COVID-19 vaccines

Foroud Shahbazi PharmD

Vaccine types

- Attenuate
- Inactivate
- Protein Subunit vaccines
- Polysaccharide
- Conjugated
- Virus particle
- Viral vector
- Nucleic acid

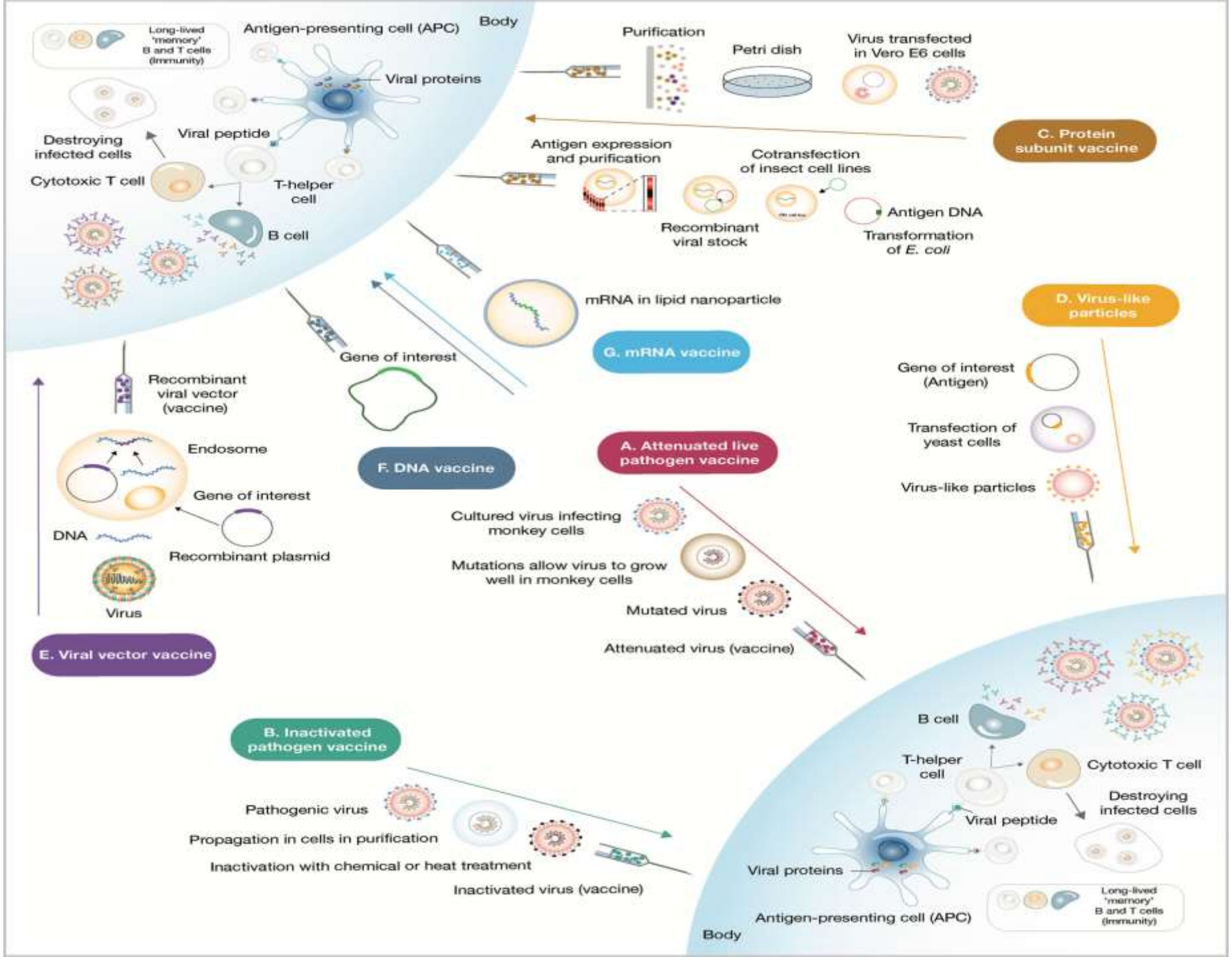
What technology do the leading SARS-CoV-2 vaccines use?

- **Viral vector vaccines**
  - Johnson & Johnson
  - Oxford-AstraZeneca
  - Gamaleya Research Institute
- **Protein based vaccines**
  - Novavax
- **mRNA vaccines**

What technology do the leading SARS-CoV-2 vaccines use?

- Pfizer-BioNTech
- Moderna
- **Inactivated vaccines**
  - Sinopharm
  - Sinovac
  - Sinopharm-Wuhan
  - Bharat Biotech

- The US Food and Drug Administration’s guidelines indicate that they would license a vaccine against the pandemic virus that showed at least 50% efficacy


Body
Long-lived 'memory' B and T cells (immunity)
Antigen-presenting cell (APC)
Viral proteins
Destroying infected cells
Viral peptide
Cytotoxic T cell
T-helper cell
B cell
Purification
Petri dish
Virus transfected in Vero E6 cells
C. Protein subunit vaccine
Antigen expression and purification
Cotransfection of insect cell lines
Recombinant viral stock
Antigen DNA
Transformation of E. coli
mRNA in lipid nanoparticle
G. mRNA vaccine
D. Virus-like particles
Gene of interest (Antigen)
Transfection of yeast cells
Virus-like particles
Gene of interest
Recombinant viral vector (vaccine)
Endosome
Gene of interest
DNA
Recombinant plasmid
Virus
F. DNA vaccine
A. Attenuated live pathogen vaccine
Cultured virus infecting monkey cells
Mutations allow virus to grow well in monkey cells
Mutated virus
Attenuated virus (vaccine)
E. Viral vector vaccine
B. Inactivated pathogen vaccine
Pathogenic virus
Propagation in cells in purification
Inactivation with chemical or heat treatment
Inactivated virus (vaccine)
B cell
T-helper cell
Cytotoxic T cell
Destroying infected cells
Viral peptide
Viral proteins
Antigen-presenting cell (APC)
Long-lived 'memory' B and T cells (immunity)
Body

Inactivated vaccines

- Sinopharm
- Bharat
- Barakat

Efficacy/ Sinopharm

Research

JAMA | Original Investigation

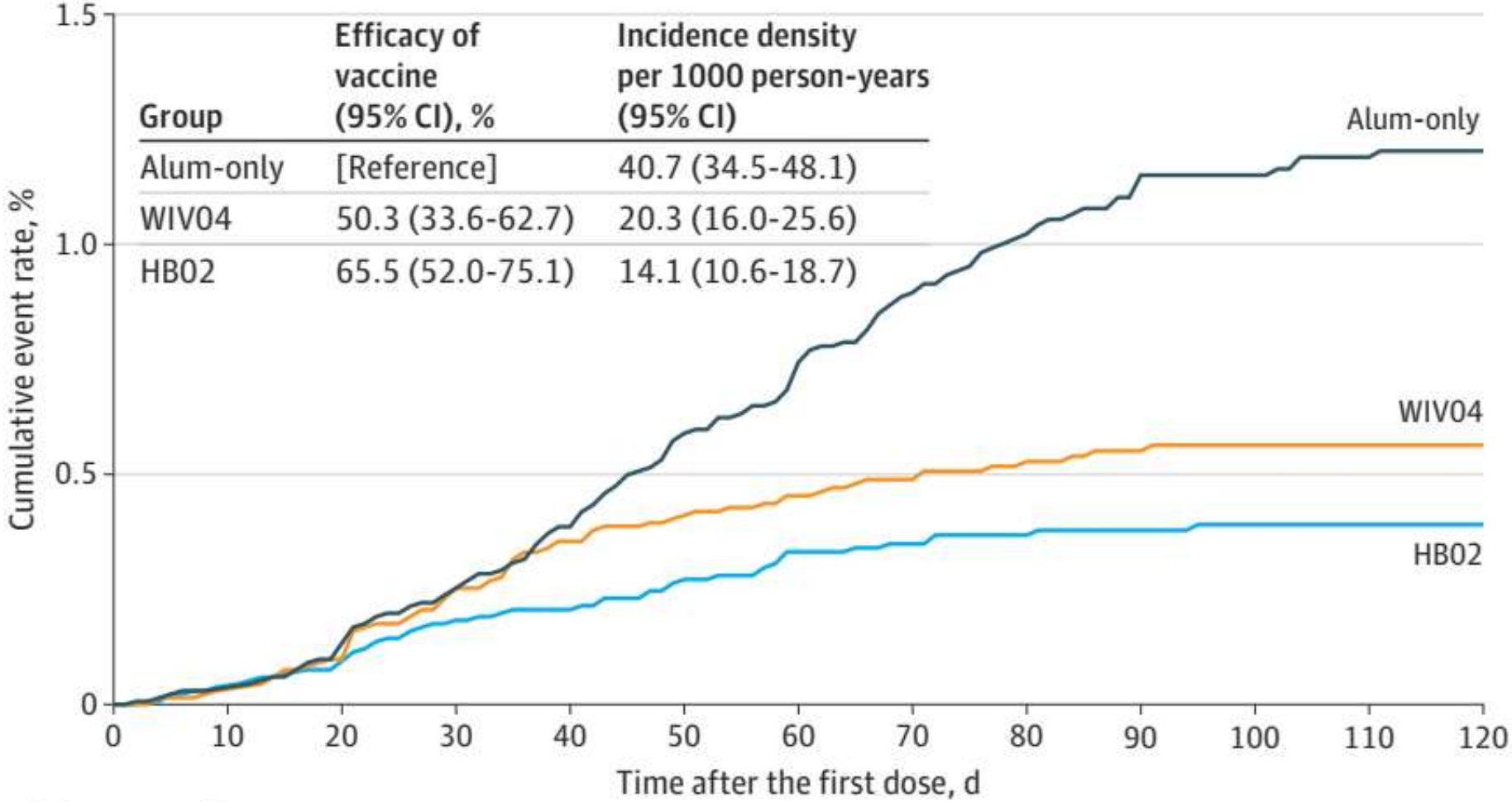
Effect of 2 Inactivated SARS-CoV-2 Vaccines on Symptomatic COVID-19 Infection in Adults

A Randomized Clinical Trial

Nawal Al Kaabi, MBBS; Yuntao Zhang, PhD; Shengli Xia, BSc; Yunkai Yang, MSc; Manaf M. Al Qahtani, MD; Najiba Abdulrazzaq, MBBS; Majed Al Nusair, MD; Mohamed Hassany, MD; Jaleela S. Jawad, MBBS; Jehad Abdalla, MBBS; Salah Eldin Hussein, MBBS; Shamma K. Al Mazrouei, MBBS; Maysoon Al Karam, MBBS; Xinguo Li, MSc; Xuqin Yang, MSc; Wei Wang, MSc; Bonan Lai, MSc; Wei Chen, MSc; Shihe Huang, PhD; Qian Wang, MSc; Tian Yang, BSc; Yang Liu, MSc; Rui Ma, MSc; Zaidoon M. Hussain, MD; Tehmina Khan, MD; Mohammed Saifuddin Fasihuddin, BSc; Wangyang You, BSc; Zhiqiang Xie, MSc; Yuxiu Zhao, MSc; Zhiwei Jiang, PhD; Guoqing Zhao, PhD; Yanbo Zhang, MSc; Sally Mahmoud, PhD; Islam ElTantawy, BSc; Peng Xiao, MSc; Ashish Koshy, MSc; Walid Abbas Zaher, PhD; Hui Wang, BSc; Kai Duan, PhD; An Pan, PhD; Xiaoming Yang, MD

- Question What is the efficacy of 2 inactivated SARS-CoV-2 vaccines for prevention of symptomatic COVID-19?
- Findings This prespecified interim analysis of a randomized clinical trial included 40 382 participants who received at least 1 dose of a 2-dose inactivated vaccine series developed from either SARS-CoV-2 WIV04 (5 μg/dose) or HB02 (4 μg/dose) strains or an aluminum hydroxide–only control, with a primary end point of the incidence of symptomatic COVID-19 at least 14 days after the second injection. The efficacy for the 2 vaccines, compared with an aluminum hydroxide–only control, was 72.8% in the WIV04 group and 78.1% in the HB02 group; both comparisons were statistically significant.
- Meaning Two inactivated SARS-CoV-2 vaccines demonstrated efficacy against symptomatic COVID-19 compared with an aluminum hydroxide–only control

B Full analysis population-1

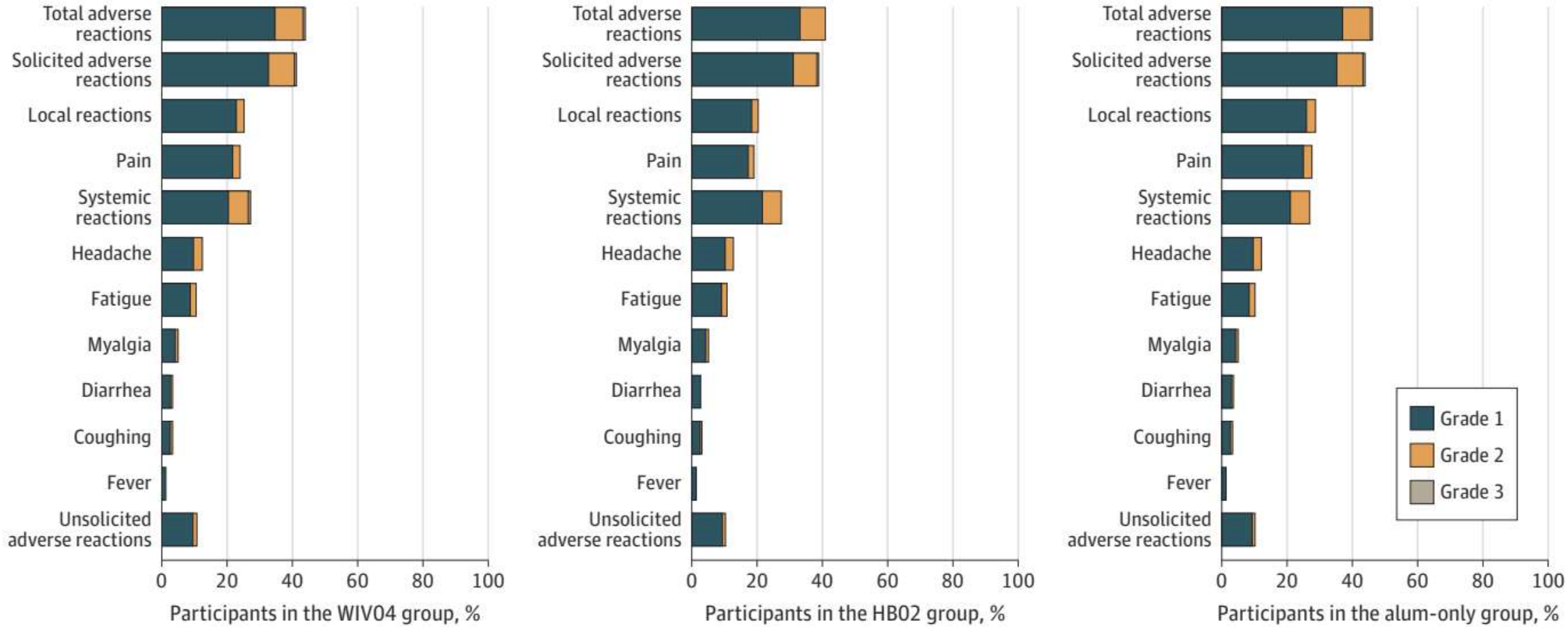


Group	Efficacy of vaccine (95% CI), %	Incidence density per 1000 person-years (95% CI)
Alum-only	[Reference]	40.7 (34.5-48.1)
WIV04	50.3 (33.6-62.7)	20.3 (16.0-25.6)
HB02	65.5 (52.0-75.1)	14.1 (10.6-18.7)

No. of participants at risk

Alum-only	13425	13273	12981	12749	12594	11857	11501	10900	9672	8041	7728	7430	665
WIV04	13428	13294	12979	12771	12622	11984	11614	11012	9780	8074	7772	7502	665
HB02	13436	13300	12993	12781	12624	11953	11618	11008	9783	8134	7844	7573	653

Figure 3. Common Adverse Reactions and Grades Within 7 Days After 2 Doses in the Safety Analysis Set



Other inactivated vaccines

- Bharat and Barakat

Safety and immunogenicity of an inactivated SARS-CoV-2 vaccine, BBV152: a double-blind, randomised, phase 1 trial

Raches Ella, Krishna Mohan Vadrevu, Harsh Jogdand, Sai Prasad, Siddharth Reddy, Vamshi Sarangi, Brunda Ganneru, Gajanan Sapkal, Pragya Yadav, Priya Abraham, Samiran Panda, Nivedita Gupta, Prabhakar Reddy, Savita Verma, Sanjay Kumar Rai, Chandramani Singh, Sagar Vivek Redkar, Chandra Sekhar Gillurkar, Jitendra Singh Kushwaha, Satyajit Mohapatra, Venkat Rao, Randeep Guleria, Krishna Ella, Balram Bhargava

Summary

Background To mitigate the effects of COVID-19, a vaccine is urgently needed. BBV152 is a whole-virion inactivated SARS-CoV-2 vaccine formulated with a toll-like receptor 7/8 agonist molecule adsorbed to alum (Algel-IMDG) or alum (Algel).

Methods We did a double-blind, multicentre, randomised, controlled phase 1 trial to assess the safety and immunogenicity of BBV152 at 11 hospitals across India. Healthy adults aged 18–55 years who were deemed healthy by the investigator were eligible. Individuals with positive SARS-CoV-2 nucleic acid and/or serology tests were excluded. Participants were randomly assigned to receive either one of three vaccine formulations (3 μg with Algel-IMDG, 6 μg with Algel-IMDG, or 6 μg with Algel) or an Algel only control vaccine group. Block randomisation was done with a web response platform. Participants and investigators were masked to treatment group allocation. Two intramuscular doses of vaccines were administered on day 0 (the day of randomisation) and day 14. Primary outcomes were solicited local and systemic reactogenicity events at 2 h and 7 days after vaccination and throughout the full study duration, including serious adverse events. Secondary outcome was seroconversion (at least four-fold increase from baseline) based on wild-type virus neutralisation. Cell-mediated responses were evaluated by intracellular staining and ELISpot. The trial is registered at ClinicalTrials.gov (NCT04471519).

Vector based vaccines

- Sputnik V
- Johnson & Johnson
- Chimpanzee adenovirus (ChAdOx1)
- Viral vector vaccines use a genetically manipulated measles or adenoviral platform to express a foreign antigen commonly resulting in robust cellular and humoral response.

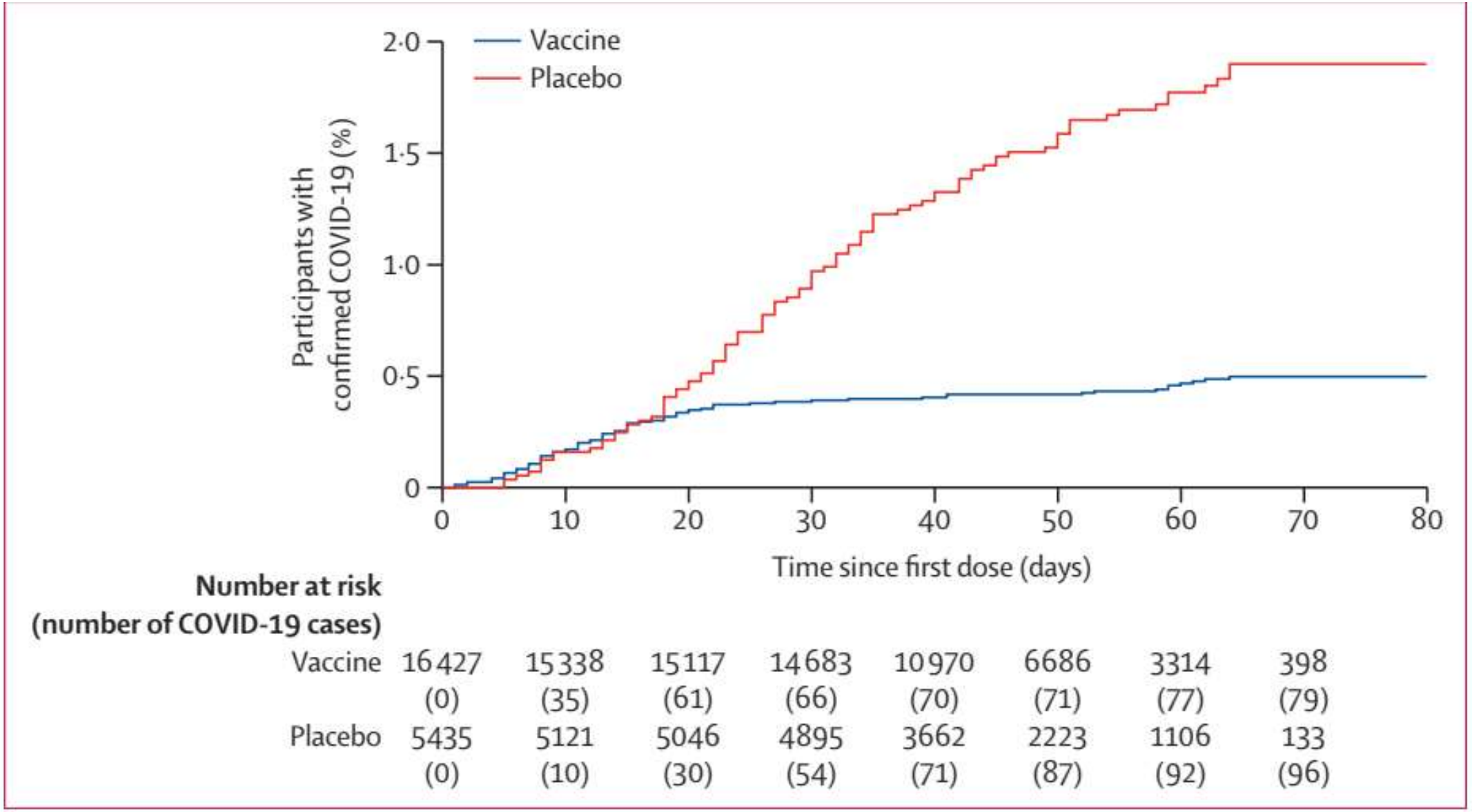
Sputnik V

Safety and efficacy of an rAd26 and rAd5 vector-based heterologous prime-boost COVID-19 vaccine: an interim analysis of a randomised controlled phase 3 trial in Russia

Denis Y Logunov, Inna V Dolzhikova*, Dmitry V Shcheblyakov, Amir I Tukhvatulin, Olga V Zubkova, Alina S Dzharullaeva, Anna V Kovyrshina, Nadezhda L Lubenets, Daria M Grousova, Alina S Erokhova, 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, Daria A Egorova, Maksim M Shmarov, Natalia A Nikitenko, Vladimir A Gushchin, Elena A Smolyarchuk, Sergey K Zyryanov, Sergei V Borisevich, Boris S Naroditsky, Alexander L Gintsburg, and the Gam-COVID-Vac Vaccine Trial Group†*

Summary

- The vaccine was administered (0·5 mL/dose) intramuscularly in a prime-boost regimen: a 21-day interval between the first dose (rAd26) and the second dose (rAd5), both vectors carrying the gene for the full-length SARS-CoV-2 glycoprotein S.
- The primary outcome was the proportion of participants with PCR-confirmed COVID-19 from day 21 after receiving the first dose



Number at risk (number of COVID-19 cases)

Vaccine	16427 (0)	15338 (35)	15117 (61)	14683 (66)	10970 (70)	6686 (71)	3314 (77)	398 (79)
Placebo	5435 (0)	5121 (10)	5046 (30)	4895 (54)	3662 (71)	2223 (87)	1106 (92)	133 (96)

Figure 2: **Kaplan-Meier cumulative incidence curves for the first symptomatic, PCR-positive COVID-19 after dose 1, in participants who received at least one dose of vaccine or placebo**

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, Shaun L Barnabas, Qasim E Bhorat, Sagida Bibi, Carmen Briner, Paola Cicconi, Andrea M Collins, Rachel Colin-Jones, Clare L Cutland, Thomas C Darton, Keertan Dheda, Christopher J A Duncan, Katherine R W Emary, Katie J Ewer, Lee Fairlie, Saul N Faust, Shuo Feng, Daniela M Ferreira, Adam Finn, Anna L Goodman, Catherine M Green, Christopher A Green, Paul T Heath, Catherine Hill, Helen Hill, Ian Hirsch, Susanne H C Hodgson, Alane Izu, Susan Jackson, Daniel Jenkin, Carina C D Joe, Simon Kerridge, Anthonet Koen, Gaurav Kwatra, Rajeka Lazarus, Alison M Lawrie, Alice Lelliott, Vincenzo Libri, Patrick J Lillie, Raburn Mallory, Ana V A Mendes, Eveline P Milan, Angela M Minassian, Alastair McGregor, Hazel Morrison, Yama F Mujadidi, Anusha Nana, Peter J O'Reilly, Sherman D Padayachee, Ana Pittella, Emma Plested, Katrina M Pollock, Maheshi N Ramasamy, Sarah Rhead, Alexandre V Schwarzbold, Nisha Singh, Andrew Smith, Rinn Song, Matthew D Snape, Eduardo Sprinz, Rebecca K Sutherland, Richard Tarrant, Emma C Thomson, M Estée Török, Mark Toshner, David P J Turner, Johan Vekemans, Tonya L Villafana, Marion E E Watson, Christopher J Williams, Alexander D Douglas*, Adrian V S Hill*, Teresa Lambe*, Sarah C Gilbert*, Andrew J Pollard* on behalf of the Oxford COVID Vaccine Trial Group†*

- Participants in the ChAdOx1 nCoV-19 group received two doses containing 5×10^{10} viral particles (standard dose; SD/SD cohort); a subset in the UK trial received a half dose as their first dose (low dose) and a standard dose as their second dose (LD/SD cohort)

	Total number of cases	ChAdOx1 nCoV-19	Control	Vaccine efficacy (95% CI)	p value for interaction
COV002 (UK), age 18–55 years*	..	..	..	..	0·019
LD/SD recipients	33	3/1367 (0·2%)	30/1374 (2·2%)	90·0% (67·3 to 97·0)	..
SD/SD recipients	49	14/1879 (0·7%)	35/1922 (1·8%)	59·3% (25·1 to 77·9)	..
COV002 (UK), age 18–55 years with >8 weeks' interval between vaccine doses*	..	..	..	..	0·082
LD/SD recipients	33	3/1357 (0·2%)	30/1362 (2·2%)	90·0% (67·3 to 97·0)	..
SD/SD recipients	34	8/1407 (0·6%)	26/1512 (1·7%)	65·6% (24·5 to 84·4)	..
All SD/SD (UK and Brazil)†	..	..	..	..	0·557
<6 weeks' interval between vaccine doses	28	9/1702 (0·5%)	19/1698 (1·1%)	53·4% (−2·5 to 78·8)	..
≥6 weeks' interval between vaccine doses	70	18/2738 (0·7%)	52/2757 (1·9%)	65·4% (41·1 to 79·6)	..

Cohorts are all subsets of the primary efficacy population. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. LD/SD=low-dose prime plus standard-dose boost. SD/SD=two standard-dose vaccines given. BMI=body-mass index. *Models adjusted for BMI (<30 *vs* ≥30 kg/m^2), health-care worker status (yes *vs* no), and ethnicity (white *vs* non-white). †Model adjusted for BMI (<30 *vs* ≥30 kg/m^2), health-care worker status (yes *vs* no), ethnicity (white *vs* non-white), age (<56 years *vs* ≥56 years), and study (COV002 *vs* COV003).

***Table 3*: Subgroup comparisons of efficacy against SARS-CoV-2 more than 14 days after a second dose of ChAdOx1 nCoV-19 vaccine in the primary efficacy population**

- The first regimen applied two full doses 4 weeks apart in 8895 adult participants and displayed a 62.1% efficacy. The second regimen, which was recognized to be the outcome of a logistics mistake, involved a half prime-dose followed by a full boost-dose with the same chronological separation between them and included 2741 individuals 18–55-year-old showing a 90% efficacy.
- It is hypothesized that this efficacy discrepancy might stem from the combination of the younger age group of the smaller cohort and the fact that a higher initial dose might promote the induction of antibodies against the viral vector, thereby hampering the intensity of the immune responses induced by the boost dose

J and J

ORIGINAL ARTICLE

Safety and Efficacy of Single-Dose Ad26.COV2.S Vaccine against Covid-19

J. Sadoff, G. Gray, A. Vandebosch, V. Cárdenas, G. Shukarev, B. Grinsztejn, P.A. Goepfert, C. Truyers, H. Fennema, B. Spiessens, K. Offergeld, G. Scheper, K.L. Taylor, M.L. Robb, J. Treanor, D.H. Barouch, J. Stoddard, M.F. Ryser, M.A. Marovich, K.M. Neuzil, L. Corey, N. Cauwenberghs, T. Tanner, K. Hardt, J. Ruiz-Guiñazú, M. Le Gars, H. Schuitemaker, J. Van Hoof, F. Struyf, and M. Douoguih, for the ENSEMBLE Study Group*

ABSTRACT

Other vaccines

The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 FEBRUARY 4, 2021 VOL. 384 NO. 5

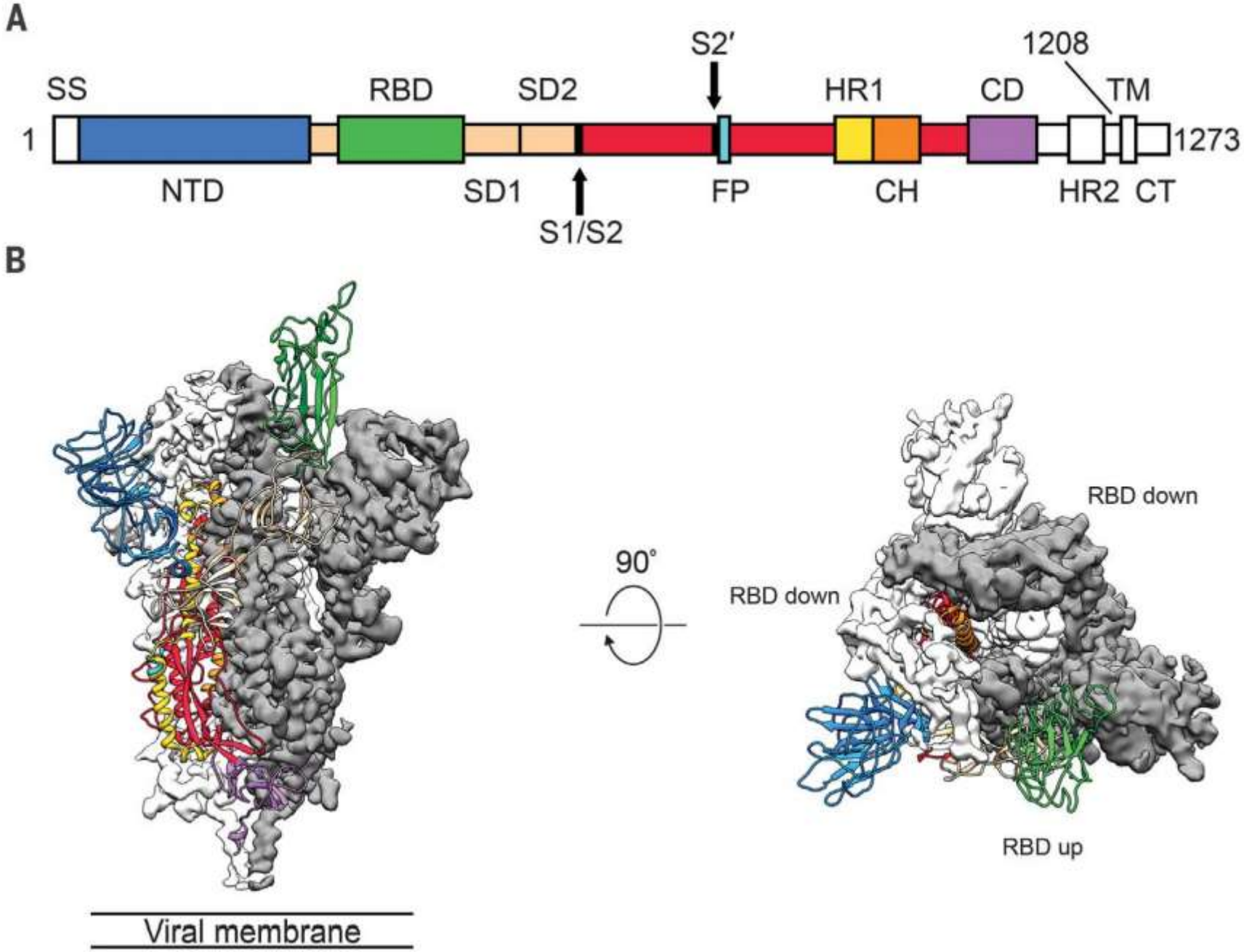
Efficacy and Safety of the mRNA-1273 SARS-CoV-2 Vaccine

L.R. Baden, H.M. El Sahly, B. Essink, K. Kotloff, S. Frey, R. Novak, D. Diemert, S.A. Spector, N. Rouphael, C.B. Creech, J. McGettigan, S. Khetan, N. Segall, J. Solis, A. Brosz, C. Fierro, H. Schwartz, K. Neuzil, L. Corey, P. Gilbert, H. Janes, D. Follmann, M. Marovich, J. Mascola, L. Polakowski, J. Ledgerwood, B.S. Graham, H. Bennett, R. Pajon, C. Knightly, B. Leav, W. Deng, H. Zhou, S. Han, M. Ivarsson, J. Miller, and T. Zaks, for the COVE Study Group*

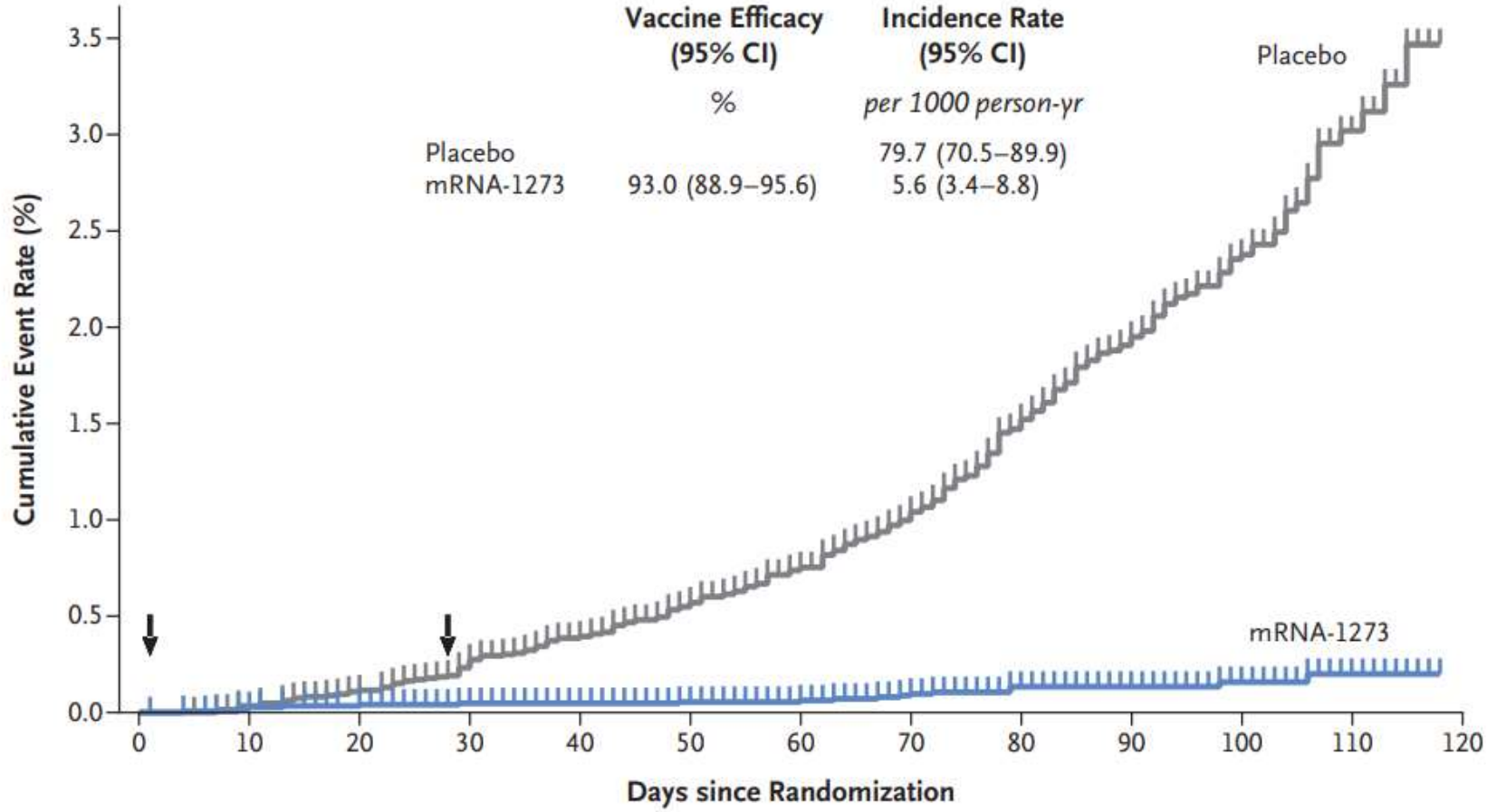
ABSTRACT

mRNA vaccines

- The vaccine is based on an mRNA molecule that contains the information for the synthesis of the stabilized prefusion form of the SARS-CoV-2 Spike (S) protein encapsulated in a lipid nanoparticle (LNP) vector that enhances uptake by host immune cells
- The administered mRNA uses the host cell transcription and translation machinery to produce the viral antigen that is afterward presented in T lymphocytes and is also directly recognized by B lymphocytes of the host, thereby initiating an adaptive immune response directed against the S protein of the virus


A
SS
RBD
SD2
S2′
HR1
CD
1208
TM
1
1273
NTD
SD1
S1/S2
FP
CH
HR2
CT
B
Viral membrane
90°
RBD down
RBD down
RBD up

B Modified Intention-to-Treat Analysis



No. at Risk

Placebo	14,598	14,590	14,567	14,515	13,806	13,352	12,694	11,450	9736	6729	4067	1200	0
mRNA-1273	14,550	14,543	14,532	14,504	13,825	13,398	12,791	11,573	9911	6871	4179	1238	0

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

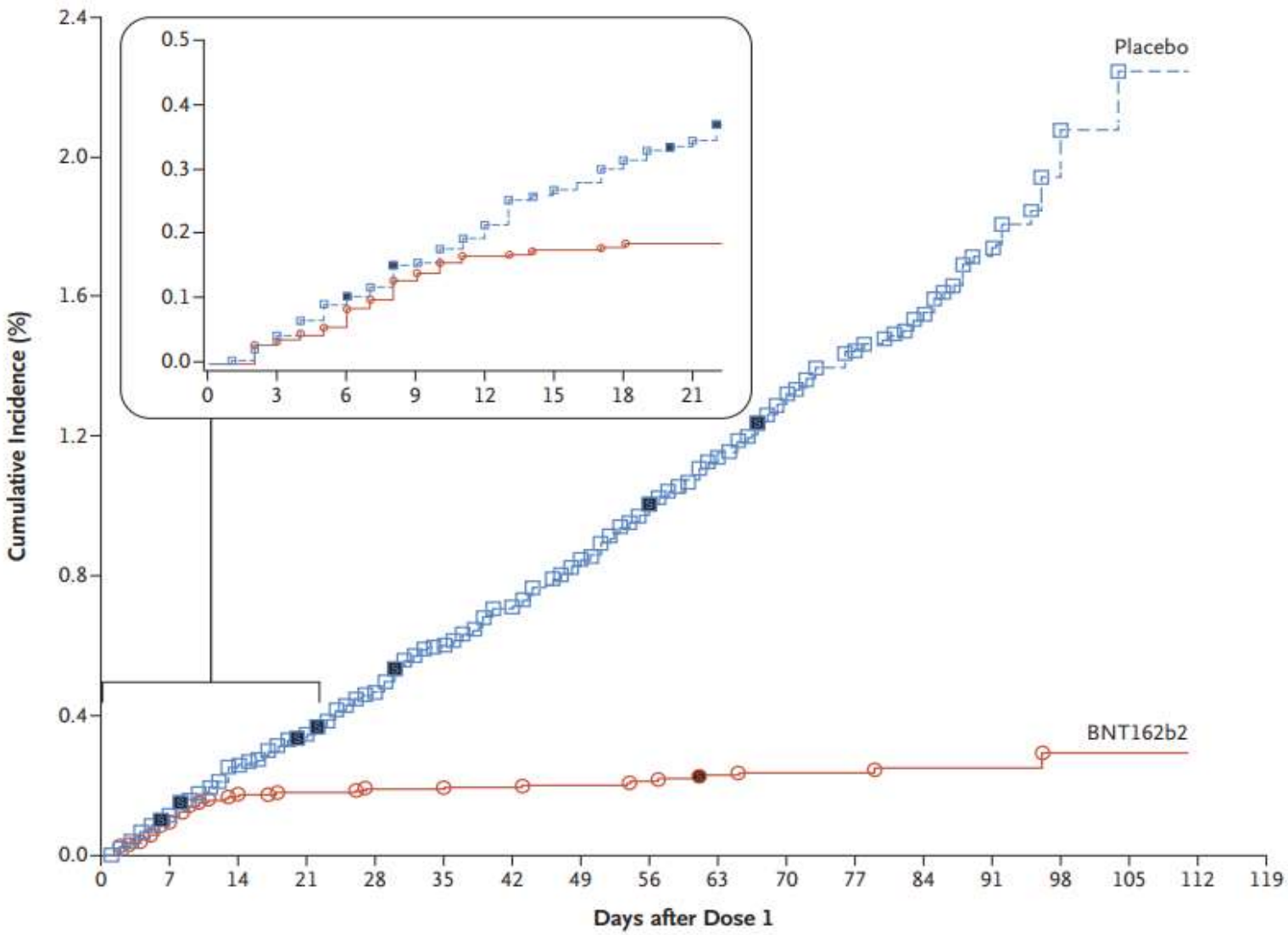
The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 31, 2020 VOL. 383 NO. 27

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

Fernando P. Polack, M.D., Stephen J. Thomas, M.D., Nicholas Kitchin, M.D., Judith Absalon, M.D., Alejandra Gurtman, M.D., Stephen Lockhart, D.M., John L. Perez, M.D., Gonzalo Pérez Marc, M.D., Edson D. Moreira, M.D., Cristiano Zerbini, M.D., Ruth Bailey, B.Sc., Kena A. Swanson, Ph.D., Satrajit Roychoudhury, Ph.D., Kenneth Koury, Ph.D., Ping Li, Ph.D., Warren V. Kalina, Ph.D., David Cooper, Ph.D., Robert W. Frenck, Jr., M.D., Laura L. Hammitt, M.D., Özlem Türeci, M.D., Haylene Nell, M.D., Axel Schaefer, M.D., Serhat Ünal, M.D., Dina B. Tresnan, D.V.M., Ph.D., Susan Mather, M.D., Philip R. Dormitzer, M.D., Ph.D., Uğur Şahin, M.D., Kathrin U. Jansen, Ph.D., and William C. Gruber, M.D., for the C4591001 Clinical Trial Group*

ABSTRACT



Efficacy End-Point Subgroup	BNT162b2, 30 μg (N=21,669)		Placebo (N=21,686)		VE (95% CI)
	No. of participants	Surveillance time *person-yr (no. at risk)*	No. of participants	Surveillance time *person-yr (no. at risk)*	*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)

The NEW ENGLAND JOURNAL of MEDICINE

CORRESPONDENCE

Three Doses of an mRNA Covid-19 Vaccine in Solid-Organ Transplant Recipients

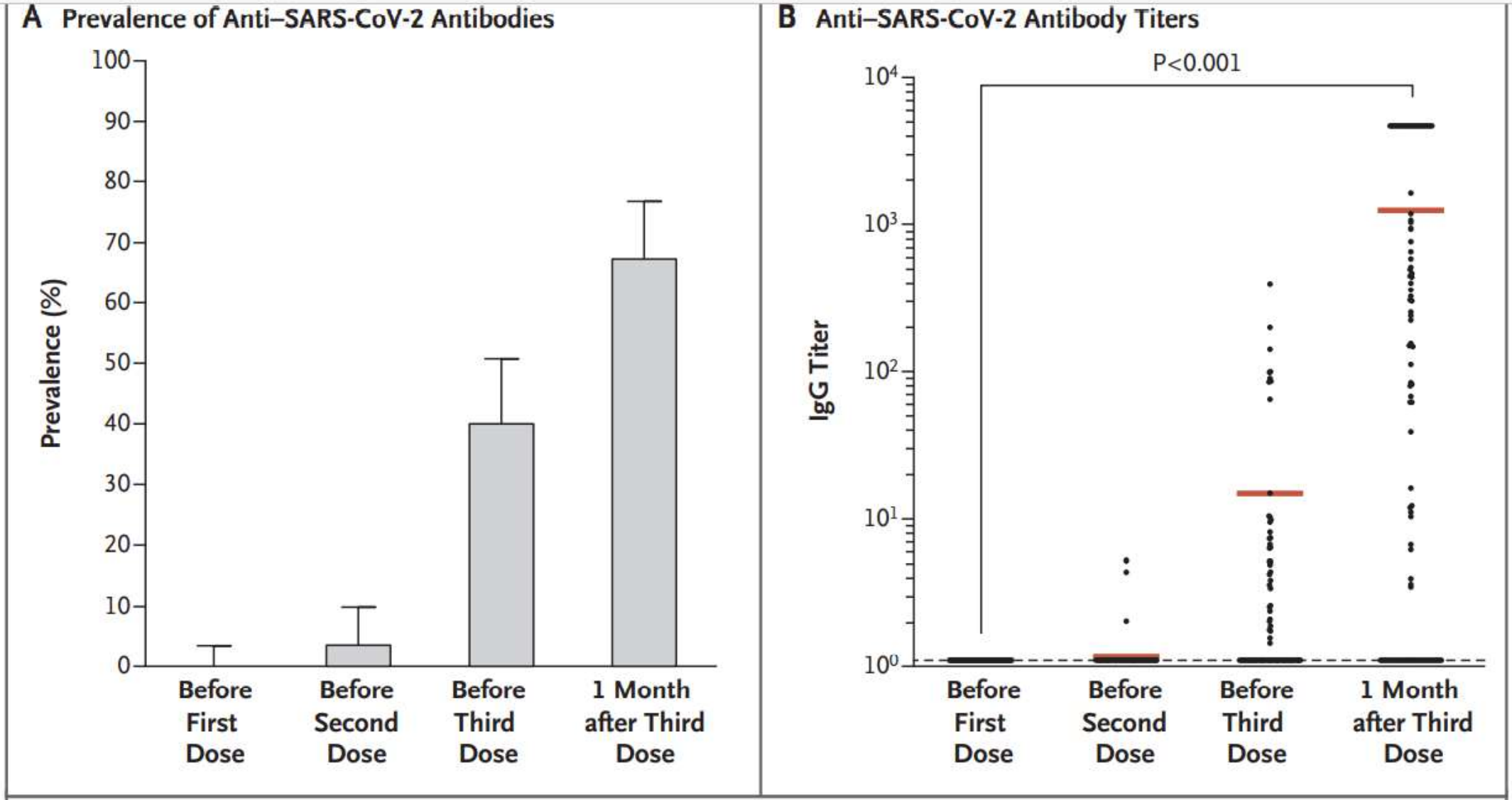


Figure 1. Immunogenicity.

Panel A shows the prevalence of anti–severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibodies before and after vaccination in the study population. Panel B shows anti–SARS-CoV-2 antibody titers before and after vaccination in the study population.

Adverse effects

Table 1 Adverse drug reactions

MedDRA SOC	Frequency	Adverse Reactions
Blood and lymphatic system disorders	Common	Thrombocytopenia[a]
	Uncommon	Lymphadenopathy
Immune system disorders	Not known	Anaphylaxis Hypersensitivity
Metabolism and nutrition disorders	Uncommon	Decreased appetite
Nervous system disorders	Very common	Headache
	Uncommon	Dizziness Somnolence
Vascular disorders	Very rare	Thrombosis with thrombocytopenia syndrome*
Gastrointestinal disorders	Very common	Nausea
	Common	Vomiting Diarrhoea
Skin and subcutaneous tissue disorders	Uncommon	Hyperhidrosis Pruritus Rash
Musculoskeletal and connective tissue disorders	Very common	Myalgia Arthralgia
General disorders and administration site conditions	Very common	Injection site tenderness Injection site pain Injection site warmth Injection site pruritus Injection site bruising[b] Fatigue Malaise Feverishness Chills
	Common	Injection site swelling Injection site erythema Fever[c]

Storage

- 6 months when stored in a refrigerator (2°C – 8°C)

- https://www.ema.europa.eu/en/documents/prac-recommendation/signal-assessment-report-embolic-thrombotic-events-smq-covid-19-vaccine-chadox1-s-recombinant-covid_en.pdf

Disseminated intravascular coagulation	IR per 100,000 Person years From FISABIO	EEA			EEA and UK		
		Expected 14d	Observed 14d From EV	OE 14d with 95% c.i.	Expected 14d	Observed 14d From EV	OE 14d with 95% c.i.
20-29	0.60	0.04	1	23.26 (0.30 - 129.41)	0.04	1	23.26 (0.30 - 129.41)
30-49	1.09	0.78	4	5.12 (1.38 - 13.11)	1.99	4	2.02 (0.54 - 5.16)
50-59	3.07	1.48	1	0.67 (0.01 - 3.75)	4.38	1	0.23 (0.00 - 1.27)
60-69	4.67	1.84	1	0.54 (0.01 - 3.03)	9.24	1	0.11 (0.00 - 0.60)
70-79	8.37	0.83	0	0.00 (0.00 - 4.42)	11.30	0	0.00 (0.00 - 0.32)
80+	11.66	0.90	0	0.00 (0.00 - 4.09)	5.37	0	0.00 (0.00 - 0.68)
Total		**5.87**	**7**	**1.19 (0.48 - 2.46)**	**32.31**	**7**	**0.22 (0.09 - 0.45)**

Cerebral Venous Sinus Thrombosis	IR per 100,000 Person years From ARS	EEA			EEA and UK		
		Expected 14d	Observed 14d From EV	OE 14d with 95% c.i.	Expected 14d	Observed 14d From EV	OE 14d with 95% c.i.
20-29	0.64	0.05	1	21.80 (0.28 - 121.32)	0.05	1	21.80 (0.28 - 121.32)
30-49	1.80	1.29	11	8.55 (4.26 - 15.31)	3.27	12	3.67 (1.89 - 6.41)
50-59	1.00	0.48	1	2.07 (0.03 - 11.53)	1.43	2	1.40 (0.16 - 5.06)
60-69	1.29	0.51	0	0.00 (0.00 - 7.23)	2.55	0	0.00 (0.00 - 1.44)
70-79	1.91	0.19	0	0.00 (0.00 - 19.37)	2.58	0	0.00 (0.00 - 1.42)
80+	1.55	0.12	0	0.00 (0.00 - 30.74)	0.71	0	0.00 (0.00 - 5.14)
Total		**2.63**	**13**	**4.94 (2.63 - 8.45)**	**10.58**	**15**	**1.42 (0.79 - 2.34)**

** Based on cases retrieved using a search in Eudravigilance with the Preferred Terms, "cerebral venous thrombosis" and "cerebral venous sinus thrombosis"*

TABLE 2 Summary of literature on suspected vaccine-induced thrombotic thrombocytopenia (VITT)

Publication	Country	Vaccine	Case number	F	M	Age (range)	Day[a] post vaccine (range)	Case fatality	General laboratory findings
									Platelet count (range) (10^9/L)
Greinacher et al[17]	Germany	AZ	9	8	1	22-49	4-16	4/8 (50%) died	9-100
Greinacher et al[18]	Germany	AZ	11	9	2	22-49	5-16	5/10 (50%) died	8-107
Schultz et al[19]	Norway	AZ	5	4	1	32-54	7-10	3/5 (60%) died	14-70
Scully et al[20]	UK	AZ	23	14	9	21-71	6-24	7/23 (30.4%) died	7-113
Mehta et al[21]	UK	AZ	2	0	2	25,32	6,9	2/2 (100%) died	30,19
Tiede et al[22]	Germany	AZ	5	5	0	41-67	5-11	0/5 (0%) died	27-105
See et al[23]	USA	JJ	12	12	0	18-60	6-15	3/12 (25%) died	9-127
Platton et al[24]	UK	AZ	43 (27 'probable'; 7 'possible'; 9 'unlikely')	NR	NR	NR	NR	NR	NR
Vayne et al[25]	France	AZ	9	7	2	24-73	9-18	NR	9-61
Althaus et al[26]	Germany	AZ	8	5	3	24-53	6-20	3/8 (37.5%) died	8-92
Castelli et al[27]	Italy	AZ	1	0	1	50	11	1/1 died	20
Muir et al[28]	USA	JJ	1	1	0	48	14	Critically ill at time of report	13
Blauenfeldt et al[29]	Denmark	AZ	1	1	0	60	7	1/1 died	118 (nadir 5)
D'Agostino et al[30]	Italy	AZ	1	1	0	54	12	1/1 died	"low"
Bjørnstad-Tuveng et al[31]	Norway	AZ	1	1	0	30's	3	1/1 died	37
Xie et al[32]	UK	AZ	1	1	0	23	7	0/1 died	73
Total or range			81-133	69	21	18-77	3-25	31/79 (39.2%)	5-127

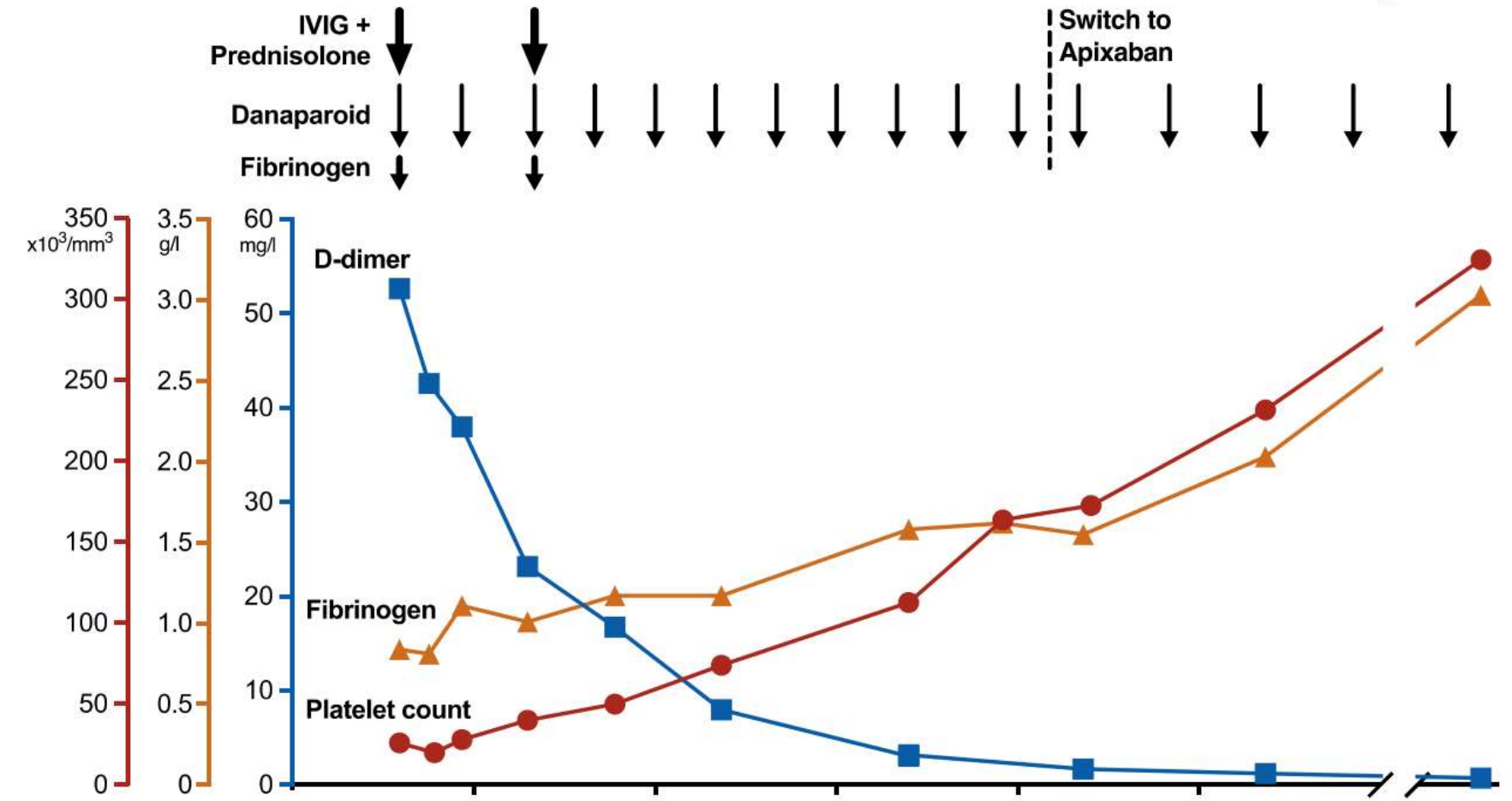


FIGURE 1 Time course of platelet count (red), fibrinogen concentration (yellow), and D-dimer (blue) during treatment of vaccine-induced prothrombotic immune thrombocytopenia

Pregnancy/lactation

Candidate	No. of Participants in Clinical Trial (Vaccine/Placebo)	Efficacy Based on Randomized Clinical Trial	DART Studies	Pregnant Persons in Trials
BioNTech–Pfizer BNT162b2	Enrolled 45,000	95%	In progress; expected completion in December 2020	Pregnant, breastfeeding, and those attempting pregnancy excluded. 23 inadvertently exposed pregnancies (12 vaccine and 11 placebo) as of November 14, 2020. Pregnancies exposed to vaccine are ongoing.
Moderna mRNA-1273	Enrolled 30,000	94.5%	Combined developmental and perinatal and postnatal reproductive toxicity study in rats submitted to the FDA on December 4, 2020; no adverse effects on female reproduction, fetal or embryonic development, or postnatal development noted	Pregnant, breastfeeding, and those attempting pregnancy excluded. 13 inadvertently exposed pregnancies (6 vaccine, 7 placebo) as of December 2, 2020. Pregnancies exposed to vaccine are ongoing.
AstraZeneca and the University of Oxford AZD1222	Enrolled 20,000	70.4%	In progress	Pregnant, breastfeeding, and those attempting pregnancy excluded. No data on unintended vaccination in pregnancy available at this time.
Johnson & Johnson–Janssen Pharmaceuticals Ad26.COV2.S	60,000 planned to be recruited	NA	In progress; preliminary report expected January 2021	Pregnant, breastfeeding, and those attempting pregnancy excluded. No data on unintended vaccination in pregnancy available at this time.

Review

COVID-19 vaccines

No authors listed

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2021 May 17.

PMID: 33355732 Bookshelf ID: NBK565969

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Manufacturers (vaccine name)	Technology used	Doses	Efficacy against symptomatic disease*	Safety profile (from phase III trials)	Efficacy against variants*		Are updated versions being made to target variants?	Reported effectiveness from mass rollout
					B.1.1.7. (first detected in UK)	B.1.351 (first detected in South Africa)		
Pfizer and BioNTech (Comirnaty)	mRNA	2	95%[1]	Of the covid-19 vaccine group, 27% of participants reported any adverse event, compared with 12% taking a placebo. This was mainly due to transient reactogenicity events, such as injection site pain. Few people in either group had severe or serious adverse events.	Unknown	Unknown	Yes	Reduced symptomatic cases by 94%, hospital admissions by 87%, and severe covid-19 by 92% in Israel[2]

Oxford and AstraZeneca (AZD1222)	Viral vector	2	82.4% (12 weeks between doses)[3]	Serious adverse events occurred in 168 participants: 79 in the vaccine group and 89 in the controls. Two cases of transverse myelitis were originally reported as potentially related to the vaccine but later determined to be unlikely to be related.	74.6%[4]	TBC (unconfirmed reports as low as 10%)[5]	Yes	In Scotland, risk of hospital admission for covid-19 fell by up to 94% four weeks after first doses administered[6]
Moderna and NIH (mRNA-1273)	mRNA	2	94.5%[7]	Solicited adverse events at the injection site occurred much more often in the vaccine than in the placebo group. Serious adverse events were rare, with incidence similar in the two groups.	Unknown (but reports of decrease in neutralising antibodies)[8]	Unknown	Yes[9]	TBC

Gamaleya (Sputnik V)	Viral vector	2	91.6%[10]	Forty five of 16 427 participants in the vaccine group and 23 of 5435 in the placebo group had serious adverse events, but none were considered associated with vaccination.	Unknown	Unknown	Unknown	TBC
CanSinoBio (Convidecia)	Viral vector	1	65.7%[11]	Unknown	Unknown	Unknown	Unknown	TBC

Manufacturers (vaccine name)	Technology used	Doses	Efficacy against symptomatic disease*	Safety profile (from phase III trials)	Efficacy against variants*		Are updated versions being made to target variants?	Reported effectiveness from mass rollout
Novavax (NVX-CoV2373)	Protein	2	95.6%[12]	A preliminary review of the safety database showed that severe, serious, and medically attended adverse events occurred at low levels and were balanced between vaccine and placebo groups.[13]	85.6%	60%	Yes[14]	TBC
Johnson & Johnson (Ad26.COV2.S)	Viral vector	1	72%	More serious adverse events were reported in participants who received placebo than in the vaccine group.[15]	Unknown	57%[16]	Unknown	TBC
Sinopharm (BBIBP-CorV)	Inactivated virus	2	79.34%[17]	Unknown	Unknown	Unknown (but reports of weekend effect)[18]	Unknown	TBC
Sinovac (CoronaVac)	Inactivated virus	2	50.4%[19]	Unknown	Unknown	Unknown	Unknown	TBC
Bharat Biotech (Covaxin)	Inactivated virus	2	Unknown	Unknown	Unknown	Unknown	Unknown	TBC

* Vaccines' efficacy cannot be directly compared because of differing clinical trial designs

Table. SARS-CoV-2 Vaccines

Vaccine	Manufacturer	Vaccine type	Antigen	Dose	Dosage	Storage conditions	Efficacy against severe COVID-19[a]	Overall efficacy	Current approvals
mRNA-1273	Moderna (US)	mRNA	Full-length spike (S) protein with proline substitutions	100 µg	2 Doses 28 d apart	−25° to −15 °C; 2-8 °C for 30 d; room temperature ≤12 h	100% 14 d After second dose (95% CI, not estimable to 1.00)	92.1% 14 d After 1 dose (95% CI, 68.8%-99.1%); 94.1% 14 d after second dose (95% CI, 89.3%-96.8%)	EUA: the US, EU, Canada, and UK
BNT162b2	Pfizer-BioNTech (US)	mRNA	Full-length S protein with proline substitutions	30 µg	2 Doses 21 d apart	−80° to −60 °C; 2-8 °C for 5 d; room temperature ≤2 h	88.9% After 1 dose (95% CI, 20.1%-99.7%)	52% After 1 dose (95% CI, 29.5%-68.4%); 94.6% 7 d after second dose (95% CI, 89.9%-97.3%)	EUA: the US, EU, Canada, and UK
Ad26.CoV2.S	Janssen/ Johnson & Johnson (US)	Viral vector	Recombinant, replication-incompetent human adenovirus serotype 26 vector encoding a full-length, stabilized SARS-CoV-2 S protein	5×10^{10} Viral particles	1 Dose	−20 °C; 2-8 °C for 3 mo	85% After 28 d; 100% after 49 d	72% in the US; 66% in Latin America; 57% in South Africa (at 28 d)	EUA: the US, EU, and Canada
ChAdOx1 (AZS1222)	AstraZeneca/ Oxford (UK)	Viral vector	Replication-deficient chimpanzee adenoviral vector with the SARS-CoV-2 S protein	5×10^{10} Viral particles (standard dose)	2 Doses 28 d apart (intervals >12 wk studied)	2-8 °C for 6 mo	100% 21 d After first dose	64.1% After 1 dose (95% CI, 50.5%-73.9%); 70.4% 14 d after second dose (95% CI, 54.8%-80.6%)	EUA: WHO/Covax, the UK, India, and Mexico
NVX-CoV2373	Novavax, Inc (US)	Protein subunit	Recombinant full-length, prefusion S protein	5 µg of protein and 50 µg of Matrix-M adjuvant	2 Doses	2-8 °C for 6 mo	Unknown	89.3% in the UK after 2 doses (95% CI, 75.2%-95.4%); 60% in South Africa (95% CI, 19.9%-80.1%)	EUA application planned
CVnCoV	CureVac/ GlaxoSmithKline (Germany)	mRNA	Prefusion stabilized full-length S protein of the SARS-CoV-2 virus	12 µg	2 Doses 28 d apart	2-8 °C for 3 mo; room temperature for 24 h	Unknown	Phase 3 trial ongoing	
Gam-COVID-Vac (Sputnik V)	Gamaleya National Research Center for Epidemiology and Microbiology (Russia)	Viral vector	Full-length SARS-CoV-2 glycoprotein S carried by adenoviral vectors	10^{11} Viral particles per dose for each recombinant adenovirus	2 Doses (first, rAd26; second, rAd5) 21 d apart	−18 °C (Liquid form); 2-8 °C (freeze dried) for up to 6 mo	100% 21 d After first dose (95% CI, 94.4%-100%)	87.6% 14 d After first dose (95% CI, 81.1%-91.8%); 91.1% 7 d after second dose (95% CI, 83.8%-95.1%)	EUA: Russia, Belarus, Argentina, Serbia, UAE, Algeria, Palestine, and Egypt
CoronaVac	Sinovac Biotech (China)	Inactivated virus	Inactivated CN02 strain of SARS-CoV-2 created from Vero cells	3 µg With aluminum hydroxide adjuvant	2 Doses 14 d apart	2-8 °C; Lifespan unknown	Unknown	Phase 3 data not published; reported efficacy 14 d after dose 2: 50.38% (mild) and 78% (mild to severe) in Brazil, 65% in Indonesia, and 91.25% in Turkey	EUA: China, Brazil, Columbia, Bolivia, Brazil, Chile, Uruguay, Turkey, Indonesia, and Azerbaijan
BBIBP-CorV	Sinopharm 1/2 (China)	Inactivated virus	Inactivated HB02 strain of SARS-CoV-2 created from Vero cells	4 µg With aluminum hydroxide adjuvant	2 Doses 21 d apart	2-8 °C; Lifespan unknown	Unknown	Phase 3 data not published; unpublished reports of 79% and 86% efficacy	EUA: China, UAE, Bahrain, Serbia, Peru, and Zimbabwe

Abbreviations: EUA, Emergency Use Authorization; UAE, United Arab Emirates; WHO, World Health Organization.

[a] Efficacy against severe disease, which includes COVID-19–related hospitalization, varies by age and by time after vaccination.