EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

COVID-19 vaccines and therapeutics

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An agency of the European Union

Therapeutics update: 4 monoclonal antibodies products with neutralising activity received scientific opinion to support emergency use before approval and have started rolling review

Currently under rolling review

- Bamlanivimab and etesevimab
- Regdanvimab
- REGN-COV2 (casirivimab / imdevimab)
- Sotrovimab

Marketing authorisation application submitted

- Olumiant (baricitinib)*
- Kineret (anakinra)*
- RoActemra (tocilizumab)*

Authorised for use in the European Union

- Veklury (remdesivir)

Early Convalescent Plasma for High-Risk Outpatients with Covid-19

- The administration of Covid-19 convalescent plasma to high-risk outpatients within one week after the onset of symptoms of Covid-19 **did not prevent** disease progression

Table 2. Primary Composite Outcome of Disease Progression within 15 Days after Randomization.*

Outcome	Intention-to-Treat Population (N=511)				Per-Protocol Population (N=497)†			
	Convalescent Plasma (N=257)	Placebo (N=254)	Risk Difference (95% Credible Interval)‡ *percentage points*	Posterior Probability of Superiority of Convalescent Plasma	Convalescent Plasma (N=246)	Placebo (N=251)	Risk Difference (95% Credible Interval)‡ *percentage points*	Posterior Probability of Superiority of Convalescent Plasma
Patients with a disease-progression event — no. (%)	77 (30.0)	81 (31.9)	1.9 (–6.0 to 9.8)	0.68	71 (28.9)	80 (31.9)	3.0 (–4.9 to 10.8)	0.76
Hospital admission for any reason	51 (19.8)	56 (22.0)			47 (19.1)	55 (21.9)		
Seeking emergency or urgent care	25 (9.7)	25 (9.8)			24 (9.8)	25 (10.0)		
Death without hospitalization	1 (0.4)	0			0	0		

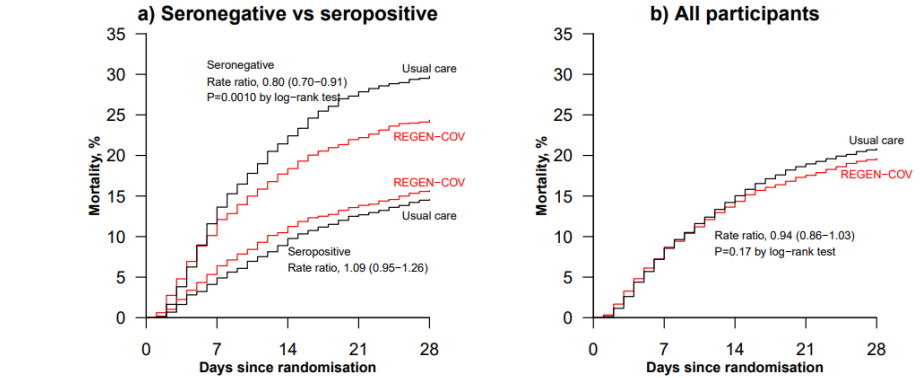
* The primary outcome was disease progression within 15 days, which was a composite of hospital admission for any reason, seeking emergency or urgent care, or death without hospitalization.
† The per-protocol population included all the patients who had undergone randomization after the exclusion of those who did not receive the assigned trial product, had an identified eligibility violation, or had a disease-progression event before the initiation of treatment.
‡ The risk difference is for the placebo group minus the convalescent-plasma group. In the intention-to-treat population, the risk difference after adjustment for age, sex, symptom duration, and enrollment site was 2.2 percentage points (95% confidence interval, –5.9 to 10.4).

Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2103784

Combination of 2 monoclonal antibodies in patients admitted to hospital with COVID-19 (RECOVERY)

- In patients hospitalised with COVID-19, the monoclonal antibody combination of casirivimab and imdevimab (REGEN-COV) **reduced** 28-day mortality among patients who were seronegative at baseline

Figure 2: Effect of allocation to REGEN–COV on 28–day mortality in: a) seronegative vs seropositive participants; and b) all participants



No. at risk, Seronegative					
REGEN–COV	1633	1429	1325	1260	1224
Usual Care	1520	1308	1173	1088	1059

No. at risk, Seropositive					
REGEN–COV	2636	2452	2322	2252	2201
Usual Care	2636	2503	2375	2292	2243

No. at risk					
REGEN–COV	4839	4388	4112	3952	3848
Usual Care	4946	4504	4182	3980	3888

Source: https://www.medrxiv.org/content/10.1101/2021.06.15.21258542v1

Combination of 2 long-acting antibodies (AZD7442) PROVENT Phase III prophylaxis trial

- AZD7442 PROVENT Phase III prophylaxis trial met primary endpoint in preventing COVID-19 – **reduction** in the incidence of symptomatic COVID-19

Company's press release on 20 August 2021

Positive high-level results from the PROVENT Phase III pre-exposure prophylaxis trial showed AstraZeneca's AZD7442 achieved a statistically significant reduction in the incidence of symptomatic COVID-19, the trial's primary endpoint.

AZD7442, a combination of two long-acting antibodies (LAAB), reduced the risk of developing symptomatic COVID-19 by 77% (95% confidence interval (CI): 46, 90), compared to placebo. The trial accrued 25 cases of symptomatic COVID-19 at the primary analysis.

There were no cases of severe COVID-19 or COVID-19-related deaths in those treated with AZD7442. In the placebo arm, there were three cases of severe COVID-19, which included two deaths.

AZD7442 is the first antibody combination (non-vaccine) modified to potentially provide long-lasting protection that has demonstrated prevention of COVID-19 in a clinical trial.

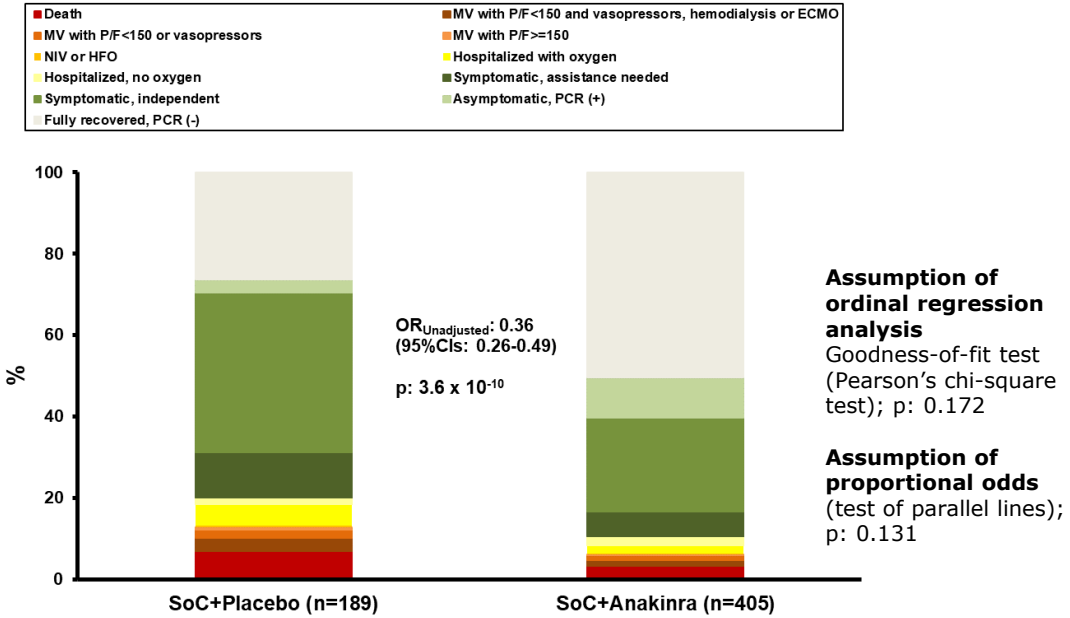
The trial included 5,197 participants in a 2:1 randomisation AZD7442 to placebo. The primary analysis was based on 5,172 participants who did not have SARS-CoV-2 infection at baseline.

More than 75% of participants had co-morbidities, which include conditions that have been reported to cause a reduced immune response to vaccination.

Source: https://www.astrazeneca.com/media-centre/press-releases/2021/azd7442-prophylaxis-trial-met-primary-endpoint.html

Early treatment of COVID-19 with interleukin 1 beta inhibitor (anakinra) – SAVE-MORE trial

- Twenty-eight-day mortality **decreased** and hospital stay was **shorter**
- Assessed by the 11-point World Health Organization Clinical Progression Scale (WHO-CPS)



Assumption of ordinal regression analysis
Goodness-of-fit test (Pearson's chi-square test); p: 0.172

Assumption of proportional odds
(test of parallel lines); p: 0.131

CIs: confidence intervals; OR: odds ratio; SoC: standard-of-care

Source: https://www.nature.com/articles/s41591-021-01499-z

COVID-19 vulnerability via autoantibodies

- Autoantibodies neutralizing type I IFNs are present in ~4% of uninfected individuals over 70 years old and account for ~20% of COVID-19 deaths

Anti-type I IFN auto-Ab positive (amount of type I IFN neutralized, in plasma diluted 1/10)	Proportion of critical patients with neutralizing auto-Abs	OR [95% CI]	*P*-value
anti-IFN-α2 and anti-IFN-ω auto-Abs (10 ng/mL)	5.6%	67 [4-1109]	$7.8x10^{-13}$
anti-IFN-α2 and/or anti-IFN-ω auto-Abs (10 ng/mL)	9.8%	17 [7-45]	$< 10^{-13}$
anti-IFN-α2 auto-Abs (10 ng/mL)	9%	45 [9-225]	$< 10^{-13}$
anti-IFN-α2 auto-Abs only (10 ng/mL)	3.4%	21 [4-107]	$1.8x10^{-09}$
anti-IFN-ω auto-Abs (10 ng/mL)	6.4%	13 [4-38]	$1.4x10^{-12}$
anti-IFN-ω auto-Abs only (10 ng/mL)	0.8%	3 [0.9-10]	0.057
anti-IFN-α2 and anti-IFN-ω auto-Abs (100 pg/mL)	7.1%	54 [11-275]	$< 10^{-13}$
anti-IFN-α2 and/or anti-IFN-ω auto-Abs (100 pg/mL)	13.6%	13 [8-21]	$< 10^{-13}$
anti-IFN-α2 auto-Abs (100 pg/mL)	10%	23 [10-55]	$< 10^{-13}$
anti-IFN-α2 auto-Abs only (100 pg/mL)	2.9%	10 [3-26]	$2.8x10^{-09}$
anti-IFN-ω auto-Abs (100 pg/mL)	10.7%	13 [7-23]	$< 10^{-13}$
anti-IFN-ω auto-Abs only (100 pg/mL)	3.6%	6 [3-12]	$3.9x10^{-10}$
anti-IFN-β auto-Abs (10 ng/mL)	1.3%	8 [2-36]	$1.7x10^{-3}$
anti-IFN-β auto-Abs only (10 ng/mL)	0.96%	5 [1-25]	0.043
anti-IFN-β auto-Abs (10 ng/mL) and, anti-IFN-α2 and/or anti-IFN-ω auto-Abs (100 pg/mL)	0.34%	16 [0.5-497]	0.018
anti-IFN-β (10 ng/mL) and, anti-IFN-α2 and anti-IFN-ω auto-Abs (100 pg/mL)	0.28%	16 [0.5-502]	0.019

Source: https://www.science.org/doi/10.1126/sciimmunol.abl4340

X-linked COVID-19 risk factor

- X-linked recessive TLR7 deficiency in ~1% of men under 60 years old with life-threatening COVID-19

Table 1. X-linked *TLR7* deleterious variants in 16 unrelated male patients with life-threatening COVID-19 pneumonia.

Patient	Genotype	Age [years]	Ethnicity	Ancestry/residence	Outcome
P1	L134P/Y	45	Admixed American	Paraguay/Spain	Survived
P2	N158Tfs11*/Y	60	European	France	Deceased
P3	L227fs*/Y	34	Middle East	Iran	Survived
P4	D244Y/Y	13	Middle East	Turkey	Survived
P5	F310L/Y	39	Middle East	Iran	Survived
P6	L372M	7	Caucasian (Central Asia based on GME Variome)	Iran	Survived
P7	I505T/Y	55	European	Italy	Survived
P8	H630Y/Y	50	European	Spain	Survived
P9	I657T/Y	18	European	Italy	Survived
P10	F670Lfs*8	31	European	Sweden	Survived
P11*	F670Lfs*8	29	European	Sweden	Survived
P12	K684*/Y	30	European	Spain	Survived
P13	P715S/Y	40	Latino	Colombia	Survived
P14	H781L/Y	13	Middle East	Russia/France	Survived
P15	L988S/Y	26	Middle East	Iran	Deceased
P16	L988S/Y	20	Middle East	Turkey	Survived
P17	M854I;L988S/Y	71	European	Italy	Survived

* P10's brother (not included in the cohort of 1,202 critical patients with critical COVID-19 pneumonia).
GME Variome, Greater Middle Eastern Variome Project

Source: https://www.science.org/doi/10.1126/sciimmunol.abl4348

Decline in pathogenic antibodies over time in vaccine-induced immune thrombotic thrombocytopenia (VITT)

- Study indicates that pathogenic antibodies (known as anti-platelet factor 4 (PF4) antibodies) are **transient in most patients** with VITT
- In a subgroup of these patients, pathogenic antibodies **may persist** for more than 12 weeks
- **Further studies are needed** to clarify whether these patients should receive prolonged anticoagulation or additional treatment

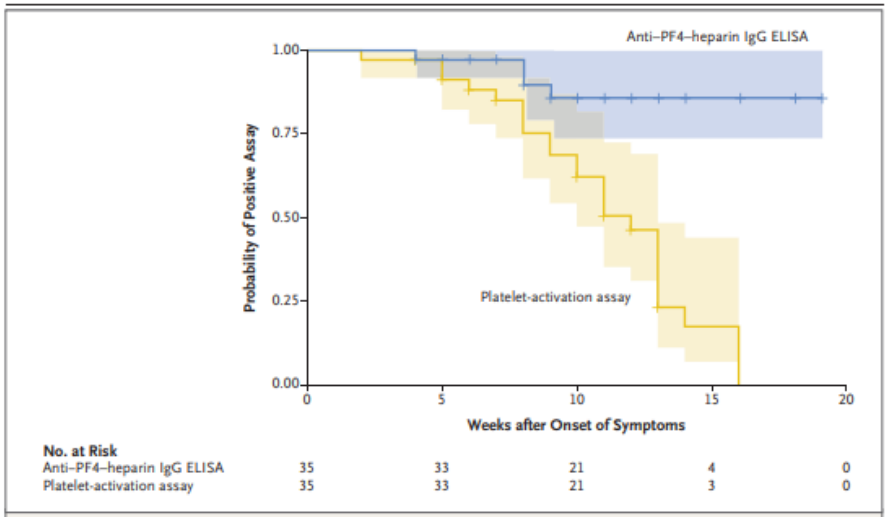
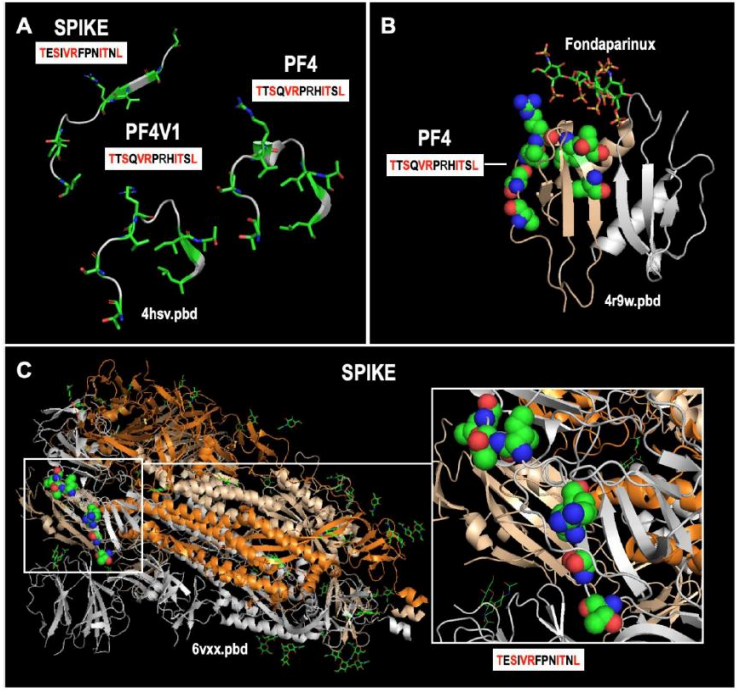


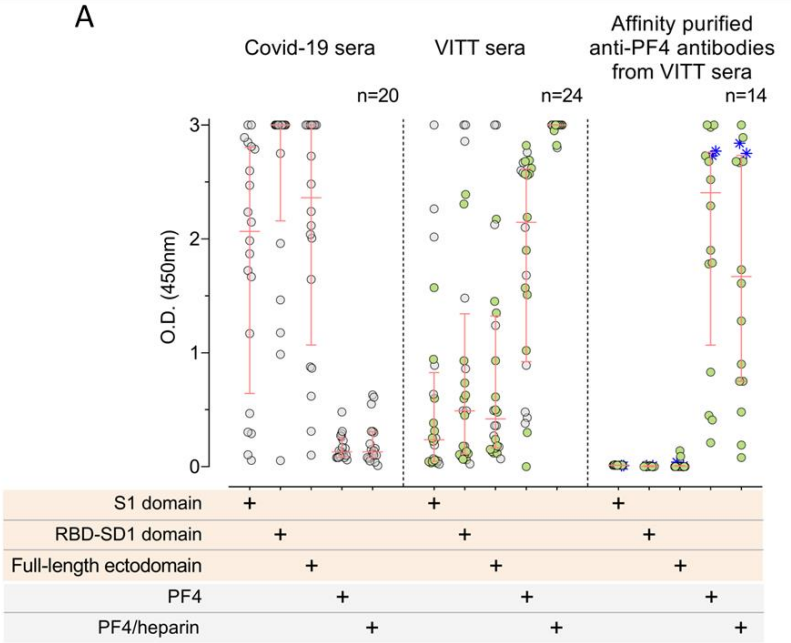
Figure 1. Kaplan–Meier Analysis of the Proportion of Patients with Positive Assay Results.

The time to an optical density of less than 0.5 on the anti–platelet factor 4 (PF4)–heparin IgG enzyme-linked immunosorbent assay (ELISA) and to a negative result on the platelet-activation assay is shown. Shaded areas indicate 95% confidence intervals. Most patients initially had very strongly positive reactivity on anti–PF4–heparin IgG ELISA, with optical densities of greater than 2.0 at the time of diagnosis of vaccine-induced immune thrombotic thrombocytopenia. Antibody levels decreased over time during follow-up but did not fall below the cutoff value. All the patients initially had positive results on an assay for PF4-dependent platelet-activating antibodies and repeatedly underwent testing (median follow-up, 11 weeks; range, 4 to 18). After 12 weeks, platelet-activating antibodies had disappeared in most patients.

Source: https://www.nejm.org/doi/full/10.1056/NEJMc2112760

Anti-platelet factor 4 antibodies causing VITT do not cross-react with SARS-CoV-2 spike protein





Source: https://www.researchsquare.com/article/rs-404769/v1

Vaccine updates

Currently under rolling review

- NVX-CoV2373
- CVnCoV
- Sputnik V (Gam-COVID-Vac)
- COVID-19 Vaccine (Vero Cell) Inactivated
- Vidprevtyn

Marketing authorisation application submitted

No marketing authorisation applications currently under evaluation

Authorised for use in the European Union

- Comirnaty
- Spikevax (previously COVID-19 Vaccine Moderna)
- Vaxzevria (previously COVID-19 Vaccine AstraZeneca)
- COVID-19 Vaccine Janssen

Safety of mRNA vaccines

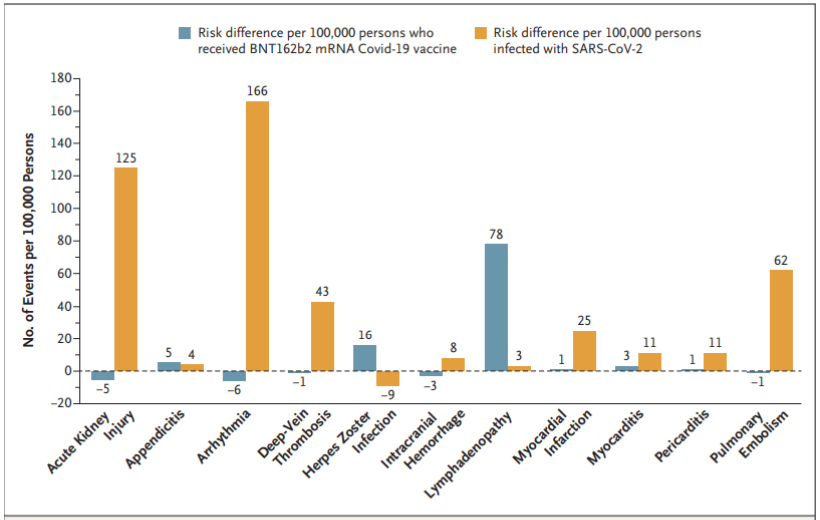


Figure 4. Absolute Excess Risk of Various Adverse Events after Vaccination or SARS-CoV-2 Infection.

Point estimates of the risk differences for selected adverse events are shown. Estimates were derived 42 days after vaccination or SARS-CoV-2 infection with the use of the Kaplan–Meier estimator. Risk differences are shown per 100,000 persons and rounded to the nearest integer. Negative differences (decreased risk) are represented as negative values on the y axis, and positive differences (increased risk) are represented as positive values on the y axis. The abbreviation mRNA denotes messenger RNA.

Source: https://www.nejm.org/doi/full/10.1056/NEJMoa2110475

- Study in a nationwide mass vaccination setting
- Results indicate SARS-CoV-2 **infection is itself a very strong risk factor for myocarditis**, and it also substantially increases the risk of multiple other serious adverse events
- Findings help to shed light on the short- and medium-term risks of the vaccine and place them in clinical context
- **Further studies needed** to estimate the potential of long-term adverse events

Anaphylaxis after mRNA vaccination

- Data suggest that **most patients** with immediate and potentially allergic reactions to mRNA COVID-19 vaccines **tolerate a second dose**

Table. Characteristics of Patients Who Experienced Potential Immediate Allergic Reactions to the First Dose of an mRNA COVID-19 Vaccine and Second Dose Outcomes

				No. (%)								
Institution	Cases, No.	Female, No. (%)	Age, mean (SD), y	Moderna	Pfizer-BioNTech	First-dose anaphylaxis[a]	Allergist skin testing performed[b]	Dose 2 administered	Dose 2 premedication given[c]	Dose 2 administered within guideline-recommended window[d]	Immediate allergic symptoms with dose 2[e]	Dose 2 tolerance[f]
MGH	76	66 (87)	39.5 (12.7)	60 (79)	16 (21)	6 (8)	34 (45)	65 (86)	7 (11)	62 (95)	8 (12)	65 (100)
BWH	54	45 (83)	43.0 (12.6)	41 (76)	13 (24)	5 (9)	30 (56)	50 (93)	11 (22)	44 (88)	7 (14)	50 (100)
VUMC	27	22 (81)	49.8 (18.2)	6 (22)	21 (78)	8 (30)	5 (19)	19 (70)	15 (79)	18 (95)	7 (37)	19 (100)
YSM	25	23 (92)	46.3 (13.3)	20 (80)	5 (20)	7 (28)	11 (44)	18 (72)	16 (64)	18 (100)	7 (29)	18 (100)
UTSW	7	7 (100)	47.0 (13.2)	3 (43)	4 (57)	6 (86)	0	7 (100)	1 (17)	6 (86)	3 (43)	7 (100)
Pooled values	189	163 (86)	43.2 (14.1)	130 (69)	59 (31)	32 (17)[g]	80 (42)	159 (84)	50 (31)	148 (93)	32 (20)	159 (100)

Abbreviations: BWH, Brigham and Women's Hospital; MGH, Massachusetts General Hospital; mRNA, messenger RNA; UTSW, University of Texas Southwestern Medical Center; VUMC, Vanderbilt University Medical Center; YSM, Yale School of Medicine.

[a] Anaphylaxis defined as meeting at least 1 of the following criteria: Brighton and/or the National Institute of Allergy and Infectious Diseases/Food Allergy and Anaphylaxis Network criteria.

[b] Skin testing was variably performed in some higher-risk patients, of whom none were positive for polyethylene glycol 3350 with percutaneous skin testing.

[c] The most common pretreatment was nonsedating oral antihistamines (47 of 50 patients).

[d] Forty-two days, US Centers for Disease Control and Prevention (https://www.cdc.gov/vaccines/covid-19/info-by-product/clinical-considerations.html).

[e] All reactions experienced with dose 2 were lower in severity compared with first-dose reactions and none required treatment with epinephrine or urgent care/emergency department visits. Reaction symptoms included: tachycardia (n = 6), dizziness/lightheadedness (n = 6), throat tightness (n = 6), flushing/erythema (n = 5), swelling (n = 4), hives (n = 3), wheezing/shortness of breath (n = 3), hypertension (n = 2), tingling (n = 2), and nausea/vomiting/abdominal pain (n = 1). Numbers do not sum to 32 because some patients had more than 1 symptom. No patients experienced hypoxia, hypotension, bradycardia, metallic taste, or tingling.

[f] Tolerance was defined as no immediate symptoms present, or if immediate symptoms were present, they were self-limited, mild, and managed with antihistamines only.

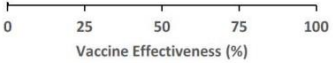
[g] Of these 32 patients, 19 (59%) received and tolerated dose 2 (2 for MGH, 4 for BWH, 6 for VUMC, 1 for YSM, and 6 for UTSW).

Source: https://jamanetwork.com/journals/jamainternalmedicine/fullarticle/2782348

Effectiveness of mRNA vaccines for preventing Covid-19 hospitalizations

- **Highly effective** for preventing Covid-19 hospitalizations among US adults
- Vaccination was **beneficial** for patients with immunosuppression, **but** effectiveness was lower in the immunosuppressed population

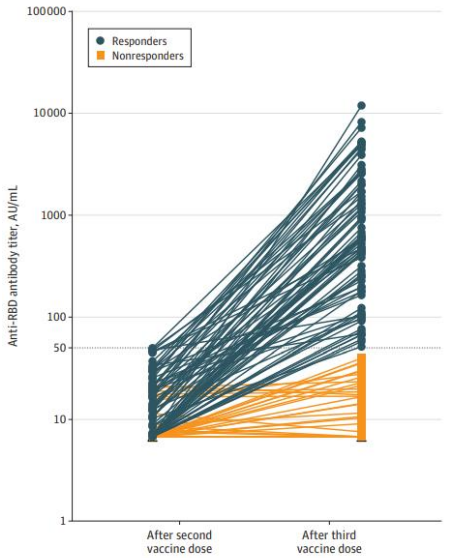
Subgroup	Vaccinated case patients / total case patients (%)	Vaccinated control patients / total control patients (%)	Vaccine effectiveness (95% confidence interval)
Full vaccination			
Overall	45/499 (9.0)	215/489 (44.0)	86.9 (80.4 to 91.2)
18 to 49 yr	1/186 (0.5)	25/140 (17.9)	97.3 (78.9 to 99.7)
50 to 64 yr	14/185 (7.6)	39/136 (28.7)	74.7 (47.2 to 87.9)
≥65 yr	30/128 (23.4)	151/213 (70.9)	87.2 (77.6 to 92.7)
Covid-19 vaccine product			
Pfizer-BioNTech	28/482 (5.8)	122/396 (30.8)	84.3 (74.6 to 90.3)
Moderna	17/471 (3.6)	93/367 (25.3)	90.0 (82.0 to 94.4)
B.1.1.7 variant lineage	7/116 (6.0)	215/489 (44.0)	92.8 (83.0 to 96.9)
Underlying medical condition			
Chronic cardiovascular disease	38/263 (14.5)	150/311 (48.2)	82.8 (72.3 to 89.3)
No chronic cardiovascular disease	7/236 (3.0)	65/178 (36.5)	95.4 (88.5 to 98.1)
Chronic lung disease	14/98 (14.3)	72/158 (45.6)	82.1 (60.3 to 91.9)
No chronic lung disease	31/398 (7.8)	143/331 (43.2)	89.0 (82.1 to 93.2)
Diabetes mellitus	19/151 (12.6)	73/162 (45.1)	81.6 (64.5 to 90.5)
No diabetes mellitus	26/347 (7.5)	142/327 (43.4)	89.8 (82.8 to 94.0)
Immunocompromising condition	20/79 (25.3)	56/116 (48.3)	59.2 (11.9 to 81.1)
No immunocompromising condition	25/417 (6.0)	159/373 (42.6)	91.3 (85.5 to 94.7)
Obesity	21/289 (7.3)	95/215 (44.2)	88.7 (79.7 to 93.8)
No obesity	24/203 (11.8)	120/273 (44.0)	84.6 (72.8 to 91.3)
Partial vaccination			
Overall	45/499 (9.0)	103/377 (27.3)	76.0 (63.7 to 84.1)



Source: https://www.medrxiv.org/content/10.1101/2021.07.08.21259776v1

Third Dose of mRNA vaccine in kidney transplant recipients

Figure. Anti-Receptor-Binding Domain (RBG) IgG Antibody Titers Measured 28 Days After the Third Dose of mRNA-1273 SARS-CoV-2 Vaccine in 159 Kidney Transplant Recipients



Horizontal dotted line indicates the cutoff for positivity (50 arbitrary units [AU]/mL). Blue lines indicate the antibody titers of kidney transplant recipients who seroconverted after the third dose (titers ≥50 AU/mL); orange lines, the evolution of antibody titers among nonresponders (titers <50 AU/mL). mRNA indicates messenger RNA.

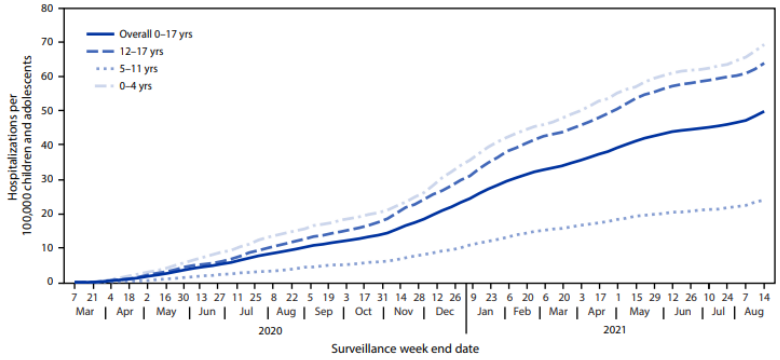
- Study found that a third dose of mRNA vaccine induced a serologic response in 49% of kidney transplant recipients who did not respond after 2 doses
- Use of a third dose of vaccine **may** be considered in organ transplant recipients

Source: https://jamanetwork.com/journals/jama/fullarticle/2782538

Hospitalisation among children and adolescents – US CDC

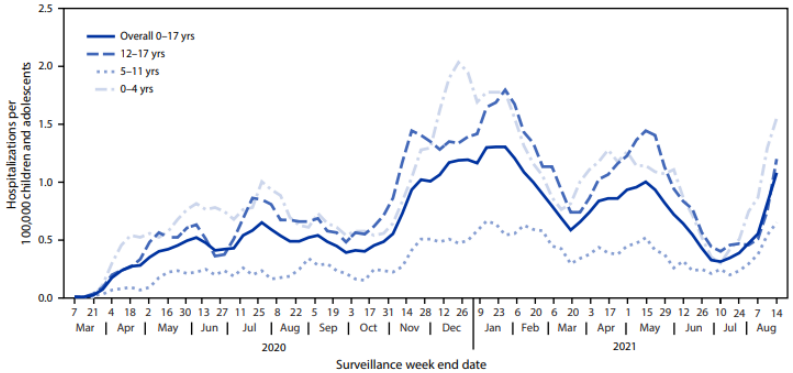
- Among adolescents aged 12–17 years, hospitalization rates were approximately 10 times higher in unvaccinated compared with fully vaccinated adolescents

FIGURE 1. COVID-19–associated cumulative hospitalizations per 100,000 children and adolescents,* by age group — COVID-NET, 14 states,† March 1, 2020–August 14, 2021



* Rates are subject to change as additional data are reported.
† Select counties in California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.

FIGURE 2. COVID-19–associated weekly hospitalizations per 100,000 children and adolescents,* by age group — COVID-NET, 14 states,† March 1, 2020–August 14, 2021 (3-week smoothed running averages)§



* Rates are subject to change as additional data are reported.
† Select counties in California, Colorado, Connecticut, Georgia, Iowa, Maryland, Michigan, Minnesota, New Mexico, New York, Ohio, Oregon, Tennessee, and Utah.
§ Smoothed running averages are used for visualization purposes only.

Source: https://www.cdc.gov/mmwr/volumes/70/wr/mm7036e2.htm

Myocarditis after mRNA vaccines – US CDC

Risk of myocarditis following SARS-CoV-2 infection is described in several recent studies

- Patients with SARS-CoV-2 infection had **16-18 times higher risk for myocarditis** compared with patients without SARS-CoV-2; risk varied by age and sex
  - Retrospective cohort using administrative data from >800 U.S. hospitals[1]
  - In a large national study from Israel[2]
- Risk of myocarditis in individuals post-SARS-CoV-2 infection was **6-34 times higher** compared to those who received mRNA vaccine
  - Administrative dataset analysis of 48 large healthcare organizations in the U.S.[3]
  - Retrospective cohort using EHR data from 42 U.S. healthcare systems[4]

[1]Boehmer & Kompaniyets, et al., Association between COVID-19 and myocarditis using hospital-based administrative data. Pre-publication; CDC authors.
[2]Barda et al. Safety of the BNT162b2 mRNA COVID-19 Vaccine in a Nationwide Setting. *NEJM*. August 25, 2021
[3]Singer ME, et al., Risk of Myocarditis from COVID-19 Infection in People Under Age 20: A Population-Based Analysis. *medRxiv*. Pre-print. July 2021.
[4]Block et al., Occurrence of myocarditis, pericarditis, and anaphylaxis in children and young adults after COVID-19 vaccination compared to SARS-CoV-2 infection. Pre-publication; CDC and university-affiliated authors.

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-08-30/06-COVID-Rosenblum-508.pdf

Myocarditis after mRNA vaccines – US CDC

Myocarditis cases and reporting rates after Pfizer-BioNTech COVID-19 vaccination

- Over 17 million 2nd Pfizer-BioNTech vaccine doses administered and 327 confirmed myocarditis cases in VAERS as of August 18, 2021 in persons aged 16-29 years

	Females			Males		
Age group	Cases	Doses admin	Reporting rate†	Cases	Doses admin	Reporting rate†
16-17 years old	15	1,834,838	8.2	124	1,689,086	73.4
18-24 years old	12	4,279,917	2.8	140	3,635,284	38.5
25-29 years old	4	3,056,893	1.3	32	2,713,481	11.8

*Source of doses administered: https://covid.cdc.gov/covid-data-tracker/#vaccinations; some age- and sex-specific doses administered data were imputed

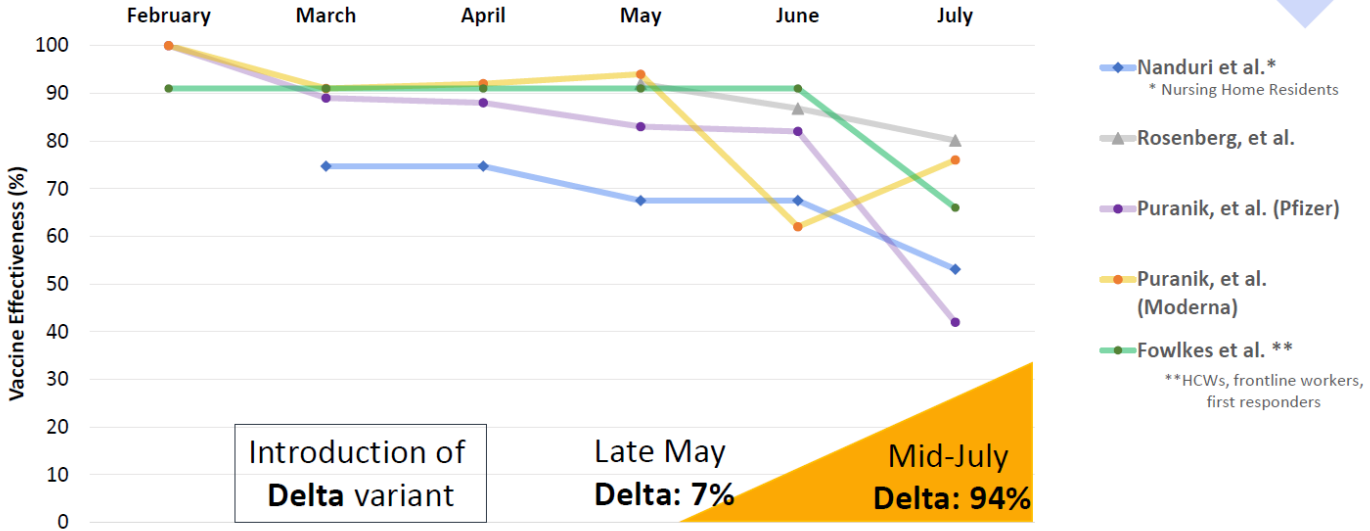
†Reporting rate = myocarditis cases per 1 million mRNA COVID-19 mRNA second vaccine doses administered

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-08-30/06-COVID-Rosenblum-508.pdf

Framework for booster doses of COVID-19 vaccines – US CDC/ACIP

Booster doses of COVID-19 vaccines:
Vaccine effectiveness against **infection**

Public Health Problem



Rosenberg ES, Holtgrave DR, Dorabawila V, et al. New COVID-19 Cases and Hospitalizations Among Adults, by Vaccination Status — New York, May 3–July 25, 2021. MMWR Morb Mortal Wkly Rep. ePub: 18 August 2021.
Nanduri S. Effectiveness of Pfizer-BioNTech and Moderna Vaccines in Preventing SARS-CoV-2 Infection Among Nursing Home Residents Before and During Widespread Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant — National Healthcare Safety Network, March 1–August 1, 2021. MMWR Morbidity and Mortality Weekly Report. 2021 2021;70.
Fowlkes A, Gaglani M, Groover K, et al. Effectiveness of COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Frontline Workers Before and During B.1.617.2 (Delta) Variant Predominance — Eight U.S. Locations, December 2020–August 2021. MMWR Morb Mortal Wkly Rep. ePub: 24 August 2021.
Puranik A, Lenehan PJ, Silvert E, et al. Comparison of two highly-effective mRNA vaccines for COVID-19 during periods of Alpha and Delta variant prevalence. medRxiv 2021.08.06.21261707.

Source: https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-08-30/09-COVID-Oliver-508.pdf

Waning immunity of the BNT162b2 vaccine

- Nationwide study from Israel
- Results indicate a strong effect of waning immunity in all age groups after six months
- Quantifying the effect of waning immunity on vaccine effectiveness is critical for policy makers worldwide facing the dilemma of administering booster vaccinations

Figure 3: Rate of documented SARS-CoV-2 infection (per 1,000 persons) from July 11, 2021 to July 31, 2021, stratified by period of second dose of COVID-19 vaccine and age group. White bars represent periods at which only persons at higher risk were allowed to receive vaccination.

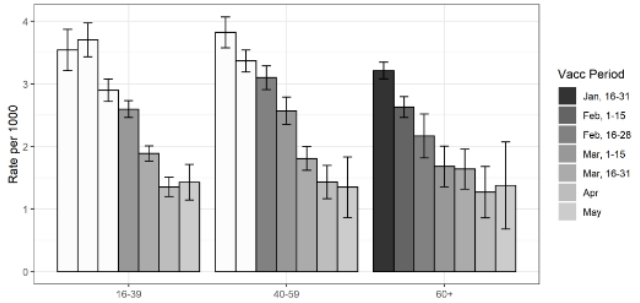
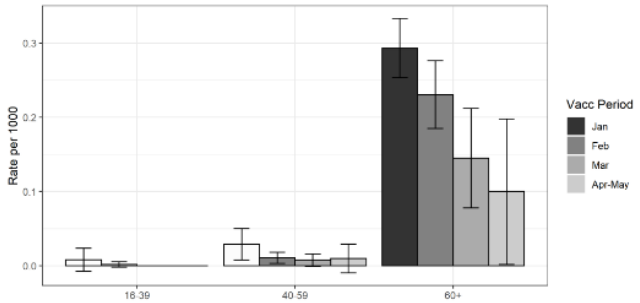


Figure 4: Rate of severe COVID-19 (per 1,000 persons) from July 11, 2021 to July 31, 2021, stratified by period of second dose of COVID-19 vaccine and age group. White bars represent periods at which only persons at higher risk were allowed to receive vaccination.



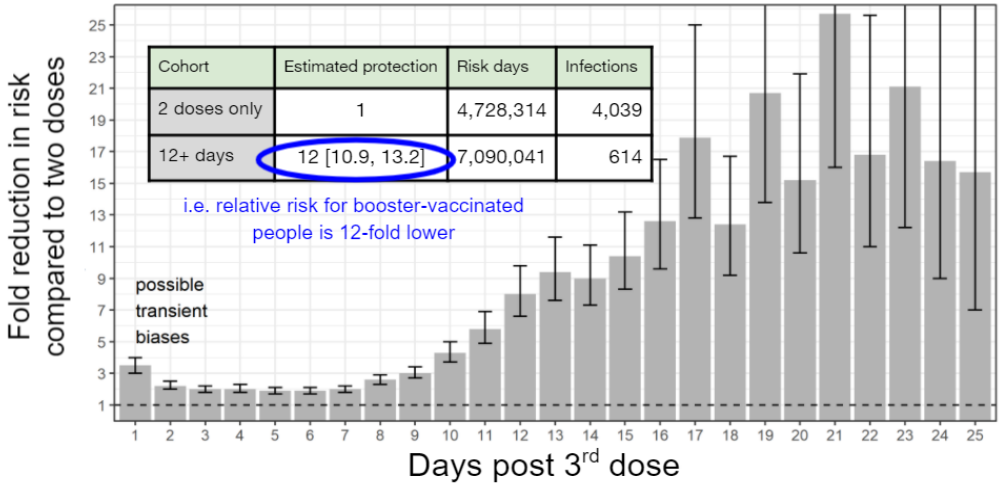
Source: https://www.medrxiv.org/content/10.1101/2021.08.24.21262423v1

BNT162b2 vaccine booster dose protection

- Nationwide study from Israel
- In conjunction with safety reports, this study demonstrates the effectiveness of a third vaccine dose in both reducing transmission and severe disease and indicates the great potential of curtailing the Delta variant resurgence by administering booster shots

Booster protection against confirmed **infection**
as a function of time post vaccination **ages 60 +**

Poisson regression adjusted for age, gender, sector, 2nd dose period and calendar day.
Based on data from August 10 to August 27 to avoid biases.



Source: https://www.medrxiv.org/content/10.1101/2021.08.27.21262679v1

Virological and serological kinetics of SARS-CoV-2 Delta variant vaccine-breakthrough infections

- Multi-center cohort study
- Study concludes that mRNA vaccines are highly effective at preventing symptomatic and severe COVID-19 associated with B.1.617.2 infection
- Vaccination is associated with faster decline in viral RNA load and a robust serological response

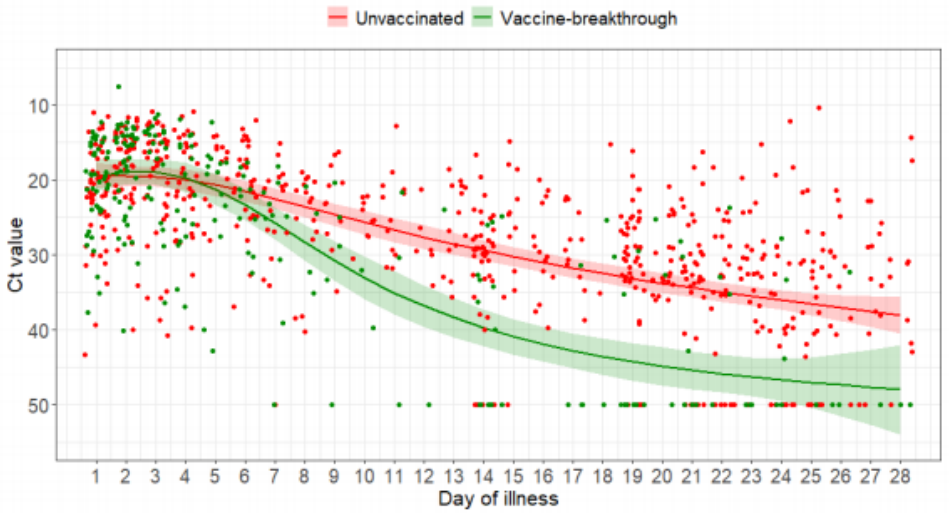


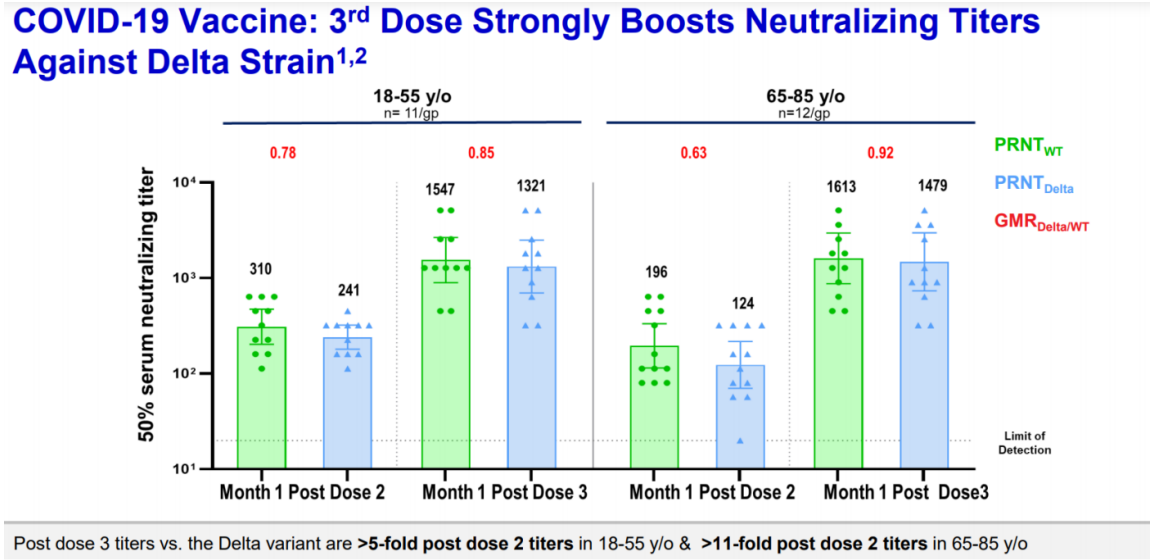
Figure 1: Scatterplot of Ct values and marginal effect of day of illness of COVID-19 B1.617.2 infected patients with 95% confidence intervals from generalized additive mixed model with interaction term between vaccination status and day of illness

Source: https://www.medrxiv.org/content/10.1101/2021.07.28.21261295v1

WHO consultation on COVID-19 vaccines research – 13 August 2021

- More studies needed to confirm the benefit of boosting strategies together with strong post-marking surveillance and pharmacovigilance
- Full report of consultation available https://cdn.who.int/media/docs/default-source/blue-print/who-vaccines-research_13aug2021_final-for-web.pdf?sfvrsn=1e52ba60_7

Comirnaty booster

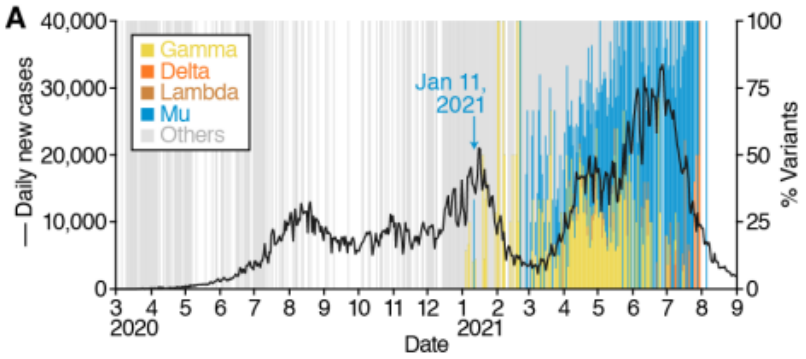


1. Initial data; 2. Samples were tested against each variant separately; PRNT: Plaque Reduction Neutralizing Test; Wt: Wild Type; GMR: Geometric Mean Ratio

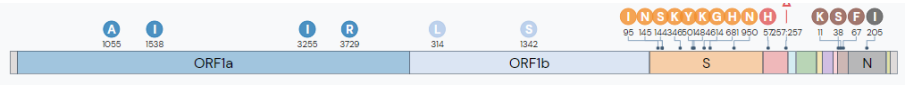
Sources: https://cdn.who.int/media/docs/default-source/blue-print/developer_pfizer_phil-dormitzer.pdf?sfvrsn=74b107d3_9
https://www.who.int/news-room/events/detail/2021/08/13/default-calendar/who-consultation-on-covid-19-vaccines-research-13-august-2021

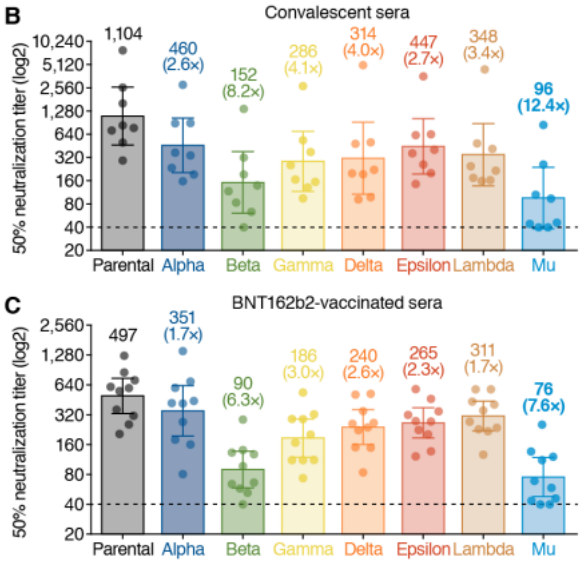
Mu variant

- Ineffective neutralization of the SARS-CoV-2 Mu variant by convalescent and vaccine sera
- Mu spike is more resistant to serum-mediated neutralization than all other currently recognized variants of interest (VOI) and concern (VOC)



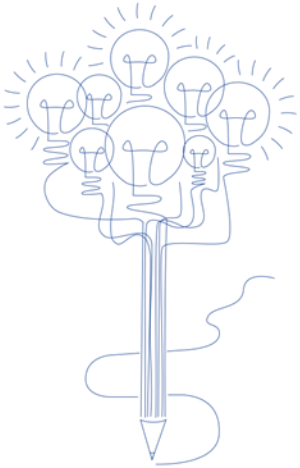
SARS-CoV-2 epidemic in Colombia





Source: https://www.biorxiv.org/content/10.1101/2021.09.06.459005v1

Summary of activities



219 therapeutics in discussion with EMA

66 vaccines identified for interaction

Rapid scientific advice proceeding for advanced vaccines and therapeutics (117 completed – 9 in the pipeline)

Booster and additional doses under assessment

Novavax, SP, Sinovac and Gamaleya under RR

EC expert group on variants and subgroup on therapeutics