Vaccination COVID-19
Données disponibles sur les ‘Prime-boost’ hétérologues

Odile Launay

Paris, 4 février 2022

Les vaccins contre la Covid-19 : un état des lieux

Groupe Vaccination et Prévention de la SPILF

4 février 2022

Espace Chaptal, 23-25 rue Chaptal, Paris 9ème

Déclaration d’intérêts de 2015 à 2022

- Intérêts financiers : aucun
- Liens durables ou permanents : aucun
- Intervention ponctuelles :
  - Recherches/essais cliniques : MSD, GSK bio, SPMSD, Sanofi Pasteur, Janssen, Pfizer
  - Aides pour des recherches : MSD, GSK bio, SPMSD, Sanofi Pasteur, Janssen, Pfizer
  - Advisory Boards/DSMB : Sanofi Pasteur, Janssen, Pfizer
  - Cours, formations : Pfizer, MSD, Sanofi Pasteur
- Intérêts indirects : aucun

Prime-boost hétérologue: définition

- ‘Prime-boost’ hétérologue: primo-vaccination avec des vaccins différents, le plus souvent **issus de plateformes vaccinales distinctes**
- Schéma différent du schéma « **homologue** » où le même vaccin est injecté deux fois successivement
- Objectifs: conjuguer les propriété immnunologiques des vaccins, eviter l’immunisation contre le vecteur, elargir la protection
- Concept étudié depuis une vingtaine d'années, dans un but d’augmenter l’immunogénicité et l’efficacité des vaccins : VIH, Ebola
- Dans le contexte du vaccin Covid:
  - En primo vaccination
  - En ‘boost’ : 3^{e} dose
  - Pour augmenter l’efficacité
  - Pour des questions de disponibilité et d’accessibilité aux vaccins
  - En raison de survenue d’effets indésirables

Prime-boost hétérologue COVID-19: primo vaccination

Vaccin Spoutnik V, Covid 19 vaccine Gamaleya

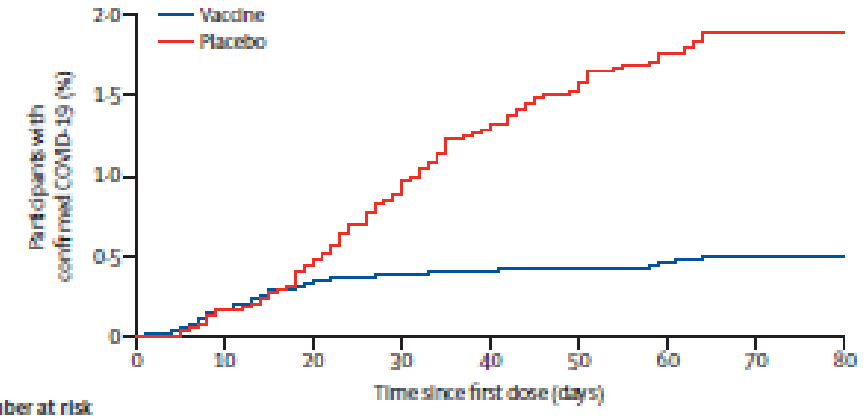
- 2 vaccins vectorisés adénovirus-protéine Spike : Ad26 puis Ad5 à 3 semaines d'intervalles
- Efficacité vaccinale résutats préliminaires:

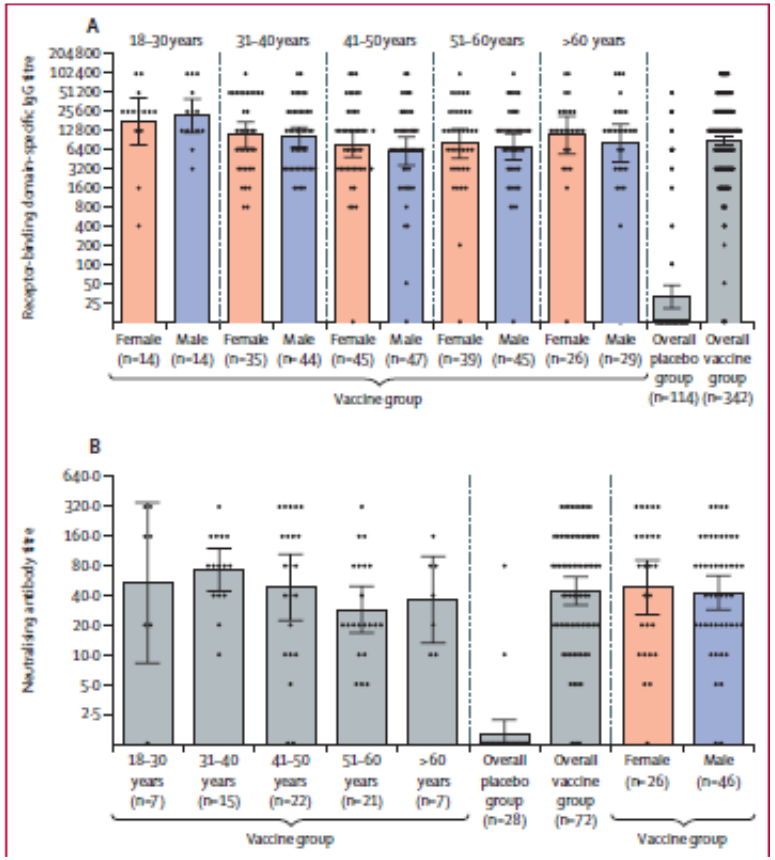
91,6% (IC05%: 85,6-95,2)

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

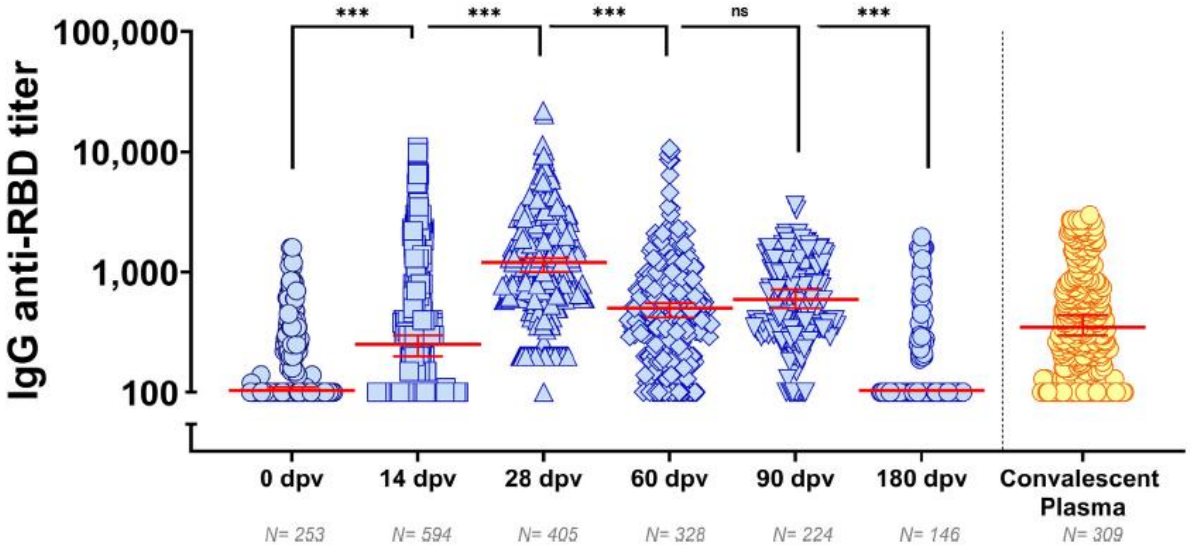
Denis Y Logunov*, Inna V Dolzhikova*, Dmitry V Shcheblyakov, Amir I Tukhvatulin, Olga V Zubkova, Alina S Dzharullaeva, Anna V Kovyrsh

Lancet 2021; 397: 671–81





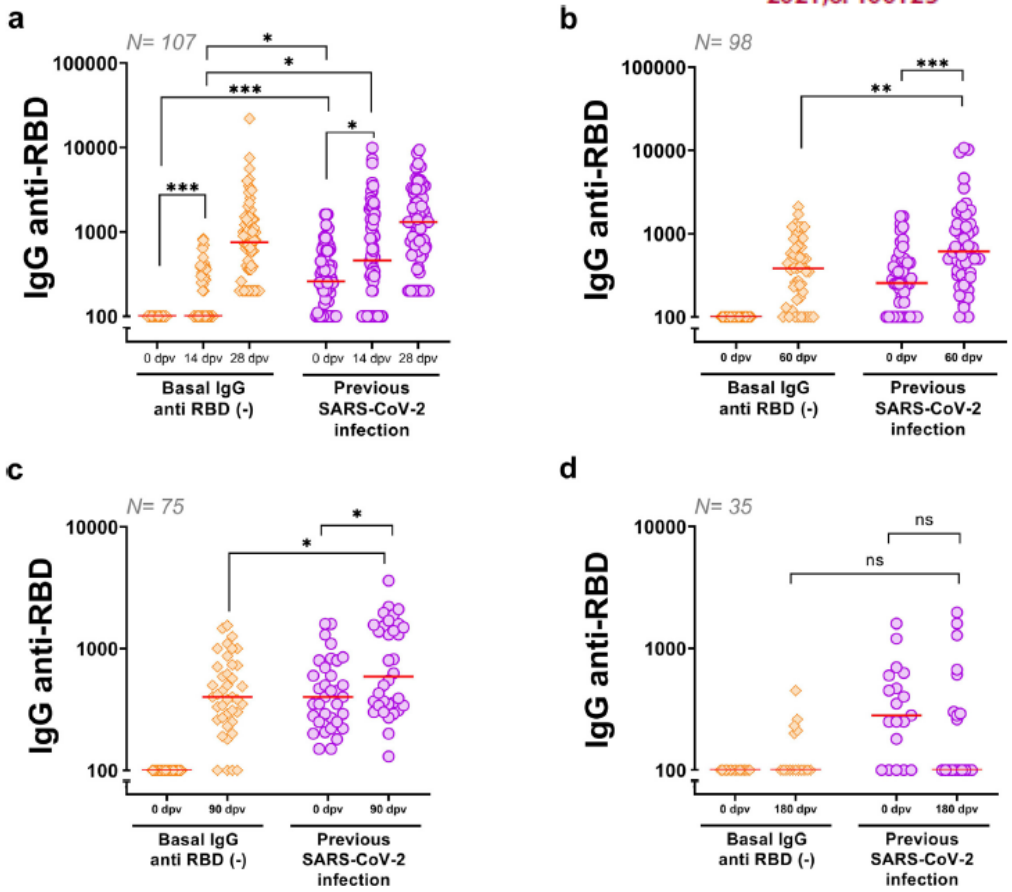
Vaccin Spoutnik V, Covid 19 vaccine Gamaleya



Long-term analysis of antibodies elicited by SPUTNIK V: A prospective cohort study in Tucumán, Argentina

Rossana Elena Chahla,[a,1] Rodrigo Hernán Tomas-Grau,[b,1] Silvia Inés Cazorla,[c,1] Diego Ploper,[b,1] Esteban Vera Pingitore,[b,1]

The Lancet Regional Health - Americas 2021;6: 100123



Vaccin Spoutnik V,
Covid 19 vaccine Gamaleya

CellPress
OPEN ACCESS

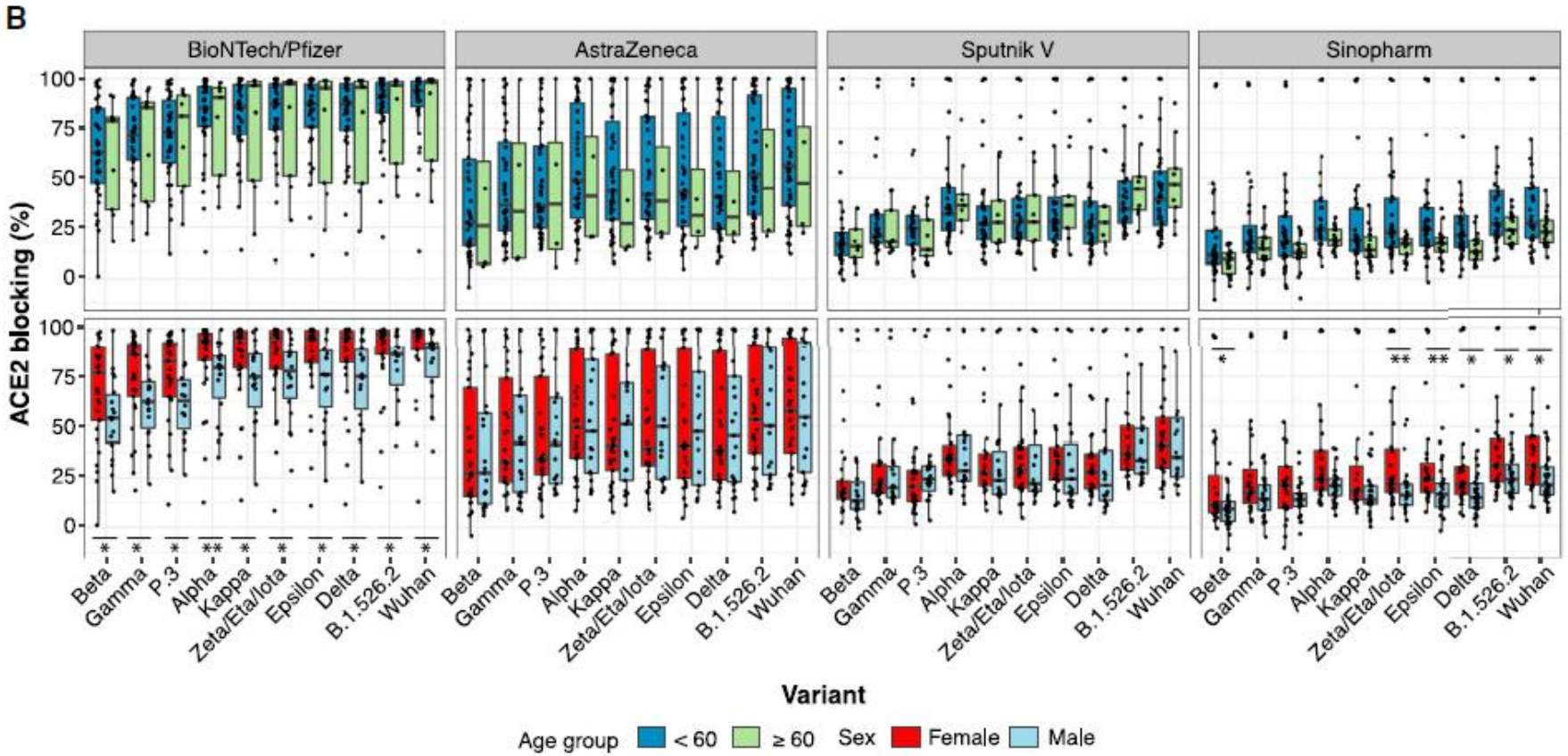
Cell Host & Microbe

Brief Report

Direct comparison of antibody responses to four SARS-CoV-2 vaccines in Mongolia

Naranjargal J. Dashdorj,[1,2,12] Oliver F. Wirz,[3,12] Katharina Röltgen,[3,12] Emily Haraguchi,[3] Anthony S. Buzzanco III,[4]

Dashdorj et al., 2021, Cell Host & Microbe 29, 1738–1743
December 8, 2021
https://doi.org/10.1016/j.chom.2021.11.004



Prime boost AZ-Pfizer/BNT162b2

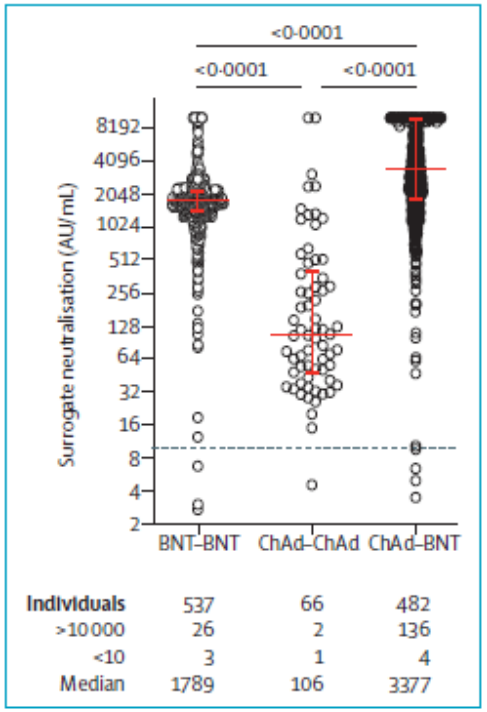


Figure: **Comparison of surrogate neutralisation activity induced by homologous and heterologous COVID-19 vaccine regimens**
Dots represent the results from individual vaccinees analysed by the two study laboratories (appendix pp 2–3). p values from a Dunn's test for multiple comparisons are shown above the graph. Median and interquartile ranges are indicated by red horizontal lines. Below the graph, the total numbers of individual participants, the numbers below the lower (<10) and above the upper (>10 000) cutoff of the surrogate neutralisation assay, and median values of each group are shown.

Heterologous prime–boost vaccination with ChAdOx1 nCoV-19 and BNT162b2

Lancet Infect Dis 2021
Published Online
July 29, 2021
https://doi.org/10.1016/
S1473-3099(21)00420-5

Matthias Tenbusch,

- Supériorité schéma AZ/Pf vs AZ/AZ
- **Sur réponse humorale et cellulaire T**

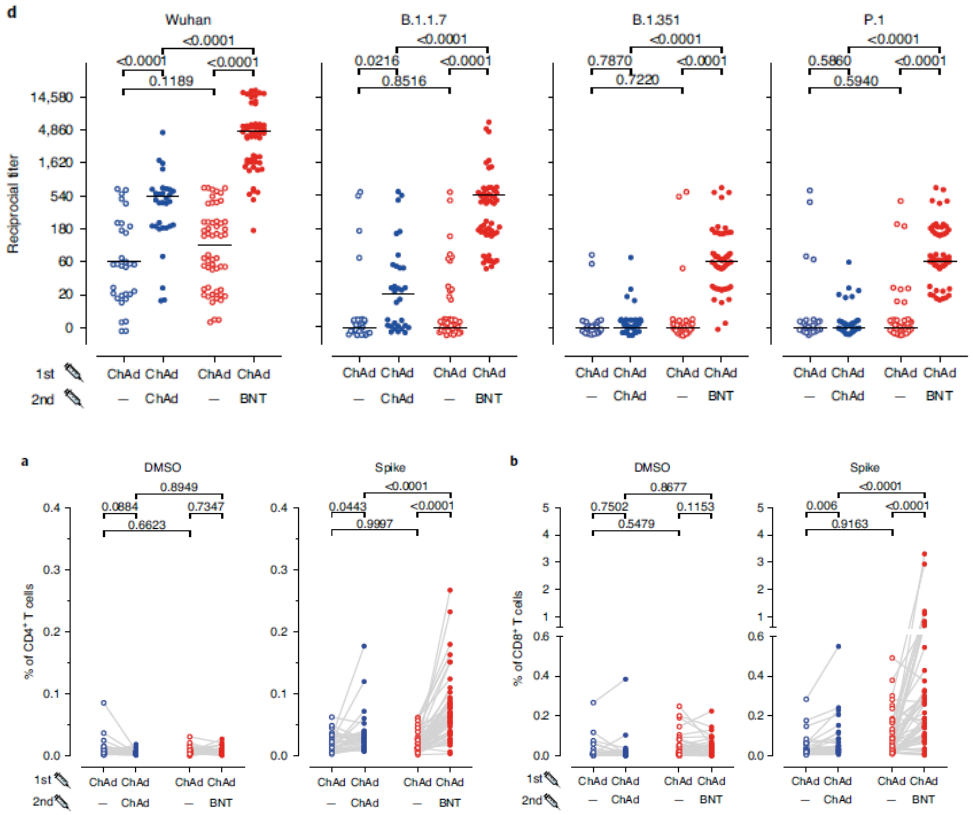
nature medicine
BRIEF COMMUNICATION
https://doi.org/10.1038/s41591-021-01449-9
Check for updates

OPEN

Immune responses against SARS-CoV-2 variants after heterologous and homologous ChAdOx1 nCoV-19/BNT162b2 vaccination

Joana Barros-Martins[1,12], Swantje I. Hammerschmidt[1,12], Anne Cossmann[2,12], Ivan Odak[1],

NATURE MEDICINE | VOL 27 | SEPTEMBER 2021 | 1525–1529 | www.nature.com/naturemedicine



Prime boost AZ-BNT162b2 ou BNT162b2-AZ: Com-COV

- **Essai Com COV- Université d'Oxford**
- Espacement entre vaccins : 4 ou 12 semaines
- 4 groupes : AZ/AZ, AZ/Pfizer, Pfizer/AZ, Pfizer/Pfizer
- Comparaison Pfizer/AZ et Pfizer/Pfizer
- **Résultats :**
  - AZ/BNT162b2 > IgG anti Spike, neutralisation et réponse cellulaire

Articles

Safety and immunogenicity of heterologous versus homologous prime-boost schedules with an adenoviral vectored and mRNA COVID-19 vaccine (Com-COV): a single-blind, randomised, non-inferiority trial

Xinxue Liu*, Robert H Shaw*, Arabella S V Stuart*, Melanie Greenland, Parvinder K Aley, Nick J Andrews, J Claire Cameron, Sue Charlton,

www.thelancet.com Vol 398 September 4, 2021

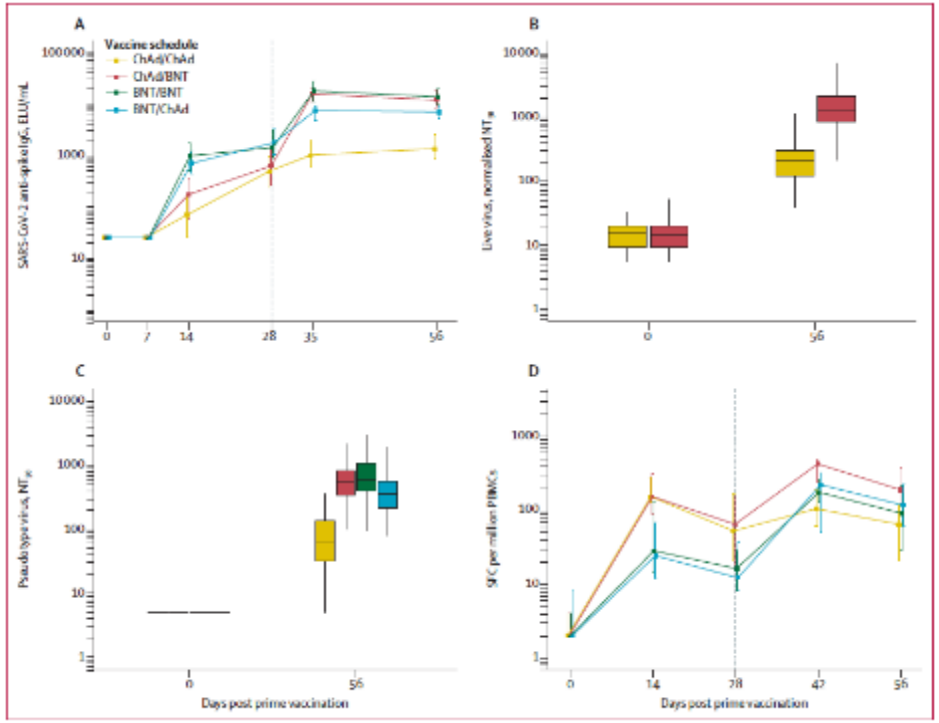


Figure 4: Kinetics of immunogenicity by vaccine schedule

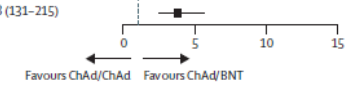
Prime boost AZ-BNT162b2 ou BNT162b2-AZ: Com-COV

Safety and immunogenicity of heterologous versus homologous prime-boost schedules with an adenoviral vectored and mRNA COVID-19 vaccine (Com-COV): a single-blind, randomised, non-inferiority trial

Xinxue Liu*, Robert H Shaw*, Arabella S V Stuart*, Melanie Greenland, Parvinder K Aley, Nick J Andrews, J Claire Cameron, Sue Charlton,

A

	ChAd/ChAd, geometric mean (95% CI)	ChAd/BNT, geometric mean (95% CI)	GMR (95% CI)	p value for interaction
SARS-CoV-2 anti-spike IgG, ELU/mL				
Age, years				0·93
50–59	1407 (1151–1721)	13578 (11804–15620)	9·5 (7·4–12·0)	
≥60	1348 (1053–1726)	12129 (9746–15095)	9·3 (6·6–13·0)	
Sex				0·34
Male	1230 (999–1516)	12312 (10421–14547)	10·0 (7·7–13·0)	
Female	1609 (1275–2031)	13976 (11772–16594)	8·4 (6·3–11·0)	
Comorbidity				0·57
Yes	1413 (1115–1791)	12055 (9159–15867)	8·5 (5·8–12·0)	
No	1371 (1111–1690)	13452 (11892–15216)	9·8 (7·7–12·0)	
Live virus neutralising antibody, normalised NT_{50}				
Age, years				0·3
50–59	192 (156–235)	1394 (1205–1614)	6·8 (5·4–8·7)	
≥60	221 (173–282)	1097 (846–1423)	5·3 (3·6–7·8)	
Sex				0·14
Male	170 (143–203)	1211 (1002–1465)	7·3 (5·6–9·4)	
Female	247 (187–326)	1351 (1114–1639)	5·4 (3·9–7·4)	
Comorbidity				0·72
Yes	187 (146–241)	1278 (977–1672)	6·5 (4·4–9·5)	
No	210 (171–259)	1265 (1079–1482)	6·2 (4·8–7·9)	
Pseudotype virus neutralising antibody, NT_{50}				
Age, years				0·48
50–59	57 (45–71)	525 (410–672)	9·1 (6·5–13·0)	
≥60	68 (48–98)	502 (387–651)	7·5 (4·6–12·0)	
Sex				0·77
Male	55 (41–74)	466 (356–608)	9·3 (6·3–14·0)	
Female	68 (54–85)	594 (481–734)	8·7 (6·3–12·0)	
Comorbidity				0·12
Yes	64 (47–87)	399 (267–598)	6·3 (3·8–10·0)	
No	58 (46–75)	583 (489–696)	10·0 (7·4–14·0)	
Cellular response, SFC per million PBMCs				
Age, years				0·097
50–59	43 (31–59)	202 (155–263)	4·8 (3·1–7·2)	
≥60	61 (42–87)	159 (121–207)	2·7 (1·7–4·3)	
Sex				0·0081
Male	36 (25–51)	197 (159–244)	5·8 (3·9–8·7)	
Female	68 (49–93)	167 (118–238)	2·6 (1·6–4·1)	
Comorbidity				0·73
Yes	54 (38–77)	224 (169–296)	4·1 (2·5–6·6)	
No	44 (32–62)	168 (131–215)	3·8 (2·5–5·7)	



Prime boost AZ-AZ-BNT162b2 ou AZ-BNT162b2-AZ: Com-COV

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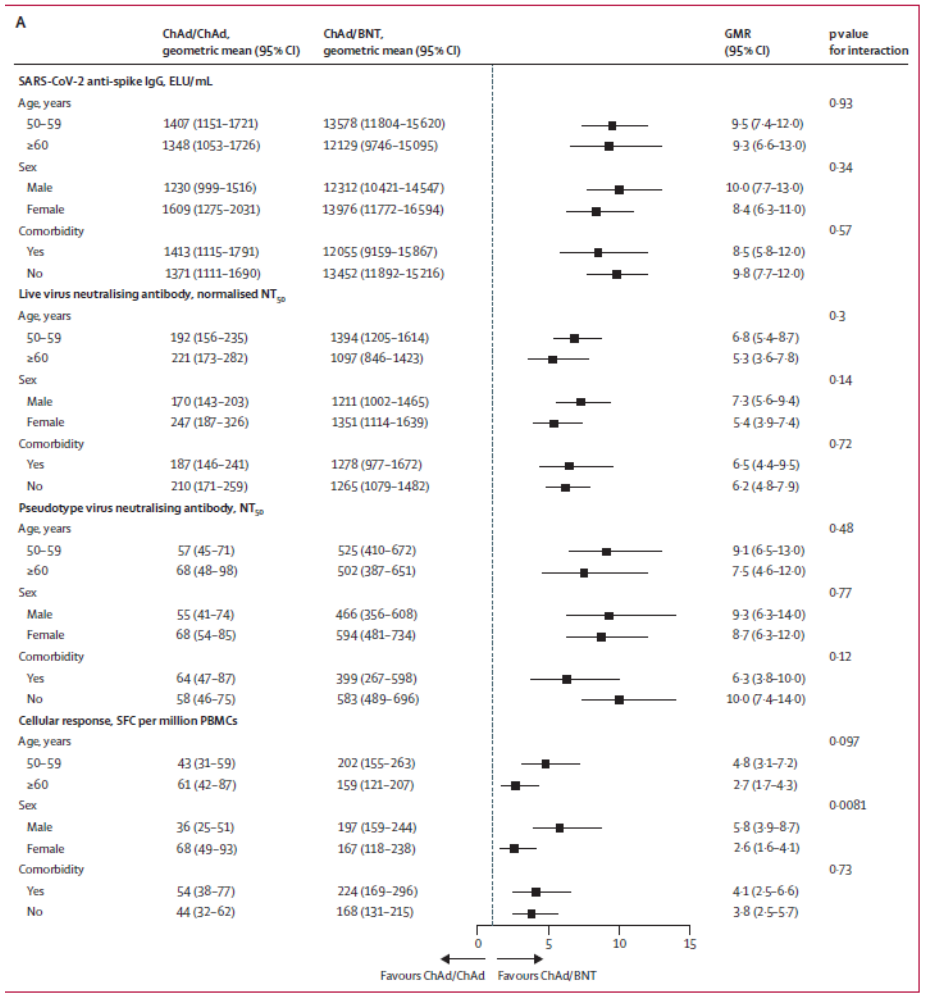
Xinxue Liu*, Robert H Shaw*, Arabella S V Stuart*, Melanie Greenland, Parvinder K Aley, Nick J Andrews, J Claire Cameron, Sue Charlton,



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Comorbidity				0·12
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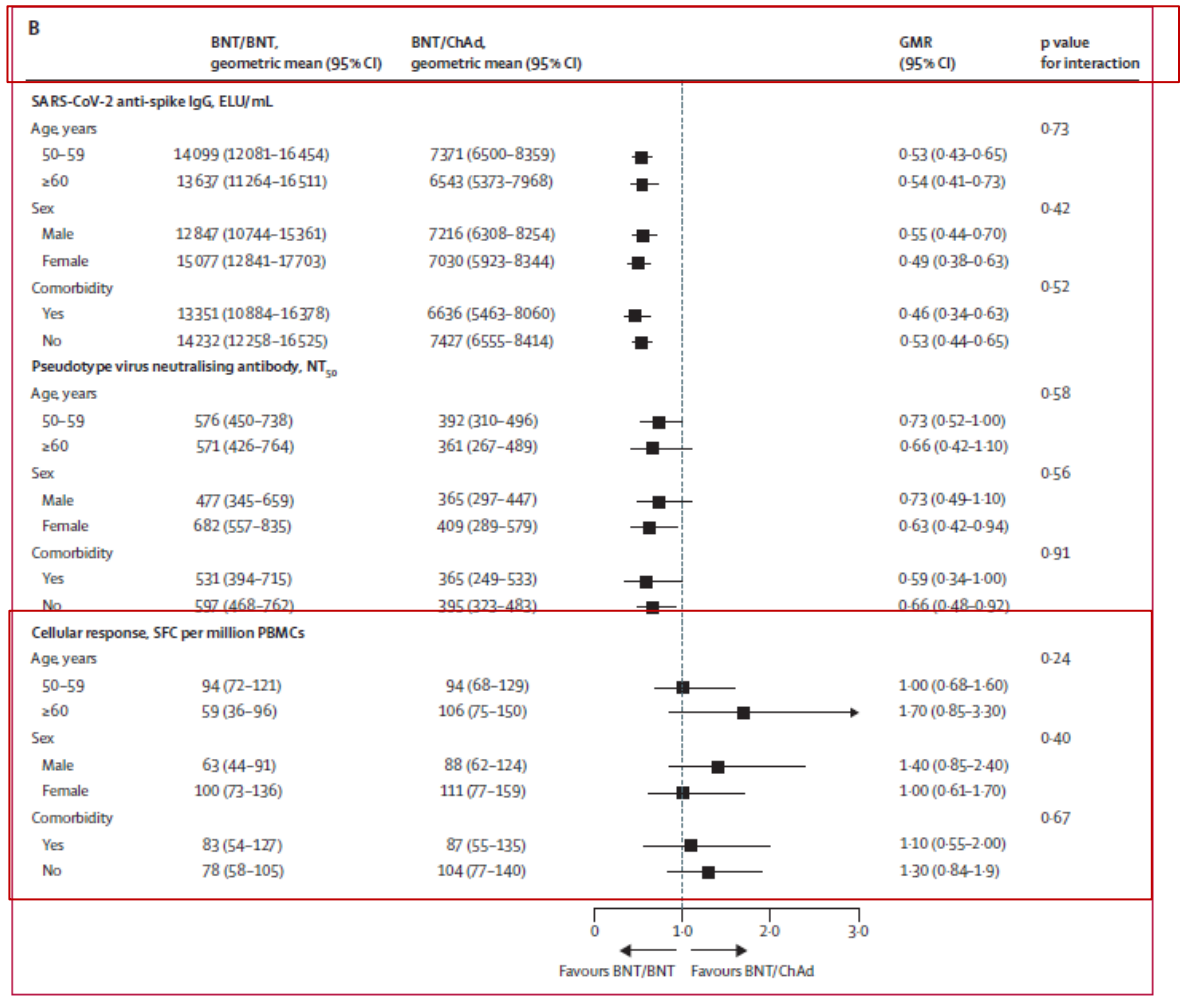
No	44 (32–62)	168 (131–215)	3·8 (2·5–5·7)	



B	BNT/BNT, geometric mean (95% CI)	BNT/ChAd, geometric mean (95% CI)	GMR (95% CI)	p value for interaction
SARS-CoV-2 anti-spike IgG, ELU/mL				
Age, years				0·73
50–59	14099 (12081–16454)	7371 (6500–8359)	0·53 (0·43–0·65)	
≥60	13637 (11264–16511)	6543 (5373–7968)	0·54 (0·41–0·73)	
Sex				0·42
Male	12847 (10744–15361)	7216 (6308–8254)	0·55 (0·44–0·70)	
Female	15077 (12841–17703)	7030 (5923–8344)	0·49 (0·38–0·63)	
Comorbidity				0·52
Yes	13351 (10884–16378)	6636 (5463–8060)	0·46 (0·34–0·63)	
No	14232 (12258–16525)	7427 (6555–8414)	0·53 (0·44–0·65)	
Pseudotype virus neutralising antibody, NT_{50}				
Age, years				0·58
50–59	576 (450–738)	392 (310–496)	0·73 (0·52–1·00)	
≥60	571 (426–764)	361 (267–489)	0·66 (0·42–1·10)	
Sex				0·56
Male	477 (345–659)	365 (297–447)	0·73 (0·49–1·10)	
Female	682 (557–835)	409 (289–579)	0·63 (0·42–0·94)	
Comorbidity				0·91
Yes	531 (394–715)	365 (249–533)	0·59 (0·34–1·00)	
No	597 (468–762)	395 (323–483)	0·66 (0·48–0·92)	
Cellular response, SFC per million PBMCs				
Age, years				0·24
50–59	94 (72–121)	94 (68–129)	1·00 (0·68–1·60)	
≥60	59 (36–96)	106 (75–150)	1·70 (0·85–3·30)	
Sex				0·40
Male	63 (44–91)	88 (62–124)	1·40 (0·85–2·40)	
Female	100 (73–136)	111 (77–159)	1·00 (0·61–1·70)	
Comorbidity				0·67
Yes	83 (54–127)	87 (55–135)	1·10 (0·55–2·00)	
No	78 (58–105)	104 (77–140)	1·30 (0·84–1·9)	

Prime boost AZ-BNT162b2

- Cohorte observationnelle, HCL
- ChAdOx1-S/BNT162b2 (n=2500) vs BNT162b2/BNT162b2 (n=10500)
- âge moyen 34 ans et 41 ans)
- Espacement entre vaccins : 12 et 4 semaines
- Analyses : réponse humorale, neutralisation et réponse cellulaire J0 et J21 post boost, neutralisation
- **Efficacité au delà de J14 post boost**

Supériorité de ChAdOx1-S/BNT162b2 par rapport a BNT162b2/BNT162b2 en termes de protection

Article

Immunogenicity and efficacy of heterologous ChAdOx1–BNT162b2 vaccination

https://doi.org/10.1038/s41586-021-04120-y
Received: 19 July 2021
Accepted: 10 October 2021
Published online: 21 October 2021
Check for updates

Bruno Pozzetto[1,2,8], Vincent Legros[1,3,8], Sophia Djebali[1,8], Véronique Barateau[1,8], Nicolas Guibert[4], Marine Villard[1], Loïc Peyrot[1], Omran Allatif[1], Jean-Baptiste Fassier[4], Amélie Massardier-Pilonchéry[4], Karen Brengel-Pesce[5], Melyssa Yaugel-Novoa[1,2], Solène Denolly[1], Bertrand Boson[1], Thomas Bourlet[1], Antonin Bal[1,6], Martine Valette[6], Thibault Andrieu[7], Bruno Lina[1,6], Covid-Ser study group*, François-Loïc Cosset[1,9,10], Stéphane Paul[1,2,9,10], Thierry Defrance[1,9,10], Jacqueline Marvel[1,9,10], Thierry Walzer[1,9,10] & Sophie Trouillet-Assant[1,2,9,10]

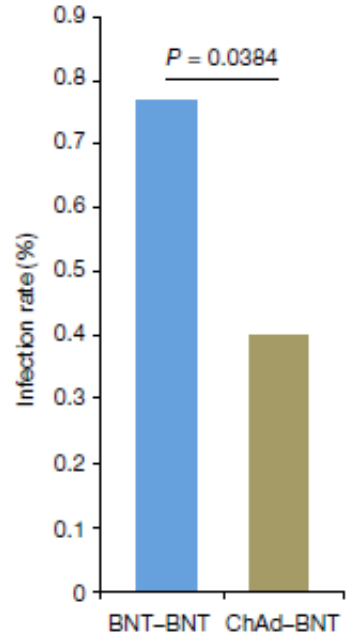
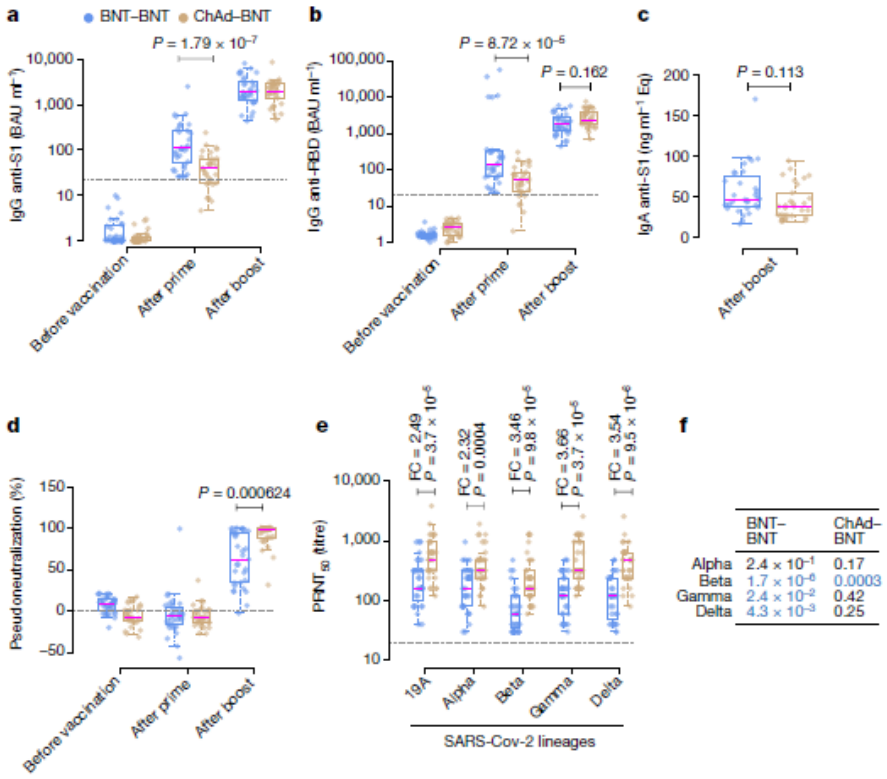


Fig. 1 | Incidence of SARS-CoV-2 infection after different vaccination regimens. Histograms show the infection rate (as documented by a positive

Prime boost AZ-BNT162b2



Reponse humorale:
Supériorité AZ-BNT162b2 sur la capacité fonctionnelle des anticorps

Article

Immunogenicity and efficacy of heterologous ChAdOx1–BNT162b2 vaccination

https://doi.org/10.1038/s41586-021-04120-y
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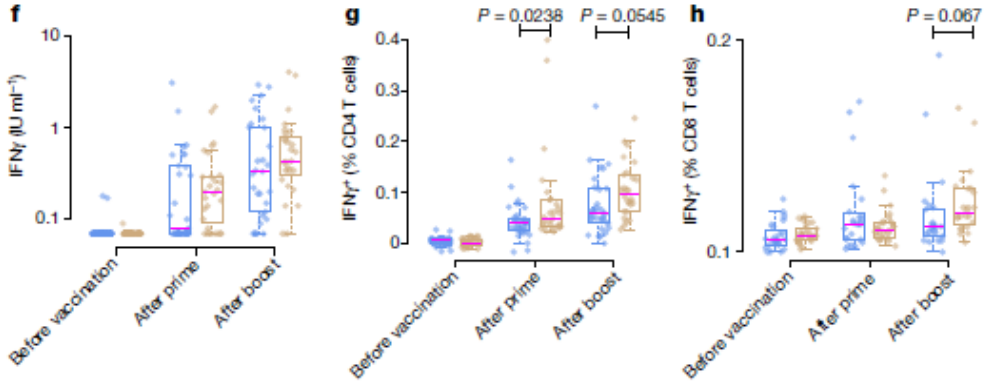
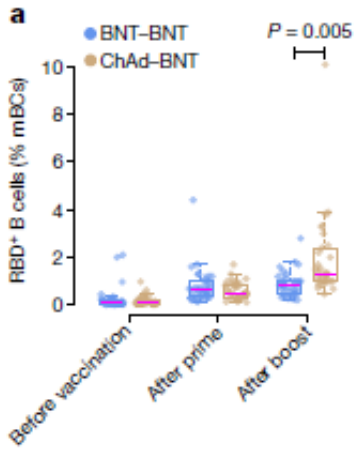
Bruno Pozzetto[1,2✉], Vincent Legros[1,3✉], Sophia Djebali[1✉], Véronique Barateau[1✉], Nicolas Guibert[4], Marine Villard[1], Loïc Peyrot[1], Omran Allatif[1], Jean-Baptiste Fassier[4], Amélie Massardier-Pilonchéry[4], Karen Brengel-Pesce[5], Melyssa Yaugel-Novoa[1,2], Solène Denolly[1], Bertrand Boson[1], Thomas Bourlet[1], Antonin Bal[1,6], Martine Valette[6], Thibault Andrieu[7], Bruno Lina[1,6], Covid-Ser study group*, François-Loïc Cosset[1,8✉], Stéphane Paul[1,2,9✉], Thierry Defrance[1,9✉], Jacqueline Marvel[1,9✉], Thierry Walzer[1,9✉] & Sophie Trouillet-Assant[1,2,9✉]

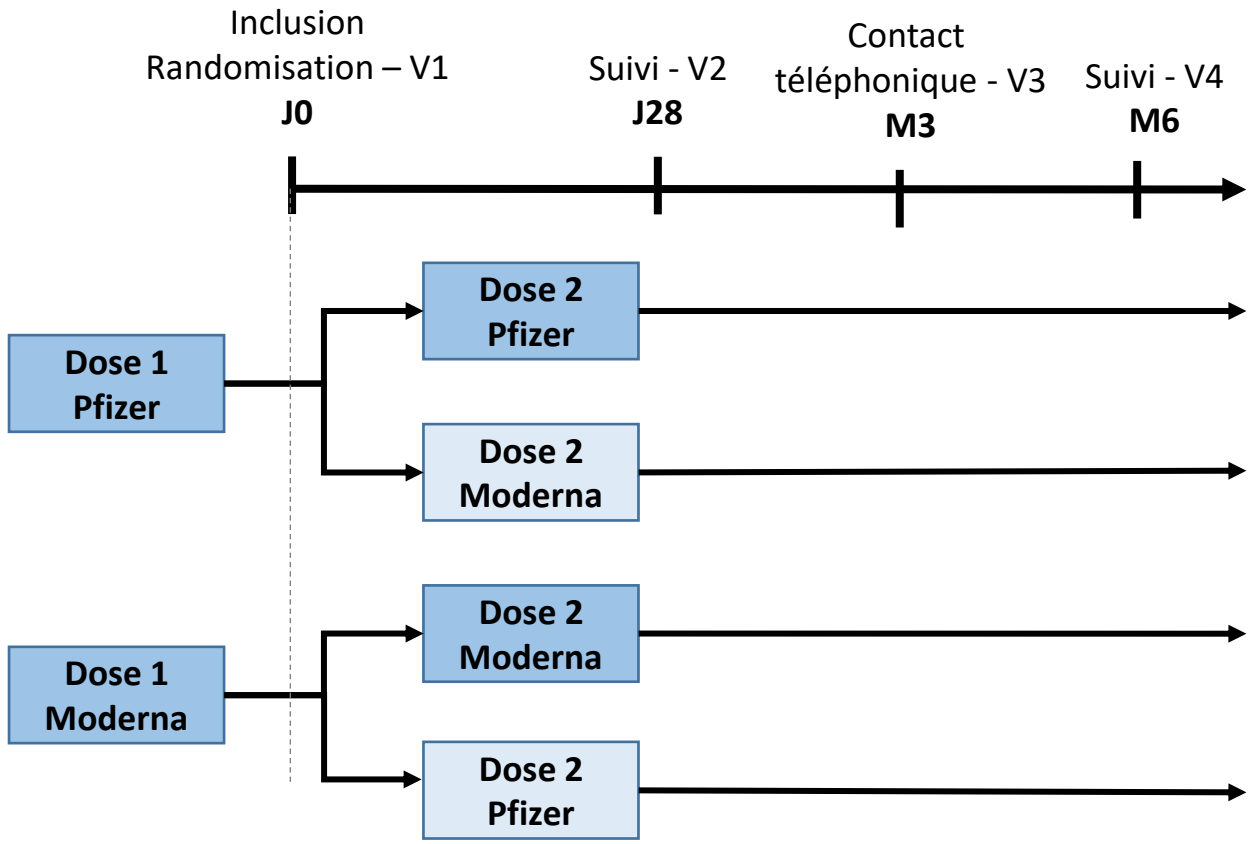




Reponse cellulaire:
Supériorité AZ-BNT162b2
réponses T et B

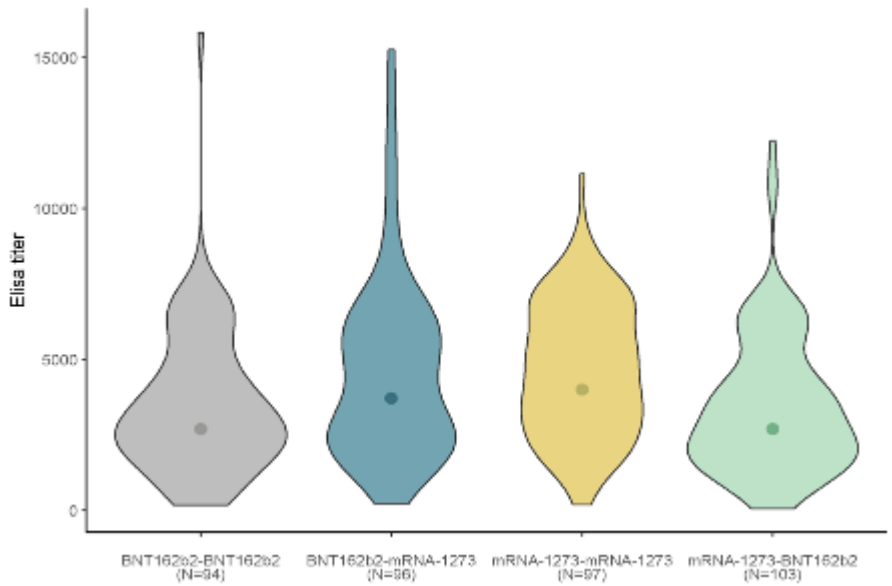
Interchangeabilité des vaccins ARNm: essai ARNcombi

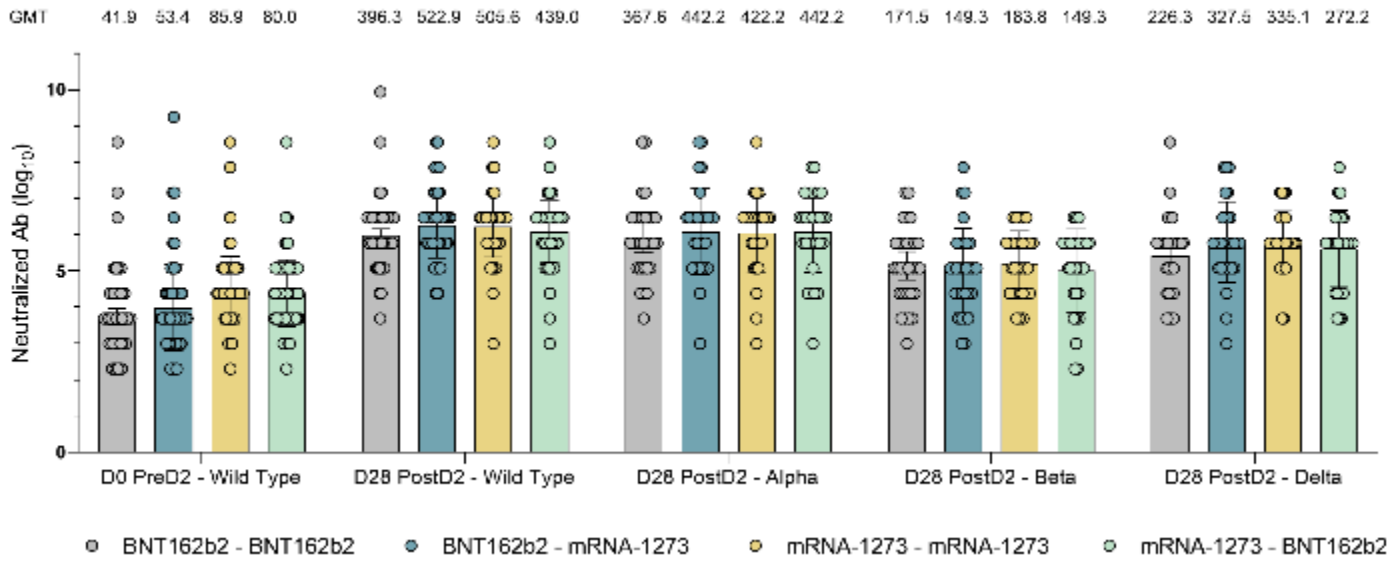
- 414 participants inclus
- 17 centres francais



Janssen C et al, submitted

Interchangeabilité des vaccins ARNm: essai ARNcombi





Janssen C et al, submitted

Prime-boost hétérologue COVID-19
3e dose

Boost hétérologue : COV BOOST study

Articles

Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial

Alasdair P S Munro*, Leila Janani*, Victoria Cornelius*, Parvinder K Aley, Gavin Babbage, David Baxter, Marcin Bula, Katrina Cathie, Krishna Chatterjee, Kate Dodd, Yvanne Enever, Karishma Gokani, Anna L Goodman, Christopher A Green, Linda Harndahl, John Haughney,

Lancet 2021; 398: 2258–76

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2878 participants inclus entre le 1er et le 30 juin 2021

Essai randomisé 12 semaines apres primo vaccination par 2 doses de AZ ou BNT162 b2

7 vaccins différents: AZ, BNT, BNT 1/2dose, NVX, NVX ½ dose, VLA, VLA ½ dose, Ad26, mRNA1273, CVn
Contrôle:MenACYW

	Prime with ChAd/ChAd					Prime with BNT/BNT				
	Control (n=106)	BNT (n=107)	VLA (n=109)	VLA half (n=111)	Ad26 (n=108)	Control (n=109)	BNT (n=110)	VLA (n=110)	VLA half (n=110)	Ad26 (n=106)
Age, years										
Mean (SD)	66·0 (14·3)	65·1 (15·3)	64·4 (15·3)	64·0 (14·9)	65·0 (14·9)	62·9 (16·9)	62·6 (17·1)	60·9 (18·1)	62·4 (16·7)	62·0 (17·4)
Median (IQR)	72·6 (57·6–77·2)	71·4 (53·8–77·0)	71·8 (51·2–76·5)	71·0 (51·2–75·9)	71·9 (51·0–76·4)	63·5 (50·4–78·3)	64·2 (49·8–77·4)	61·2 (46·2–77·7)	62·0 (51·8–76·2)	61·6 (49·2–78·3)
Intervals between first and second doses, days	68·5 (63·0–77·0)	73·0 (66·0–77·0)	70·0 (63·0–77·0)	72·0 (64·0–77·0)	74·5 (68·0–77·0)	64·0 (24·0–74·0)	65·0 (28·0–74·0)	64·5 (27·2–73·0)	63·5 (27·2–74·0)	62·0 (25·2–74·0)
Intervals between second and third doses, days	78·0 (75·0–84·0)	77·0 (73·0–84·8)	79·0 (73·0–85·0)	77·0 (73·0–84·0)	77·0 (72·0–83·0)	101·0 (89·0–147·0)	100·0 (91·0–135·0)	100·5 (91·0–146·8)	101·5 (90·2–141·5)	106·0 (91·0–143·8)
Age groups, years										
<70	48 (45·3%)	50 (46·7%)	51 (46·8%)	51 (45·9%)	50 (46·3%)	62 (56·9%)	60 (54·5%)	63 (57·3%)	61 (55·5%)	59 (55·7%)
≥70	58 (54·7%)	57 (53·3%)	58 (53·2%)	60 (54·1%)	58 (53·7%)	47 (43·1%)	50 (45·5%)	47 (42·7%)	49 (44·5%)	47 (44·3%)
Gender										
Female	53 (50·0%)	50 (46·7%)	50 (45·9%)	54 (48·6%)	48 (44·4%)	52 (47·7%)	61 (55·5%)	59 (53·6%)	49 (44·5%)	60 (56·6%)
Male	53 (50·0%)	57 (53·3%)	59 (54·1%)	57 (51·4%)	60 (55·6%)	57 (52·3%)	49 (44·5%)	51 (46·4%)	61 (55·5%)	46 (43·4%)

Added value of this study

This was, to our knowledge, the first randomised trial of third dose booster vaccines given 10–12 weeks after an initial course of ChAd/ChAd or BNT/BNT COVID-19 immunisation. This trial has demonstrated the potential of all vaccines tested (ChAd, BNT, mRNA1273, NVX-CoV2373 [Novavax; hereafter referred to as NVX], Ad26, CVnCov [CureVac; hereafter referred to as CVn], and VLA2001 [Valneva; hereafter referred to as VLA]) to boost immunity after an initial course of ChAd/ChAd and of six vaccines (ChAd, BNT, mRNA1273, NVX, Ad26, and CVn) after an initial course of BNT/BNT. All vaccines showed acceptable side-effect profiles, although some schedules were more reactogenic than others.

Boost hétérologue : COV BOOST study

Safety and immunogenicity of seven COVID-19 vaccines as a third dose (booster) following two doses of ChAdOx1 nCov-19 or BNT162b2 in the UK (COV-BOOST): a blinded, multicentre, randomised, controlled, phase 2 trial

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	Prime with ChAd/ChAd				Prime with BNT/BNT			
	Control (n=93)	ChAd (n=100)	NVX (n=96)	NVX half (n=97)	Control (n=111)	ChAd (n=98)	NVX (n=103)	NVX half (n=99)
SARS-CoV-2 anti-spike IgG, ELU/mL								
GMC*	801 (664–967; n=91)	2457 (2058–2933; n=99)	6975 (5829–8347; n=95)	4634 (3794–5660; n=97)	2541 (2110–3060; n=111)	13 424 (11 702–15 399; n=97)	10 862 (9009–13 097; n=101)	8550 (7210–10 138; n=98)
GMR†	Ref	3·25 (2·52–4·20)	8·75 (6·77–11·31)	5·82 (4·50–7·51)	Ref	5·33 (4·23–6·73)	4·78 (3·80–6·02)	3·07 (2·43–3·88)

	Prime with ChAd/ChAd					Prime with BNT/BNT				
	Control (n=93)	BNT (n=96)	V1A (n=95)	V1A half (n=107)	Ad26 (n=101)	Control (n=97)	BNT (n=96)	V1A (n=99)	V1A half (n=98)	Ad26 (n=89)
SARS-CoV-2 anti-spike IgG, ELU/mL										
GMC*	763 (630–924; n=91)	20 517 (17 718–23 757; n=93)	1835 (1514–2224; n=93)	1430 (1198–1707; n=103)	5517 (4642–6548; n=98)	3197 (2714–3767; n=94)	27 242 (24 148–30 731; n=96)	4204 (3640–4856; n=98)	3721 (3200–4326; n=98)	17 079 (14 488–20 133; n=87)
GMR†	Ref	24·48 (19·50–30·79)	2·20 (1·75–2·77)	1·81 (1·45–2·27)	5·84 (4·65–7·33)	Ref	8·11 (6·59–9·99)	1·31 (1·07–1·62)	1·25 (1·01–1·54)	5·63 (4·55–6·97)
Pseudotype virus neutralising antibody (wild-type), NT_{50}										

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	Prime with ChAd/ChAd				Prime with BNT/BNT			
	Control (n=102)	BNT half (n=105)	m1273 (n=98)	CVn (n=105)	Control (n=100)	BNT half (n=94)	m1273 (n=92)	CVn (n=94)
SARS-CoV-2 anti-spike IgG, ELU/mL								
GMC*	852 (697–1041; n=101)	16 045 (13 449–19 143; n=103)	31 111 (26 363–36 714; n=97)	3996 (3397–4700; n=103)	3029 (2556–3589; n=98)	23 082 (19 971–26 678; n=92)	33 768 (27 816–40 993; n=91)	7613 (6515–8897; n=91)
GMR†	Ref	16·80 (12·97–21·76)	32·30 (24·84–42·01)	5·05 (3·90–6·54)	Ref	6·78 (5·51–8·35)	11·49 (9·36–14·12)	2·30 (1·87–2·83)
Pseudotype virus neutralising antibody (wild-type) NT_{50}								

Boost hétérologue

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Homologous and Heterologous Covid-19 Booster Vaccinations

R.L. Atmar, K.E. Lyke, M.E. Deming, L.A. Jackson, A.R. Branche, H.M. El Sahly,

This article was published on January 26,2022, at NEJM.org.DOI:10.1056/NEJMoa2116414

- 458 participants vaccinés par 1 dose Ad26 ou 2 doses mRNA1273 ou BNT162 b2
- Essai randomisé
- 12 semaines après primovaccination
- 3 vaccins différents : mRNA1273, Ad26 ou BNT

Table 1. Characteristics of the Participants at Enrollment.*

Characteristic	mRNA-1273 Booster			Ad26.COV2.S Booster			BNT162b2 Booster		
	Primary Ad26.COV2.S	Primary mRNA-1273	Primary BNT162b2	Primary Ad26.COV2.S	Primary mRNA-1273	Primary BNT162b2	Primary Ad26.COV2.S	Primary mRNA-1273	Primary BNT162b2
Group no.	1	2	3	4	5	6	7	8	9
No. of participants	53	51	50	50	49	51	53†	51	50
Sex — no. (%)									
Female	26 (49)	32 (63)	29 (58)	27 (54)	16 (33)	23 (45)	29 (55)	26 (51)	23 (46)
Male	27 (51)	19 (37)	21 (42)	23 (46)	33 (67)	28 (55)	24 (45)	25 (49)	27 (54)
Age — yr									
Mean	57±14	53±16	55±17	50±14	50±17	50±15	48±14	54±17	50±18
Range	24–81	24–76	22–85	24–77	20–75	20–76	22–74	23–75	19–80

Boost hétérologue

Augmentation des titres en anticoprs neutraliosants

- Boosts homologues: facteur entre 4 - 20,
- Boosts heterologues faceur: 6 - 73.

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Table 2. Binding and Neutralizing Antibody Responses.*

Variable	mRNA-1273 Booster			Ad26.COV2.S Booster			BNT162b2 Booster		
	Primary Ad26.COV2.S	Primary mRNA-1273	Primary BNT162b2	Primary Ad26.COV2.S	Primary mRNA-1273	Primary BNT162b2	Primary Ad26.COV2.S	Primary mRNA-1273	Primary BNT162b2
Group no.	1	2	3	4	5	6	7	8	9
No. of participants on day 15	53	51	50	50	49	50	52	51	49
IgG serum binding antibody titer†									
GMT (95% CI)									
Day 1	59 (46–76)	872 (680–1117)	357 (262–484)	71 (48–106)	639 (514–794)	321 (251–410)	75 (55–103)	534 (445–642)	224 (177–282)
Day 15	3244 (2540–4142)	6865 (5840–8070)	6155 (4895–7739)	326 (236–451)	3029 (2433–3772)	1905 (1498–2422)	2563 (2052–3201)	5256 (4513–6120)	3345 (2711–4127)
Day 29	2986 (2478–3598)	6224 (5282–7333)	5231 (4274–6402)	369 (291–467)	4560 (3544–5867)	2600 (2086–3240)	2277 (1833–2828)	5273 (4567–6088)	3164 (2649–3779)
Percent with ≥2 factor increase from baseline titer on day 15 (95% CI)	100 (93–100)	96 (86–100)	98 (89–100)	86 (73–94)	84 (70–93)	92 (81–98)	98 (90–100)	100 (93–100)	100 (93–100)
Increase in GMT from baseline (95% CI)	55 (40–75)	8 (6–10)	17 (13–22)	5 (4–6)	5 (4–6)	6 (5–8)	34 (26–45)	10 (8–12)	15 (12–19)
Pseudovirus neutralizing antibody‡									
GMT (95% CI)									
Day 1	9 (6–13)	89 (68–116)	25 (18–34)	8 (5–12)	62 (45–85)	19 (13–26)	9 (6–14)	58 (45–74)	21 (15–30)
Day 15	676 (518–883)	902 (728–1118)	786 (596–1035)	31 (22–44)	382 (290–503)	216 (158–297)	344 (244–484)	694 (578–832)	437 (334–573)
Day 29	432 (323–578)	700 (569–862)	496 (370–663)	30 (22–40)	528 (383–729)	267 (196–362)	242 (190–309)	515 (436–609)	306 (244–384)
Percent with ≥4 factor increase from baseline titer on day 15 (95% CI)	100 (93–100)	84 (71–93)	100 (93–100)	50 (36–64)	61 (46–75)	82 (69–91)	98 (90–100)	94 (84–99)	98 (89–100)
Increase in GMT from baseline (95% CI)	73 (52–101)	10 (8–13)	32 (24–42)	4 (3–6)	6 (4–9)	12 (9–18)	36 (25–53)	12 (9–15)	20 (15–27)

Boost hétérologue

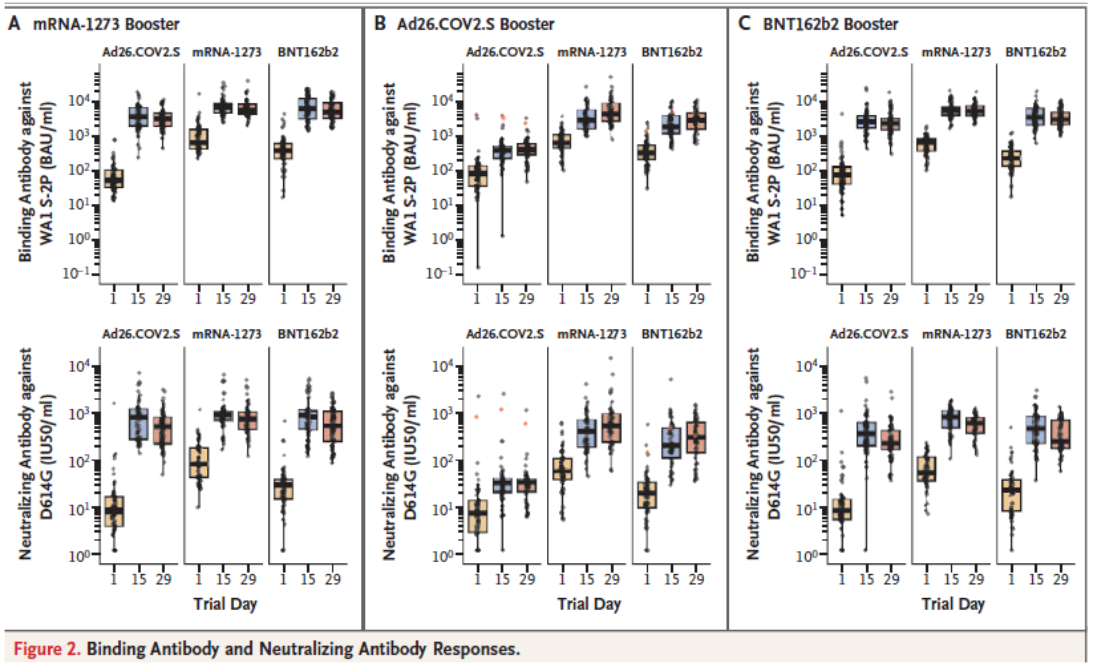

Figure 2. Binding Antibody and Neutralizing Antibody Responses.

Reponses T augmentées sauf dans le groupe homologueAd26

Réponse CD8 plus durable chez les primo vaccinés Ad26

Boost avec Ad26 augmente CD8T cell chez les primo vaccinés ARNm

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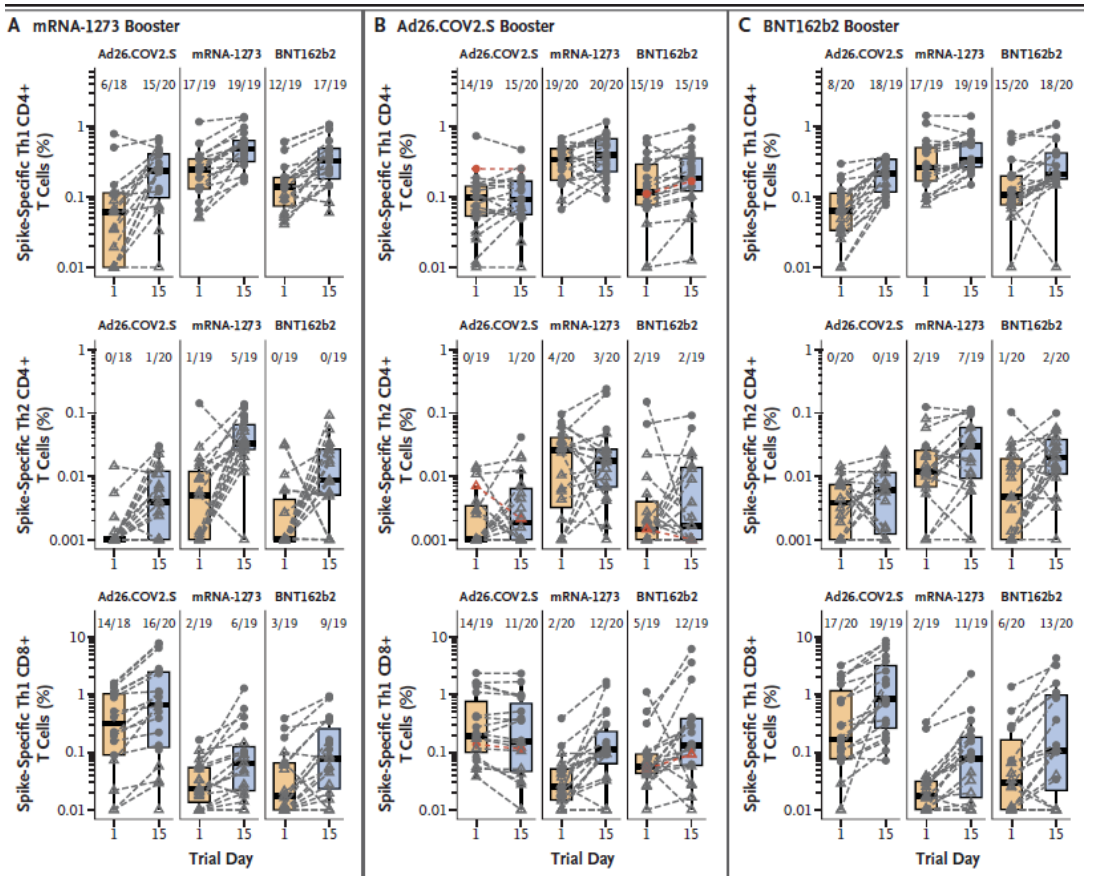

Figure 3. CD4+ and CD8+ T-Cell Responses.

Boost hétérologue

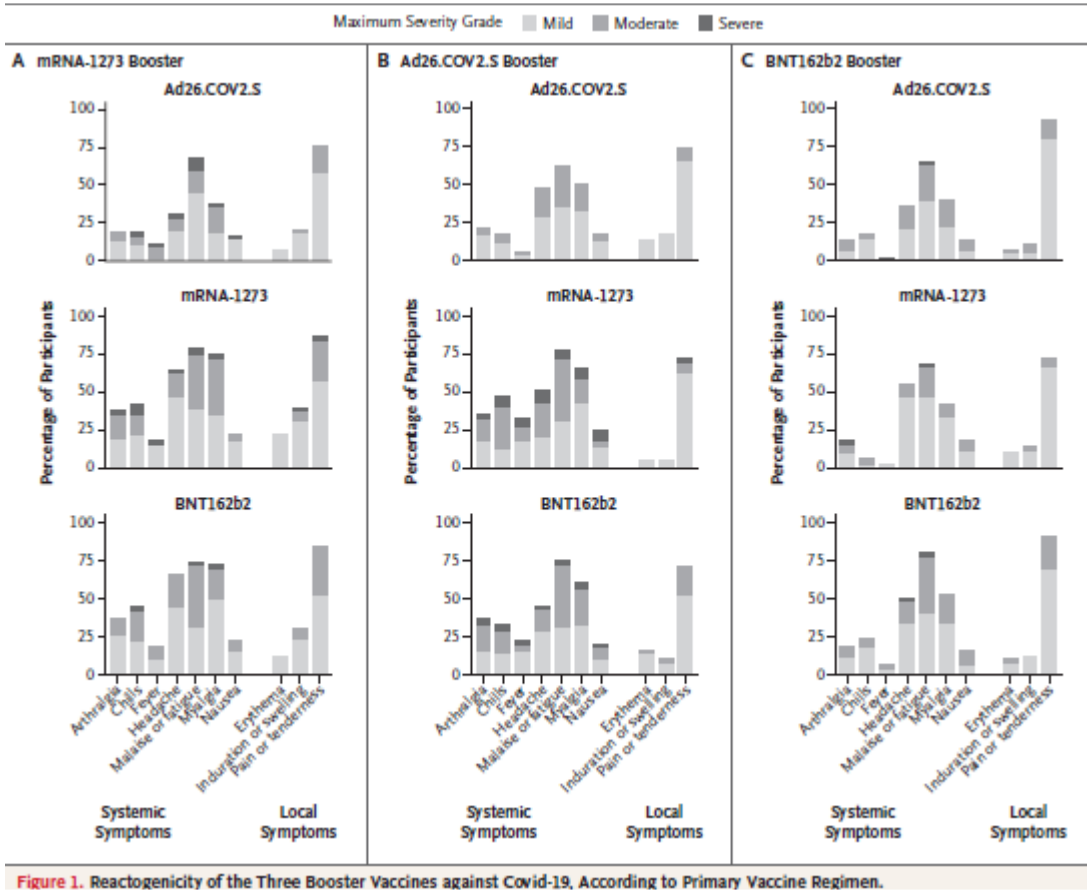

Figure 1. Reactogenicity of the Three Booster Vaccines against Covid-19, According to Primary Vaccine Regimen.

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Reactogenicité similaire à celle de la primo vaccination

50% des participants : douleurs au site d'injection, malaise, cephalées ou myalgies

Conclusion

- Acquis
  - Possibilité de ‘mixer’ les vaccins en primo vaccination
  - Intérêt des boost hétérologues en particulier après vaccination par vaccin vectorisés

- Questions:
  - Place des autres plateformes vaccinales (vaccins inactivés, sous unitaires) sur la réponse vis a vis des variants
  - Intérêt du boost hétérologue sur la réponse muqueuse
  - Place chez les immunodéprimés
  - ….