Module AFRANUM #1 : COVID-19 (1)

Modération : Charlotte Charpentier / Louise Fortès

- Introduction — *Gilles Wandeler*
- Actualités virologiques — *Charlotte Charpentier et Ahidjo Ayouba*
- Aspects cliniques et thérapeutiques — *Guillaume Martin-Blondel*
- Vaccination — *Brigitte Autran*

Chaque intervention sera suivie d'une séance de Q&R

Vaccins anti-SARS-Cov2

Où en est-on aujourd'hui ?

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Liens d'intérêt: Janssen: vaccin VIH (Consultations)

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Inserm

Développement rapide des Vaccins anti-SARS-Cov2

Développement clinique

Développement préclinique :
Souris / Macaques

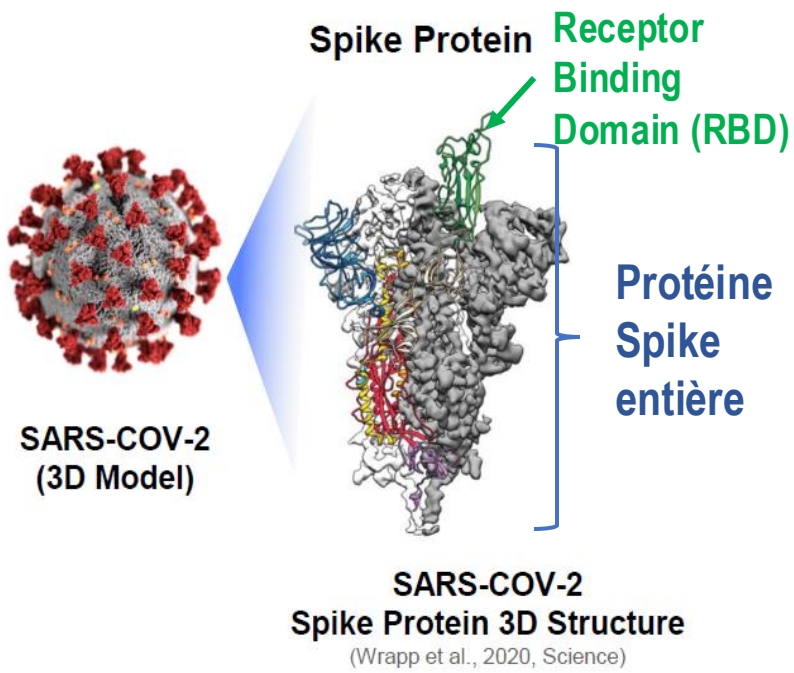
Développement Pharmaceutique :
Candidat Vaccin

Recherche :
Virus
Immunité Protectrice ?

1) Quelle Immunité anti-SARS-CoV2 ?

➢ **Séquence SARS-CoV2 et Structure 3D Spike**

(Zhou P et al. Nature 2020; Wrapp et al. Science 20)



Jiang HW et al. doi: https://doi.org/10.1101/2020.03.20.20039495 medRxiv;
Jiang S et al. Trends in Immunology, May 2020;
Kai-Wang To K et al. www.thelancet.com/infection 2020
Long QX et al. Nat.Med. 2020.; Peng Y,.bioRxiv. 2020.; Wajnberg A et al., Science 2020).
Sun B et al.Emerg Microbes Infect. 2020; Ni L et al Immunity. 2020
Grifoni A et al. Cell. 2020; Vabret N et al. Immunity 2020, 52, 910.

➢ **Réponses Anticorps:**

- chez >95% sujets infectés
- **taux << chez A-symptomatiques**
- **pic à J30 puis décroissance**
- anti- Spike (100%), Nucléocapside (95%) …

➢ **Anticorps Neutralisants = Anti-Spike (RBD)**

- chez les convalescents, **persistent > 5 mois**
- taux corrélés aux Ac anti-SARS-CoV2
- **ne croisent pas avec autres CoronaVirus**
- *(standardisation???)*

Réponses Protectrices?
d'après autres infections à CoronaV

➢ **Réponses cellulaires**

- chez 95% sujets infectés
- anti- Spike, NC et protéines non structurales
  - peuvent croiser avec autres CoronaV
- de type Th1 (Interferon-gamma) => Protection ?
- ou Th2 (IL-6, TNF, IL-4…) => **Inflammation**

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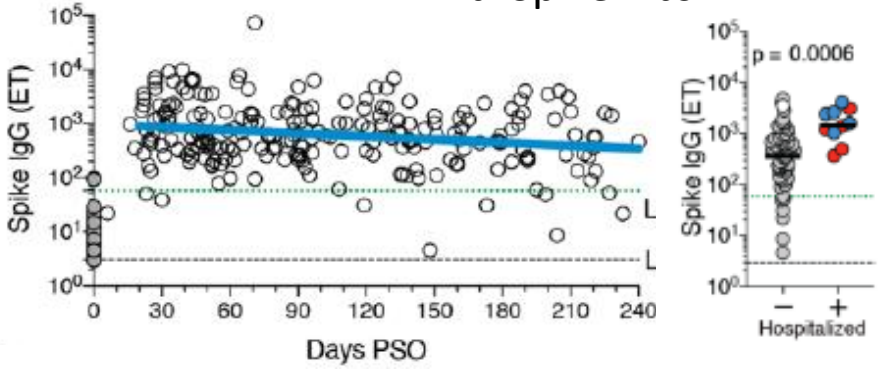
Durability of SARS-CoV2 specific Immune Memory ?

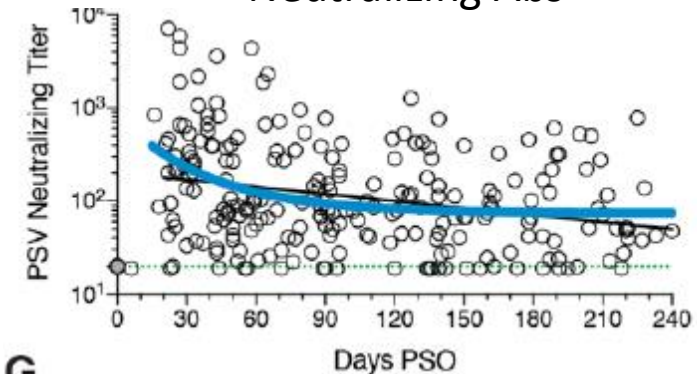
Immunological memory to SARS-CoV-2 assessed for up to 8 months after infection

Cite as: J. M. Dan *et al.*, *Science* 10.1126/science.abf4063 (2021).

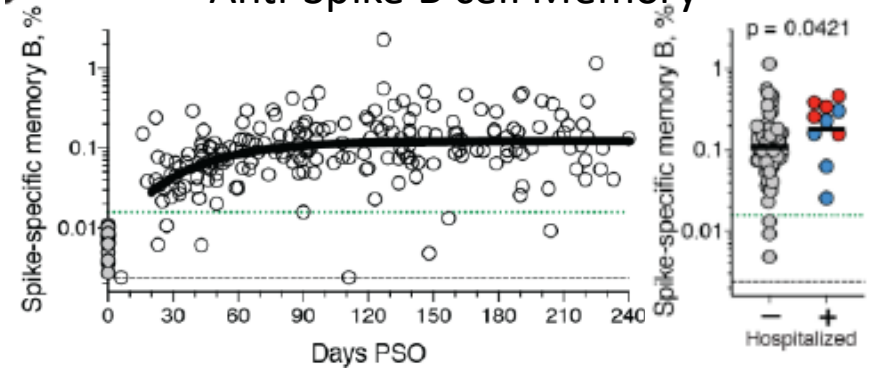
Anti-Spike Abs



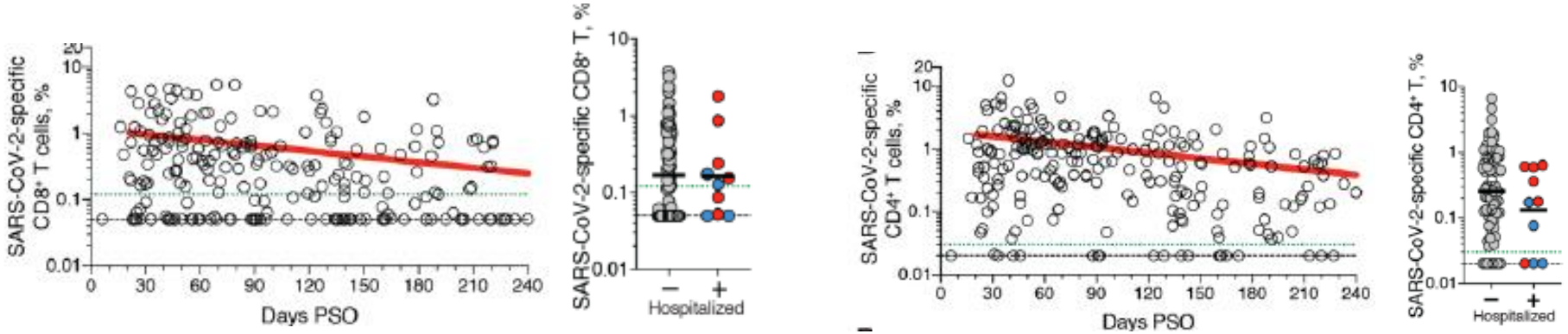
Neutralizing Abs



Anti-Spike B cell Memory



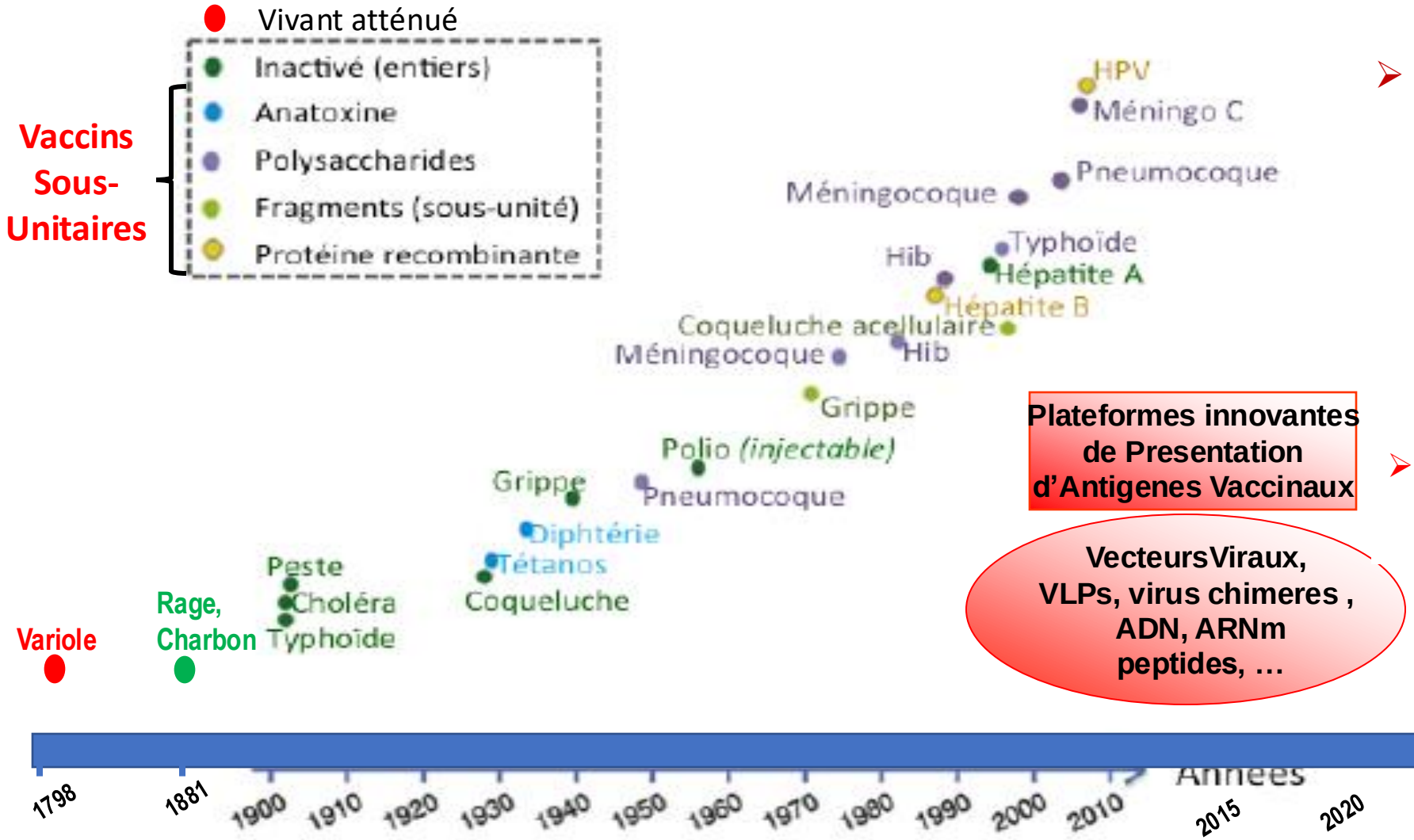
Anti-SARS-CoV2 CD8 and CD4 T cells



- Mid-term Durability (about 1y) = similar to other acute viral infections
- Higher Magnitude of Memory in Severe patients (as for Flu)

Développement rapide de Vaccins anti-SARS-Cov2

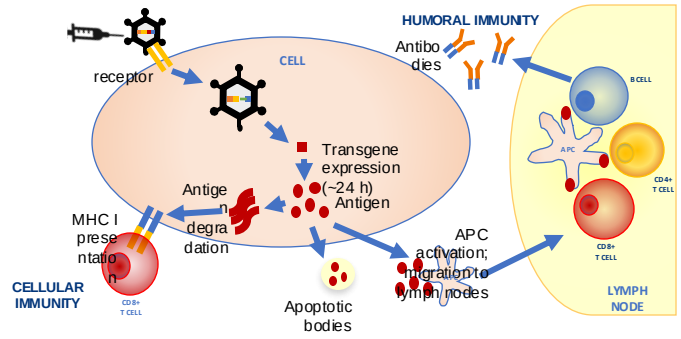
Vaccins classiques du 20e siècle et Innovations vaccinales du 21e



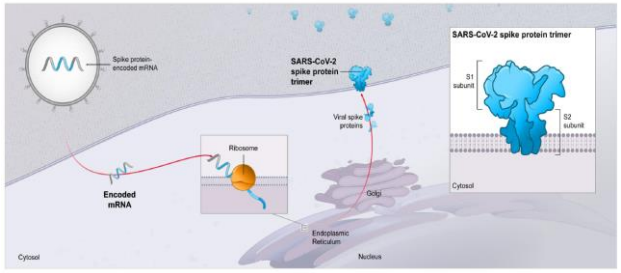
Plateformes innovantes de Presentation d'Antigenes Vaccinaux

VecteursViraux, VLPs, virus chimeres , ADN, ARNm peptides, …

➢ **Vecteur vaccinal recombinant**



➢ **Vaccin ARN messager**



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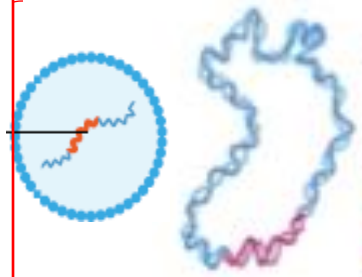
Plateformes de développement rapide de Vaccins anti-SARS-Cov2

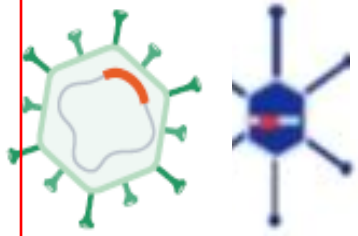
« Plateformes » Vaccinales : versatiles, adaptées à divers pathogènes :

Plateformes innovantes de Presentation d'Antigenes Vaccinaux



Immunisation génétique :
Vaccins ARN ou ADN «nu»

SARS, MERS, West Nile, Zika, RSV



Vecteurs viraux recombinants :

Ebola, Marburg, Zika

Nanoparticules :
(protéine virale sur particules)

Influenza, Malaria, RSV

Virus-like particules :
(sans ADN ni ARN)
Non infectieuses

Chikungunya, Zika, WEVEE

Protéines recombinantes :

Influenza, RSV

Adjuvants
(e.g., AS01, MF59)

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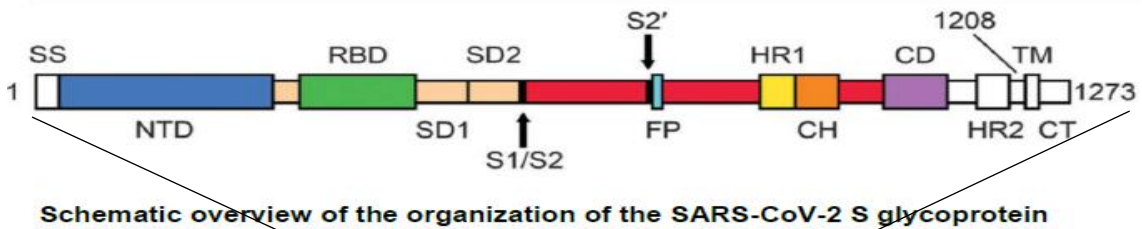
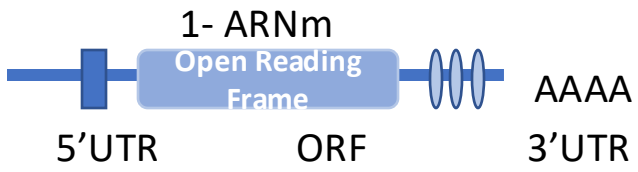
From F Krammer Nature2020 and T Fauci, J Hopkins Conf. Oct2020

Vaccins ARNm



Schematic overview of the organization of the SARS-CoV-2 S glycoprotein



1- Modifications des ARNm:

Pseudo-uridine au lieu de l'Uridine

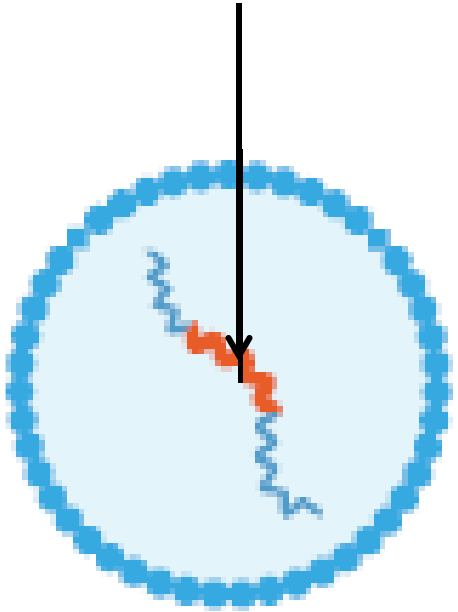
⇒ diminution de réponse intra-cellulaire anti-ARNm

⇒ stabilisation des messagers

⇒ traduction augmentée

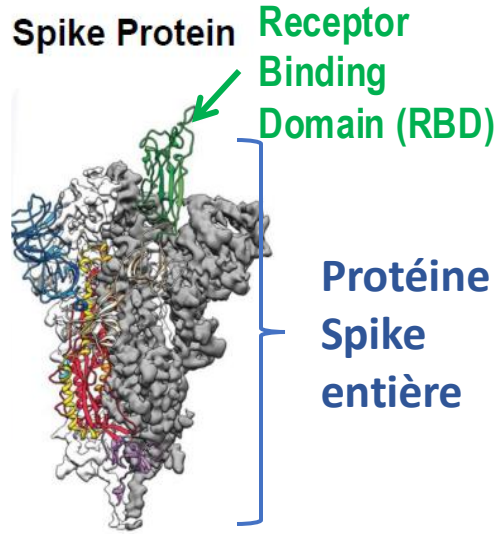
2- Insertion des ARNm dans des LipoNanoParticules:

- Protègent ARNm
- Augmentent endocytose par cell. Dendritiques
- Augmentent l'immunogénicité



IIM

3- Synthese *in-vivo* de la protéine Spike



SARS-COV-2
Spike Protein 3D Structure
(Wrapp et al., 2020, Science)

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Vaccins ARNm : Réponses immunes anti-SARS-CoV2

RNA-Based COVID-19 Vaccine BNT162b2 Selected for a Pivotal Efficacy Study

RE Walsh, R Frenck et al. 2020, at NEJM.org.

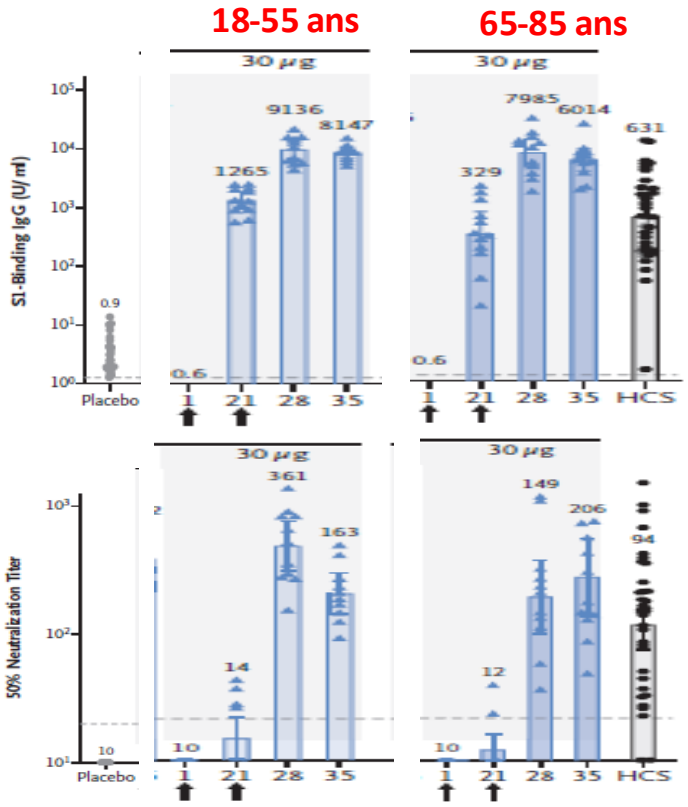
DOI: 10.1056/NEJMoa2027906

➢ **Vaccin Pfizer : ARNm** modifié de **Spicule** en Liponanoparticules

X Doses vs Placebo en **2 injections à J0, J21, 2 populations** (N=12/bras)

➢ **Anticorps anti-S**

➢ **Ac Neutralisants**



➢ **Anticorps Neutralisants :**

< chez >65 ans mais **équivalents aux convalescents**

➢ **Réponses cellulaires T**

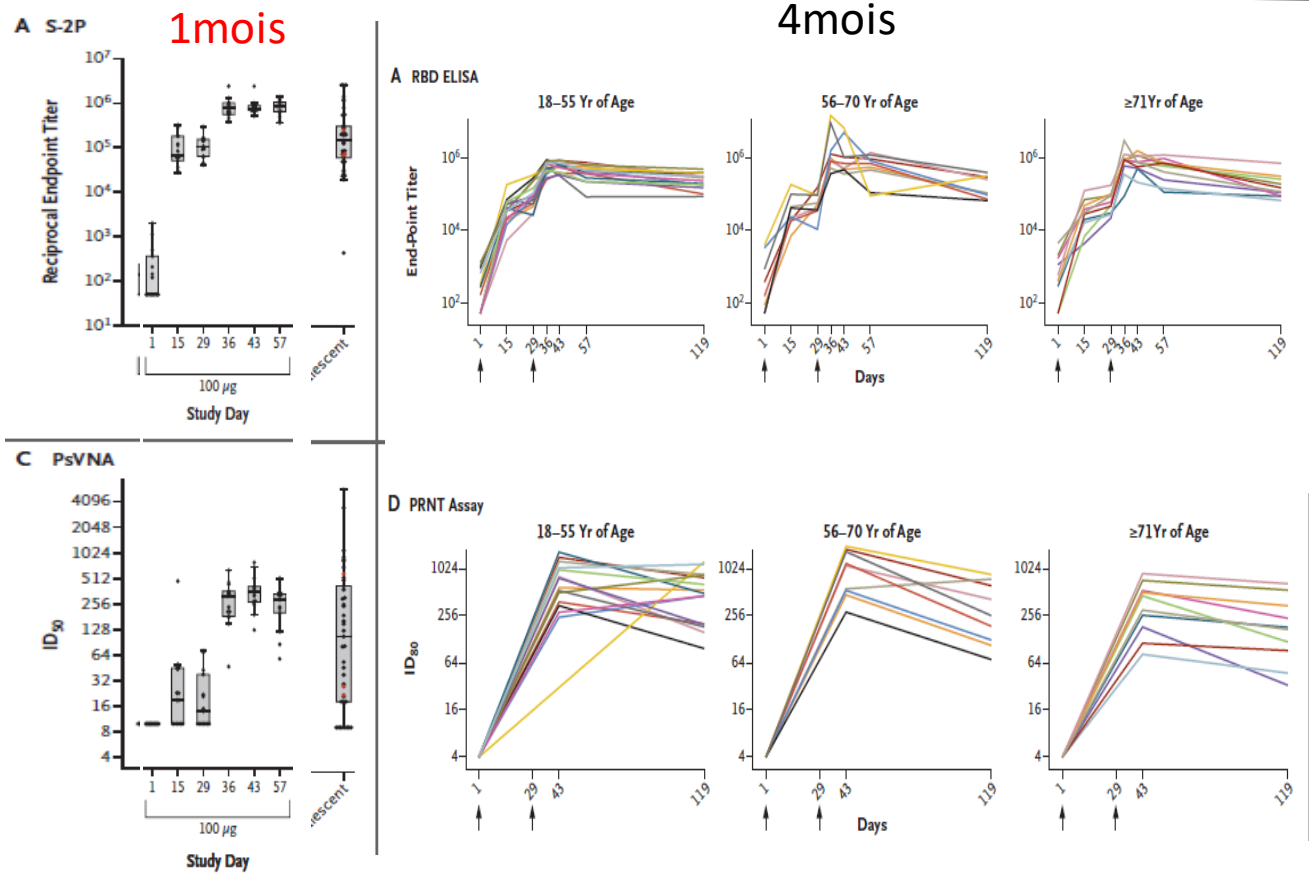
An m-RNA vaccine against SARS-CoV2 : Ph 2

Jackson L, Anderson EJ, Rouphael NG, et al. N Engl J Med. 14 Jul 2020; DOI: 10.1056/NEJMoa2022483

Adrian B. McDermott, *N. Engl. J. Med Dec 2020*

➢ **Vaccin Moderna**: ARNm modifié de **Spicule** en LNP :

➢ 100µg, **2 injections**: J0-J29; 3 gp d'**Adultes sains 18-55 / 56-70 / >71 ans**



➢ **Anticorps Neutralisants : équivalents**

➢ **Durabilité : sur 4-8 mois**

➢ **Réponses cellulaires T**

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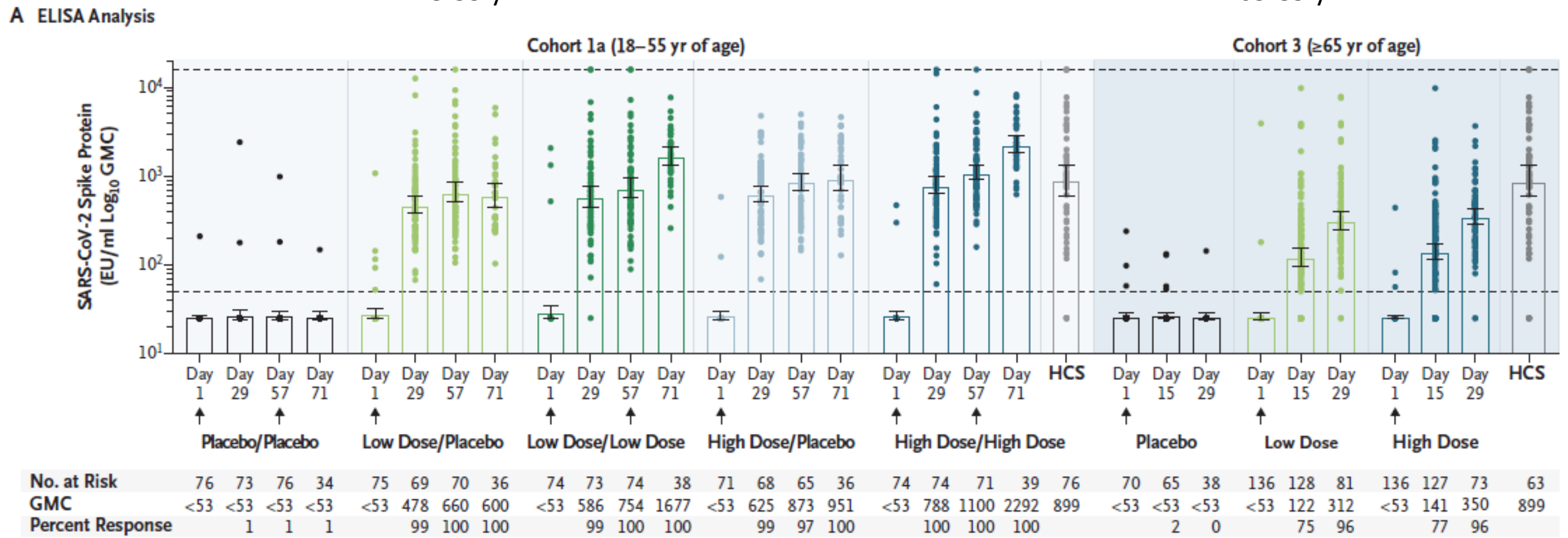
JANSSEN Phase I Immunogenicity results:

18-55 y 65-85 y



No. at Risk	76	73	76	34	75	69	70	36	74	73	74	38	71	68	65	36	74	74	71	39	76	70	65	38	136	128	81	136	127	73	63
GMC	<53	<53	<53	<53	<53	478	660	600	<53	586	754	1677	<53	625	873	951	<53	788	1100	2292	899	<53	<53	<53	<53	122	312	<53	141	350	899
Percent Response		1	1	1		99	100	100		99	100	100		99	97	100		100	100	100			2	0		75	96		77	96	

Vaccine: Ad26-recombinant / Spike : in 1 or 2 injections, High dose vs Low dose

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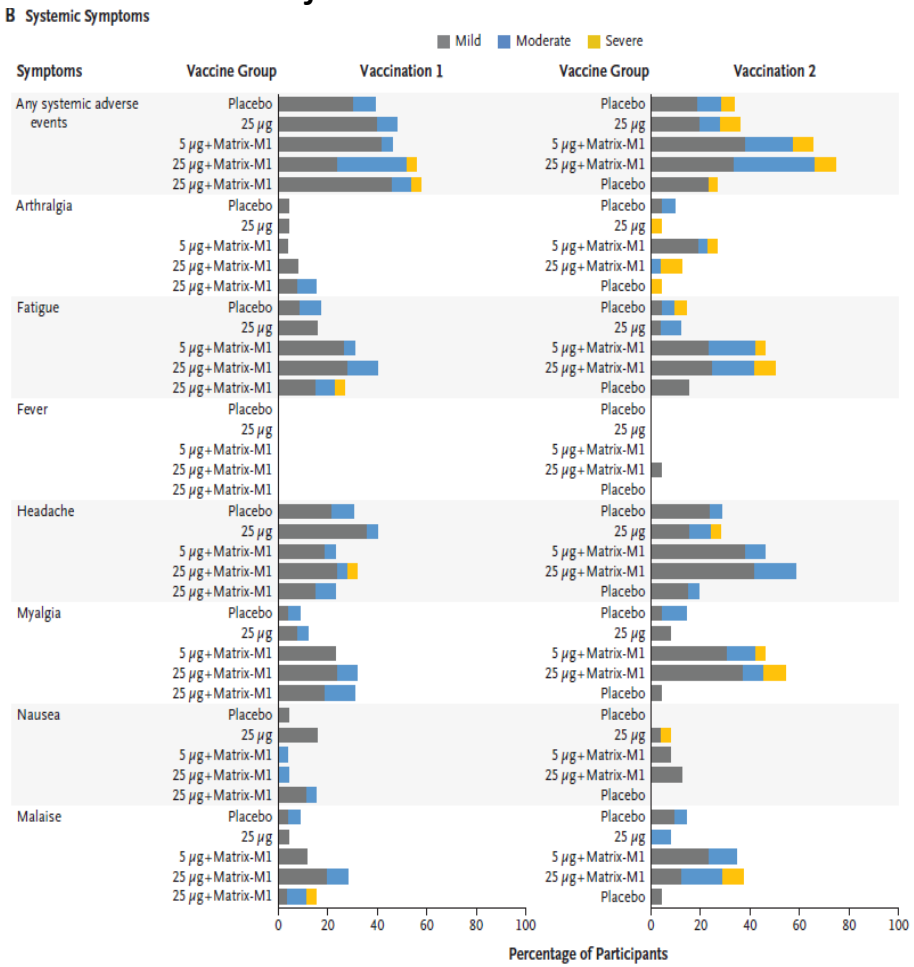
Phase 1-2 Trial of a SARS-CoV-2 recombinant Spike Protein Nanoparticle vaccine

C Keech et al. N.Engl.J.Med 2020

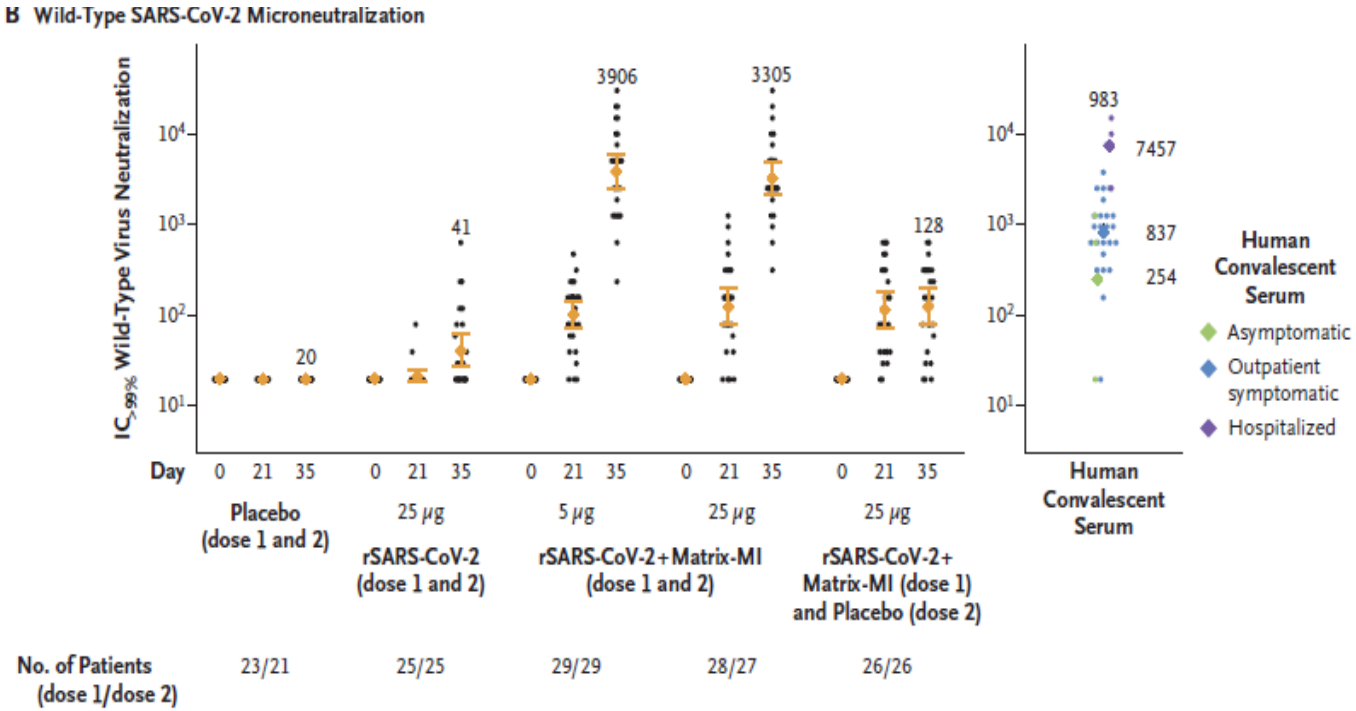
- **Vaccine**: NVX-CoV2373 : **Nanoparticule recombinante Spike +/- adjuvant**
- **Phase I-II**: 5 vs 25µg; **2 injections** : J0, J21; 131 adultes sains

- **Tolerance**:
  - **Pas d'EI sévères**
  - EI > avec adjuvant



- **Ac Neutralisants:**
  - **Titres élevés** : à 5 et 25µg; 2 injections > 1 inj.:
    = taux de convalescents (Asx; Sx; Sévères)

\+ Réponses cellulaires T CD4 Th1



- **Progression en Phase III :** débutée en Octobre 2020

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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

This article was published on December 10, 2020, at NEJM.org.

DOI: 10.1056/NEJMoa2034577

Safety and Efficacy of the BNT162b2 mRNA Covid-19 Vaccine

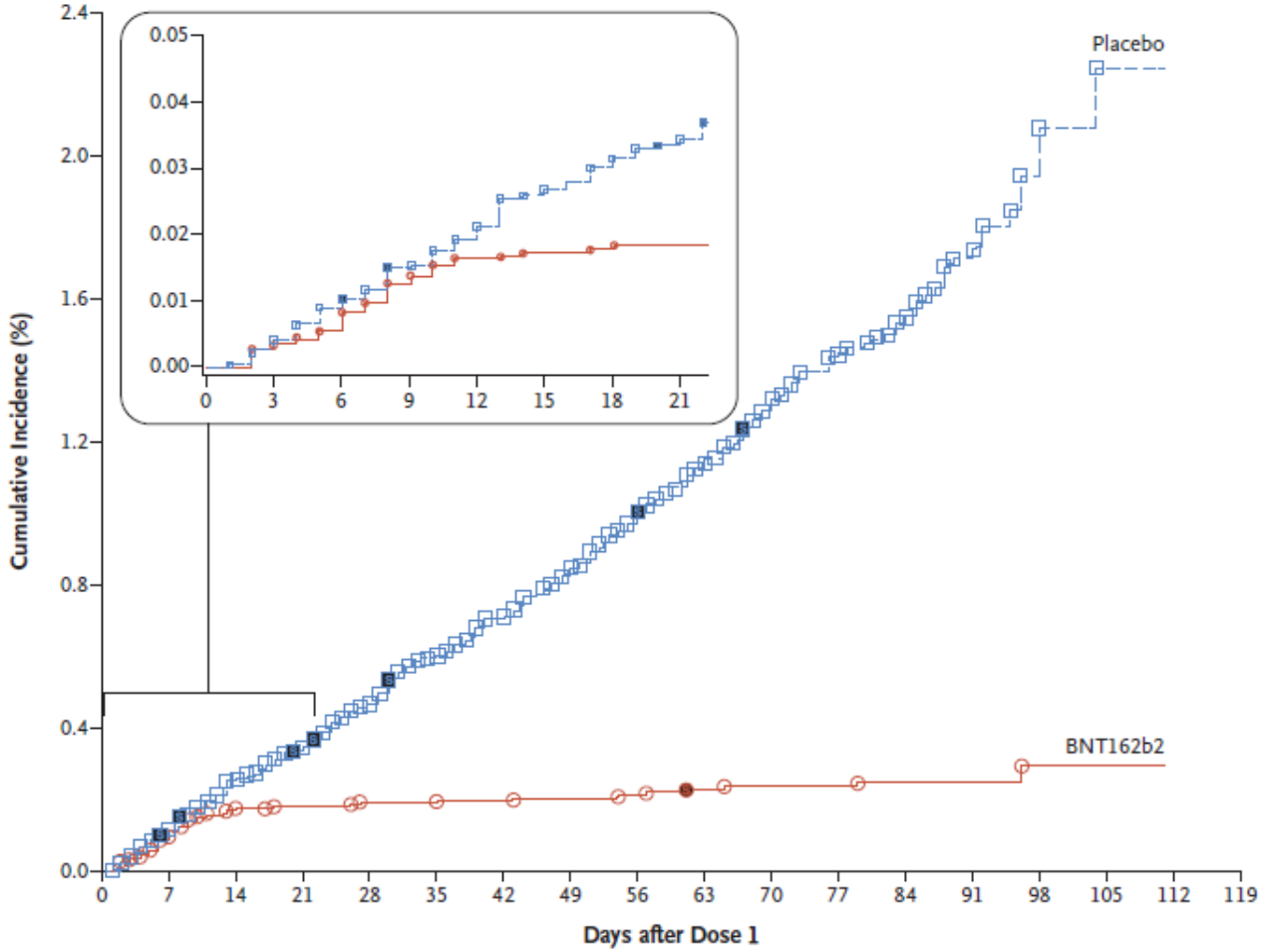
FP Polack et al.

N = 37 706 participants

Succès de tous critères Primaires d'efficacité :

Depuis le 7e jour après 2e Dose à fin de l'analyse:

- **Efficacité vaccinale (VE) sans Covid19 antérieur : 95%** (p<0.0001) :
  - **162 cas : bras placebo**
  - **8 cas : bras vaccin**
- **VE avec et sans Covid19 or infection antérieure: 94,6%**
- VE reproductible avec l'âge**, genre, et ethnicité:**
  - **>65 ans : >94%.**
- **VE: Prevention de la maladie sévère:**
  - **9 vs 1 : placebo vs vaccinés**.
- **Pas d'evènements indésirables graves** liés au vaccin.



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)

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The NEW ENGLAND JOURNAL of MEDICINE

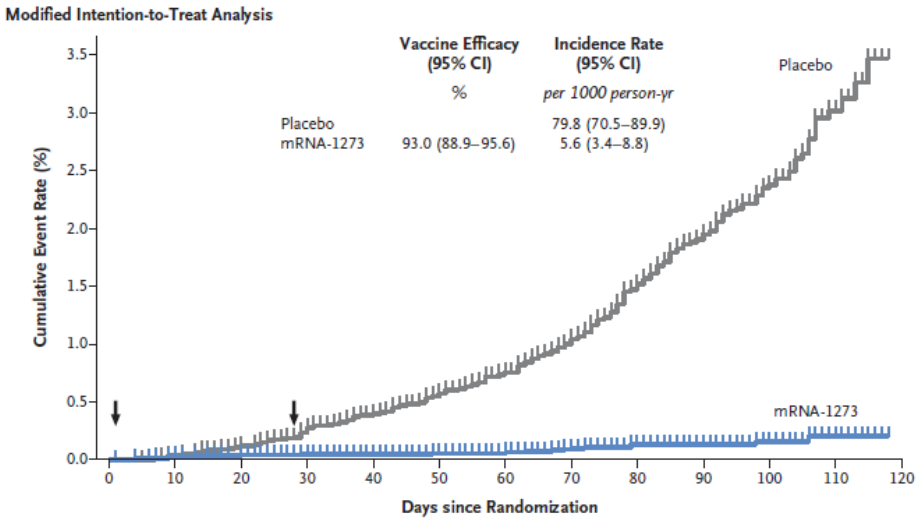
This article was published on December 30, 2020, at NEJM.org.

DOI: 10.1056/NEJMoa2035389

ORIGINAL ARTICLE

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*



- Primary endpoint: prevention of symptomatic COVID-19
  N= > 7,000 > 65, and > 5,000 <65 with high-risk diseases

- **1st interim analysis :**
  - **90 cases vs 5 in placebo vs vaccinees,**
    - **VE of 94.5%** (p <0.0001).
  - 2ry endpoint : severity :
    - **11 severe cases** (as per protocol): **All in Placebo**
    - vs 0 inthe mRNA-1273 vaccinated group.
  - No significant safety concerns

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

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

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

	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)

Développement clinique « raté »

1er essai de Ph3 : en fait 2 avec **design peu clair :**

2 doses différentes (LD vs HD

2 populations d'âge différent

(fD: <55 ans, FD: 18->70 ans t 79%<55)

2 efficacités : fD: 90% vs FD: 62%

2e essai Ph3: Af Sud: Pb des variants

3e essai Ph3 : US

Communiqué Presse: 79% VE/ f. Symptom.

100ù VE/Décès

Rappel à l'ordre NIAID

Correctif: 76% VE/ f. Symptom.

100ù VE/Décès

- **EMA : autorisation 29/1 : > 18 ans**
- **HAS: 2/2: seulement <65 an**

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Vaccine effectiveness after 1st and 2nd dose of the BNT162b2 mRNA Covid-19 Vaccine in long-term care facility residents and healthcare workers – a Danish cohort study

Ida Rask Moustsen-Helms[1]

Table 2 – Vaccine effectiveness with accompanying 95 % confidence intervals for LTCF residents and HCW after first and second vaccine dose

				Unadjusted VE[2]		Adjusted VE[3]	
	No. of persons with SARS-CoV-2[1]	PYRS	IR	VE	95% CI	VE	95% CI
Nursing home residents							
Unvaccinated	488	1059.09	0.46	-	-	-	-
0-14 days after 1st dose	760	1388.32	0.55	-0.19	-0.44;0.01	-0.40	-0.62;-0.02
> 14 days after 1st dose until 2nd dose	184	1008.17	0.18	0.60	0.46;0.71	0.21	-0.11;0.44
0-7 days after 2nd dose	57	633.5	0.09	0.80	0.70;0.88	0.52	0.27;0.69
> 7 days after 2nd dose	27	1435.9	0.02	0.96	0.91;0.98	0.64	0.14;0.84
Health care workers							
Unvaccinated	5663	37599.85	0.15	-	-	-	-
0-14 days after 1st dose	1189	3425.09	0.35	-1.13	-1.69;-0.97	-1.04	-1.18;-0.91
> 14 days after 1st dose until 2nd dose	213	2821.84	0.08	0.50	0.29;0.66	0.17	0.04;0.28
0-7 days after 2nd dose	52	1525.19	0.03	0.77	0.57;0.90	0.46	0.28;0.59
> 7 days after 2nd dose	10	2468.95	0.00	0.97	0.90;100	0.90	0.82;0.95

[1]Laboratory confirmed SARS-CoV-2 test
[2]Crude VE estimate
[3]VE adjusted for calendar time

B Autran

Astra-Zeneca & Pfizer: Effectiveness

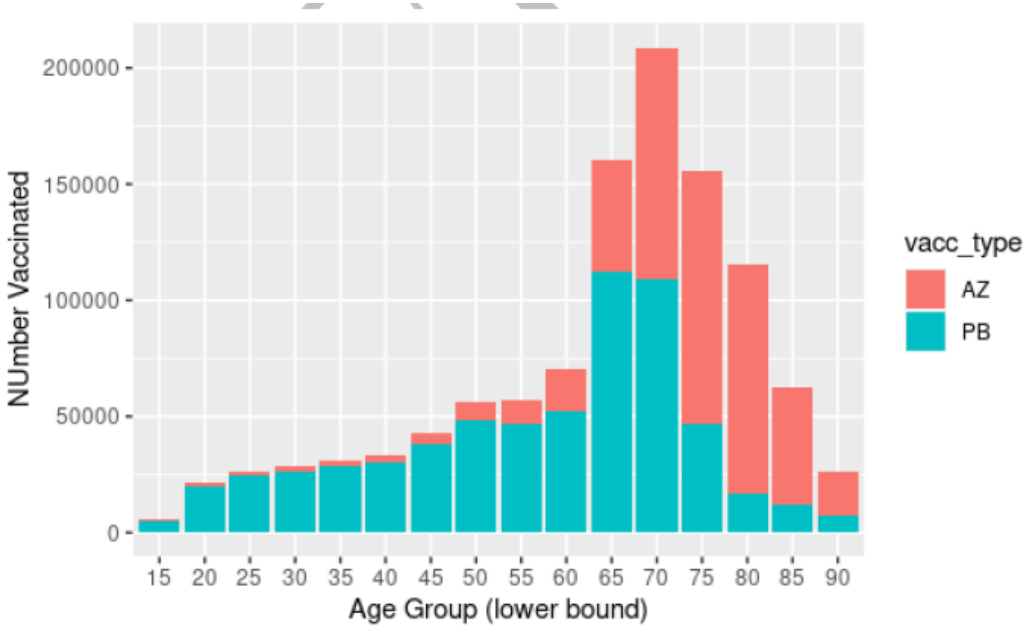
Ecosse E Vasileiou et al. (not peer-reviewed)

Prospective cohort of 1 137 775 people Tous vaccins = 39057: Pfizer = 27675

Peak Effectiveness Pfizer 1st dose = 85% for Covid Hosp.

AZ 1st dose = 94%

Peaks at 28-34d post-vacc



- (more AZ >80yo)

Vaccination status	Person years	Number of events	Age-adjusted Hazard Ratios (95% CI)*	Full-adjusted Hazard Ratios (95% CI)**	Full and inverse propensity adjusted Hazard Ratios (95% CI)***	Vaccine effect (95% CI)
Vaccinated overall						
Unvaccinated	787518	7472	1	1	1	NA
Vaccine dose 1 (7-13 days)	13487	212	0.73 (0.64 to 0.84)	0.74 (0.64 to 0.86)	0.53 (0.47 to 0.61)	47% (39 to 53)
Vaccine dose 1 (14-20 days)	9191	120	0.61 (0.5 to 0.73)	0.63 (0.52 to 0.76)	0.4 (0.34 to 0.48)	60% (52 to 66)
Vaccine dose 1 (21-27 days)	6343	52	0.43 (0.33 to 0.56)	0.44 (0.33 to 0.58)	0.3 (0.23 to 0.38)	70% (62 to 77)
Vaccine dose 1 (28-34 days)	3867	20	0.34 (0.22 to 0.52)	0.31 (0.2 to 0.48)	0.16 (0.1 to 0.26)	84% (74 to 90)
Vaccine dose 1 (35-41 days)	2326	17	0.6 (0.38 to 0.97)	0.46 (0.28 to 0.76)	0.39 (0.26 to 0.58)	61% (42 to 74)
Vaccine dose 1 (42+ days)	3843	21	0.52 (0.34 to 0.81)	0.51 (0.33 to 0.79)	0.42 (0.3 to 0.61)	58% (39 to 70)
BNT162b2 or Pfizer-BioNTech						
Unvaccinated	708129	6690	1	1	1	NA
Vaccine dose 1 (7-13 days)	7766	104	0.71 (0.58 to 0.86)	0.56 (0.46 to 0.68)	0.62 (0.53 to 0.72)	38% (28 to 47)
Vaccine dose 1 (14-20 days)	5758	60	0.61 (0.47 to 0.78)	0.42 (0.32 to 0.55)	0.4 (0.32 to 0.5)	60% (50 to 68)
Vaccine dose 1 (21-27 days)	4688	34	0.43 (0.31 to 0.6)	0.29 (0.21 to 0.41)	0.28 (0.21 to 0.38)	72% (62 to 79)
Vaccine dose 1 (28-34 days)	3346	18	0.33 (0.21 to 0.53)	0.22 (0.14 to 0.35)	0.15 (0.09 to 0.24)	85% (76 to 91)
Vaccine dose 1 (35-41 days)	2275	17	0.46 (0.28 to 0.73)	0.29 (0.18 to 0.48)	0.32 (0.21 to 0.47)	68% (53 to 79)
Vaccine dose 1 (42+ days)	3842	21	0.38 (0.25 to 0.58)	0.32 (0.21 to 0.51)	0.36 (0.25 to 0.51)	64% (49 to 75)
ChAdOx1nCoV-19 or Oxford-AstraZeneca						
Unvaccinated	700859	7090	1	1	1	NA
Vaccine dose 1 (7-13 days)	5721	108	0.49 (0.41 to 0.6)	0.51 (0.42 to 0.62)	0.3 (0.24 to 0.37)	70% (63 to 76)
Vaccine dose 1 (14-20 days)	3433	60	0.4 (0.31 to 0.52)	0.46 (0.35 to 0.6)	0.26 (0.19 to 0.34)	74% (66 to 81)
Vaccine dose 1 (21-27 days)	1655	18	0.24 (0.15 to 0.38)	0.29 (0.18 to 0.47)	0.16 (0.1 to 0.28)	84% (72 to 90)
Vaccine dose 1 (28-34 days)	521	2	0.08 (0.02 to 0.33)	0.1 (0.03 to 0.41)	0.06 (0.01 to 0.27)	94% (73 to 99)
Vaccine dose 1 (35-41 days)	51	0	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	NA
Vaccine dose 1 (42+ days)	1	0	0.00 (0.00)	0.00 (0.00)	0.00 (0.00)	NA

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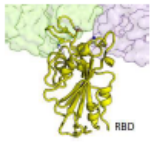
Is vaccine neutralisation impacted by 501Y.V2?

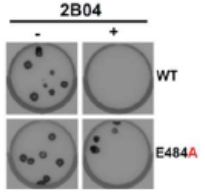
	Pseudovirion and live virus Lab assays
* Single dose Johnson & Johnson	-
Pfizer	1 to 3 fold ↓
moderna	6.4 fold ↓
THE GAMALEYA NATIONAL CENTER	-
AstraZeneca	3 to 86 fold↓ / ko
NOVAVAX	-
Sinopharm	1.6 fold ↓
sinovac	-

Lab assays:

- Pseudovirion mutant assay



- Live virus plaque assay



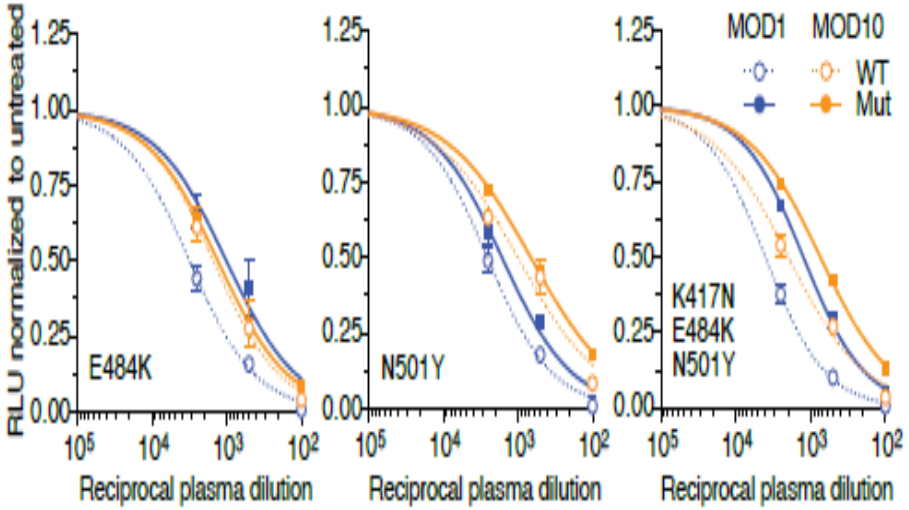
20 volontaires 8 semaines après 2e vaccination

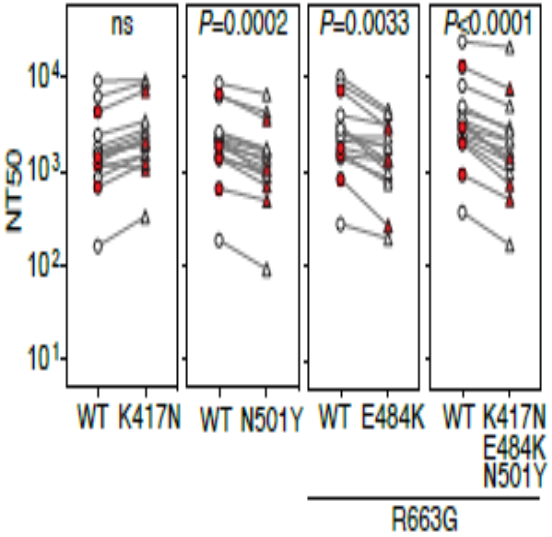
/ Moderna (n=14) ou Pfizer (n=6):

Neutralisation / E484K ou N501Y

ou K417N:E484K:N501Y

= réduite de 1 à 3 fois.





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Are vaccines clinically effective against 501Y.V2?

	Pseudovirion and live virus Lab assays	Clinical efficacy (mild / mod)	Clinical efficacy (mod / severe)	Clinical efficacy (hosp / severe)
* Single dose Johnson & Johnson	-	-	57%	85%
Pfizer	1 to 3 fold ↓	-	-	-
moderna	6.4 fold ↓	-	-	-
THE GAMALEYA NATIONAL CENTER OF EPIDEMIOLOGY AND MICROBIOLOGY	-	-	-	-
AstraZeneca	3 to 86 fold↓ / ko	22%	-	-
NOVAVAX	-	49%	-	-
Sinopharm	1.6 fold ↓	-	-	-
sinovac	-	-	-	-

Of the primary endpoint cases :
93% = B.1.351

VE = 10.4% as a secondary objective.

SA Madhi et al.
doi: https://doi.org/10.1101/2021.02.10.21251247

CAPRISA

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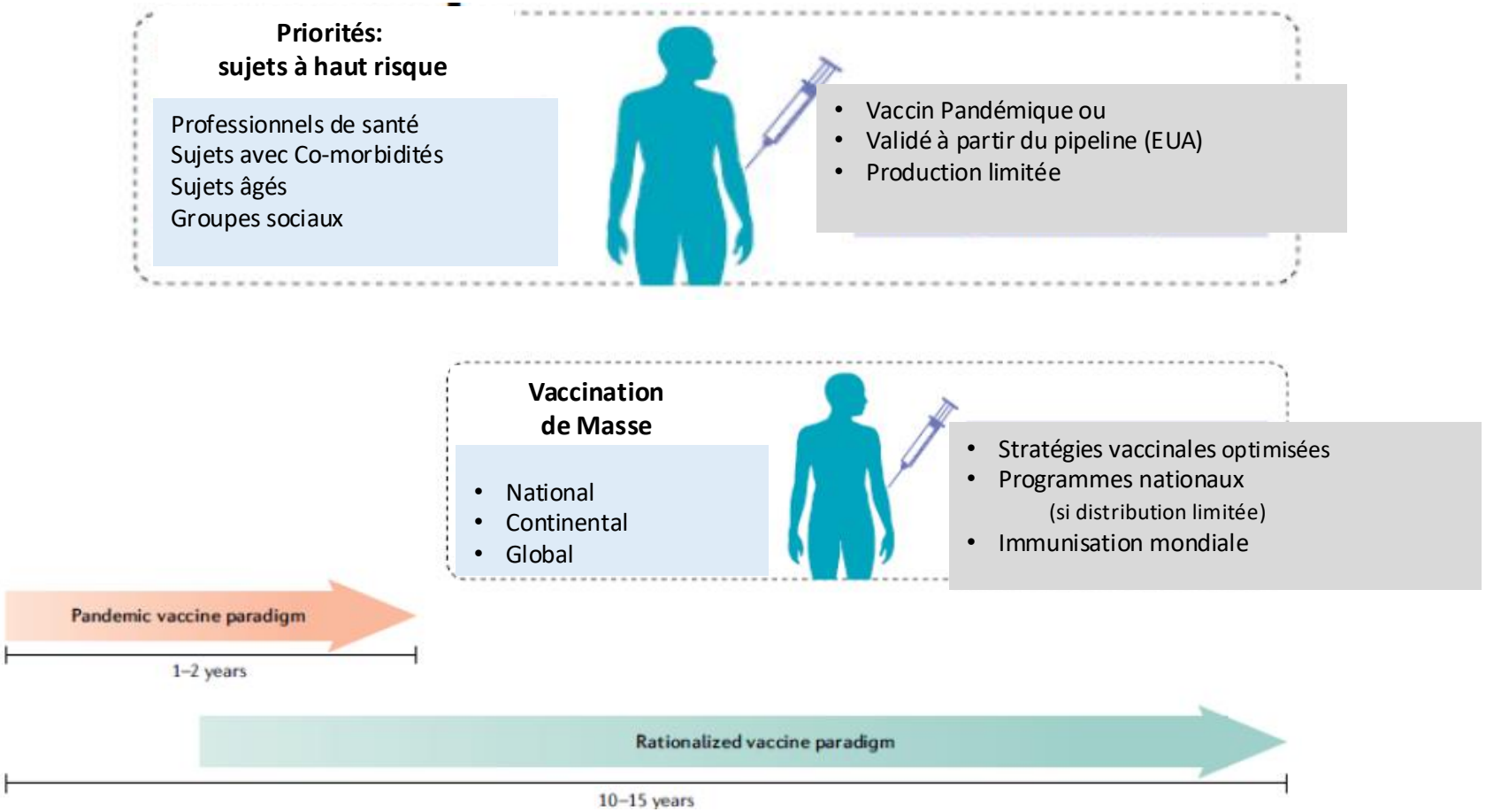
Qui et comment vacciner contre Covid19 ou SARS-CoV2 ?

Scénarios possibles de vaccination anti-Covid19

From M Jeyanathan et al. Nature Rev. Immunol. Oct.2020



B Autran

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Sécurité en vie réelle des vaccins anti-SARS-CoV2: les accidents thrombo-emboliques liés au ChAd3-CoV2

22 / 3 / 2021 : 86 cas dont 18 décès (EudraVigilance): sur 25 millions de vaccines EEA + UK
62 cas de **thrombose du sinus caverneux** + 24 cas de **thrombose veines splanchniques**
4 / 4 / 2021: 169 cas de CVST + 53 cas SVT sur 34 millions de vaccinés
chez sujets **< 60 ans, majoritairement des femmes, après 1e injection**

Mécanisme ? Réponse immune Ac anti-plaquettes (anti-Pf4) ? Proche des thrombopathies à l'héparine?

Thrombotic Thrombocytopenia after ChAdOx1 nCov-19 Vaccination

Andreas Greinacher, M.D., Thomas Thiele, M.D., Theodore E. Warkentin, M.D., Karin Weisser, Ph.D., Paul A. Kyrle, M.D., and Sabine Eichinger, M.D.

NEJM, 2021, **DOI: 10.1056/NEJMoa2104840**

Thrombosis and Thrombocytopenia after ChAdOx1 nCoV-19 Vaccination

Nina H. Schultz, M.D., Ph.D., Ingvild H. Sørvoll, M.D., Annika E. Michelsen, Ph.D., Ludvig A. Munthe, M.D., Ph.D., Fridtjof Lund-Johansen, M.D., Ph.D., Maria T. Ahlen, Ph.D., Markus Wiedmann, M.D., Ph.D., Anne-Hege Aamodt, M.D., Ph.D., Thor H. Skattør, M.D., Geir E. Tjønnfjord, M.D., Ph.D., and Pål A. Holme, M.D., Ph.D.

NEJM, 2021, **DOI: 10.1056/NEJMoa2104882**

20 / 4 / 2021 : COVID-19 Vaccine Janssen:
EMA : possible link to very rare cases of unusual blood clots with low blood platelets

Effet de classe ? Mais risques <<< bénéfices des vaccins
Indication maintenue chez > 55 / 60 ans

COVAX : collaborer pour un accès mondial et équitable aux vaccins anti-COVID-19

- **Axe Vaccins de l'Accelerator Act** (Access to COVID-19 Tools):
  - **Accélérer la recherche de vaccins** COVID-19 **efficaces & accessibles**:
    - Identification des vaccins les + efficaces et adaptés (rigueur des études & passage à l'echelle)
  - **Contribuer à développer des capacités de fabrication et acheter à l'avance**:
    - 78 pays à hauts/moyens revenus participant
  - **Distribuer équitablement ≥ 2 milliards de doses** (Prof.Santé+F.Risque Ind.) d'ici fin 2021:
    - Dès qu'un vaccin = Efficace et bien toléré
      - **Distribué à tous pays** participants **au même rythme et proportionnellement aux populations**
      - **Doses de vaccins pour 10-50% populations**

        MAIS aucun pays ne reçoit pour > 20% populations tant que autres pays ne sont pas servis,
      - **Stock de 5% pour urgences humanitaires**

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