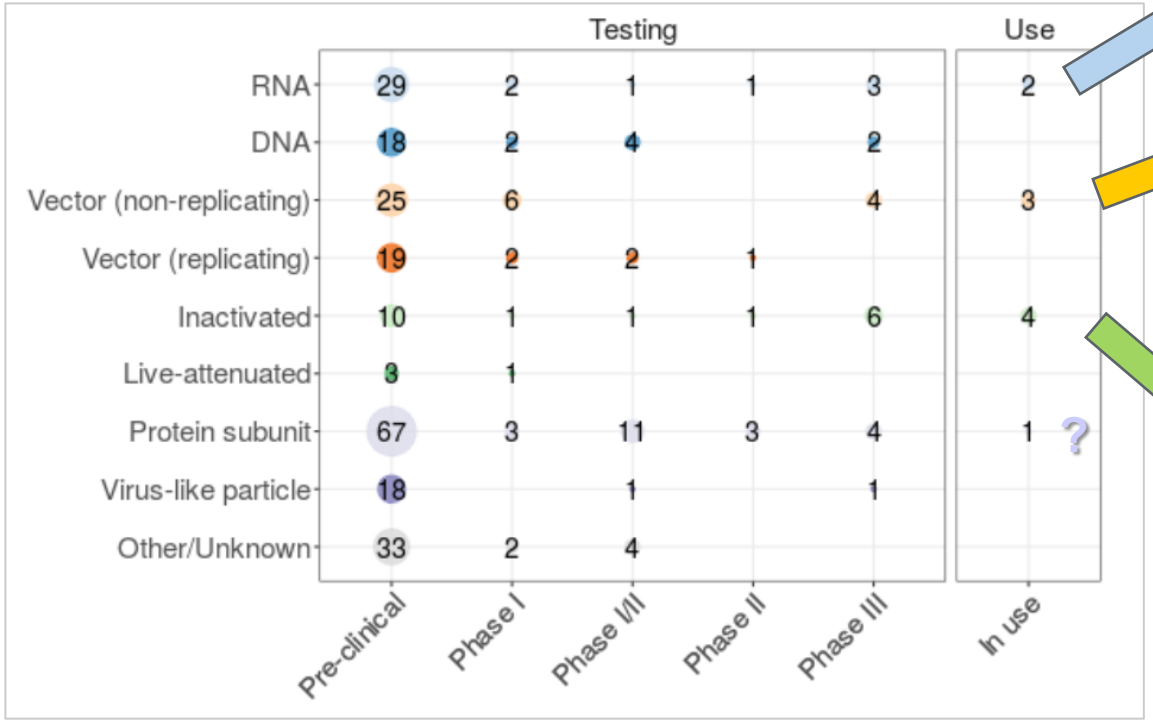
Vaccine pipeline Ende Januar 2021



Moderna
BioNTech/Pfizer

AstraZeneca
Gamaleya (Sputnik V)
Janssen - Cilag
CanSino

Bharat Biotech ICMR
Nat. Institute for Virology

Beijing Institute of Biological Products/Sinopharm

Sinovac

Wuhan Institute of Biological Products/Sinopharm

https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

Contains Nonbinding Recommendations

Development and Licensure of Vaccines to Prevent COVID-19

Guidance for Industry

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Biologics Evaluation and Research
June 2020

E. Statistical Considerations

- To ensure that a widely deployed COVID-19 vaccine is effective, the primary efficacy endpoint point estimate for a placebo-controlled efficacy trial should be at least 50%, and the statistical success criterion should be that the lower bound of the appropriately alpha-adjusted confidence interval around the primary efficacy endpoint point estimate is >30%.
  - The same statistical success criterion should be used for any interim analysis designed for early detection of efficacy.
  - A lower bound ≤30% but >0% may be acceptable as a statistical success criterion for a secondary efficacy endpoint, provided that secondary endpoint hypothesis testing is dependent on success on the primary endpoint.

Einreichung an FDA nur wenn «Mindest-Wirksamkeit im Mittel 50%»

https://www.fda.gov/media/139638/download

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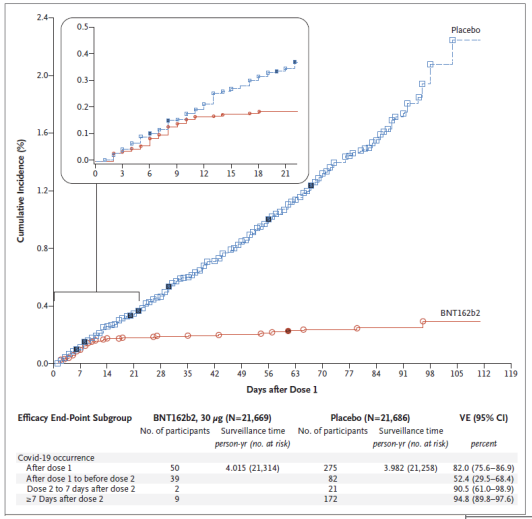
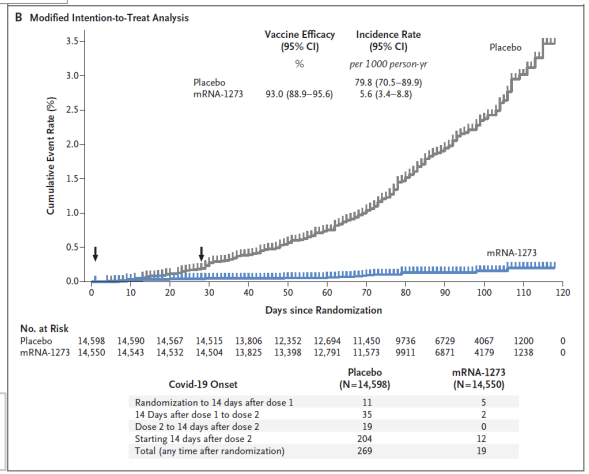
Pfizer/BioNTech	VE
nach Dosis 1	82% (76% - 87%)
zwischen Dosis 1 und Dosis 2	52% (30% - 68%)
≥7 Tage nach Dosis 2	**95% (90% - 98%)**

Moderna	VE
nach Dosis 1	95% (91% - 97%)
zwischen Dosis 1 und Dosis 2	? – visuell um 50%
≥14 Tage nach Dosis 2	**95% (91% - 97%)**



Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669) No. of participants	BNT162b2, 30 μg (N=21,669) Surveillance time person-yr (no. at risk)	Placebo (N=21,686) No. of participants	Placebo (N=21,686) Surveillance time person-yr (no. at risk)	VE (95% CI) percent
Covid-19 occurrence					
After dose 1	50	4.015 (21,314)	275	3.982 (21,258)	82.0 (75.6–86.9)
After dose 1 to before dose 2	39		82		52.4 (29.5–68.4)
Dose 2 to 7 days after dose 2	2		21		90.5 (61.0–98.9)
≥7 Days after dose 2	9		172		94.8 (89.8–97.6)

NEJM December 10,2020



Covid-19 Onset	Placebo (N=14,598)	mRNA-1273 (N=14,550)
Randomization to 14 days after dose 1	11	5
14 Days after dose 1 to dose 2	35	2
Dose 2 to 14 days after dose 2	19	0
Starting 14 days after dose 2	204	12
Total (any time after randomization)	269	19

This article was published on December 30, 2020, at NEJM.org.

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

Merryn Voysey*, Sue Ann Costa Clemens*, Shabir A Madhi*, Lily Y Weckx*, Pedro M Folegatti*, Parvinder K Aley, Brian Angus, Vicky L Baillie,

Und dann das gute aber nicht so perfekte Resultat:

Astra Zeneca	VE
nach Dosis 1	64% (91% - 97%)
LD/SD	90% (67% - 97%)
SD/SD	62% (41% - 76%)
insgesamt	**70% (55% - 81%)**

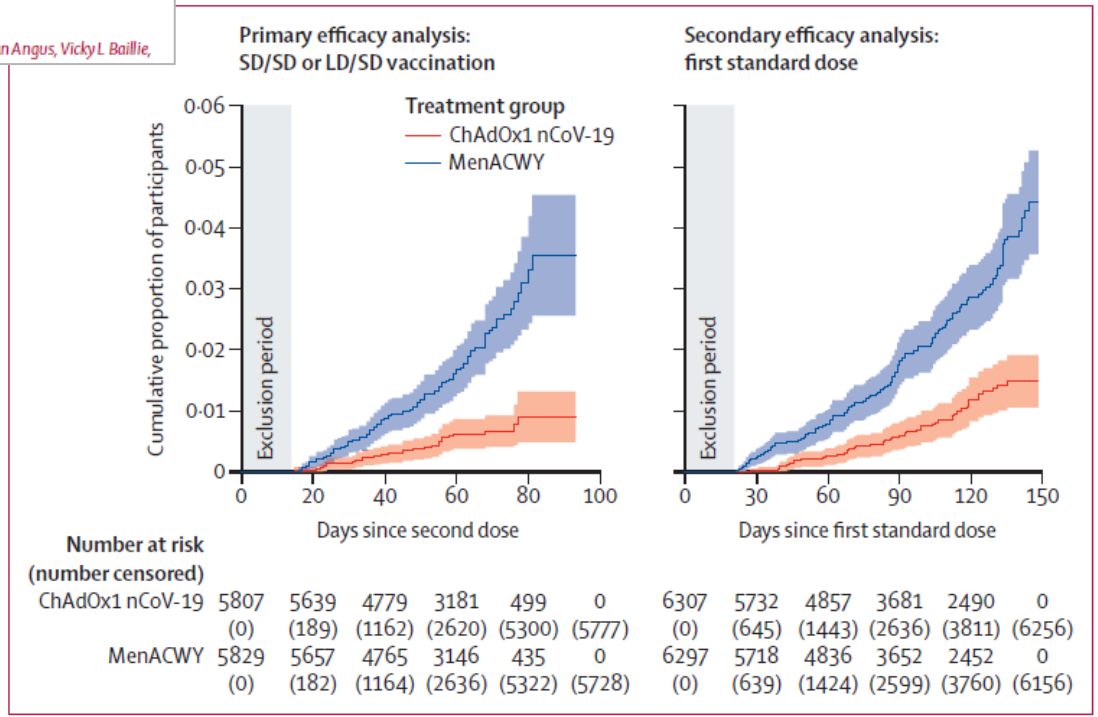
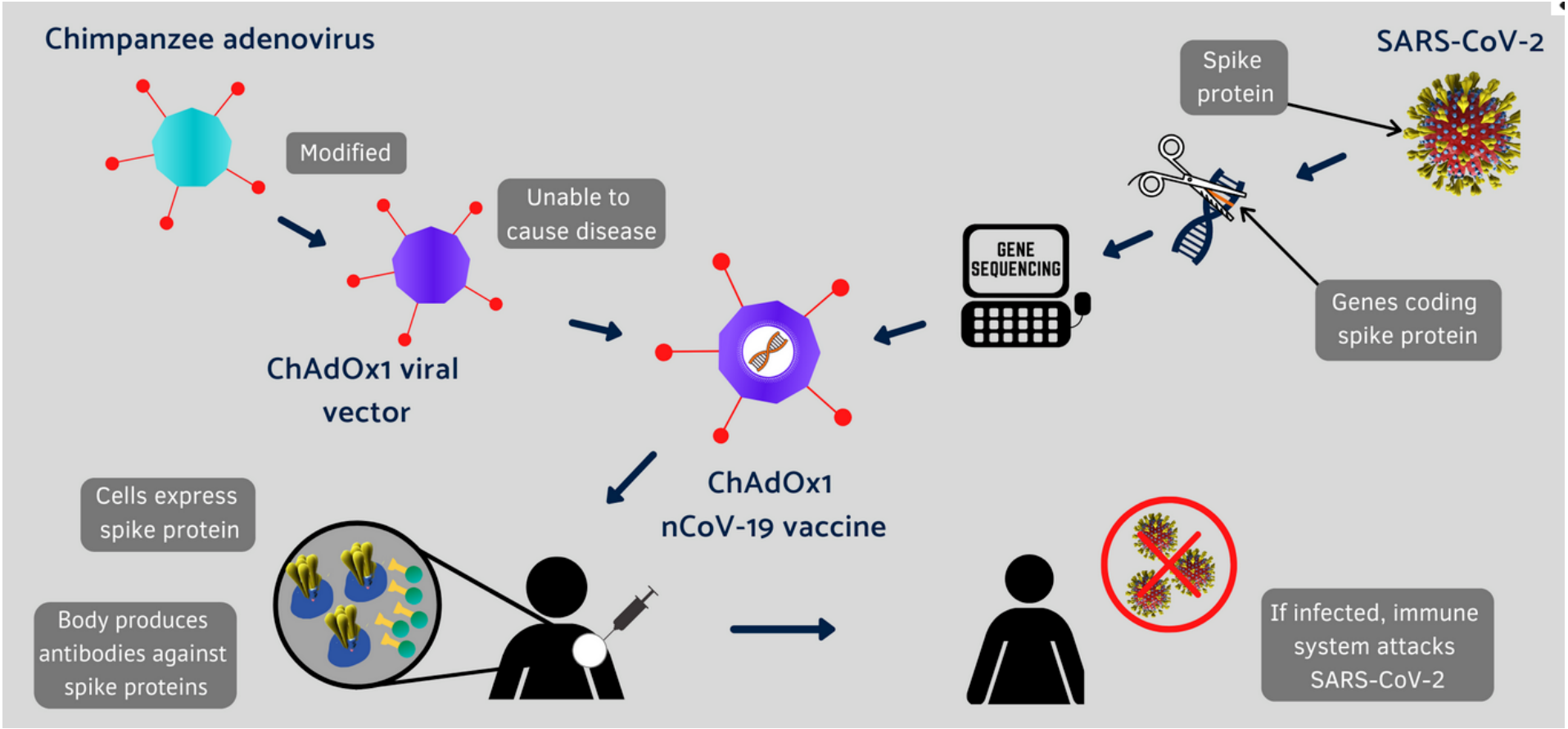


Figure: Kaplan-Meier cumulative incidence of primary symptomatic, NAAT-positive COVID-19

Published online December 8, 2020 https://doi.org/10.1016/S0140-6736(20)32661-1


Chimpanzee adenovirus
Modified
Unable to cause disease
ChAdOx1 viral vector
SARS-CoV-2
Spike protein
GENE SEQUENCING
Genes coding spike protein
ChAdOx1 nCoV-19 vaccine
Cells express spike protein
Body produces antibodies against spike proteins
If infected, immune system attacks SARS-CoV-2

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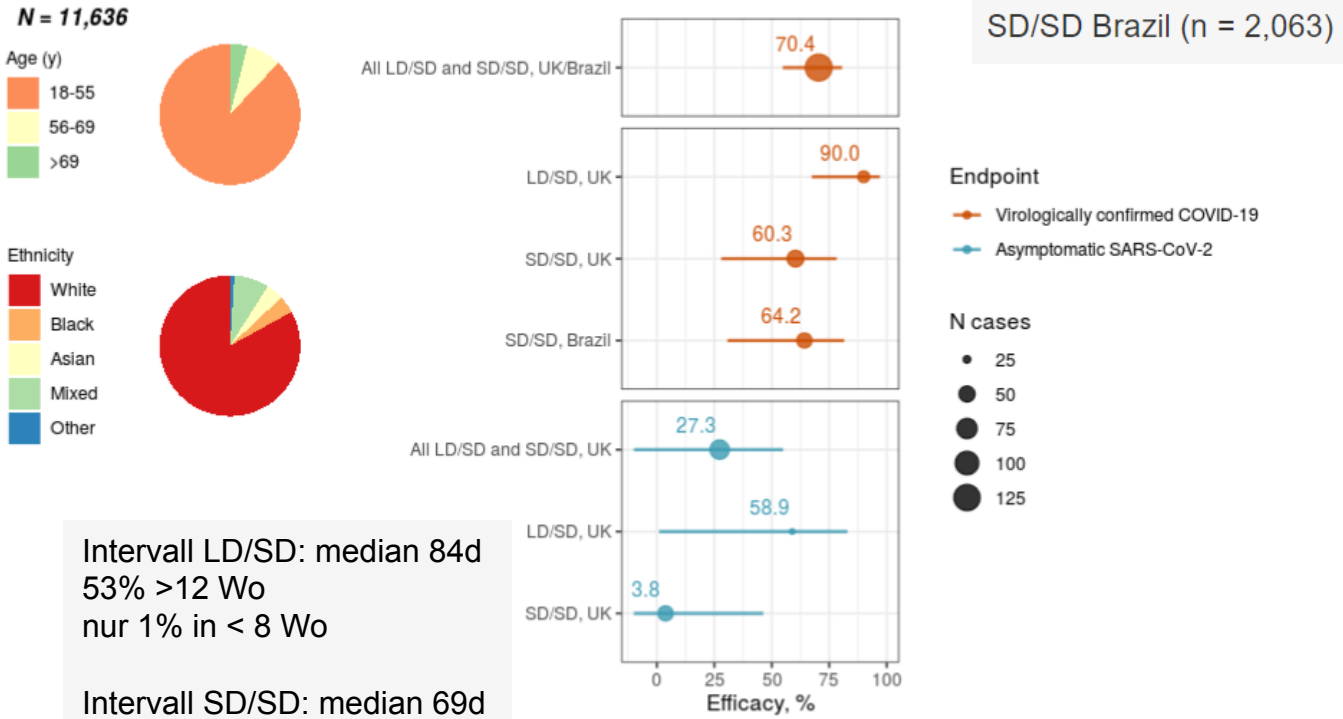
Primary endpoint: Symptomatic COVID-19 in seronegative participants with a nucleic acid test-positive swab >14 days after second dose
Asymptomatic SARS-CoV-2: Weekly self-administered nose and throat swabs for nucleic acid testing from 1 week after first dose
Severe COVID-19: Hospitalisation due to COVID-19

Plot | Table | Population profile

Interim efficacy subset:
LD/SD UK (n = 1,367)
SD/SD UK (n = 2,377)
SD/SD Brazil (n = 2,063)

18–55y: 10,218 (88%)
56–69y: 974 (8%)
>69y: 444 (4%)

efficacy in >55 year olds ?



Vaccine efficacy VE

VE von LD/SD >> SD/SD

VE gemäss Intervall D1-D2:
< 6 Wochen = ≥ 6 Wochen

Intervall LD/SD: median 84d
53% >12 Wo
nur 1% in < 8 Wo

Intervall SD/SD: median 69d

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«serendipity»

"The reason we had the half dose is serendipity," said Mene Pangalos, executive vice-president of biopharmaceuticals research and development at AstraZeneca.

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World ▸ Europe US Americas Asia Australia Middle East Africa Inequality Global development
Coronavirus

Oxford Covid vaccine hit 90% success rate thanks to dosing error

Participants given first shot at half strength by mistake were found to be better protected

Jessica Murray and agency
Mon 23 Nov 2020 23.24 GMT

Coronavirus - latest updates
See all our coronavirus coverage

Instead of restarting the trial, he said researchers decided to continue with the half dose and administer the full dose booster shot at the scheduled time.

About 3,000 people were given the half dose and then a full dose four weeks later, with data showing 90% were protected. In the larger group, who were given two full doses also four weeks apart, efficacy was 62%.

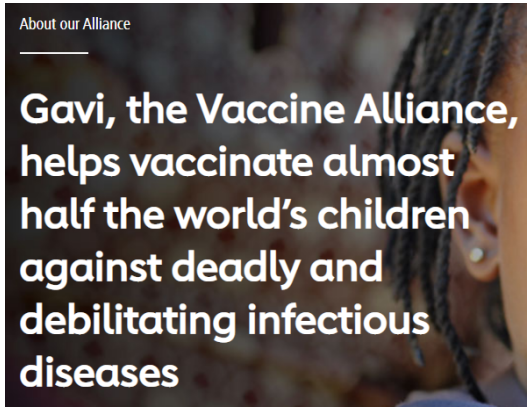
Scientists said they still could not fully explain why the half dose gave better protection, but said it may be that it triggers the immune system differently.

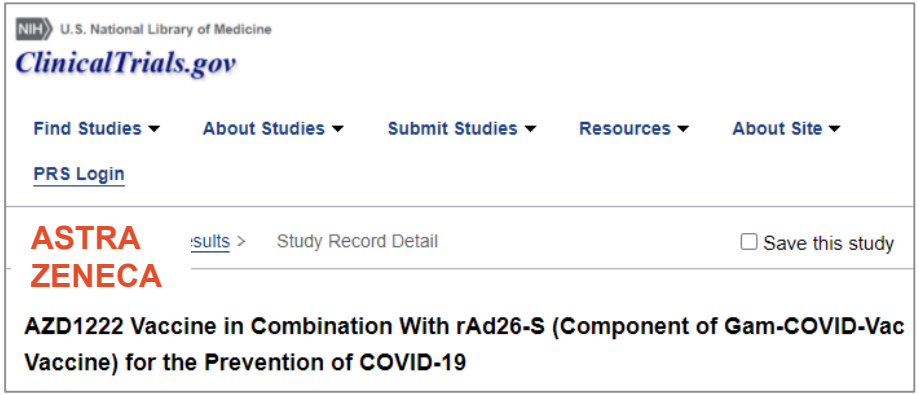
< BACK TO #VACCINESWORK

Coronavirus: why combining the Oxford vaccine with Russia's Sputnik V vaccine could make it more effective

Vaccines that use harmless viruses as a delivery mechanism are vulnerable to being attacked by our immune system – but experimenting with how they are given could get around this.

24 January 2021 – by Jameel Inal

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ASTRA ZENECA
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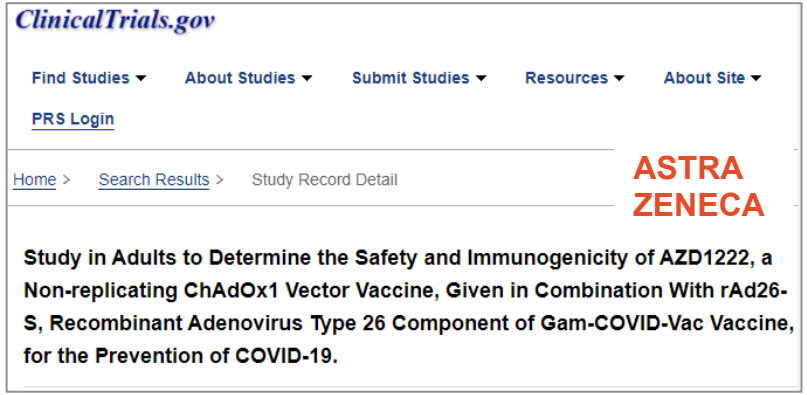
Study Record Detail
Save this study
AZD1222 Vaccine in Combination With rAd26-S (Component of Gam-COVID-Vac Vaccine) for the Prevention of COVID-19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Submit Studies
Resources
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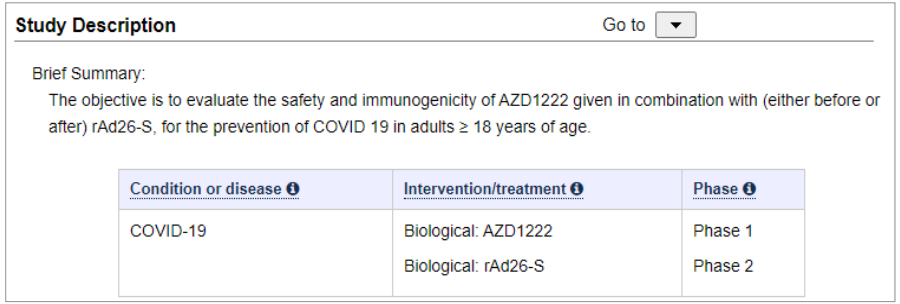
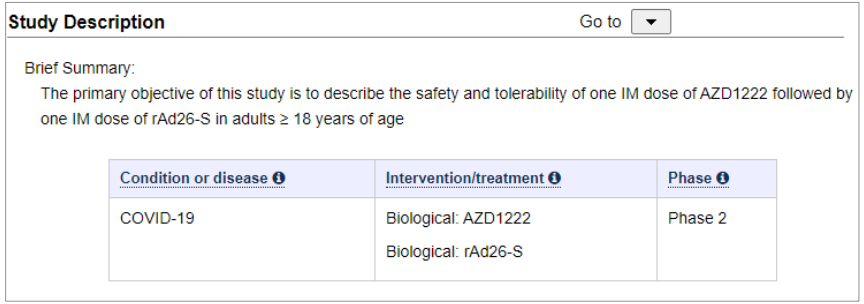
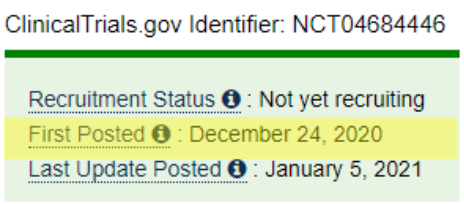
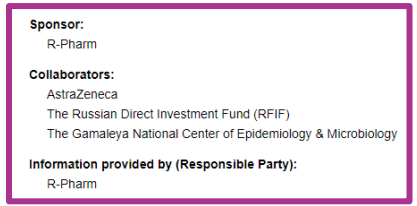
Home >
Search Results >
Study Record Detail
ASTRA ZENECA
Study in Adults to Determine the Safety and Immunogenicity of AZD1222, a Non-replicating ChAdOx1 Vector Vaccine, Given in Combination With rAd26-S, Recombinant Adenovirus Type 26 Component of Gam-COVID-Vac Vaccine, for the Prevention of COVID-19.

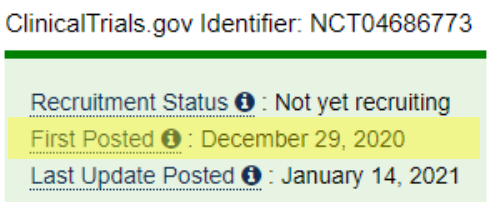

Study Description
Go to
Brief Summary:
The objective is to evaluate the safety and immunogenicity of AZD1222 given in combination with (either before or after) rAd26-S, for the prevention of COVID 19 in adults ≥ 18 years of age.
Condition or disease
Intervention/treatment
Phase
COVID-19
Biological: AZD1222
Biological: rAd26-S
Phase 1
Phase 2


Study Description
Go to
Brief Summary:
The primary objective of this study is to describe the safety and tolerability of one IM dose of AZD1222 followed by one IM dose of rAd26-S in adults ≥ 18 years of age
Condition or disease
Intervention/treatment
Phase
COVID-19
Biological: AZD1222
Biological: rAd26-S
Phase 2


ClinicalTrials.gov Identifier: NCT04684446
Recruitment Status : Not yet recruiting
First Posted : December 24, 2020
Last Update Posted : January 5, 2021


Sponsor:
AstraZeneca
Collaborators:
R-Pharm
The Russian Direct Investment Fund (RDIF)
The Gamaleya National Center of Epidemiology & Microbiology
Information provided by (Responsible Party):
AstraZeneca


Sponsor:
R-Pharm
Collaborators:
AstraZeneca
The Russian Direct Investment Fund (RFIF)
The Gamaleya National Center of Epidemiology & Microbiology
Information provided by (Responsible Party):
R-Pharm


ClinicalTrials.gov Identifier: NCT04686773
Recruitment Status : Not yet recruiting
First Posted : December 29, 2020
Last Update Posted : January 14, 2021

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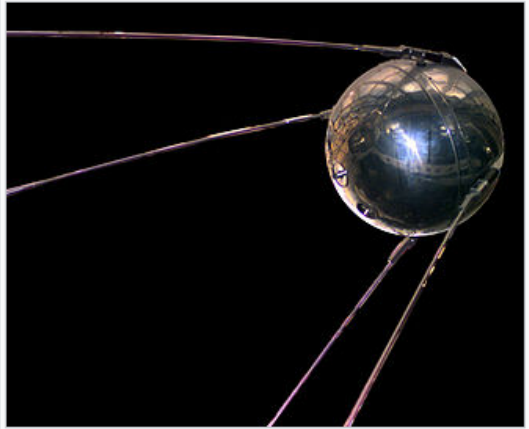
Sputnik V

«The vaccine is named after the first Soviet space satellite. The launch of Sputnik-1 in 1957 reinvigorated space research around the world, creating a so called “Sputnik moment” for the global community..»



Modell des Sputnik 1

Sputnik V

THE FIRST REGISTERED COVID-19 VACCINE

PROVEN HUMAN ADENOVIRAL VECTOR TECHNOLOGY

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Sputnik V

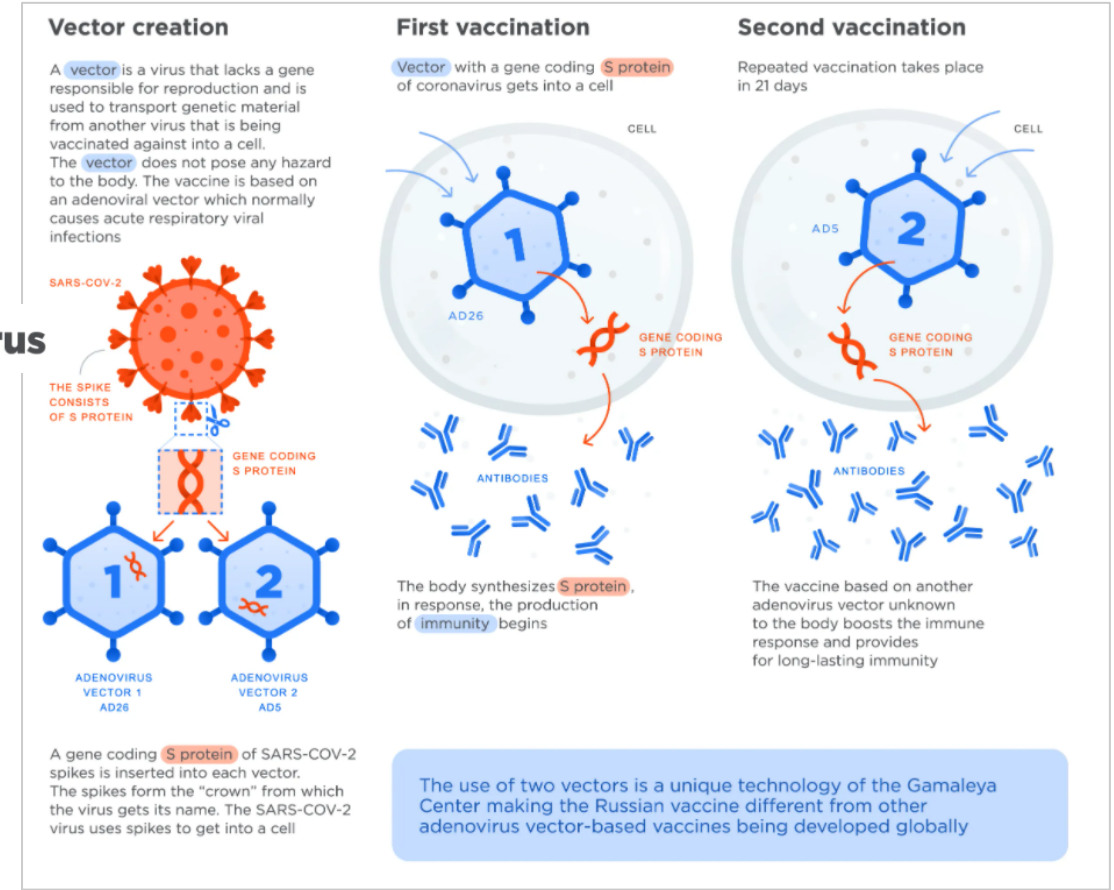
THE FIRST REGISTERED COVID-19 VACCINE

PROVEN HUMAN ADENOVIRAL VECTOR TECHNOLOGY

Two-vector vaccine against coronavirus

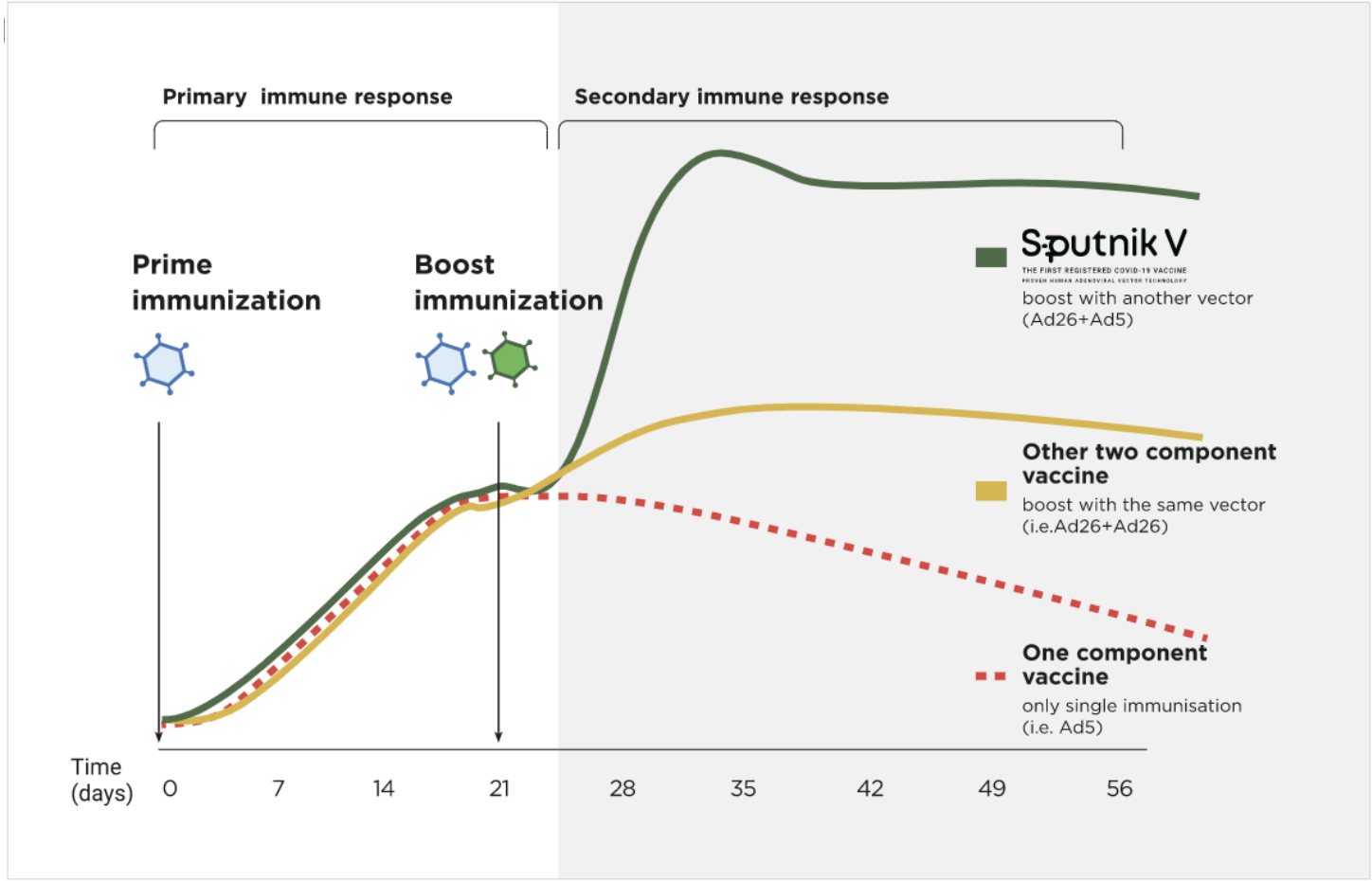
Dosis 1: rAd26-S
Dosis 2: rAd5-S

“The gene from adenovirus, which causes the infection, is removed while a gene with the code of a protein from another virus spike is inserted. --
The technological platform of adenovirus-based vectors makes it easier and faster to create new vaccines through modifying the initial carrier vector with genetic material from new emerging viruses that helps to create new vaccines in relatively short time.”



Source: Gamaleya Center, RDIF, 2020

https://sputnikvaccine.com/about-vaccine/



https://sputnikvaccine.com/about-vaccine/

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

Denis Y Logunov, Inna V Dolzhikova*, Olga V Zubkova, Amir I Tukhvatullin, Dmitry V Shcheblyakov, Alina S Dzharullaeva, Daria M Grousova, Alina S Erokhova, Anna V Kovyrshina, Andrei G Botikov, Fatima M Izhaeva, Olga Popova, Tatiana A Ozharovskaya, Ilias B Esmagambetov, Irina A Favorskaya, Denis I Zrelkin, Daria V Voronina, Dmitry N Shcherbinin, Alexander S Semikhin, Yana V Simakova, Elizaveta A Tokarskaya, Nadezhda L Lubenets, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Lola F Morozova, Elena A Smolyarchuk, Evgeny V Kryukov, Vladimir F Babira, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg*

Summary

Background We developed a heterologous COVID-19 vaccine consisting of two components, a recombinant adenovirus type 26 (rAd26) vector and a recombinant adenovirus type 5 (rAd5) vector, both carrying the gene for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spike glycoprotein (rAd26-S and rAd5-S). We aimed to assess the safety and immunogenicity of two formulations (frozen and lyophilised) of this vaccine.

Methods We did two open, non-randomised phase 1/2 studies at two hospitals in Russia. We enrolled healthy adult volunteers (men and women) aged 18–60 years to both studies. In phase 1 of each study, we administered intramuscularly on day 0 either one dose of rAd26-S or one dose of rAd5-S and assessed the safety of the two components for 28 days. In phase 2 of the study, which began no earlier than 5 days after phase 1 vaccination, we administered intramuscularly a prime-boost vaccination, with rAd26-S given on day 0 and rAd5-S on day 21. Primary outcome measures were antigen-specific humoral immunity (SARS-CoV-2-specific antibodies measured by ELISA on days 0, 14, 21, 28, and 42) and safety (number of participants with adverse events monitored throughout the study). Secondary outcome measures were antigen-specific cellular immunity (T-cell responses and interferon-γ concentration) and change in neutralising antibodies (detected with a SARS-CoV-2 neutralisation assay). These trials are registered with ClinicalTrials.gov, NCT04436471 and NCT04437875.

Lancet 2020; 396: 887–97

Published Online
September 4, 2020
https://doi.org/10.1016/S0140-6736(20)31866-3

See Comment page 868

*Contributed equally

Federal State Budget Institution "National Research Centre for Epidemiology and Microbiology named after Honorary Academician N F Gamaleya" of the Ministry of Health of the Russian Federation, Moscow, Russia (D Y Logunov DSc, I V Dolzhikova PhD, O V Zubkova PhD,

Added value of this study

We designed a COVID-19 vaccine with two different adenoviral vectors (recombinant Ad26 [rAd26] and recombinant Ad5 [rAd5]), both carrying the gene for SARS-CoV-2 spike glycoprotein (rAd26-S and rAd5-S), and we implemented a prime-boost regimen. We did two open, phase 1/2 non-randomised trials of two formulations (frozen and lyophilised) of the vaccine in healthy adult volunteers. Safety of

Since boosting vaccination is necessary for formation of a more powerful immune response, the effectiveness of such vaccination can be reduced when using a homologous vector (because of formation of an immune response not only to the target antigen but also to the vector components after priming vaccination).

Phase	Vaccine	Platform	N	Age (years)	N doses	Rand.	Design	Location	Start date	Primary completion date	Trial number	Status
Phase I/II	Gamaleya Gam-COVID-Vac/Sputnik V (Lyo)	Non-replicating viral vector	38	18–60	1 or 2	No	Open-label	Russia	17/06/2020	03/08/2020	NCT04437875	Completed
Phase III	Gamaleya Gam-COVID-Vac/Sputnik V	Non-replicating viral vector	40,000	≥18	2	Yes	Double-blind	Russia	07/09/2020	01/05/2021	NCT04530396	Recruiting
Phase III	Gamaleya Gam-COVID-Vac/Sputnik V	Non-replicating viral vector	2,000	≥18	2	Yes	Double-blind	Venezuala	01/11/2020	31/10/2021	NCT04642339	Not yet recruiting
Phase II/III	Gamaleya Gam-COVID-Vac/Sputnik V	Non-replicating viral vector	1,600	≥18	2	Yes	Double-blind	India	01/12/2020	30/08/2021	NCT04640233	Not yet recruiting
Phase II	Gamaleya Gam-COVID-Vac/Sputnik V	Non-replicating viral vector	110	≥60	2	No	Open-label	Russia	22/10/2020	30/12/2020	NCT04587219	Recruiting
Phase III	Gamaleya Gam-COVID-Vac/Sputnik V	Non-replicating viral vector	100	18–60	2	Yes	Double-blind	Belarus	28/09/2020	28/03/2021	NCT04564716	Active, not recruiting
Phase I/II	Gamaleya Gam-COVID-Vac/Sputnik V	Non-replicating viral vector	38	18–60	1 or 2	No	Open-label	Russia	17/06/2020	03/08/2020	NCT04436471	Completed

Showing 1 to 7 of 7 entries (filtered from 122 total entries)

Previous 1 Next

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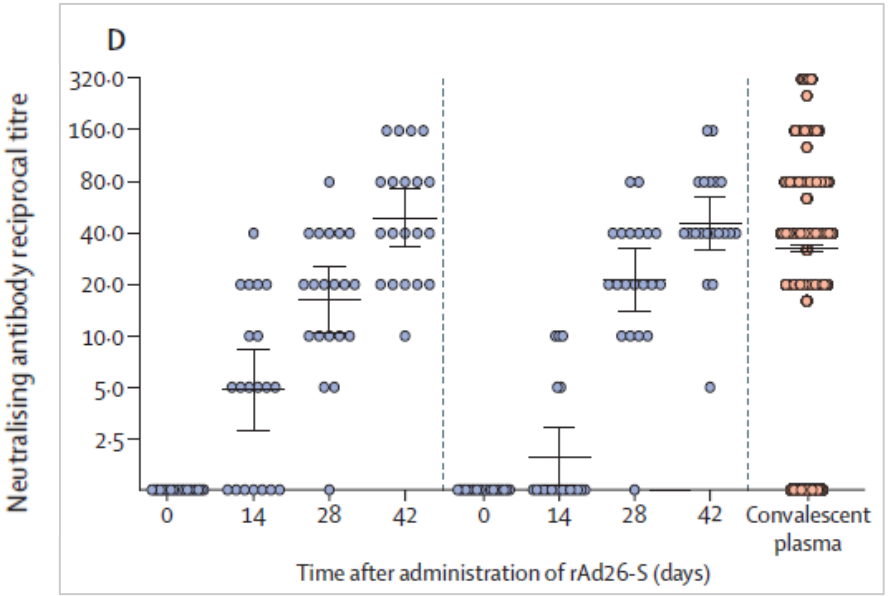
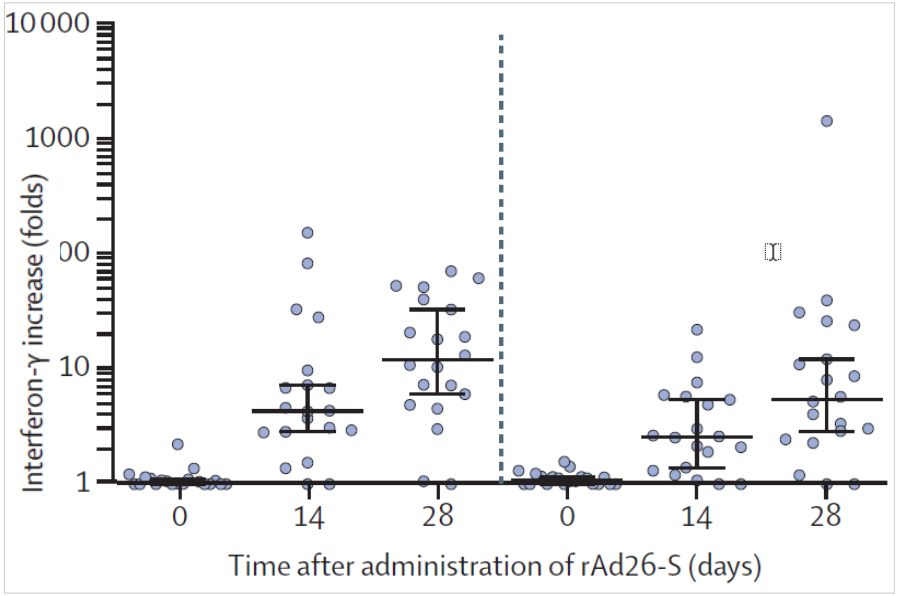
humorale Antwort

gefroren lyophilisiert



zelluläre Antwort

gefroren lyophilisiert



lyophylisiert = getrocknet durch Gefrieren in hohem Vakuum

Logunov; Lancet Sept. 2020

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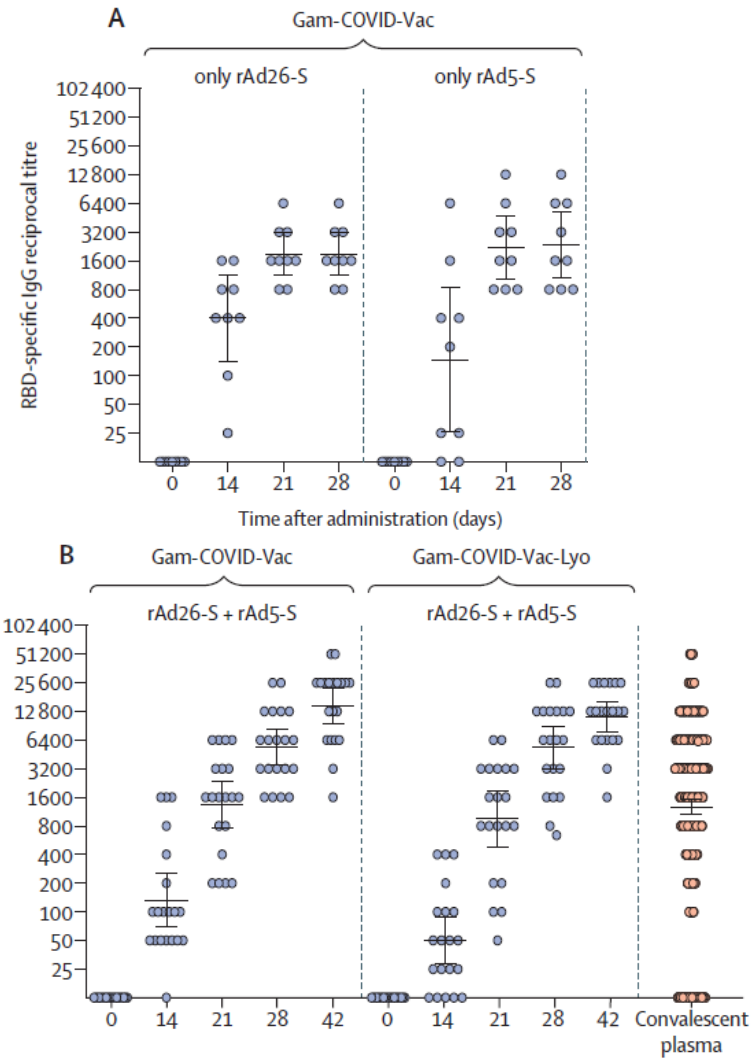
Präformierte Ak gegen Adenoviren?

To investigate the effect of the pre-existing immune response to adenoviral vectors, neutralising antibodies to recombinant vectors were measured in all participants on days 0 and 28 in both studies (figure 4). After one injection of vaccine components, not only is an immune response to target antigen formed but also an immune response is seen to components of the vaccine vector.

Kreuz-reagierende Ak gegen das andere Adenovirus?

Administration of rAd26 did not increase the titre of neutralising antibodies to rAd5 on day 28, and vice versa, which indicates the absence of cross-reactivity with respect to vaccine components (figure 4). Thus, the



List of clinical trials on human adenovirus-based vector vaccines

№	NCT Number	Start Date	Enrollment	URL
1	NCT00004779	1993	12	https://ClinicalTrials.gov/show/NCT0000477
2	NCT00004498	1998	21	https://ClinicalTrials.gov/show/NCT00004498
3	NCT00406939	1998	4	https://ClinicalTrials.gov/show/NCT00406939
4	NCT00003167	1998	24	https://ClinicalTrials.gov/show/NCT00003167
5	NCT00003257	1998	39	https://ClinicalTrials.gov/show/NCT00003257
6	NCT00003147	1998	30	https://ClinicalTrials.gov/show/NCT00003147
7	NCT00003450	1998	20	https://ClinicalTrials.gov/show/NCT00003450
8	NCT00003649	1998	-	https://ClinicalTrials.gov/show/NCT00003649
9	NCT00003588	1998	30	https://ClinicalTrials.gov/show/NCT00003588
10	NCT00048386	1999	13	https://ClinicalTrials.gov/show/NCT00048386

№	NCT Number	Start Date	Enrollment	URL
245	NCT04398147	2020	696	https://ClinicalTrials.gov/show/NCT04398147
246	NCT04111172	2020	81	https://ClinicalTrials.gov/show/NCT04111172
247	NCT04100889	2020	100	https://ClinicalTrials.gov/show/NCT04100889
248	NCT04505722	2020	60 000	https://ClinicalTrials.gov/show/NCT04505722
249	NCT04509947	2020	125	https://ClinicalTrials.gov/show/NCT04509947
250	NCT04436276	2020	1 045	https://ClinicalTrials.gov/show/NCT04436276
251	NCT04228783	2020	916	https://ClinicalTrials.gov/show/NCT04228783
252	NCT04354480	2020	36	https://ClinicalTrials.gov/show/NCT04354480
253	NCT04453202	2020	128	https://ClinicalTrials.gov/show/NCT04453202
254	NCT02928094	2021	320	https://ClinicalTrials.gov/show/NCT02928094

Sputnik V clinical trials

An Open Study of the Safety, Tolerability and Immunogenicity of "Gam-COVID-Vac Lyo" Vaccine Against COVID-19

An Open Study of the Safety, Tolerability and Immunogenicity of the Drug "Gam-COVID-Vac" Vaccine Against COVID-19

Clinical Trial of Efficacy, Safety, and Immunogenicity of Gam-COVID-Vac Vaccine Against COVID-19 (RESIST)

Demnächst in diesem Theater: randomisierte doppelt verblindete Phase III soll Ende Januar im Lancet publiziert werden

Sputnik V im Orbit

- Ongoing post-registration trial Russland: 40’000 Probanden
- Seit Anfang Dez. 2020 gemäss staatlichen Angaben 1.5 Mio. Menschen geimpft – bis Sommer sollen 60% der Bevölkerung geimpft werden.

- Vorzeitige Zulassung in weiteren Ländern
  - Argentinien, 30.12.2020 → bereits 240’000 Personen geimpft
  - Ungarn, 22.01.2021
  - Serbien, Venezuela, Bolivien → ? ob Massenimpfungen schon gestartet
    Weitere Studien «announced» in Weissrussland, Venezuela, Indien, UAE
- Produktion für globalen Markt soll erfolgen in Indien, Brasilien, China, Südkorea.
- Der getrocknete (lyophilisierte) Impfstoff kann bei +2 bis +8°C gelagert werden.
- Kosten einer Dosis sollen $10 sein ($20 für eine Impfung)
- Bestellungen von > 1.2 Mia. Dosen aus > 50 Ländern

HEALTH AND SCIENCE

Germany's Merkel 'open' to producing Russian Covid vaccine in the EU

PUBLISHED THU, JAN 7 2021•8:54 AM EST

Silvia Amaro
@SILVIA_AMARO

KEY POINTS

- The EU has been criticized for a slow rollout of Covid-19 vaccines in comparison with other parts of the world, with the U.S., China and Israel among those leading the way in terms of the number doses administered.
- Merkel discussed the response to the Covid-19 pandemic with Russia's President Vladimir Putin on Tuesday.

German Chancellor Angela Merkel is "open" to the idea of producing Russia's coronavirus vaccine in the European Union, according to a spokesperson for her office.

Test studies of the Covid-19 vaccine candidate Sputnik V are being carried out in Russia.
Sefa Karacan | Anadolu Agency | Getty Images

Germany has made it clear that this would only happen if the European Medicines Agency (EMA) were to give its approval to the Sputnik V vaccine.

INSELGRUPPE

Neu, 7.12.2020

EMA starts rolling review of Janssen's COVID-19 vaccine Ad26.COV2.S

Share

News 01/12/2020

EMA's human medicines committee (CHMP) has started a rolling review of Ad26.COV2.S, a COVID-19 vaccine from Janssen-Cilag International N.V.

The CHMP's decision to start the rolling review is based on preliminary results from laboratory studies and early clinical studies in adults. These studies suggest that the vaccine triggers the production of antibodies and immune cells that target the SARS-CoV-2 coronavirus.

The company is currently conducting trials in people to assess safety and immunogenicity (how well the vaccine triggers a response against the virus), and effectiveness. EMA will evaluate data from these and other clinical trials as they become available.

Schweiz prüft weiteren Corona-Impfstoff

Mit der Janssen-Cilag AG hat das vierte Unternehmen ein Impfstoff-Gesuch bei Swissmedic eingereicht im Kampf gegen das Coronavirus. Das Schweizerische Heilmittelinstitut prüft auch dieses beschleunigt im rollenden Verfahren, wie es am Montagabend mitteilte.

07.12.2020 / 20:16 / von: abl/sda **Seite drucken** **Kommentare** 0

Mit der Janssen-Cilag AG hat das vierte Unternehmen ein Impfstoff-Gesuch bei Swissmedic eingereicht. (Bild: KEYSTONE/PETER KLAUNZER)

Zuvor hatten bereits die schwedische-britische AstraZeneca sowie die deutsche Biontech mit ihrem US-Partner Pfizer und Moderna aus den USA Gesuche eingereicht.

Die Janssen-Cilag AG ist ein deutsches Tochterunternehmen des US-Gesundheitskonzerns Johsnon&Johnson. Janssen-Cilang habe den Antrag für den Vektor-basierten Impfstoff-Kandidaten fast zeitgleich auch in Europa und Kanada gestellt, erklärte Swissmedic.


Select vaccine:
Janssen Ad26.COV2.S
Selection location:
USA (1-dose)
USA (1-dose)
Argentina (1-dose)
Brazil (1-dose)
Chile (1-dose)
Colombia (1-dose)
Mexico (1-dose)
Peru (1-dose)
South Africa (1-dose)
USA (2-dose)
Belgium (2-dose)
Colombia (2-dose)
France (2-dose)
Germany (2-dose)
Philippines (2-dose)
South Africa (2-dose)
Spain (2-dose)
UK (2-dose)
NORTH AMERICA
SOUTH AMERICA
ASIA
AFRICA
OCEANIA
Atlantic Ocean
Pacific Ocean
Indian Ocean
Southern Ocean
recruiting
not yet recruiting

Ad26.COV2.S Impfung versus Placebo

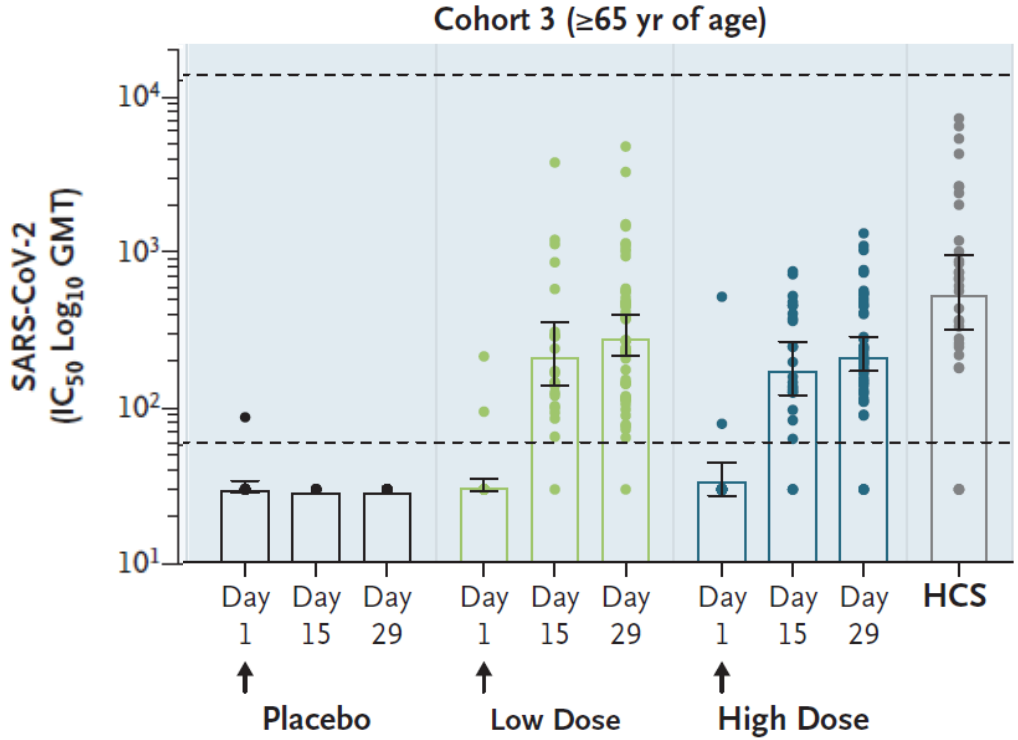
Low dose: 5×10^{10} viral particles /ml

High dose: 1×10^{11} viral particles /ml

Zelluläre Immunantwort mit gleichem

Muster: low dose ca. = high dose

ules, a single dose of Ad26.COV2.S elicited a strong humoral response in a majority of vaccine recipients, with the presence of S-binding and neutralizing antibodies in more than 90% of the participants, regardless of either age group or vaccine dose. In addition, during 71 days of follow-up after



No. at Risk	25	12	25	49	23	50	25	25	50	32
GMT	<58	<58	<58	<58	212	277	<58	172	212	522
Percent Response		0	0		91	96		84	88	

ORIGINAL ARTICLE

Interim Results of a Phase 1–2a Trial of Ad26.COV2.S Covid-19 Vaccine

J. Sadoff, M. Le Gars, G. Shukarev, D. Heerwegh, C. Truyers, A.M. de Groot, J. Stoop, S. Tete, W. Van Damme, I. Leroux-Roels, P.-J. Berghmans, M. Kimmel, P. Van Damme, J. de Hoon, W. Smith, K.E. Stephenson, S.C. De Rosa, K.W. Cohen, M.J. McElrath, E. Cormier, G. Scheper, D.H. Barouch, J. Hendriks, F. Struyf, M. Douoguih, J. Van Hoof, and H. Schuitemaker

This article was published on January 13, 2021, and last updated on January 21, 2021, at NEJM.org.

DOI: 10.1056/NEJMoa2034201

Our interim analysis indicates that vaccine candidate Ad26.COV2.S is safe and immunogenic in both younger and older adults. This finding, in combination with the results in preclinical challenge studies,[12,13] has supported our decision to proceed with two phase 3 trials (NCT04505722 and NCT04614948) to evaluate the efficacy of either a single-dose or two-dose regimen of the lower dose (5×10^{10} viral particles) of Ad26.COV2.S.

Supported by Johnson & Johnson and by a contract (HHS0100201700018C) with the Biomedical Advanced Research and Development Authority of the Department of Health and Human Services.

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NIH U.S. National Library of Medicine

ClinicalTrials.gov

Find Studies | About Studies | Submit Studies | Resources

Home > Search Results > Study Record Detail

A Study of Ad26.COV2.S for the Prevention of SARS-CoV-2-Mediated COVID-19 in Adult Participants (ENSEMBLE)

Brief Summary:

The study will enroll up to 60,000 participants in order to evaluate the efficacy of Ad26.COV2.S in the prevention of molecularly confirmed moderate to severe/critical COVID-19, as compared to placebo, in adult participants.

Condition or disease	Intervention/treatment	Phase
Participants With or Without Stable Co-morbidities Associated With Progression to Severe COVID-19 at Different Stages of the Protocol	Biological: Ad26.COV2.S Other: Placebo	Phase 3

ClinicalTrials.gov Identifier: NCT04505722

Recruitment Status : Recruiting
First Posted : August 10, 2020
Last Update Posted : December 3, 2020

Arm

Experimental: Ad26.COV2.S

Participants will receive intramuscular (IM) injection of Ad26.COV2.S at a dose level of 5*10^10 virus particles (vp) as single dose vaccine on Day 1.

Placebo Comparator: Placebo

Participants will receive IM injection of placebo on Day 1.

Phase	Vaccine	Platform	N	Age (years)	N doses	Rand.	Design	Location	Start date	Primary completion date	Trial number	Status
Phase III	Janssen Ad26.COV2.S	Non-replicating viral vector	60,000	≥18	1	Yes	Double-blind	USA, Argentina, Brazil, others	07/09/2020	10/03/2023	NCT04505722	Recruiting
Phase III	Janssen Ad26.COV2.S	Non-replicating viral vector	30,000	≥18	2	Yes	Double-blind	USA, Belgium, Colombia, others	15/11/2020	10/05/2022	NCT04614948	Recruiting
Phase I/II	Janssen Ad26.COV2.S	Non-replicating viral vector	1,045	≥18	1 or 2	Yes	Double-blind, dose-ranging	USA, Belgium	15/07/2020	15/09/2021	NCT04436276	Recruiting
Phase II	Janssen Ad26.COV2.S	Non-replicating viral vector	550	≥18	1 or 2	Yes	Double-blind, dose-ranging	Belgium, USA	28/08/2020	15/12/2021	NCT04535453	Recruiting

Rekombinantes Spike-Protein

Adjuvantiert

UK: 89.3% VE

- 95.6% WT
- 85.5% VOC

RSA (93% escape mutant):

60% VE (HIV-)

49.4% (HIV+ und HIV-)

Novavax COVID-19 Vaccine Demonstrates 89.3% Efficacy in UK Phase 3 Trial

Jan 28, 2021 at 4:05 PM EST

	Pfizer-BioNTech		Moderna		Astra Zeneca	
Typ	mRNA | SARS CoV-2 spike protein		mRNA | SARS CoV-2 spike protein		ChAdOx1 nCoV-19 (Chimp.Adenovirus Vektor)	
Adjuvans	keine		keine		keine	
Dosis	2 x 30 µg (0, 21d) praktisch auch 0, 28d		2 x 100 µg (0, 28d)		2 unterschiedliche Dosierungsschemata	
Teilnehmer Phase 3	Fast 44'000		>30'000		>84'000 (kumulativ Ph. I-III)	
Zulassung	>16 J.		≥ 18 J. (Studie für 12- 17-jährige am Laufen*)		≥ 18 Jahre	
Bestellte Dosen CH	3 Mio.	~20 CHF/Dosis	7.5 Mio.	~15-25 CHF/Dosis	5.3 Mio	~2.50 CHF/Dosis
6 Monate Haltbarkeit bei	- 75°		- 20°C		2 - 8°C	
Haltbarkeit bei 2-8°C	5 Tage		30 Tage		6 Monate	
Kleinste Bestellmenge (Verpackung)	195 Vials à 5 Dosen (=975 Dosen)		10 Vials à 10 Dosen (=100 Dosen)		10 Vials à 8/10 Dosen (80/100 Dosen)	

https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html

*https://investors.modernatx.com/news-releases/news-release-details/moderna-announces-first-participants-dosed-phase-23-study-covid

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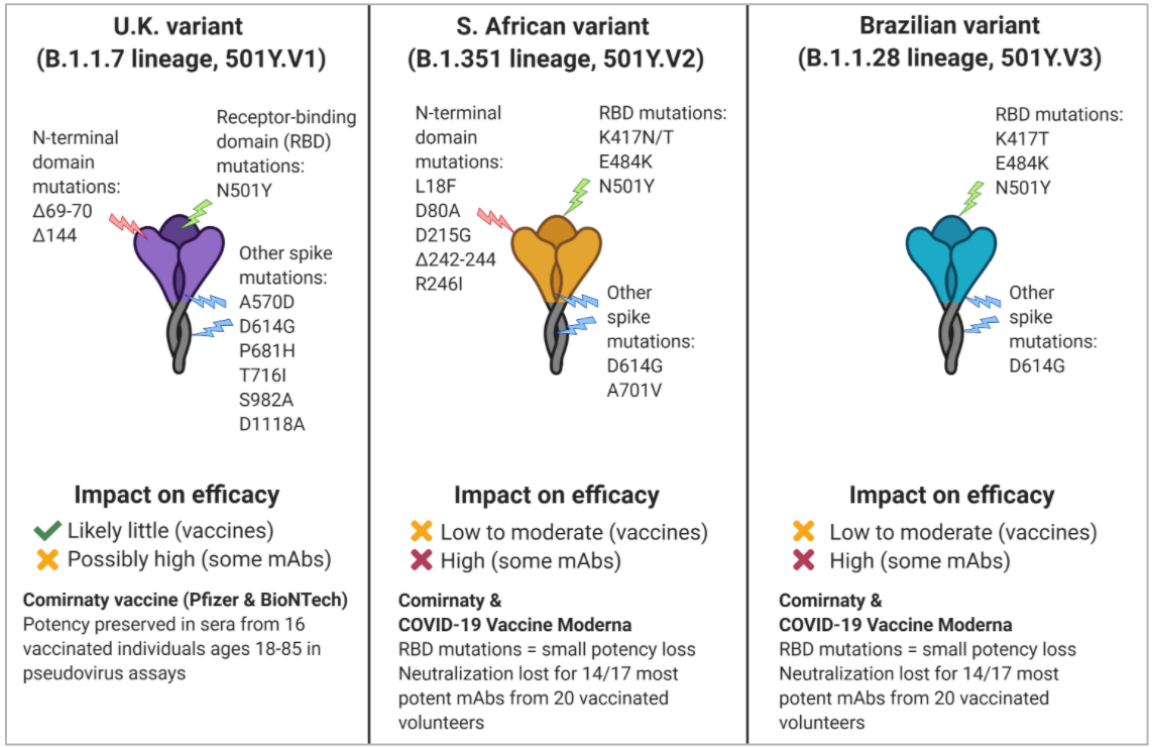
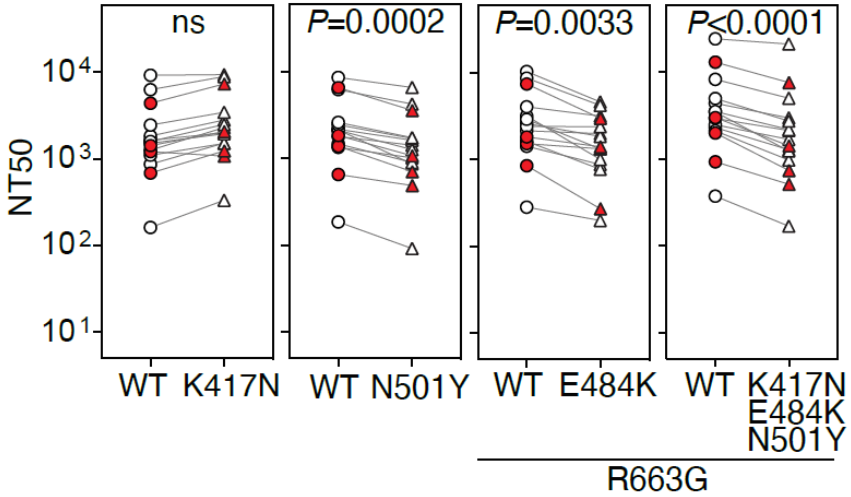
«next level» Herausforderungen



https://www.biocentury.com/article/633630/how-spike-mutations-in-sars-cov-2-variants-affect-vaccines-therapies-data-byte?return_feed=%2Fcoronavirus

mRNA vaccine-elicited antibodies to SARS-CoV-2 and circulating variants

Zijun Wang[1,*], Fabian Schmidt[2,*], Yiska Weisblum[2,*], Frauke Muecksch[2,*], Christopher O. Barnes[3,*], Shlomo Finkin[1,*], Dennis Schaefer-Babajew[1,*], Melissa Cipolla[1*], Christian Gaebler[1*], Jenna A. Lieberman[4,*], Zhi Yang[3], Morgan E. Abernathy[3], Kathryn E. Huey-Tubman[3], Arlene Hurley[5], Martina Turroja[1], Kamille A. West[6], Kristie Gordon[1], Katrina G. Millard[1], Victor Ramos[1], Justin Da Silva[2], Jianliang Xu[4], Robert A. Colbert[7], Roshni Patel[1], Juan Dizon[1], Cecille Unson-O'Brien[1], Irina Shimeliovich[1], Anna Gazumyan[1], Marina Caskey[1], Pamela J. Bjorkman[3,#], Rafael Casellas[4,8,#], Theodora Hatziioannou[2,#], Paul D. Bieniasz[2,9,#], Michel C. Nussenzweig[1,9,#]



«taken together, the results suggest that the monoclonal antibodies in clinical use should be tested against newly arising variants, and that mRNA vaccines may need to be updated regularly to avoid potential loss of clinical efficacy.»

The report comes two weeks after Pfizer and University of Texas Medical Branch researchers presented data in *bioRxiv* showing Comirnaty's humoral immunogenicity **isn't affected by the N501Y** mutation.

mRNA-1273 vaccine induces neutralizing antibodies against spike mutants from global SARS-CoV-2 variants

Kai Wu[1*], Anne P. Werner[2*], Juan I. Moliva[2], Matthew Koch[1], Angela Choi[1], Guillaume B. E. Stewart-Jones[1], Hamilton Bennett[1], Seyhan Boyoglu-Barnum[2], Wei Shi[2], Barney S. Graham[2], Andrea Carfi[1#], Kizzmekia S. Corbett[2#], Robert A. Seder[2#], Darin K. Edwards[1#]

[1]Moderna Inc., Cambridge, MA, USA

[2]National Institutes of Health, National Institute of Allergy and Infectious Diseases, Vaccine Research Center, Bethesda, MD, USA

the B.1.351 variant remained at ~1/300. Taken together these data demonstrate reduced but still significant neutralization against the full B.1.351 variant following mRNA-1273 vaccination.

https://doi.org/10.1101/2021.01.25.427948

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- 2. gleicher Booster nach 6-12 Monaten (Aktien +12%...)
- Neuer Booster mit aktualisierter mRNA-Sequenz (mRNA-1273.351) gegen Variante aus RSA (B.1.351)

Moderna's two-pronged approach to combating emerging SARS-CoV-2 variants

BY SANDI WONG, ASSISTANT EDITOR

JAN 26, 2021 | 3:30 AM CET

Moderna is taking a two-pronged approach to addressing potentially weakened vaccine protection against SARS-CoV-2 variants by evaluating an additional booster shot of its current vaccine — a solution that could apply to multiple mutants — and a new booster candidate designed against a specific variant.

In a tweet, Acting FDA Commissioner Janet Woodcock said the agency is considering regulatory pathways for authorized COVID-19 vaccines or other products that would require changes in response to emerging variants, but hasn't announced specific plans. FDA has longstanding experience with mutating viruses through its oversight of flu vaccines, which are updated on an annual basis.

Moderna Inc. (NASDAQ:MRNA) gained $15.96 (12%) to $147 Monday when it announced plans to test a second booster shot of Moderna COVID-19 Vaccine (mRNA-1273). On a conference call Monday, CMO Tal Zaks said third injection would likely be given 6-12 months after the initial two in the vaccination schedule, but not sooner.

The company also plans to advance mRNA-1273.351, designed as a booster against the B.1.351 (501Y.V2) variant first identified in South Africa, into preclinical and Phase I testing; its development timeline is not disclosed.

The biotech also published Monday, with NIH's National Institute of Allergy and Infectious Diseases, a ***bioRxiv*** paper showing antibodies evoked by Moderna COVID-19 Vaccine were less potent against pseudoviruses with spikes bearing all the B.1.351 mutations vs. the D614G mutation alone.

Neutralizing geometric mean titers (GMTs) in sera from eight Phase I volunteers fell 6.4-fold (p=0.0078) against the variant's spike, but remained above thresholds that protected non-human primates in SARS-CoV-2 challenge titers.

On Monday's call, Moderna President Stephen Hoge pointed out that all eight trial participants' sera remained "able to completely neutralize" the pseudovirus variant, suggesting Moderna COVID-19 Vaccine will remain effective against B.1.351.

The participants' titers were also 2.7 times lower in assays using spikes that had only D614G plus the three receptor-binding domain (RBD) mutations, which are also present in the P.1 variant — also known as 501Y.V3 —first identified in Brazil.

https://www.biocentury.com/article/633630/how-spike-mutations-in-sars-cov-2-variants-affect-vaccines-therapies-data-byte?return_feed=%2Fcoronavirus

Offene Fragen

- Dauer der Immunität
- Notwendigkeit eines Boosters?
- Potenzielle Langzeitfolgen?
- Schutz bei Immunsupprimierten?
- Altersabhängige Wirksamkeit oder Wirkdauer?
- Mukosale Immunität? i.e. nur «disease-preventing» oder auch «transmission-blocking»?
- Kosten…
- Impfprioritäten in der CH?

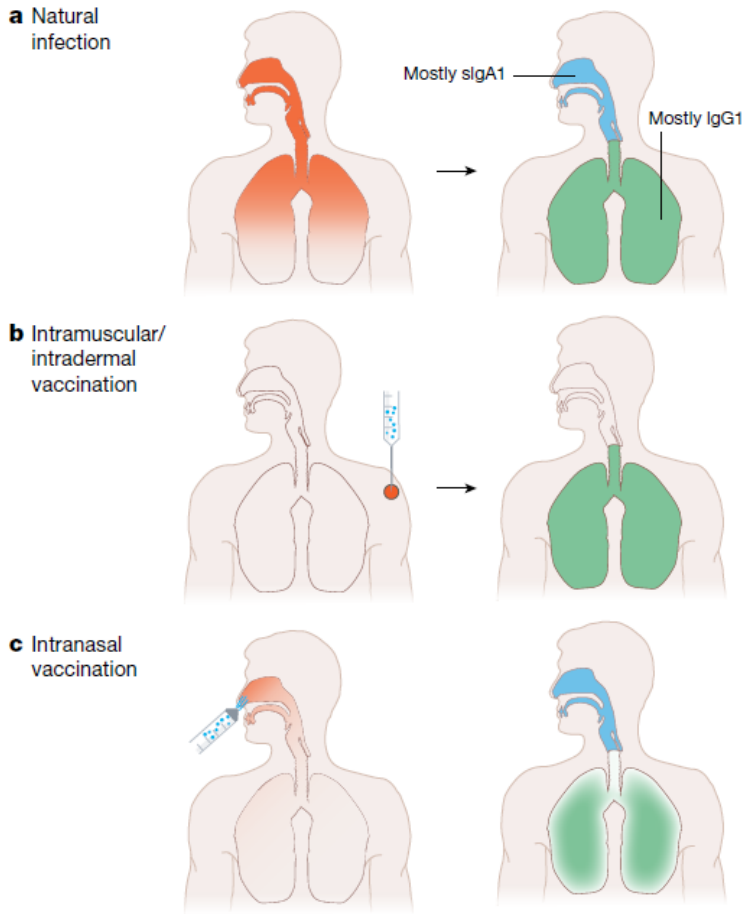
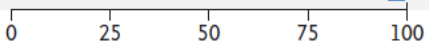


Fig. 2 | Mucosal and systemic immune responses to natural infection with respiratory viruses and to vaccination. The lower human respiratory tract

Moderna - Subgruppenanalysen

Subgroup	Placebo (N=14,073)	mRNA-1273 (N=14,134)	Vaccine Efficacy (95% CI)
	no. of events/total no.		
All patients	185/14,073	11/14,134	94.1 (89.3–96.8)
Age			
≥18 to <65 yr	156/10,521	7/10,551	95.6 (90.6–97.9)
≥65 yr	29/3552	4/3583	86.4 (61.4–95.2)
Age, risk for severe Covid-19			
18 to <65 yr, not at risk	121/8403	5/8396	95.9 (90.0–98.3)
18 to <65 yr, at risk	35/2118	2/2155	94.4 (76.9–98.7)
≥65 yr	29/3552	4/3583	86.4 (61.4–95.2)
Sex			
Male	87/7462	4/7366	95.4 (87.4–98.3)
Female	98/6611	7/6768	93.1 (85.2–96.8)
At risk for severe Covid-19			
Yes	43/3167	4/3206	90.9 (74.7–96.7)
No	142/10,906	7/10,928	95.1 (89.6–97.7)
Race and ethnic group			
White	144/8916	10/9023	93.2 (87.1–96.4)
Communities of color	41/5132	1/5088	97.5 (82.2–99.7)



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Vaccine pipeline implementation worldwide

	BioNTech BNT162 (b1/b2)	Moderna mRNA-1273	Oxford ChAdOx1-S
Developer(s)	BioNTech, Fosun Pharma, Pfizer	Moderna, NIAID	University of Oxford, AstraZeneca
Platform	RNA	RNA	Non-replicating viral vector
Dosing	2 doses, intramuscular	2 doses, intramuscular	2 doses, intramuscular
Description	Lipid nanoparticle-formulated mRNA encoding full-length spike (S) protein	Lipid nanoparticle-encapsulated mRNA encoding pre-fusion spike (S) protein	Simian adenovirus vector containing codon-optimised spike (S) protein
Efficacy data	Vaccine efficacy against COVID-19 reported to be 95% based on primary efficacy analysis of 170 confirmed cases (18 Nov 2020). These included 10 cases of severe COVID-19, 9 of which occurred in the placebo group.	Vaccine efficacy against COVID-19 reported to be 94.5% based on interim data from 95 cases (16 Nov 2020). These included 11 cases of severe COVID-19, all of which occurred in the placebo group.	Vaccine efficacy against COVID-19 reported to be 62–90% based on interim data from 131 cases (23 Nov 2020).
Storage requirements	Ultra-cold (-60°C to -80°C)	Refrigeration (2°C to 8°C) for up to 30 days or frozen (-15°C to -25°C) for long-term storage	Refrigeration (2°C to 8°C)
ONE Vaccine Access Test score	BioNTech and Pfizer given scores of 1 out of 15 and 2.8 out of 15, respectively	Moderna given score of 1.7 out of 15	AstraZeneca given score of 8.6 out of 15
Manufacture projections	50 million doses in 2020 and up to 1.3 billion doses in 2021 (09 Nov 2020)	500 million to 1 billion doses per year (26 Oct 2020)	3 billion doses in 2021 (23 Nov 2020)
Approval/licensure	Not yet approved for widespread use	Not yet approved for widespread use	Not yet approved for widespread use

Vaccines undergoing phase III efficacy testing are included (see **Clinical trials** and **Trial mapper** tabs for further details). Information on storage requirements obtained from Poland et al (2020).

https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

INSELGRUPPE

Landscape of candidate vaccines in clinical development

Dienstag, 26. Januar 2021

DISCLAIMER: These landscape documents have been prepared by the World Health Organization (WHO) for information purposes only concerning the 2019-2020 pandemic of the novel coronavirus. Inclusion of any particular product or entity in any of these landscape documents does not constitute, and shall not be deemed or construed as, any approval or endorsement by WHO of such product or entity (or any of its businesses or activities). While WHO takes reasonable steps to verify the accuracy of the information presented in these landscape documents, WHO does not make any (and hereby disclaims all) representations and warranties regarding the accuracy, completeness, fitness for a particular purpose (including any of the aforementioned purposes), quality, safety, efficacy, merchantability and/or non-infringement of any information provided in these landscape documents and/or of any of the products referenced therein. WHO also disclaims any and all liability or responsibility whatsoever for any death, disability, injury, suffering, loss, damage or other prejudice of any kind that may arise from or in connection with the procurement, distribution or use of any product included in any of these landscape documents.

New information that has been added this week is highlighted in yellow

(NCT04510207) This Phase 3 trial assesses both the Wuhan and Beijing vaccine in the same study.

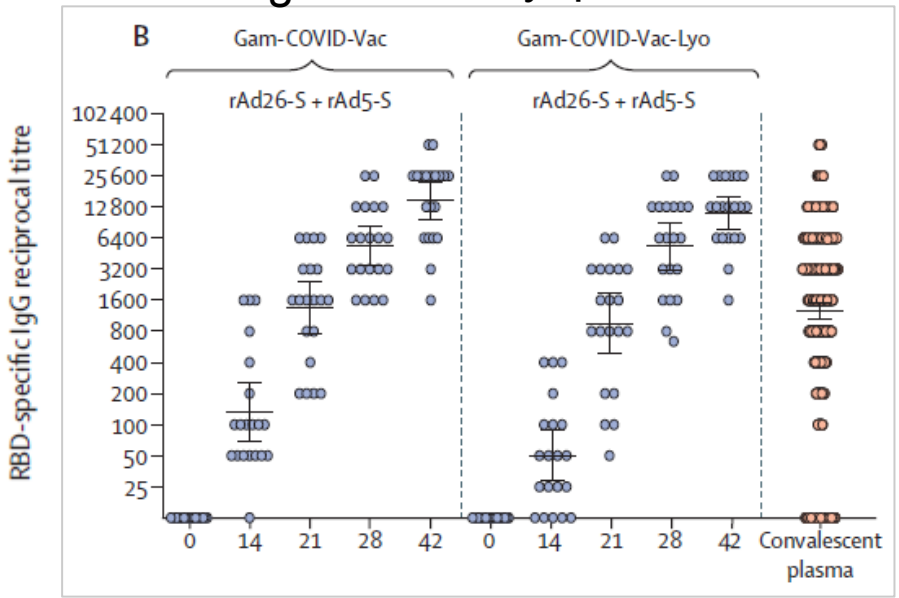
Information highlighted in red indicates a change in the development of the vaccine

									Current status of clinical evaluation (Trial registries and public reports)				
ID	Vaccine platform acronym	Vaccine platform description	Type of candidate vaccine	Number of doses	Dosing schedule	Route of administration	Developers	Phase	Phase 1	Phase 1/2	Phase 2	Phase 2/3	Phase 3
3	IV	Inactivated virus	Inactivated SARS-CoV-2 vaccine (Vero cell)	2	Day 0 + 21	IM	Sinopharm + China National Biotec Group Co + Beijing Institute of Biological Products	Phase 3		ChiCTR2000032459 Study Report			NCT04560881 NCT04510207*
4	VVnr	Viral vector (Non-replicating)	ChAdOx1-S - (AZD1222) (Covishield)	1-2	Day 0 + 28	IM	AstraZeneca + University of Oxford	Phase 3	PACTR202005681895696	PACTR202006922165132 2020-001072-15 Interim Report NCT04568031 Study Report NCT04444674 NCT04324606 Study Report Study Report Study Report NCT04684446	NCT04686773	NCT04400838 Study Report CTRI/2020/08/027170	ISRCTN89951424 NCT04516746 NCT04540393 NCT04536051 EUCTR2020-005226-28- Study Report
5	VVnr	Viral vector (Non-replicating)	Recombinant novel coronavirus vaccine (Adenovirus type 5 vector)	1	Day 0	IM	CanSino Biological Inc./Beijing Institute of Biotechnology	Phase 3	ChiCTR2000030906 NCT04313127 NCT04568811 NCT04552366 Study Report	NCT04398147	ChiCTR2000031781 NCT04566770 NCT04341389 Study Report		NCT04526990 NCT04540419
6	VVnr	Viral vector (Non-replicating)	Gam-COVID-Vac Adeno-based (rAd26-S+rAd5-S)	2	Day 0 + 21	IM	Gamaleya Research Institute ; Health Ministry of the Russian Federation	Phase 3		NCT04436471 NCT04437875 NCT04713488 Study Report	NCT04587219	NCT04640233	NCT04530396 NCT04564716 NCT04642339 NCT04656613
7	VVnr	Viral vector (Non-replicating)	Ad26.COV2.S	1-2	Day 0 or Day 0 +56	IM	Janssen Pharmaceutical	Phase 3	NCT04509947	NCT04436276 Study Report Study Report	EUCTR2020-002584-63-DE NCT04535453		NCT04505722 NCT04614948
8	PS	Protein subunit	SARS-CoV-2 rS/Matrix M1-Adjuvant (Full length recombinant SARS CoV-2 glycoprotein nanoparticle vaccine adjuvanted with Matrix M)	2	Day 0 + 21	IM	Novavax	Phase 3		NCT04368988	NCT04533399		NCT04611802

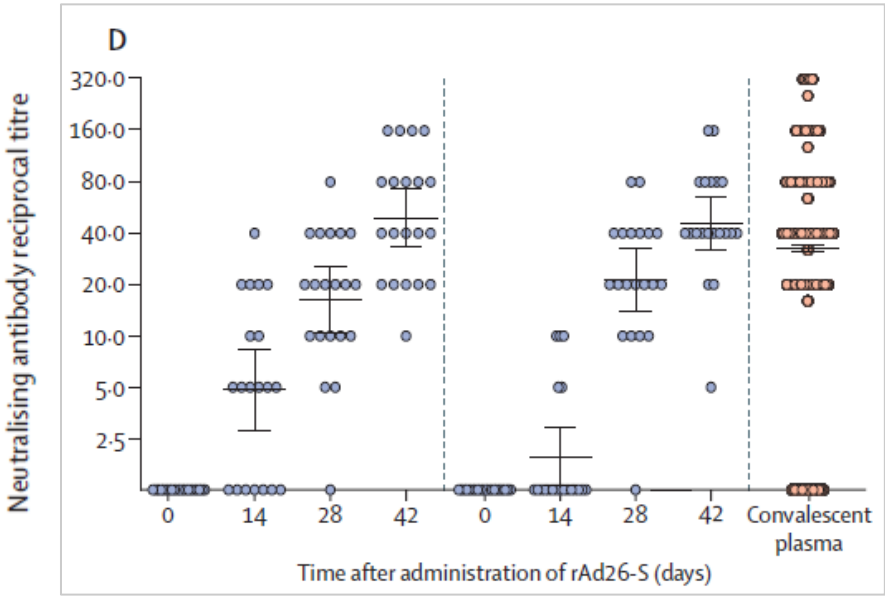
https://www.who.int/publications/m/item/draft-landscape-of-covid-19-candidate-vaccines

Humorale Antwort

gefroren lyophilisiert



gefroren lyophilisiert



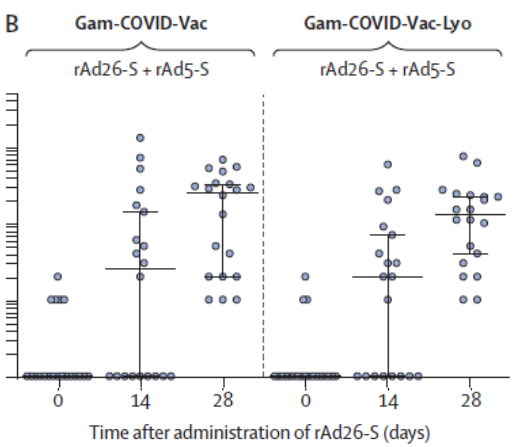
lyophylisiert = getrocknet durch Gefrieren in hohem Vakuum

Logunov; Lancet Sept. 2020

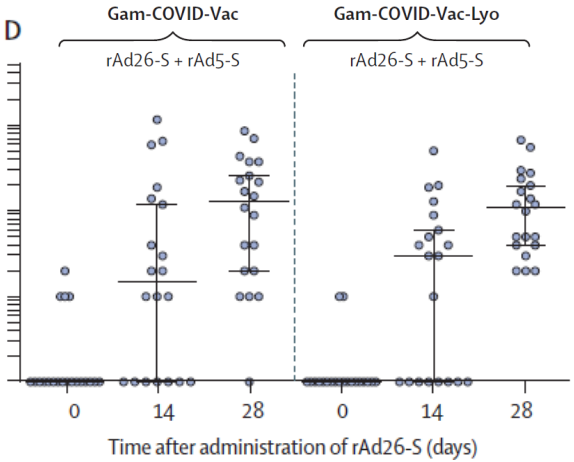
INSELGRUPPE

Zelluläre Antwort

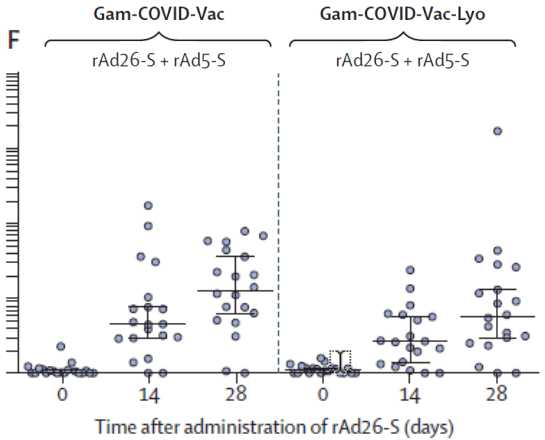
gefroren lyophilisiert



CD4+-proliferation



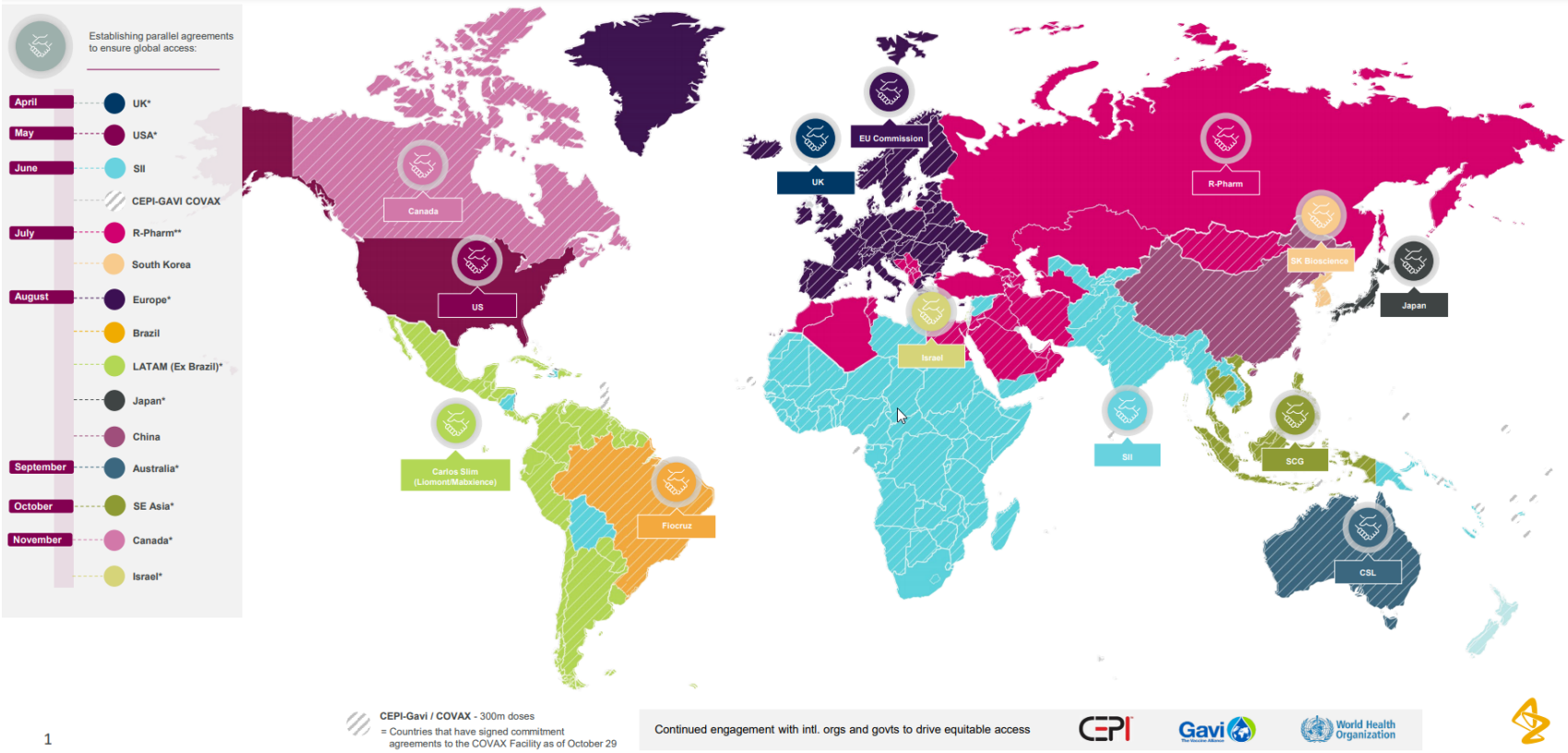
CD8+-proliferation



INF-γ increase (folds)

Logunov; Lancet Sept. 2020

Astra Zeneca candidate vaccine



scape/