COREB
mission nationale
Coordination Opérationnelle
Risque Epidémique et Biologique

https://www.coreb.infectiologie.com/

VACCINE

REACTing
research & action
targeting emerging infectious diseases

https://reacting.inserm.fr/

Scientific update on COVID-19

Updated on February 20th 2021

Redaction committee

Boris Lacarra – *ANRS MIE*

F-Xavier Lescure – *Inserm, AP-HP Bichat, COREB*

Guillaume Mellon – *AP-HP Bichat, COREB*

Inmaculada Ortega Perez – *ANRS MIE*

Eric D'Ortenzio – *ANRS MIE*

Erica Telford – *ANRS MIE*

Reviewing committee

Jean-Marc Chapplain – *CHU Rennes, COREB*

Flavie Chatel – *COREB*

Hélène Coignard – *HCL, COREB*

Dominique Costagliola – *Inserm, ANRS MIE*

Marie-Paule Kieny – *Inserm, ANRS MIE*

Quentin Le Hingrat – *Inserm, AP-HP Bichat*

Jean-Christophe Lucet – *Inserm, AP-HP Bichat*

Claire Madelaine – *Inserm, ANRS MIE*

Matthieu Mahevas – *Inserm, AP-HP Henri-Mondor*

Emmanuelle Vidal Petiot – *Inserm, AP-HP Bichat*

Benoit Visseaux – *Inserm, AP-HP Bichat*

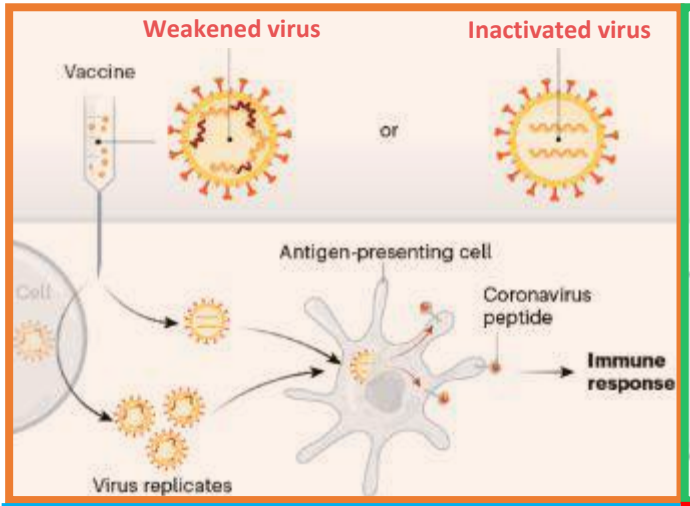
VACCINE

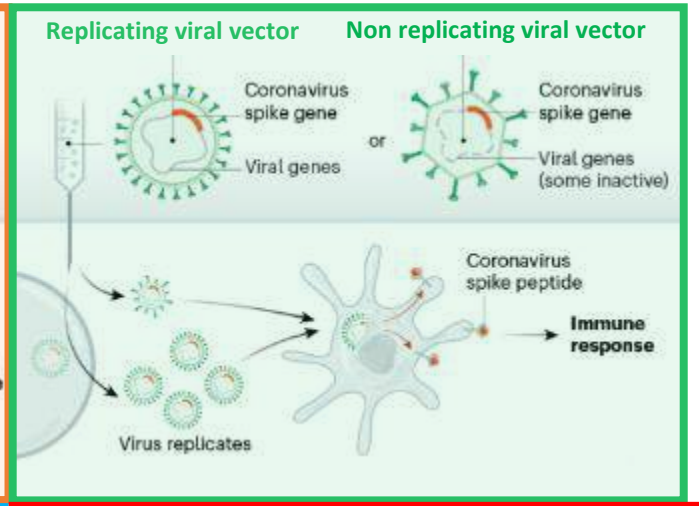
Question:

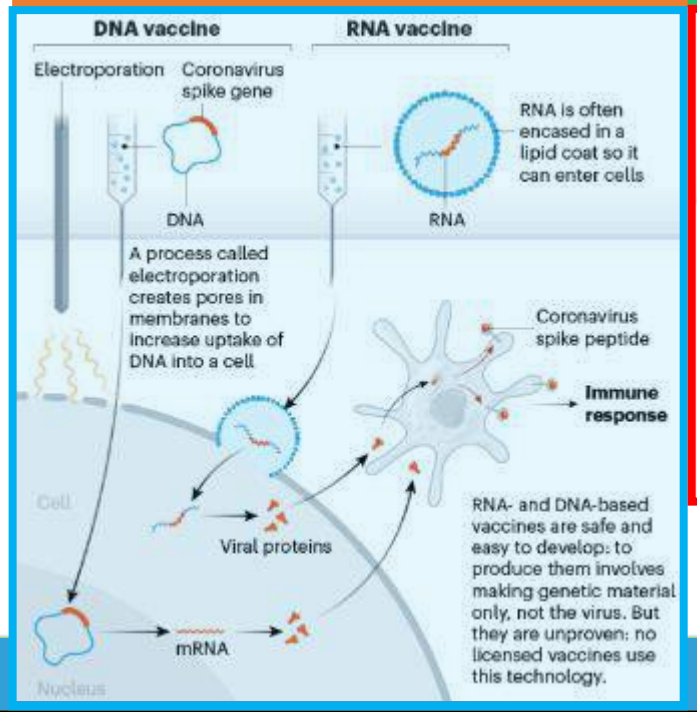
- What are the types of vaccines in clinical evaluation?
- Which are the results of immunogenicity safety and efficacy of SARS CoV-2 vaccines?
- May they protect against arising viral variants?

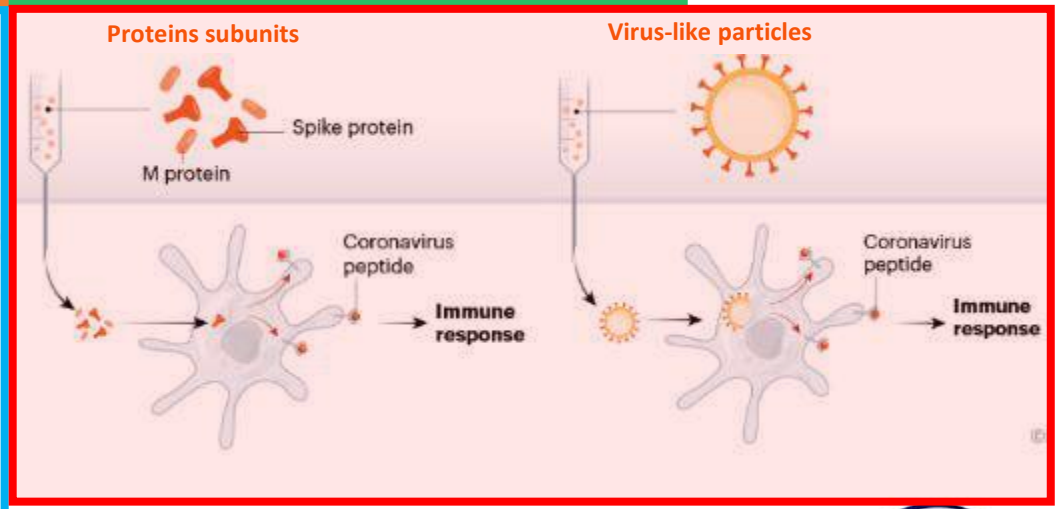
Vaccine

- **Vaccines aims**: expose the immune system to an antigen that won't cause disease, provoke an immune response (able to block/kill the virus)
- **Eight types of vaccines**:
  - virus (inactivated, weakened),
  - viral vector (replicating, non replicating)
  - nucleic acid (DNA, RNA)
  - protein based (protein subunit, virus like particles)









Callaway E. *Nature* Apr 2020

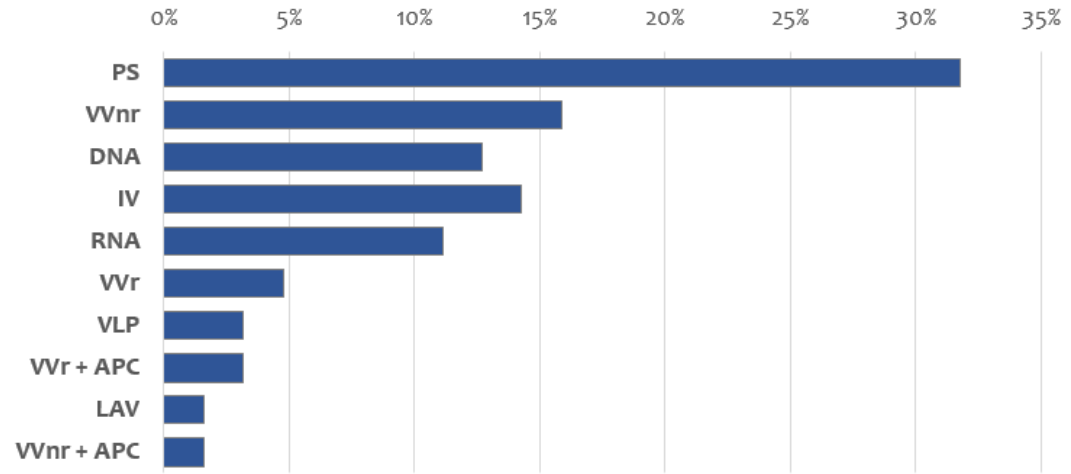
Vaccine

- **R&D landscape**: WHO lists 177 candidates in preclinical development, 63 candidate vaccines in clinical evaluation (February 8th 2021); update available at :

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

3. - Candidates in clinical phase

Filter	All	Select phase of development (default is all)	
Platform		**Candidate vaccines (no. and %)**	
PS	Protein subunit	20	32%
VVnr	Viral Vector (non-replicating)	10	16%
DNA	DNA	8	13%
IV	Inactivated Virus	9	14%
RNA	RNA	7	11%
VVr	Viral Vector (replicating)	3	5%
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	



4 vaccines abandoned after trials: MSD-IAVI, MSD-Pasteur, Imperial College, University of Queensland

From WHO COVID19 vaccine tracker

Phase III COVID-19 Vaccines (Feb 8th 2021)

Developer	Vaccine Platform	Description
BioNTech – Pfizer – Fosun Pharma 🟥🟨	RNA	**BNT162b2*:** Lipid nanoparticle-formulated, nucleoside **modified mRNA** vaccine encoding **full-length spike (S) protein**
Moderna – NIAID 🟥🟨	RNA	**mRNA-1273:** Lipid nanoparticle encapsulated, mRNA vaccine encoding **pre fusion spike (S) protein**
CureVac	RNA	**CVnCoV:** Lipid nanoparticle encapsulated, mRNA (non modified) vaccine encoding **pre fusion spike (S) protein**
Inovio-IVI	DNA	**INO-4800:** DNA plasmid vaccine with electroporation
Osaka University-Takara Bio	DNA	**AG0302-COVID19:** DNA plasmid vaccine + Adjuvant
CanSino Biologicals Inc – Beijing Institute of Biotechnology 🟩	Non replicating viral vector	**Ad5-nCoV:** Replication-deficient **Ad5** vector containing optimised **full-length spike (S) protein**
Gamaleya Research Institute 🟩	Non replicating viral vector	**Spoutnik V:** Recombinant **Ad26 (prime)** and recombinant **Ad5 (boost)** viruses expressing the gene for **spike (S) protein**
Janssen Pharmaceutical Companies – Beth Israel Deaconness Medical Center	Non replicating viral vector	**Ad26COVS1:** Recombinant adenovirus vaccine **(Ad26)** incorporating SARS-CoV-2 full stabilized **Spike (S)** protein
University of Oxford – AstraZeneca 🟨🟩	Non replicating viral vector	**AZD1222:** Replication-deficient **simian adenovirus (ChAdOx1)** vector containing **codon-optimised spike (S) protein**

🟥 *FDA approved* 🟨 *EMA approved* 🟩 *Approved by other national regulatory agencies*

Phase III COVID-19 Vaccines (Feb 8th 2021)

Developer	Vaccine Platform	Description
Novavax	Protein subunit	**NVX-COV2373:** Recombinant **nanoparticle** vaccine consisting of **full-length spike (S) protein**, with or without **Matrix-M1 adjuvant**
Medicago Inc	Protein subunit	**CoVLP: Plant-derived** VLP **adjuvanted** with AS03
Anhui Zhifei Logcom Biopharmaceutical-Chinese Academy of Sciences	Protein subunit	**ZF2001: Adjuvanted** recombinant protein (**RBD-Dimer**) expressed in CHO cells
Clover Biopharmaceutical Inc **GSK** **Dynavax**	Protein subunit	**SCB-2019: Native** like **trimeric subunit Spike** Protein (AS03 or CpG1018 plus alum **adjuvanted**)
Covaxx **University of Nebraska**	Protein subunit	**UB-6212: Multiepitope** peptide based **S1-RBD** protein based vaccine

FDA approved *EMA approved* *Approved by other national regulatory agencies*

Phase III COVID-19 Vaccines (Feb 8th 2021)

Developer	Vaccine Platform	Description
Sinovac – Institute Butantan	Inactivated	**CoronaVac: β-propiolactone inactivated** vaccine adiministered with **aluminium hydroxide adjuvant**
Beijing Institute of Biological Products – Sinophram	Inactivated	**BBIBP-CorV**: **β-propiolactone i**nactivated vaccine adiministered with **aluminium hydroxide adjuvant**
Wuhan Institute of Biological products– Sinopharm	Inactivated	**SARS-CoV-2 Vaccine: β-propiolactone inactivated** vaccine adsorbed to 0.5-mg **aluminum**
Bharat Biotech- ICMR- National Institut of Virology	Inactivated	**COVAXIN:** whole-virion inactivated vaccine
Research Institute for Biological Safety Problems	Inactivated	**QazCovid-in:** Inactivated vaccine
Institute of Medical Biology Chine Academy of Medical Sciences	Inactivated	Inactivated Vaccine:

FDA approved *EMA approved* *Approved by other national regulatory agencies*

mRNA vaccine

BNT162 b2

IMMUNOGENICITY AND SAFETY DATA

BioNTech/Pfizer

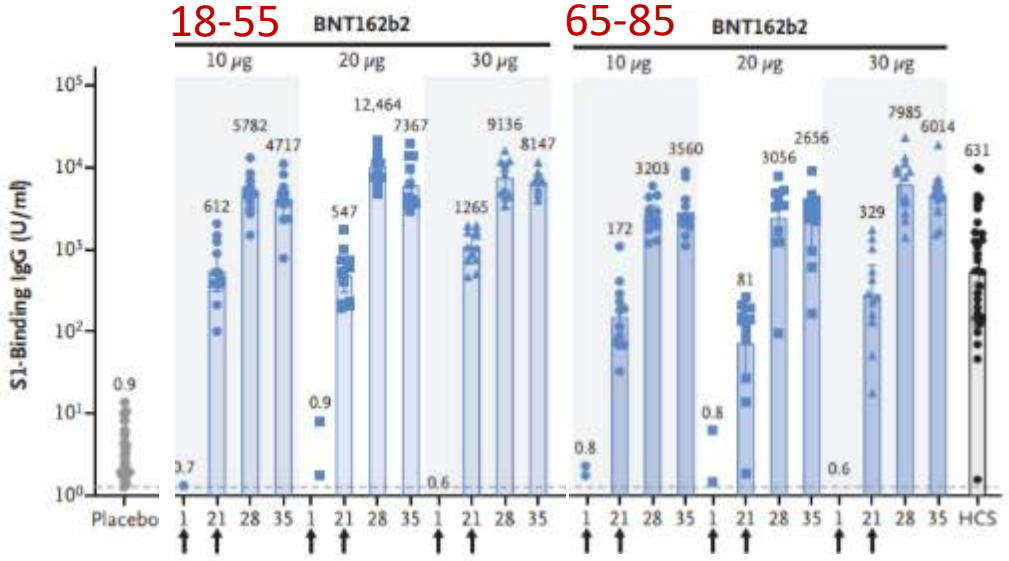
Phase I: NCT04368728

Study Designw	Phase I randomized controlled, dose-finding trial
Age range	18 – 55 or 65 – 85
Nb of participants	195
Nb of doses/route	2 (days 1/21)-IM
Vaccine groups	10 µg BNT162b2 (S) 18–55y (n = 12) 20 µg BNT162b2 (S) 18–55y (n = 12) 30 µg BNT162b2 (S) 18–55y (n = 12) 10 µg BNT162b2 (S) 65–85y (n = 12) 20 µg BNT162b2 (S) 65–85y (n = 12) 30 µg BNT162b2 (S) 65–85y (n = 12) *+BNT1621b (not used in Phase III)*
SAE	None
Local AE	Injection site pain, swelling
Systemic AE	Headache, fatigue, chills, muscle pain, fever, joint pain, diarrhoea

IMMUNOGENICITY 1/2

1. S1 specific binding responses

Assay: Luminex immunoassay
Units: Geometric mean concentration, U/mL (95% CI)



Antigen-binding IgG and virus-neutralizing responses to vaccination with 10 µg to 30 µg of BNT162b2 **boosted by the second dose** in both the younger adults and the older adults (**lower** antigen-binding **IgG in elderly** group)

mRNA vaccine

BNT162 b2

IMMUNOGENICITY AND SAFETY DATA

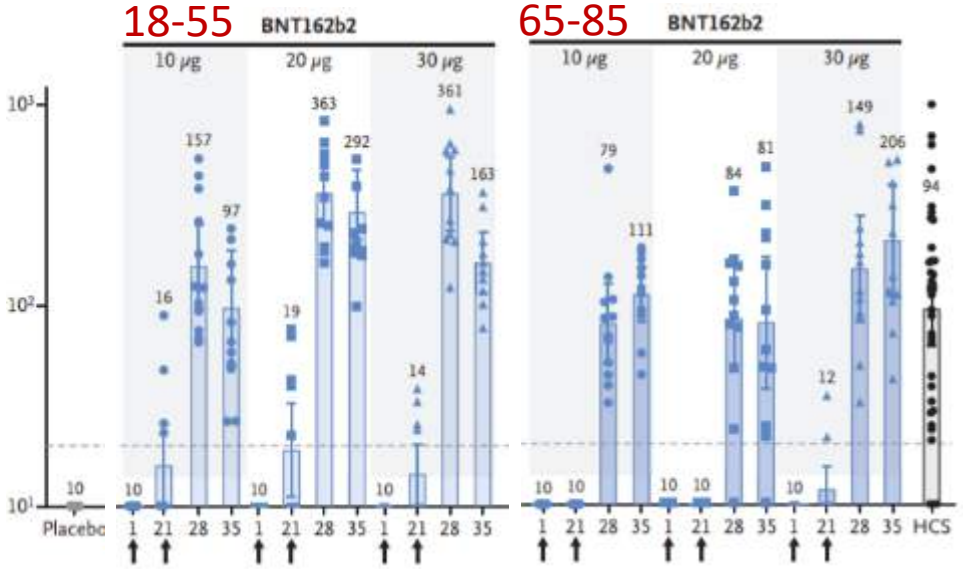
IMMUNOGENICITY 2/2

2. Neutralizing responses

Assay: SARS-CoV-2 virus neutralisation test (mNeonGreen reporter strain), 50% inhibitory dilution

Units: Geometric mean response, ID50 (95% CI)

The **50% neutralizing** at the 30-µg dose level on day 28 or day 35 ranged from **1.7 to 4.6 times the GMT of the convalescent serum panel** among participants **18 to 55** years of age and from 1.1 to 2.2 times the GMT of the convalescent serum panel among those **65 to 85** years of age.



Phase I/II results are presented ONLY for vaccines with phase III published results

Walsh EE et al. NEJM Oct 2020

Adenoviral vector vaccine

AZD1222

IMMUNOGENICITY AND SAFETY DATA

AstraZeneca-Oxford University

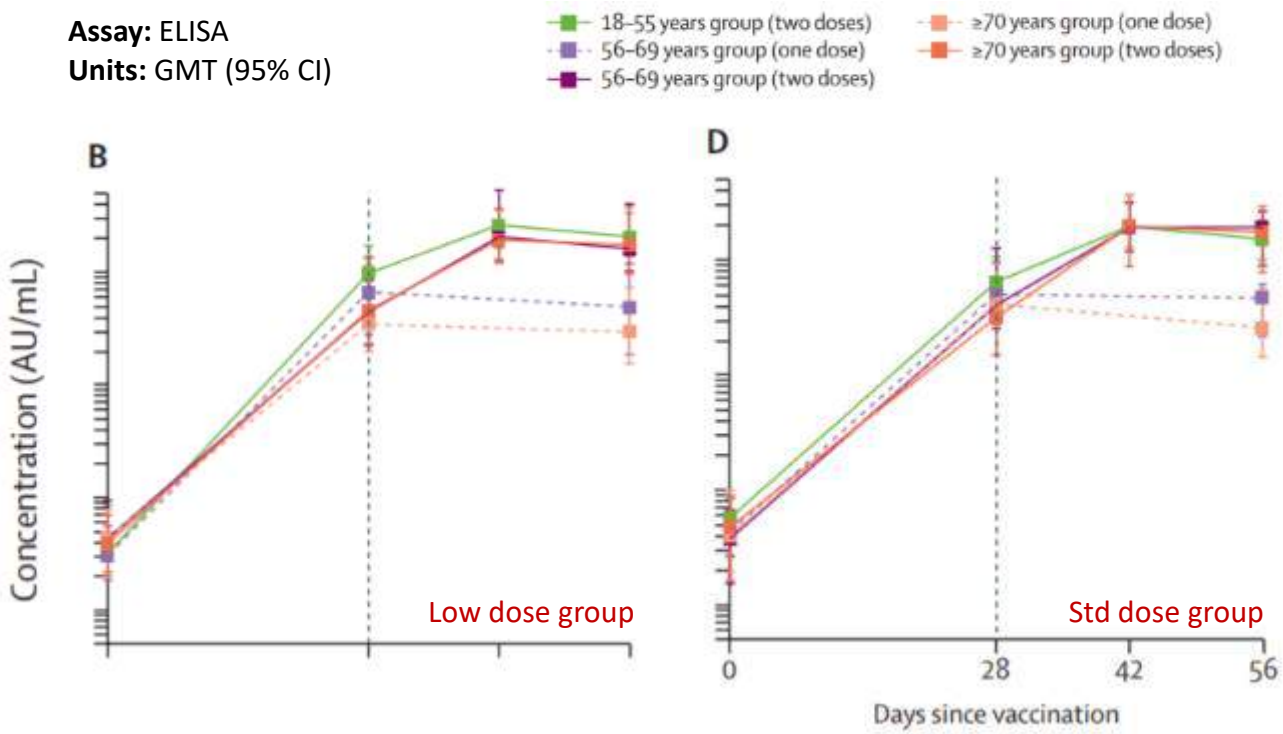
Phase II: NCT04400838

Study Design	Phase II randomised controlled trial
Age range	1: 18–55; 2: 56–69; 3: ≥70
Nb of participants	560
Nb of doses/route	1 (day 0) or 2 (days 0/28)- IM
Vaccine groups	18–55y: 2 x low dose (n = 50) 56–69y: 1 x low dose (n = 30) 56–69y: 2 x low dose (n = 30) ≥70y: 1 x low dose (n = 50) ≥70y: 2 x low dose (n = 50) 18–55y: 2 x std dose (n = 50) 56–69y: 1 x std dose (n = 30) 56–69y: 2 x std dose (n = 30) ≥70y: 1 x std dose (n = 50) ≥70y: 2 x std dose (n = 50) **Control group:** MenACWY (n = 534)
SAE	13 serious adverse events have occurred none of which are considered related to either study vaccine as assessed by the investigators *(Ph III trial suspended and resumed in Sep 2020 due to 2 cases of tranverse myelitis among participants, found not to be related to vaccination)*
Local AE	Tenderness, injection site pain; reported for participants who received 2 doses of vaccine; adverse events were less frequent in older adults (≥56y)
Systemic AE	Fatigue, headache, muscle ache, malaise, feverish, chills, joint pain; reported for participants who received 2 doses of vaccine; adverse events were less frequent in older adults (≥56y)

IMMUNOGENICITY 1/2

1. SARS-CoV-2 IgG response to spike protein

Assay: ELISA
Units: GMT (95% CI)



Total IgGs against the Spike protein **were similar in all age groups regardless the dose.** **Responses** at day 28 **decreased with increasing age** (low: 18–55 years, median 6439[AU]/mL; 56–69 years, 4553 AU/mL; ≥70 years, 3565 AU/mL. Std: 18–55 years, median 9807 AU/mL; 56–69 years, 5496 AU/mL; ≥70 years, 4156 AU/mL)

Adenoviral vector vaccine

AZD1222

IMMUNOGENICITY AND SAFETY DATA

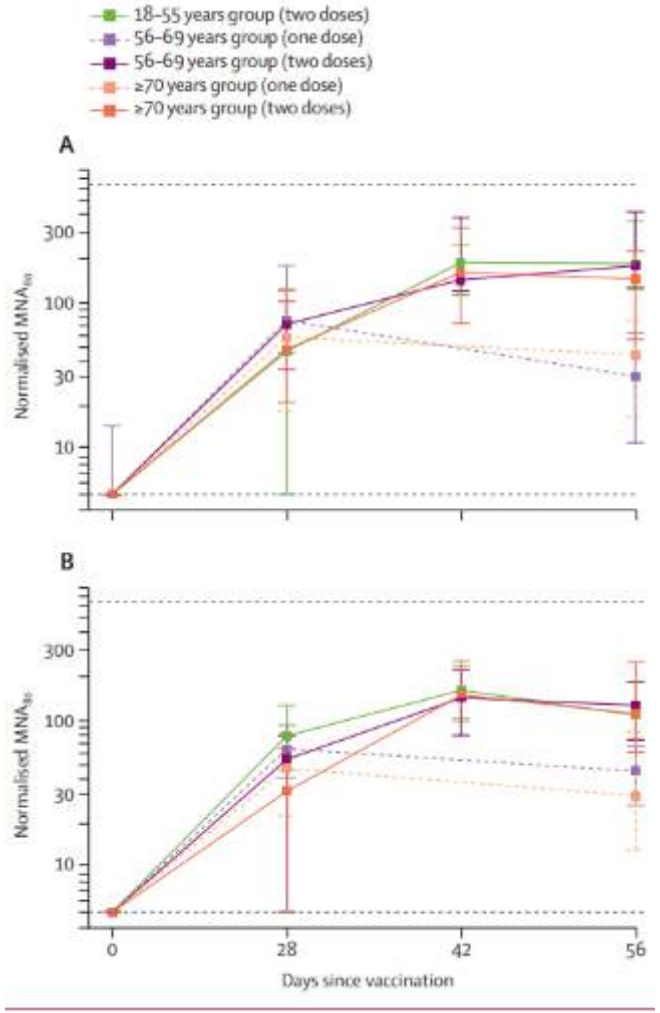
IMMUNOGENICITY 2/2

2. Live SARS-CoV-2 microneutralisation assay (MNA_{80})

Assay: Microneutralisation test (80% inhibitory dilution) tion)
Units: Median titre, ID80 (IQR)

Neutralizing antibody responses: Median titres peaked by day 42 in groups receiving two vaccinations.

There are **no significant differences** in normalized titers **between age groups at day 42** (low: 18–55 years, median 161; 56–69 years, 143; ≥70 years, 150. Std: 18–55 years, median 193; 56–69 years, 144; and ≥70 years, 161.



3. Induction of T cell responses and increase of IFN-γ expression

IFN-γ ELISpot responses against SARS-CoV-2 spike protein peaked 14 days after the prime vaccination

mRNA vaccine

mRNA 1273

IMMUNOGENICITY AND SAFETY DATA

Moderna-NIH

Phase I: NCT04283461

Study Design	Phase I open-label, non-randomised, dose-finding trial
Age range	18 – 55
Nb of participants	45
Nb of doses/route	2 (days 1/29)-IM
Vaccine groups	25 µg (n = 15) 100 µg (n = 15) 250 µg (n = 15)
SAE	None
Local AE	Injection site pain *(67–100% at ds1, 77–100% at ds 2)*
Systemic AE	Headache *(20–47% at ds1, 23–100% at ds2)*, myalgia *(7–27% at ds1, 23–93% at ds2)*, chills *(8–86% at ds2)*, fatigue *(27–33% at ds1, 39–80% at ds2)*, fever *(0–57% at ds2)*, nausea *(0–47% at ds 2)*

IMMUNOGENICITY 1/2

1. GMHI* assay to spike protein in trial participants.

Assay: ELISA
Units: Geometric mean titre (95% CI)

Time Point	25-µg Group		100-µg Group		250-µg Group		Convalescent Serum	
	no.	GMT (95% CI)	no.	GMT (95% CI)	no.	GMT (95% CI)	no.	GMT (95% CI)
ELISA anti–S-2P							38	142,140 (81,543–247,768)
Day 1	15	116 (72–187)	15	131 (65–266)	15	178 (81–392)		
Day 15†	15	32,261 (18,723–55,587)	15	86,291 (56,403–132,016)	15	163,449 (102,155–261,520)		
Day 29	15	40,227 (29,094–55,621)	15	109,209 (79,050–150,874)	14	213,526 (128,832–353,896)		
Day 36	13	391,018 (267,402–571,780)	15	781,399 (606,247–1,007,156)	14	1,261,975 (973,972–1,635,140)		
Day 43	13	379,764 (281,597–512,152)	14	811,119 (656,336–1,002,404)	14	994,629 (806,189–1,227,115)		
Day 57	13	299,751 (206,071–436,020)	14	782,719 (619,310–989,244)	13	1,192,154 (924,878–1,536,669)		

Binding antibody IgG geometric mean titers (GMTs) to S protein: **seroconversion in all participants by day 15.**

A recent study shows that mRNA 1273 vaccine induces specific IgG responses and NAbs in adults older than 70 years of age. *(Anderson EJ, NEJM 2020)*

mRNA vaccine

mRNA 1273

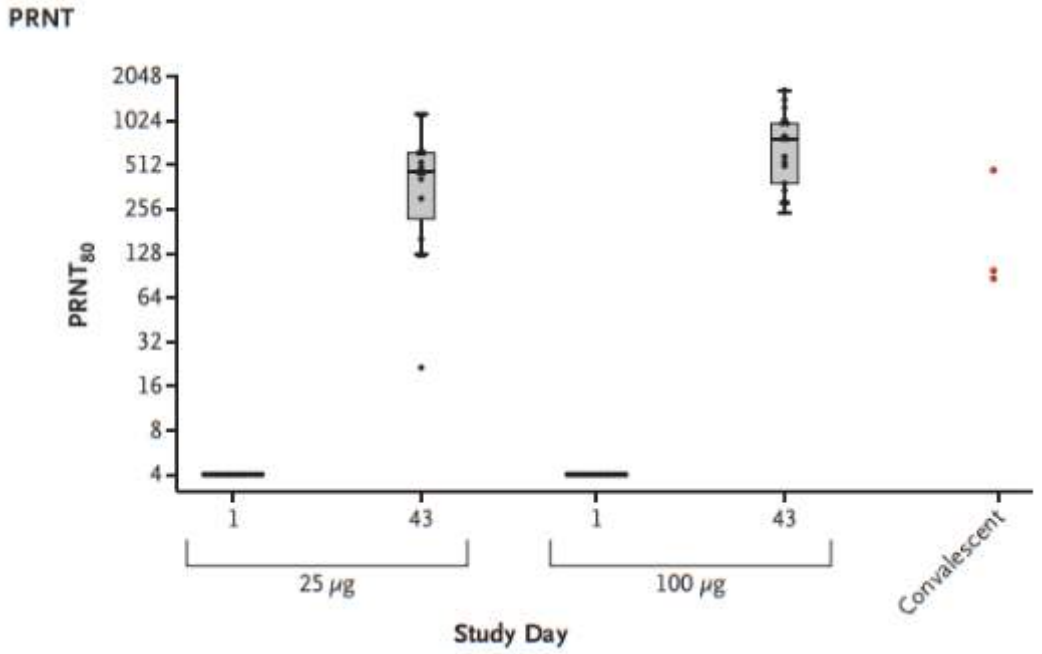
IMMUNOGENICITY AND SAFETY DATA

IMMUNOGENICITY 2/2

2. Neutralizing responses

Assay: Plaque-reduction neutralization test (80% inhibitory dilution)
Units: Geometric mean response, ID80 (95% CI)

At day 43, **wild-type virus–neutralizing activity capable of reducing SARS-CoV-2 infectivity by 80%** or more ($PRNT_{80}$) detected in all participants, with geometric mean $PRNT_{80}$ responses of 339.7 (95% CI, 184.0 to 627.1) in the 25-µg group and 654.3 (95% CI, 460.1 to 930.5) in the 100-µg group



3. Cellular responses: 25-µg and 100-µg doses elicit CD4 T-cell responses **biased toward expression of Th1** cytokines (TNFα > IL2> IFNγ).

Adenoviral vector vaccine

Sputnik V

IMMUNOGENICITY AND SAFETY DATA

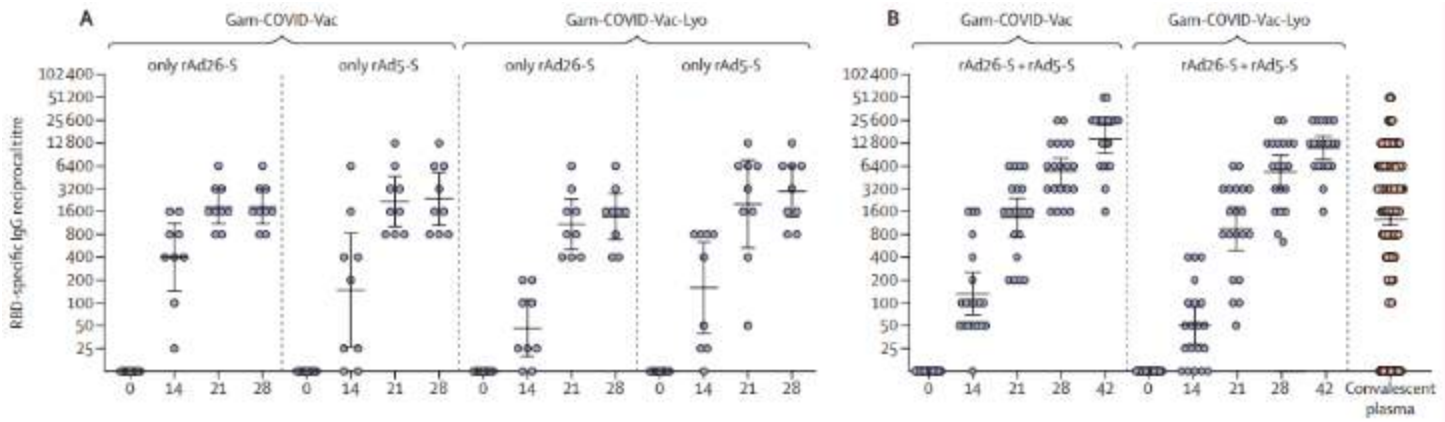
Phase I/II: NCT04436471 *(frozen product)*
NCT04437875 *(lyo product)*

Study Design	Phase I/II open-label, non-randomised trial
Age range	18 – 60
Nb of participants	76
Nb of doses/route	1 (day 0) or 2 (rAd26 on day 0, rAd5 on day 21) -IM
Vaccine groups	Frozen 1 x 10^{11} rAd26 (n = 9) Frozen 1 x 10^{11} rAd5 (n = 9) Frozen 10^{11} rAd26/10^{11} rAd5 (n = 20) Lyo 1 x 10^{11} rAd26 (n = 9) Lyo 1 x 10^{11} rAd5 (n = 9) Lyo 10^{11} rAd26/10^{11} rAd5 (n = 20)
SAE	None
Local AE	Injection site pain *(40–78%)*
Systemic AE	Changes in laboratory variables *(67–100%),* hyperthermia *(11–100%),* headache *(25–67%),* asthenia *(0–55%),* muscle or joint pain *(11–33%),* subjective heartbeat palpitation *(0–33%)*

IMMUNOGENICITY 1/2

1. SARS-CoV-2 RBD-specific IgGs

Assay: ELISA
Units: Geometric mean titre (95% CI)



Anti-RBD IgG responses detected **from day 14** for both products and in all vaccine administration schemes . At **day 21** RBD-specific IgGs were detected in **100% of vaccinated** participants. ([GMT] 1629 with the frozen formulation and 951 with the lyophilized one). **Heterologous boosting** with rAd5-S led to an **increase in SARS-CoV-2 RBD specific IgG** titres; 7 days after boost.

COREB mission nationale Coordination Opérationnelle Risque Epidémique et Biologique

Phase I/II results are presented ONLY for vaccines with phase III published results

Logunov DY et al *Lancet*. Sep 2020

anrs MALADIES INFECTIEUSES ÉMERGENTES

Adenoviral vector vaccine

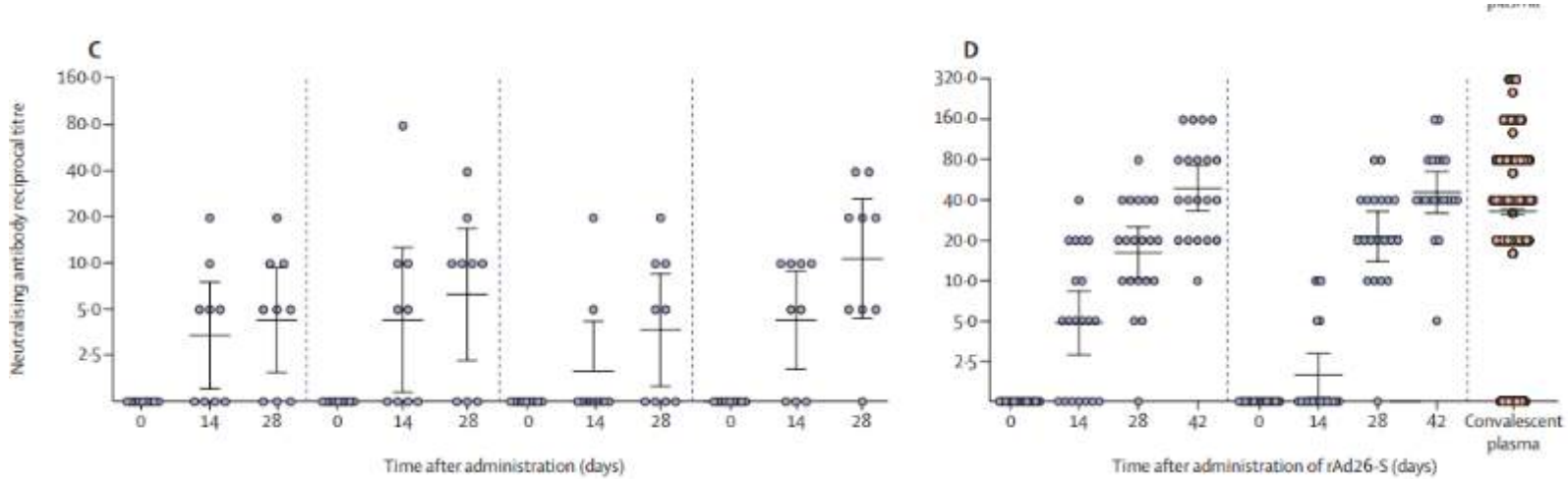
Sputnik V

IMMUNOGENICITY AND SAFETY DATA

IMMUNOGENICITY 2/2

2. Neutralizing responses

Assay: Microneutralisation assay (50% inhibitory dilution, Vero E6 cells)
Units: Geometric mean titre, ID50 (95% CI)



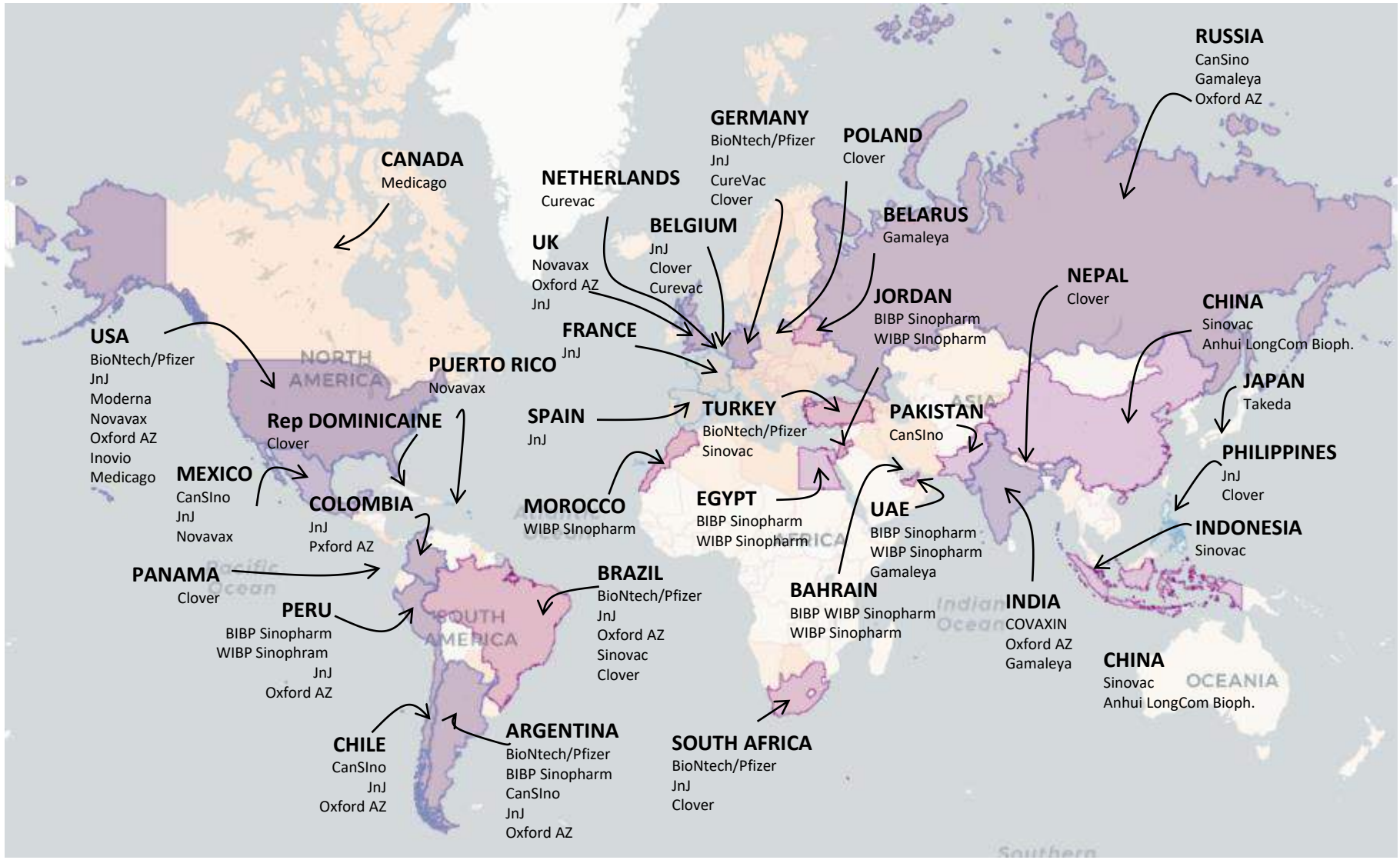
Administration of **both rAd26-S and rAd5-2** led to production of **neutralizing antibodies in 100% of participants**, whereas administration of only rAd26-S led to a lower seroconversion rate

3. T cell response: induction of **CD4+** and **CD8+** cells and an increase in the concentration of **interferon-γ secretion**

Summary of immunogenicity data

Vaccine & Developer	Phase III regimen	Specific IgG titers (14 - 28 days after 2nd dose) *as per Phase I or II published results*	NAb titers (14 - 28 days after 2nd dose) *as per Phase I or II published results*	Publication
BNT162b2 BioNTech – Pfizer – Fosun Pharma	2 doses (d1 and d22) 30µg/dose	8147 GMT *Test: Luminex anti S1 IgG*	163 GMT *Test: $wtVNA_{50}$*	Walsh EE et al. *NEJM* Oct 2020
mRNA-1273 Moderna – NIAID	2 doses (d1 and d29) 100µg/dose	782 719 GMT *Test: ELISA anti S IgG*	654.3 GMT *Test: $PRNT_{80}$*	Jackson LA *et al. NEJM* Jul 2020
SputnikV Gamaleya Research Institute	d1 0,5 mL rAd26 d21 0,5 mL rAd5	14 703 GMT *Test: ELISA anti RBD IgG*	49.25 GMT *Test: MNA_{50}*	Logunov DY *et al. Lancet* Sep 2020
AZD-1222 University of Oxford – AstraZeneca	2 doses (d1 and d29) $5x10^{10}$ vp	639 EU *Test: ELISA anti S IgG*	136 MT *Test: MNA_{80}*	*Ramasay MN et al. Lancet Nov 2020*

Efficacy Trial Map (Feb 8th 2021)



Adapted from LSHTM COVID19 vaccine tracker https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape/

COREB mission nationale Coordination Opérationnelle Risque Epidémique et Biologique

anrs MALADIES INFECTIEUSES ÉMERGENTES

VACCINE EFFICACY DATA

First data regarding vaccine efficacy has been made public by the means of **PRESS RELEASES** by pharmaceutical companies

Date of Press release	Company	Vaccine	Analysis
November 9th 2020	BioNTech/Pfizer	BNT162b2	1st interim analysis; 28 days after 1st dose 94 confirmed cases of COVID19 • **> 90% Efficacy**
November 11th 2020	Gamaleya	Sputnik V	1st interim analysis; 21 days after 1st dose 20 confirmed cases of COVID19 • **> 92% Efficacy**
November 16th 2020	Moderna	mRNA 1273	1st interim analysis; 42 days after 1st dose 95 confirmed cases of COVID19 • **94.5% Efficacy**
November 18th 2020	BioNTech/Pfizer	BNT162b2	**Final analysis**; 28 days after 1st dose 170 confirmed cases of COVID19 • **95% Efficacy**
November 23rd 2020	AstraZeneca/Oxford	AZD1222	**1st interim analysis** 14 days after 2nd dose 131 confirmed cases of COVID19 • **90% Efficacy when given as half dose/full dose** • **62% Efficacy when given as full dose/full dose** • **Overall 70% efficacy**
November 24th 2020	Gamaleya	Sputnik V	**2nd interim analysis**; 42 days after 1st dose 39 confirmed cases of COVID19 *(10 severe)* • **95% Efficacy**
November 30th 2020	Moderna	mRNA 1273	**Final analysis**; 42 days after 1st dose 196 confirmed cases of COVID19 *(30 severe)* • **94.1% Efficacy**

VACCINE EFFICACY DATA

Date of press release	Company	Vaccine	Analysis
January 28th 2021	NOVAVAX	NVX-COV2373:	1st interim analysis; Onset of COVID 7 days after 2nd dose 28 days after 1st dose (one dose vaccine) 62 confirmed cases of COVID19 (56 on the placebo group) • Efficacy by strain was calculated to be **95.6% against the original COVID-19** strain and **85.6% against the UK variant strain**
January 29th 2021	Janssen	Ad26COVS1	1st interim analysis 28 days after vaccination (one dose) Etude multinational ENSEMBLE. • **72% Effective** in the US and **66% Effective** Overall at Preventing Moderate to Severe COVID-19 • **85% Effective** overall in preventing severe disease. • **Complete protection** against COVID-19 related Hospitalisation and Death • Protection against the SARS-CoV-2 Variant from the B.1.351 Lineage Observed in South Africa
February 2nd 2021	Sinovac	CoronaVac	1st interim analysis; 14 days after 2nd dose vaccination 253 confirmed cases of COVID19 Efficacy rate against diseases caused by COVID-19 for: • **all** cases: **50.65%** • cases requiring **medical treatment:** 83.70% **hospitalized, severe** and **fatal** cases: **100%** Efficacy by strain: • **85.6%** against the **UK variant** strain

First data regarding vaccine efficacy has been made public by the means of **PRESS RELEASES** by pharmaceutical companies

mRNA vaccine

BNT162 b2

EFFICACY AND SAFETY DATA

- Efficacy data from ongoing double blind, randomized phase III trial across Argentina, Brazil, South Africa and USA (43 548 participants randomized 1:1)
- Two 30 µg doses of BNT162b2 vaccine, 21 days apart
- **Inclusion criteria:** healthy adults or stable chronic medical conditions, including HIV, HBV or HCV aged of 16y or more.
- **Exclusion criteria:** medical history of Covid-19, treatment with immunosuppressive therapy, or diagnosis with an immunocompromising condition
- Primary **efficacy** endpoint: efficacy of BNT162b2 against confirmed Covid-19 with onset at least 7 days after the second dose
- Primary **safety** end points: solicited, specific local or systemic adverse events and use of antipyretic or pain medication within 7 days after the receipt of each dose

Table 1. Demographic Characteristics of the Participants in the Main Safety Population.*

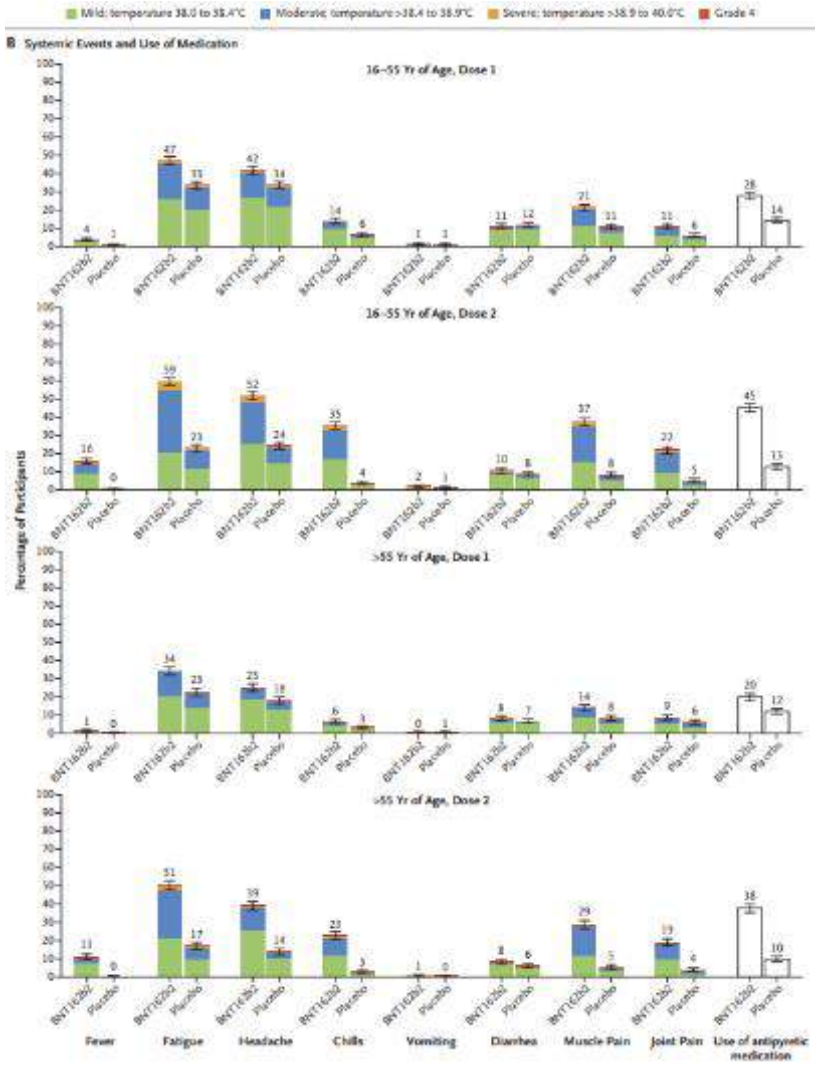
Characteristic	BNT162b2 (N=18,860)	Placebo (N=18,846)	Total (N=37,706)
Sex — no. (%)			
Male	9,639 (51.1)	9,436 (50.1)	19,075 (50.6)
Female	9,221 (48.9)	9,410 (49.9)	18,631 (49.4)
Race or ethnic group — no. (%)†			
White	15,636 (82.9)	15,630 (82.9)	31,266 (82.9)
Black or African American	1,729 (9.2)	1,763 (9.4)	3,492 (9.3)
Asian	801 (4.2)	807 (4.3)	1,608 (4.3)
Native American or Alaska Native	102 (0.5)	99 (0.5)	201 (0.5)
Native Hawaiian or other Pacific Islander	50 (0.3)	26 (0.1)	76 (0.2)
Multiracial	449 (2.4)	406 (2.2)	855 (2.3)
Not reported	93 (0.5)	115 (0.6)	208 (0.6)
Hispanic or Latinx	5,266 (27.9)	5,277 (28.0)	10,543 (28.0)
Country — no. (%)			
Argentina	2,883 (15.3)	2,881 (15.3)	5,764 (15.3)
Brazil	1,145 (6.1)	1,139 (6.0)	2,284 (6.1)
South Africa	372 (2.0)	372 (2.0)	744 (2.0)
United States	14,460 (76.7)	14,454 (76.7)	28,914 (76.7)
Age group — no. (%)			
16–55 yr	10,889 (57.7)	10,896 (57.8)	21,785 (57.8)
>55 yr	7,971 (42.3)	7,950 (42.2)	15,921 (42.2)
Age at vaccination — yr			
Median	52.0	52.0	52.0
Range	16–89	16–91	16–91
Body-mass index‡			
≥30.0: obese	6,556 (34.8)	6,662 (35.3)	13,218 (35.1)

* Percentages may not total 100 because of rounding.
† Race or ethnic group was reported by the participants.
‡ The body-mass index is the weight in kilograms divided by the square of the height in meters.

mRNA vaccine

BNT162 b2

EFFICACY
AND SAFETY DATA



- The BNT162b2 vaccine is reactogenic, but the side effects remain acceptable in all populations studied.
- The short-term safety profile of the BNT162b2 vaccine is characterized by mild to moderate pain at the injection site, fatigue and headache. These manifestations disappear after 24 to 48 hours.
- The only grade 3 adverse events with a frequency greater than 2% after the second vaccine administration are fatigue (97/2405 participants; 4.6%) and headache (7/2015; 3.2%).
- No grade 4 adverse side effects observed.

Six deaths were reported during the clinical trials, including four in the placebo group, but no relation with vaccination was found.

<u>Limits :</u>

Just 2 month follow up safety data

Data for over 75 is scarce and absent for children, pregnant women or immunocompromised

Polack FP *et al. NEJM* Dec 2020

mRNA vaccine

BNT162 b2

EFFICACY AND SAFETY DATA

Table 2. Vaccine Efficacy against Covid-19 at Least 7 days after the Second Dose.*

Efficacy End Point	BNT162b2		Placebo		Vaccine Efficacy, % (95% Credible Interval)‡	Posterior Probability (Vaccine Efficacy >30%)§
	No. of Cases	Surveillance Time (n)†	No. of Cases	Surveillance Time (n)†		
		(N=18,198)		(N=18,325)		
Covid-19 occurrence at least 7 days after the second dose in participants without evidence of infection	8	2.214 (1,7411)	162	2.222 (17,511)	95.0 (90.3–97.6)	>0.9999
		(N=19,965)		(N=20,172)		
Covid-19 occurrence at least 7 days after the second dose in participants with and those without evidence of infection	9	2.332 (18,559)	169	2.345 (18,708)	94.6 (89.9–97.3)	>0.9999

TOTAL OF CASES: 170

- 8 in the BNT162b2 group/162 in the Control
- 10 severe cases, 9 within the Placebo group

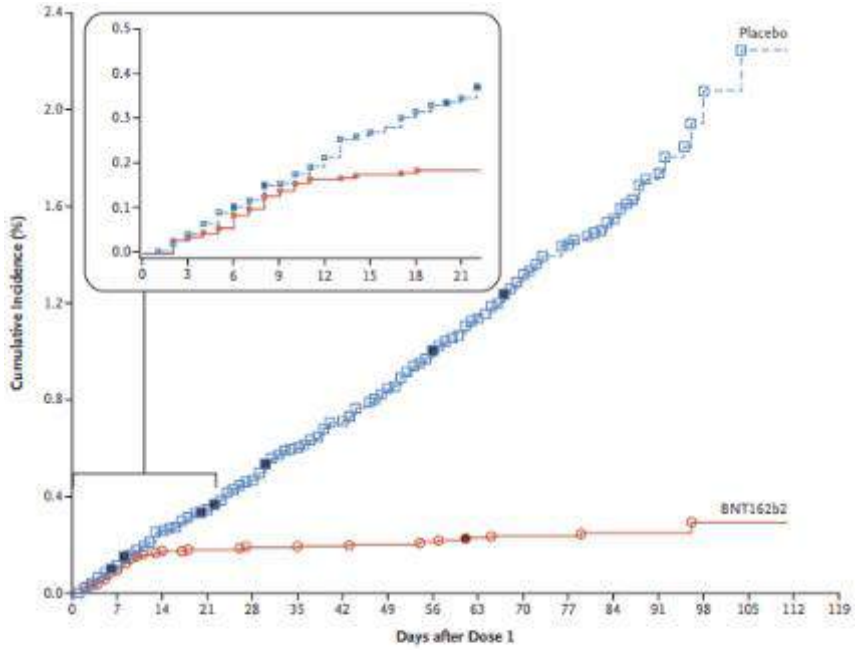
Vaccine efficacy: 95%

Limits:

Efficacy measured in symptomatic patients

No evidence of an potential effect against viral shedding

- Protection occurs as early as the second week after the first vaccine administration, with an increase of protection level up to 95% after the second administration



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)

Polack FP *et al. NEJM* Dec 2020

COREB mission nationale Coordination Opérationnelle Risque Epidémique et Biologique

MALADIES INFECTIEUSES ÉMERGENTES

mRNA vaccine

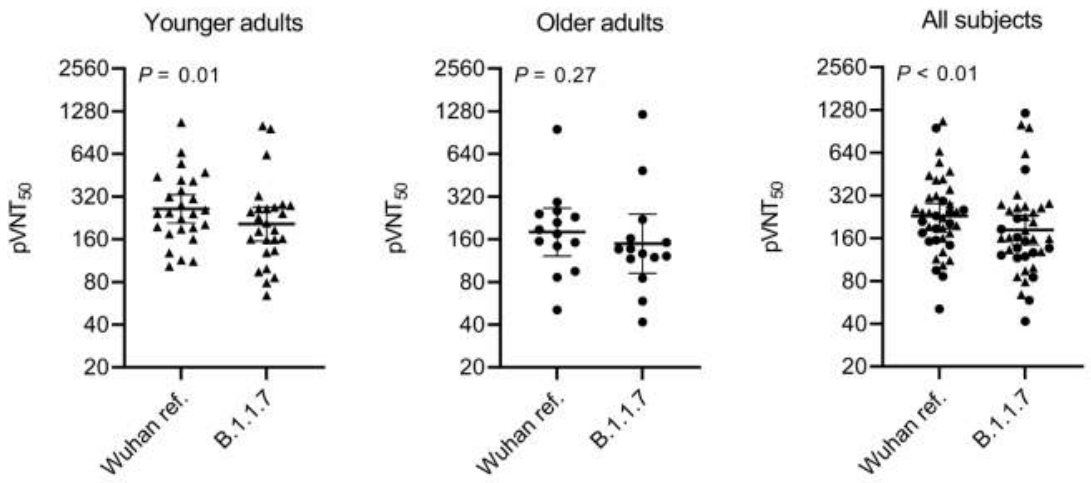
BNT162 b2

NEUTRALIZATION OF VIRAL VARIANTS

Sera of BNT162b2 vaccinated subjects tested against lab generated VSV pseudovirus bearing B.1.1.7 SARS CoV2 mutations

Description of tested sera:

- 40 participants from Phase I
  - 26 younger (23-55 years of age)
  - 14 older (57-73 years of age)
- 7 or 21 days after booster immunization



The 50% neutralization GMT of the sera against the SARS-CoV-2 lineage B.1.1.7 pseudovirus were slightly, statistically significantly reduced compared to the GMTs against the Wuhan reference pseudovirus

The largely preserved neutralization of pseudoviruses bearing the B.1.1.7 spike by BNT162b2-immune sera makes it unlikely that the UK variant virus will escape BNT162b2-mediated protection.

Limitation of the work: use of a non-replicating pseudovirus system

Adenoviral vector vaccine

AZD1222

EFFICACY AND SAFETY DATA

- Efficacy data from ongoing blinded, randomized, controlled trials across UK and Brazil
  - **COV 002:**Phase II/III study in UK. Two dosage groups:
    - LD/SD: prime **$2{,}2\times10^{10}$** vp; boost **5×10^{10}** vp at **28 days**
    - SD/SD: prime **5×10^{10}** vp; boost **5×10^{10}** vp at **28 days**
  - **COV 003:**Phase III study in Brazil. Dosage:
    - SD/SD: prime/boost **$3{\cdot}5–6{\cdot}5\times10^{10}$** vp up to **12 weeks** apart (target 4 weeks)
- **Inclusion criteria:** healthy adults aged of 18y or more.
  - **COV 002:** healthy adults
  - **COV 003:** healthy and stable pre-existing health conditions individuals
- **Main outcome**: virologically confirmed, symptomatic COVID-19 (positive swab combined with at least one qualifying symptom)
- The interim **efficacy** is assessed by **combining data from COV002 and COV003**

	COV002 (UK; LD/SD; N=2741)		COV002 (UK; SD/SD; N=4807)		COV003 (Brazil; all SD/SD; N=4088)	
	ChAdOx1 nCoV-19 (n=1367)	MenACWY (n=1374)	ChAdOx1 nCoV-19 (n=2377)	MenACWY (n=2430)	ChAdOx1 nCoV-19 (n=2063)	MenACWY plus saline (n=2025)
Age, years						
18–55	1367 (100·0%)	1374 (100·0%)	1879 (79·0%)	1922 (79·1%)	1843 (89·3%)	1833 (90·5%)
56–69	0	0	285 (12·0%)	293 (12·1%)	209 (10·1%)	187 (9·2%)
≥70	0	0	213 (9·0%)	215 (8·8%)	11 (0·5%)	5 (0·2%)
Sex						
Female	886 (64·8%)	927 (67·5%)	1378 (58·0%)	1437 (59·1%)	1261 (61·1%)	1156 (57·1%)
Male	481 (35·2%)	447 (32·5%)	999 (42·0%)	993 (40·9%)	802 (38·9%)	869 (42·9%)
BMI, kg/m²	25·2 (22·8–28·7)	25·3 (22·7–28·8)	25·4 (22·9–28·7)	25·5 (22·9–29·1)	25·6 (22·8–29·1)	25·6 (23·1–29·0)
Ethnicity						
White	1257 (92·0%)	1278 (93·0%)	2153 (90·6%)	2214 (91·1%)	1357 (65·8%)	1366 (67·5%)
Black	6 (0·4%)	2 (0·1%)	17 (0·7%)	14 (0·6%)	230 (11·1%)	210 (10·4%)
Asian	76 (5·6%)	59 (4·3%)	137 (5·8%)	138 (5·7%)	54 (2·6%)	53 (2·6%)
Mixed	19 (1·4%)	22 (1·6%)	48 (2·0%)	42 (1·7%)	410 (19·9%)	386 (19·1%)
Other	9 (0·7%)	13 (0·9%)	22 (0·9%)	22 (0·9%)	12 (0·6%)	10 (0·5%)
Health and social care setting workers	1236 (90·4%)	1253 (91·2%)	1441 (60·6%)	1513 (62·3%)	1833 (88·9%)	1775 (87·7%)
Comorbidities						
Cardiovascular disease	104 (7·6%)	92 (6·7%)	264 (11·1%)	266 (10·9%)	271 (13·1%)	244 (12·0%)
Respiratory disease	158 (11·6%)	176 (12·8%)	285 (12·0%)	316 (13·0%)	215 (10·4%)	210 (10·4%)
Diabetes	18 (1·3%)	15 (1·1%)	58 (2·4%)	60 (2·5%)	59 (2·9%)	60 (3·0%)

Data are n (%) or median (IQR). The primary efficacy population (LD/SD and SD/SD) includes randomly assigned participants who were seronegative at baseline and received LD/SD or SD/SD or were in the corresponding control group, and remained on study more than 14 days after their second dose without having had a previous virologically confirmed severe acute respiratory syndrome coronavirus 2 infection. In addition, for groups in COV002, only efficacy groups (ie, groups 4, 6, 9, and 10) are included. LD/SD=low-dose prime plus standard-dose boost. SD/SD=two standard-dose vaccines given. MenACWY=meningococcal group A, C, W, and Y conjugate vaccine. BMI=body-mass index.

Table 1: **Baseline characteristics of participants included in the primary efficacy population, by study and dosing strategy**

Limits:

Immunocompromised volunteers not included in the trial

Elderly participants are low represented

Heterogenicity between trials (concentration and schedule)

Adenoviral vector vaccine

AZD1222

EFFICACY AND SAFETY DATA

	Total number of cases	ChAdOx1 nCoV-19		Control		Vaccine efficacy (CI*)
		n/N (%)	Incidence rate per 1000 person-years (person-days of follow-up)	n/N (%)	Incidence rate per 1000 person-years (person-days of follow-up)	
All LD/SD and SD/SD recipients	131	30/5807 (0·5%)	44·1 (248 299)	101/5829 (1·7%)	149·2 (247 228)	70·4% (54·8 to 80·6)†
COV002 (UK)	86	18/3744 (0·5%)	38·6 (170 369)	68/3804 (1·8%)	145·7 (170 448)	73·5% (55·5 to 84·2)
LD/SD recipients	33	3/1367 (0·2%)	14·9 (73 313)	30/1374 (2·2%)	150·2 (72 949)	90·0% (67·4 to 97·0)‡§
SD/SD recipients	53	15/2377 (0·6%)	56·4 (97 056)	38/2430 (1·6%)	142·4 (97 499)	60·3% (28·0 to 78·2)
COV003 (Brazil; all SD/SD)	45	12/2063 (0·6%)	56·2 (77 930)	33/2025 (1·6%)	157·0 (76 780)	64·2% (30·7 to 81·5)‡
All SD/SD recipients	98	27/4440 (0·6%)	56·4 (174 986)	71/4455 (1·6%)	148·8 (174 279)	62·1% (41·0 to 75·7)
Other non-primary symptomatic COVID-19 disease¶	18	7/5807 (0·1%)	10·3 (248 299)	11/5829 (0·2%)	16·3 (247 228)	36·4% (−63·8 to 75·3)‡
Any symptomatic COVID-19 disease	149	37/5807 (0·6%)	54·4 (248 299)	112/5829 (1·9%)	165·5 (247 228)	67·1% (52·3 to 77·3)
Asymptomatic or symptoms unknown (COV002)	69	29/3288 (0·9%)	69·8 (151 673)	40/3350 (1·2%)	96·0 (152 138)	27·3% (−17·2 to 54·9)
LD/SD recipients	24	7/1120 (0·6%)	41·4 (61 782)	17/1127 (1·5%)	100·6 (61 730)	58·9% (1·0 to 82·9)‡
SD/SD recipients	45	22/2168 (1·0%)	89·4 (89 891)	23/2223 (1·0%)	92·9 (90 408)	3·8% (−72·4 to 46·3)
Any NAAT-positive swab	221	68/5807 (1·2%)	100·0 (248 299)	153/5829 (2·6%)	226·0 (247 228)	55·7% (41·1 to 66·7)

Vaccine efficacy was calculated from the robust Poisson model. The primary efficacy population (LD/SD and SD/SD) includes randomly assigned participants who were seronegative at baseline and received LD/SD or SD/SD or were in a corresponding control group, and remained on study more than 14 days after their second dose without having had a previous virologically confirmed SARS-CoV-2 infection. In addition, for groups in COV002, only efficacy groups (ie, groups 4, 6, 9, and 10) are included. 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. NAAT=nucleic acid amplification test. *CIs are 95% unless indicated otherwise. †95·8% CI used for primary analysis. ‡Vaccine efficacy calculated from a reduced robust Poisson model that was not adjusted for age. All other models included an adjustment for age. §p value for interaction term comparing LD/SD with SD/SD is p=0·010. ¶Other non-primary symptomatic COVID-19 disease includes cases who have symptoms other than the five main symptoms that are required for inclusion in the primary analysis (eg, a participant who has diarrhoea and malaise but no fever, cough, shortness of breath, anosmia, or ageusia).

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

Primary Efficacy Analysis: 2weeks after second dose

- 98 cases in the ***SD/SD*** group (2 trials)
  - 27 within the ChAdOx1 nCov19 group
  - 71 within the Control group
  - ***Vaccine Efficacy in SD/SD: 62,1%***
- 33 cases in the ***LD/SD*** group
  - 3 within the ChAdOx1 nCov19 group
  - 33 within the Control group
  - ***Vaccine Efficacy in LD/SD: 90%***

TOTAL OF CASES: 131
30 in the ChAdOx1 nCov /101 in the Control
Vaccine efficacy: 70,4%

Limits:

Is aggregation of SD/LD and SD/SD data for efficacy analysis possible? (different doses, different vaccination schedules schedules)

COREB mission nationale Coordination Opérationnelle Risque Epidémique et Biologique

Voysey M *et al. The Lancet* Dec 2020

anrs MALADIES INFECTIEUSES ÉMERGENTES

Adenoviral vector vaccine

AZD1222

EFFICACY AND SAFETY DATA

	Total number of cases	ChAdOx1 nCoV-19		Control		Vaccine efficacy (95% CI)
		n/N (%)	Incidence per 1000 person-years (person-days of follow-up)	n/N (%)	Incidence per 1000 person-years (person-days of follow-up)	
COV002 (UK)	90	28/3060 (0·9%)	35·4 (288 955)	62/3064 (2·0%)	78·5 (288 395)	55·0% (29·7 to 71·1)
COV003 (Brazil)	102	23/3247 (0·7%)	46·7 (179 743)	79/3233 (2·4%)	162·4 (177 693)	71·2% (54·2 to 81·9)
Primary symptomatic COVID-19*	192	51/6307 (0·8%)	39·7 (468 698)	141/6297 (2·2%)	110·5 (466 088)	64·1% (50·5 to 73·9)
Other non-primary symptomatic COVID-19†	21	12/6307 (0·2%)	9·4 (468 698)	9/6297 (0·1%)	7·1 (466 088)	−32·8% (−214·8 to 44·0)‡
Any symptomatic COVID-19	213	63/6307 (1·0%)	49·1 (468 698)	150/6297 (2·4%)	117·5 (466 088)	58·3% (44·0 to 68·9)
Asymptomatic or symptoms unknown (COV002)	71	34/2751 (1·2%)	46·8 (265 142)	37/2760 (1·3%)	51·0 (264 994)	7·8% (−46·7 to 42·1)
Any NAAT-positive swab	291	102/6307 (1·6%)	79·5 (468 698)	189/6297 (3·0%)	148·1 (466 088)	46·3% (31·8 to 57·8)

Vaccine efficacy was calculated from the robust Poisson model. The first-standard-dose efficacy population includes participants seronegative at baseline who received only standard dose vaccines or were in the corresponding control group, and remained on study 22 days after their first dose without having had a previous virologically confirmed SARS-CoV-2 infection. In addition, for groups in COV002, only efficacy groups (ie, groups 4, 6, 9, and 10) are included. SARS-CoV-2=severe acute respiratory syndrome coronavirus 2. NAAT=nucleic acid amplification test. *NAAT-positive swab plus at least one of cough, shortness of breath, fever higher than 37·8°C, anosmia, or ageusia. †Other non-primary symptomatic COVID-19 disease includes cases that have symptoms other than the five main symptoms required for inclusion in the primary analysis (eg, a participant who has diarrhoea and malaise but no fever, cough, shortness of breath, anosmia, or ageusia). ‡Vaccine efficacy was calculated from a reduced robust Poisson model (excluding the age group category due to the full model failing to converge). Participants with a low-dose prime were excluded.

Table 4: **Efficacy against SARS-CoV-2 more than 21 days after the first standard dose in seronegative participants who received only standard doses**

Primary Efficacy Analysis at more than 21 days after second dose

TOTAL OF CASES: 192
(only SD/SD group; two trials, *different vaccination schedules*)
51 in the ChAdOx1 nCov / 141 in the Control
Vaccine efficacy: 64,1%

Limits: No evidence of an potential effect against viral shedding

From 21 days after the first dose: there were ten cases hospitalized for COVID-19, all in the control arm; two were classified as severe COVID-19, including one death

	ChAdOx1 nCoV-19 (n=12 021)	MenACWY or saline control (n=11 724)
Hospitalisation (WHO clinical progression score ≥4)		
≤21 days after the first dose	2*	6
>21 days after the first dose and ≤14 days after the second dose	0	5
>14 days after the second dose	0	5
Severe COVID-19 (WHO clinical progression score ≥6)		
≤21 days after the first dose	0	0
>21 days after the first dose and ≤14 days after the second dose	0	1
>14 days after the second dose	0	1

The safety population includes all randomisation participants who received at least one dose of vaccine. Severe COVID-19 (WHO score ≥6) is a subset of hospitalisations (WHO score ≥4). Cases were eligible for inclusion in efficacy if the first symptom or first NAAT-positive result was on or before the data cutoff date (Nov 4, 2020). Two cases appear in this table that do not appear in the table for serious adverse events in appendix 1 (pp 15–20) as the adverse event reporting date was after the data cutoff date. MenACWY=meningococcal group A, C, W, and Y conjugate vaccine. NAAT=nucleic acid amplification test. *One case on the day of the first vaccination and one case 10 days after the first dose.

Table 5: **Hospitalisation for COVID-19 and severe COVID-19 in the safety population**

COREB mission nationale
Coordination Opérationnelle Risque Epidémique et Biologique

Voysey M *et al. The Lancet* Dec 2020

MALADIES INFECTIEUSES ÉMERGENTES

mRNA vaccine

mRNA 1273

EFFICACY AND SAFETY DATA

- Efficacy data from Phase III blinded, randomized, controlled trials at 99 US sites
- 2 doses of 100 µg of mRNA 1273 or placebo 28 days apart
  - 30 420 participants randomized (1:1)
  - >96% received 2nd dose
- Inclusion criteria: healthy adults aged of 18y or more with no history of SARS CoV 2 and high risk of severe COVID19

Primary endpoint: efficacy of the mRNA-1273 vaccine in preventing a first occurrence of symptomatic Covid-19 with onset at least 14 days after the second injection (virologically confirmed, symptomatic COVID-19: positive swab combined with at least two qualifying symptom)

Secondary end point: efficacy of mRNA-1273 in the prevention of severe Covid-19

Safety assessments: monitoring of solicited local and systemic adverse events for 7 days after each injection; unsolicited adverse reactions for 28 days after each injection

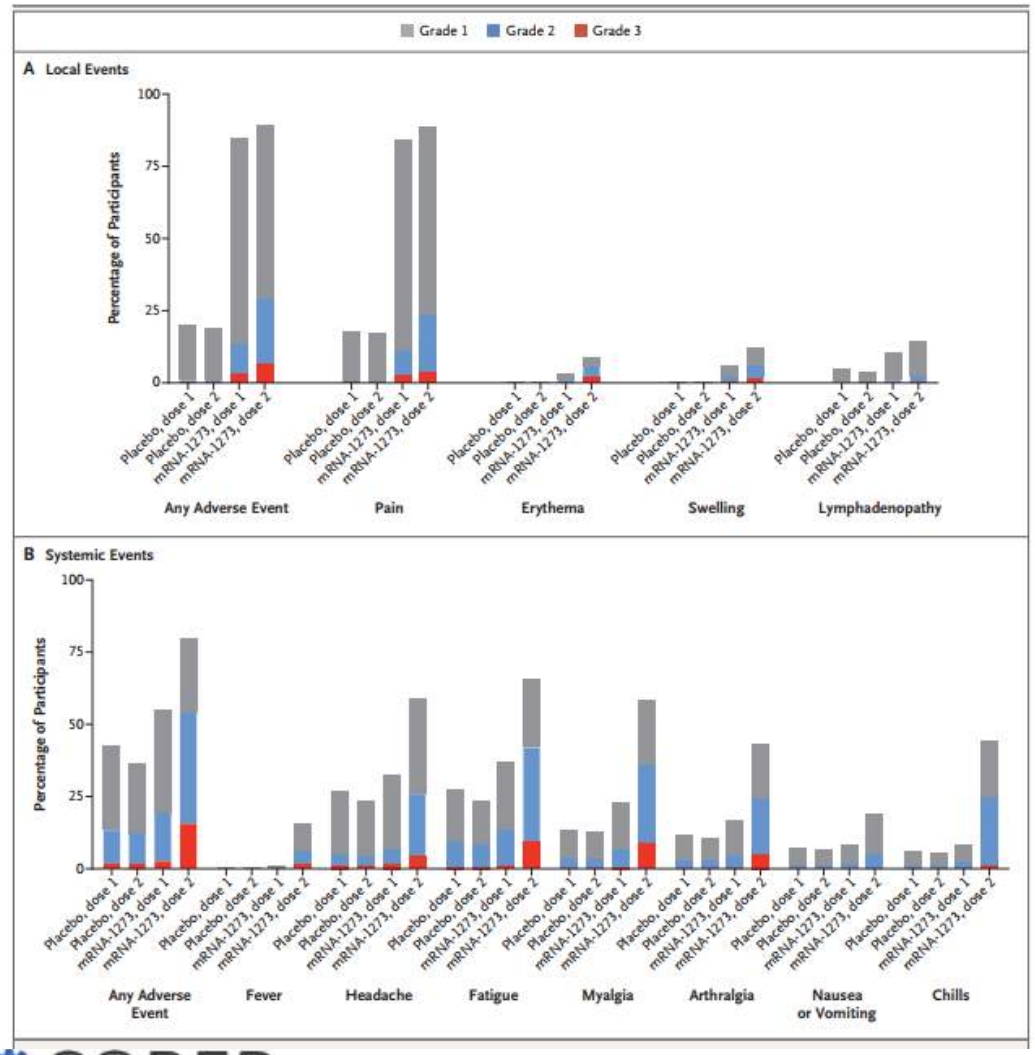
Table 1. Demographic and Clinical Characteristics at Baseline.*

Characteristics	Placebo (N=15,170)	mRNA-1273 (N=15,181)	Total (N=30,351)
Sex — no. of participants (%)			
Male	8,062 (53.1)	7,923 (52.2)	15,985 (52.7)
Female	7,108 (46.9)	7,258 (47.8)	14,366 (47.3)
Mean age (range) — yr	51.3 (18–95)	51.4 (18–95)	51.4 (18–95)
Age category and risk for severe Covid-19 — no. of participants (%)†			
18 to <65 yr, not at risk	8,886 (58.6)	8,888 (58.5)	17,774 (58.6)
18 to <65 yr, at risk	2,535 (16.7)	2,530 (16.7)	5,065 (16.7)
≥65 yr	3,749 (24.7)	3,763 (24.8)	7,512 (24.8)
Hispanic or Latino ethnicity — no. of participants (%)‡			
Hispanic or Latino	3,114 (20.5)	3,121 (20.6)	6,235 (20.5)
Not Hispanic or Latino	11,917 (78.6)	11,918 (78.5)	23,835 (78.5)
Not reported and unknown	139 (0.9)	142 (0.9)	281 (0.9)
Race or ethnic group — no. of participants (%)‡			
White	11,995 (79.1)	12,029 (79.2)	24,024 (79.2)
Black or African American	1,527 (10.1)	1,563 (10.3)	3,090 (10.2)
Asian	731 (4.8)	651 (4.3)	1,382 (4.6)
American Indian or Alaska Native	121 (0.8)	112 (0.7)	233 (0.8)
Native Hawaiian or Other Pacific Islander	32 (0.2)	35 (0.2)	67 (0.2)
Multiracial	321 (2.1)	315 (2.1)	636 (2.1)
Other	316 (2.1)	321 (2.1)	637 (2.1)
Not reported and unknown	127 (0.8)	155 (1.0)	282 (0.9)
Baseline SARS-CoV-2 status — no. of participants (%)§			
Negative	14,598 (96.2)	14,550 (95.8)	29,148 (96.0)
Positive	337 (2.2)	343 (2.3)	680 (2.2)
Missing data	235 (1.5)	288 (1.9)	523 (1.7)
Baseline RT-PCR test — no. of participants (%)			
Negative	14,923 (98.4)	14,917 (98.3)	29,840 (98.3)
Positive	95 (0.6)	87 (0.6)	182 (0.6)
Missing data	152 (1.0)	177 (1.2)	329 (1.1)
Baseline bAb anti–SARS-CoV-2 assay — no. of participants (%)			
Negative	14,726 (97.1)	14,690 (96.8)	29,416 (96.9)
Positive	303 (2.0)	305 (2.0)	608 (2.0)
Missing data	141 (0.9)	186 (1.2)	327 (1.1)
Risk factor for severe Covid-19 — no. of participants (%)			
Chronic lung disease	744 (4.9)	710 (4.7)	1,454 (4.8)
Significant cardiac disease	744 (4.9)	752 (5.0)	1,496 (4.9)
Severe obesity	1,021 (6.7)	1,025 (6.8)	2,046 (6.7)
Diabetes	1,440 (9.5)	1,435 (9.5)	2,875 (9.5)
Liver disease	96 (0.6)	100 (0.7)	196 (0.6)
Human immunodeficiency virus infection	87 (0.6)	92 (0.6)	179 (0.6)

mRNA vaccine

mRNA 1273

EFFICACY
AND SAFETY DATA



- **Solicited adverse events at the injection site:** more frequent in the mRNA-1273 group after both the 1st (84.2%, vs. 19.8%) and the 2nd dose (88.6%, vs. 18.8%). Mainly grade 1 or 2
- **Solicited systemic adverse events:** more often in the mRNA-1273 group after both the 1st (54.9%, vs. 42.2%) and the 2nd dose (79.4%, vs. 36.5%). Increase proportions of grade 2 and 3 events after 2nd Dose (from 16.5% vs 38.1% and from 2.9% to 15.8%).
- Both solicited injection-site and systemic adverse events were more common among younger participants (18 to <65y) than among older participants (≥65 y)
- The frequency **of unsolicited adverse events, unsolicited severe adverse events, and serious adverse events** 28 days after injection similar among age groups
- **Hypersensitivity reactions** reported in 1.5% and 1.1% of participants in the vaccine and placebo groups. 3 **Bell's palsy** in the vaccine group and 1 in the placebo group
- 5 deaths, including 3 in the mRNA 1273 group with no link to vaccine

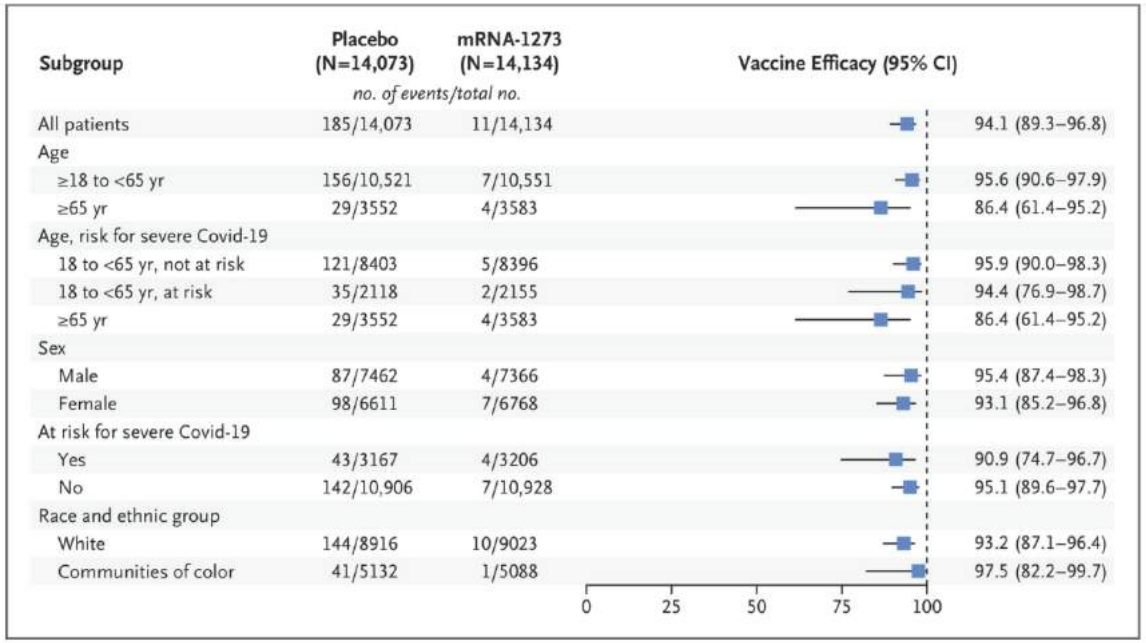
Key limitations: short duration of safety and efficacy follow-up

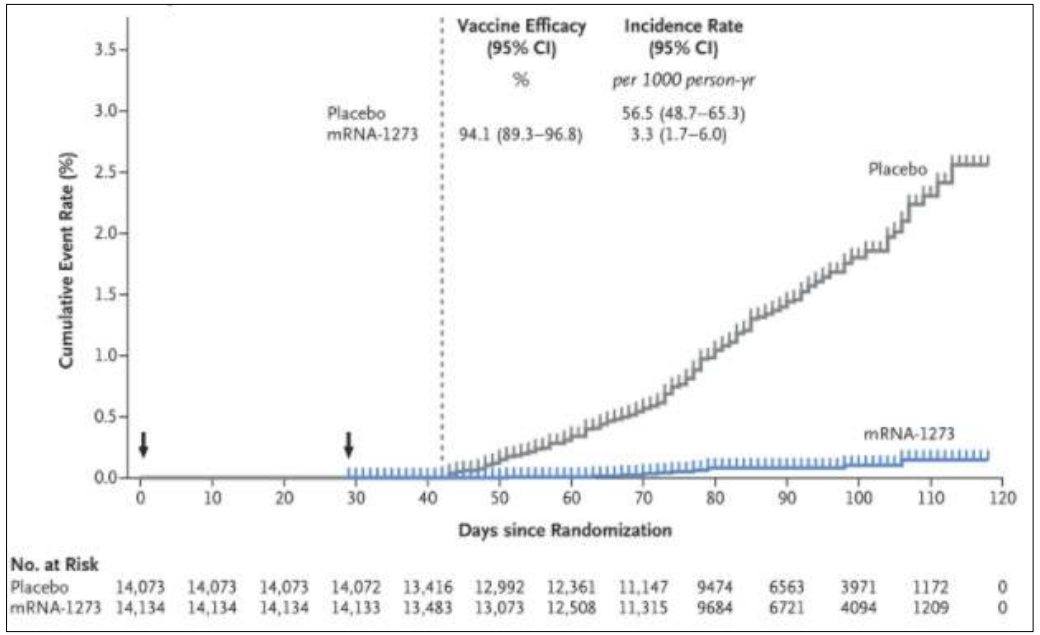
mRNA vaccine

mRNA 1273

EFFICACY AND SAFETY DATA

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)





TOTAL OF CASES: 196

- 11 in the mRNA 1273 group /185 in the placebo group
- 30 severe cases all within the placebo group

Vaccine efficacy: 94.1% (100% protection against severe cases)

data not sufficient to assess asymptomatic infection

Limits: efficacy tested in a setting of national recommendations for masking and social distancing, which may have translated into lower levels of infectious inoculum.

mRNA vaccine

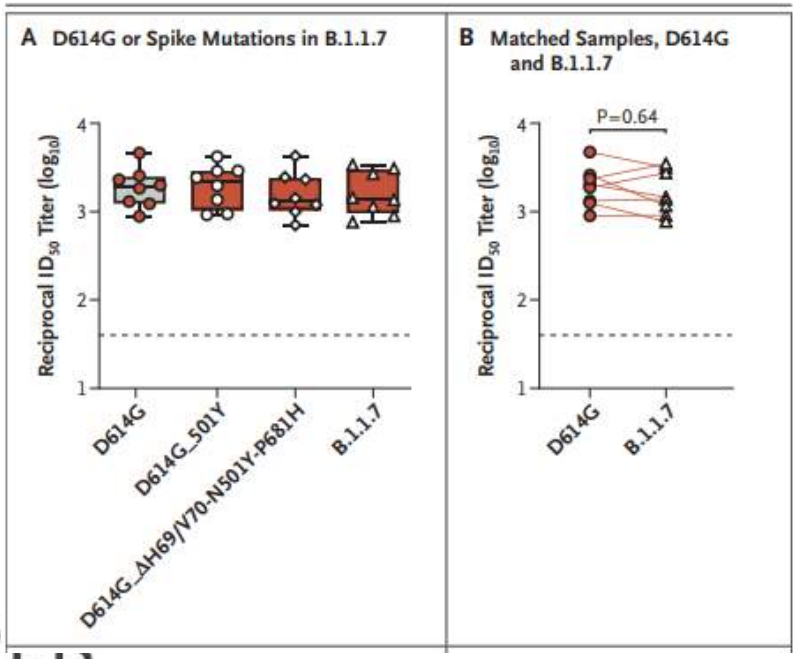
mRNA 1273

NEUTRALIZATION OF VIRAL VARIANTS

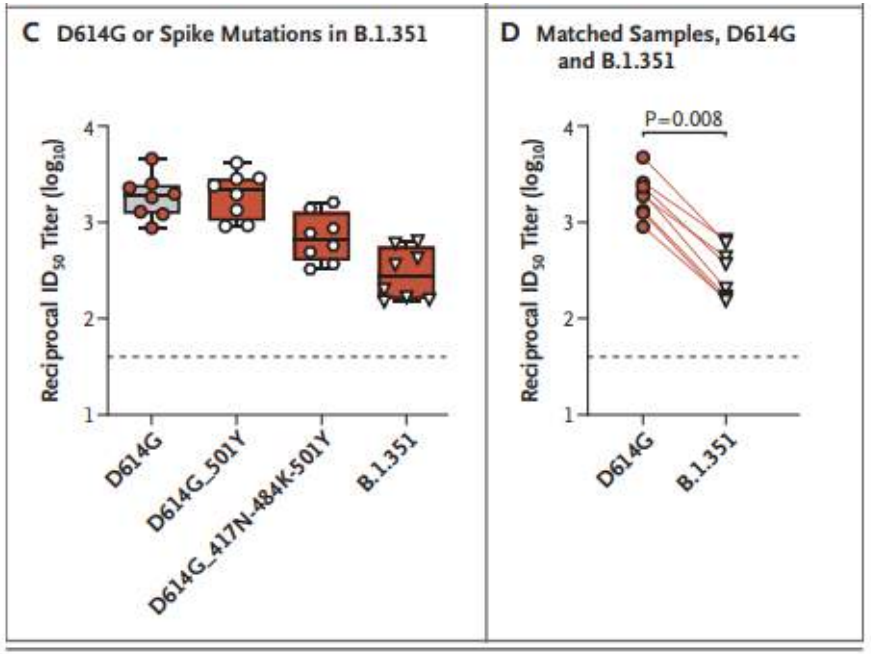
Serum neutralizing activity against recombinant vesicular stomatitis virus (rVSV)–based SARS-CoV-2 bearing the spike protein from the original Wuhan-Hu-1 isolate, the D614G variant, the B.1.1.7 and B.1.351 variants

Description of tested sera: participants from Phase I trial of the mRNA-1273 vaccine, 7 days after second dose

Full panel of mutations and a subset of mutations affecting the RBD of the B.1.1.7 variant had no significant effect on neutralization by serum from vaccinated patients



Decrease in titers of neutralizing antibodies against the B.1.351 variant and a subset of its mutations affecting the RBD.



Wu K., *et al NEJM* Feb 2021.

Adenoviral vector vaccine

Sputnik V

EFFICACY AND SAFETY DATA

- Sputnik vaccine comprises two vector components, rAd26-S and rAd5-S.
- Efficacy data from Phase III blinded, randomized, controlled trials at 25 sites in Moscow-Russia
- 2 doses of 10^{11} recombinant vp each at 21 d interval (d26 first, Ad5 later)
  - 21 977 participants randomized (3:1)
  - >90% received 2nd dose
- Inclusion criteria: healthy adults aged of 18y negative for HIV, Hepatitis B and C and no history of SARS CoV 2

Primary outcome: proportion of participants with COVID-19 confirmed by PCR from day 21 after receiving the first dose

Secondary outcomes: end point: severity of COVID-19; changes in antibody levels against SARS-CoV-2 glycoprotein S; proportion of participants with antibodies against SARS-CoV-2 N-protein; changes in SARS-CoV-2 neutralising antibody titres; changes in antigen-specific cellular immunity level; and incidence and severity of adverse events

	Vaccine (n=14 964)	Placebo (n=4902)
Sex		
Female	5821 (38·9%)	1887 (38·5%)
Male	9143 (61·1%)	3015 (61·5%)
Race		
White	14 741 (98·5%)	4830 (98·5%)
Asian	217 (1·5%)	69 (1·4%)
Other*	6 (<0·1%)	3 (<0·1%)
Age group, years		
18–30	1596 (10·7%)	521 (10·6%)
31–40	3848 (25·7%)	1259 (25·7%)
41–50	4399 (29·4%)	1443 (29·4%)
51–60	3510 (23·5%)	1146 (23·4%)
>60	1611 (10·8%)	533 (10·9%)
Age, years	45·3 (12·0)	45·3 (11·9)
Bodyweight, kg	81·3 (17·5)	81·6 (17·7)
Height, cm	173·1 (9·1)	173·3 (9·0)
Body-mass index, kg/m²	26·75 (4·56)	26·75 (4·55)
Concomitant diseases (diabetes, hypertension, ischaemic heart disease, obesity)†	3687/14 944 (24·7%)	1235/4892 (25·2%)
Risk of infection in volunteers†‡		
High	65/14 567 (0·4%)	23/4778 (0·5%)
Medium	3853/14 567 (26·5%)	1280/4778 (26·8%)
General	10649/14 567 (73·1%)	3475/4778 (72·7%)

Data are n (%) and mean (SD). *Includes Black or African American, Native Hawaiian or other Pacific Islander, or undefined. †Denominator shows number of participants for whom these data were available. ‡High risk denotes those whose work involves interaction with patients with a confirmed diagnosis of COVID-19; medium risk is those who have professional contact with a large number of people, such as general practitioners, social workers, and shop assistants; and general risk denotes those with no additional risks associated with their professional activities.

Table 1: Baseline characteristics of participants who received two doses of assigned treatment and were included in primary outcome analysis

Adenoviral vector vaccine

Sputnik V

EFFICACY AND SAFETY DATA

Primary Efficacy Analysis

	Total cases	Vaccine group	Placebo group	Vaccine efficacy (95% CI)	p value
First COVID-19 occurrence from 21 days after dose 1 (day of dose 2)*					
Overall	78	16/14 964 (0·1%)	62/4902 (1·3%)	91·6% (85·6–95·2)	<0·0001
Age group (years)					
18–30	5	1/1596 (0·1%)	4/521 (0·8%)	91·9% (51·2–99·3)	0·0146
31–40	17	4/3848 (0·1%)	13/1259 (1·0%)	90·0% (71·1–96·5)	<0·0001
41–50	19	4/4399 (0·1%)	15/1443 (1·0%)	91·3% (73·7–96·9)	<0·0001
51–60	27	5/3510 (0·1%)	22/1146 (1·9%)	92·7% (81·1–97·0)	<0·0001
>60	10	2/1611 (0·1%)	8/533 (1·5%)	91·8% (67·1–98·3)	0·0004
Sex					
Female	32	9/5821 (0·2%)	23/1887 (1·2%)	87·5% (73·4–94·2)	<0·0001
Male	46	7/9143 (0·1%)	39/3015 (1·3%)	94·2% (87·2–97·4)	<0·0001
Moderate or severe cases	20	0/14 964	20/4902 (0·4%)	100% (94·4–100·0)	<0·0001
First COVID-19 occurrence after dose 1†					
Any time after dose 1	175	79/16 427 (0·5%)	96/5435 (1·8%)	73·1% (63·7–80·1)	<0·0001
From 14 days after dose 1	109	30/14 999 (0·2%)	79/4950 (1·6%)	87·6% (81·1–91·8)	<0·0001
First COVID-19 occurrence after dose 2 (28 days after dose 1)*					
All	60	13/14 094 (0·1%)	47/4601 (1·0%)	91·1% (83·8–95·1)	<0·0001

Data are n/N (%), unless otherwise stated. *Includes those who received both doses. †Includes participants who received at least one dose.

Table 2: **Interim results on vaccine efficacy**

Limitations of the interim analysis: the small sample sizes within age strata

From 21 days after the first dose of vaccine (the day of dose 2)

TOTAL OF CASES: confirmed cases78
16 in the vaccinated group /62 in the Placebo
20 moderate of severe cases all in the Placebo
4 deaths unrelated to vaccine
Vaccine efficacy: 91,6%
(greater that 87% for all studied groups including >60)

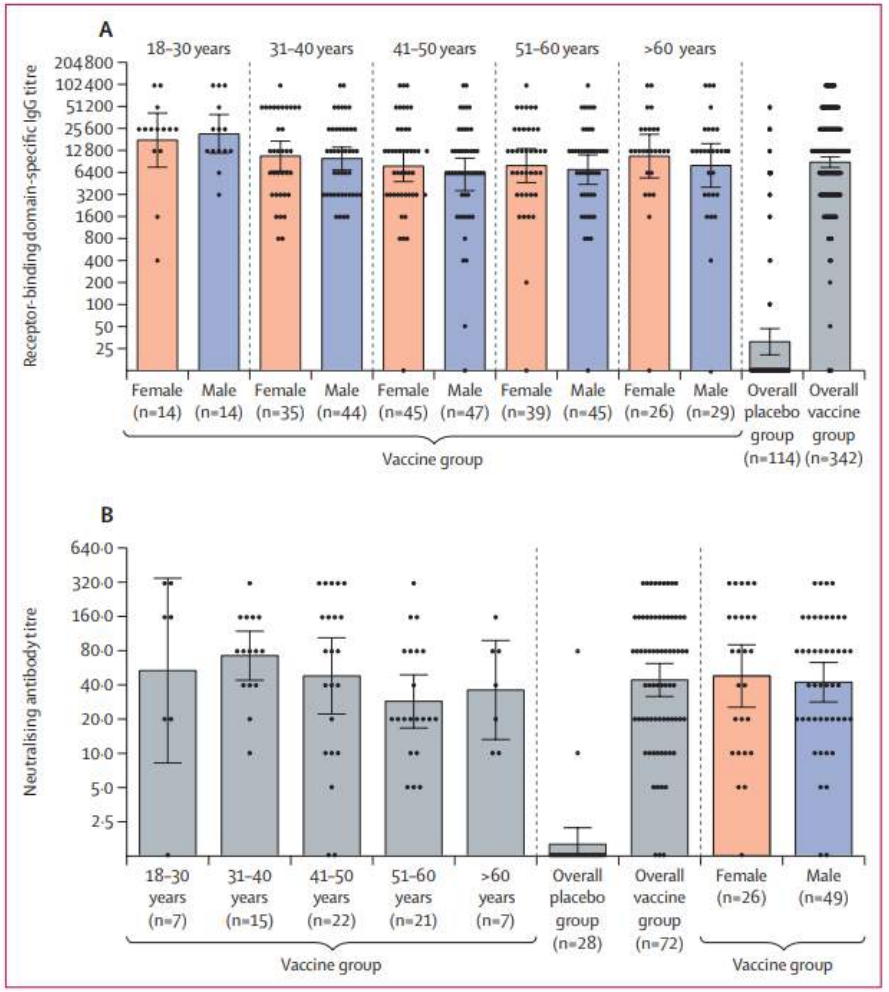
SAFETY:

- Most of the reported adverse events (7485 [94·0%] of 7966) were grade 1; 451 were grade 2 (5·66%) and 30 were grade 3 (0·38%) (*flu-like illness, injection site reactions, headache, and asthenia).*
- 122 rare adverse events (91 in the vaccine group and 31 in the placebo group
- 70 episodes of serious adverse events, considered not related to COVID-19 (68 participants, 45 from the vaccine group and 23 from the placebo group)

Adenoviral vector vaccine

Sputnik V

EFFICACY AND SAFETY DATA



- **Presence of IgGs** specific to RBD 42 days from the start of vaccination
  - In the vaccine group, : detected in 336 (98%) of 342 samples, with a GMT of 8996 (95% CI 7610–10 635). Seroconversion rate: 98·25%.
  - In the placebo group: detected in 17 (15%) of 114 samples, with a GMT of 30,55 (20,18–46,26), and a seroconversion rate of 14·91%
  - 18–30 years group had a significantly higher GMT than the other age groups
- **Presence of neutralizing antibodies** on day 42 after first vaccination
  - In vaccine group: GMT of 44,5 (95% CI 31,8–62,2) and the seroconversion level was 95,83%
  - In the placebo group: GMT 1,6 (1,12–2,19) and the seroconversion rate was 7·14%

- All participants in the vaccine group had significantly higher levels of IFN-γ secretion upon antigen stimulation

VACCINE (February 20 th 2020)

1. What are the types of vaccines in clinical evaluation?

- 63 candidates vaccines are in an ongoing clinical evaluation
- Published Phase I/II data suggests that vaccine candidates on trial are immunogenic and mostly well tolerated in young adults. Data is emerging on elderly, globally keeping the trend described in young adults
- Induced titers of NAb are variable depending on the vaccine candidate. Comparison of Nab titers among candidates should not be made at this stage
- No data on ADE risk on humans nor virus clearance in upper respiratory tract after human vaccination has been published yet
- 12 vaccines are already in Phase III for efficacy evaluation and data has come out for 4 of them. Overall efficacy results are good and rang between 62% and 95% depending on the vaccine studies. mRNA vaccines perform the best although sterilization capacity and long term protection remains largely unknown
- SARS COV 2 variants represent a challenge for current vaccines with preliminary results showing and variable level of crossreaction depending on the viral strain.