Perspectives vaccinales

Pr Odile Launay
Hôpital Cochin, Paris

Actualisation des connaissances en vaccinologie clinique
Veyrier du Lac, 3 avril 2025

Déclaration d'intérêts de 2020 à 2025

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

Histoire de la vaccination

Revue des Maladies Respiratoires (2019) 36, 74—81

Disponible en ligne sur ScienceDirect www.sciencedirect.com

Elsevier Masson France EM|consulte www.em-consulte.com

SÉRIE « VACCINATIONS » COORDONNÉE PAR E. BLANCHARD ET A. BERGERON (GREPI)

Histoire et principes de la vaccination

History and principles of vaccination

E. Canouï[a,*], O. Launay[a,b]

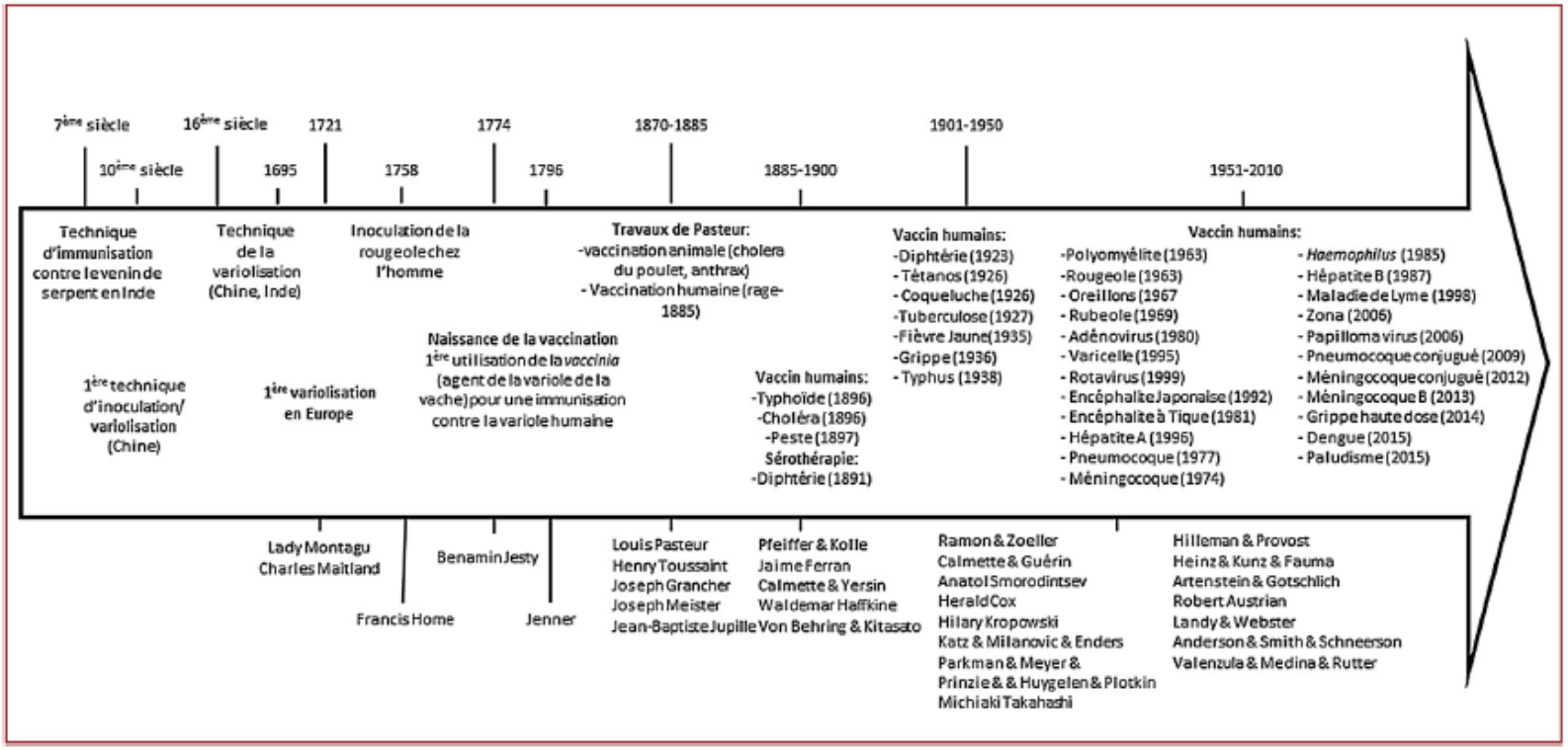
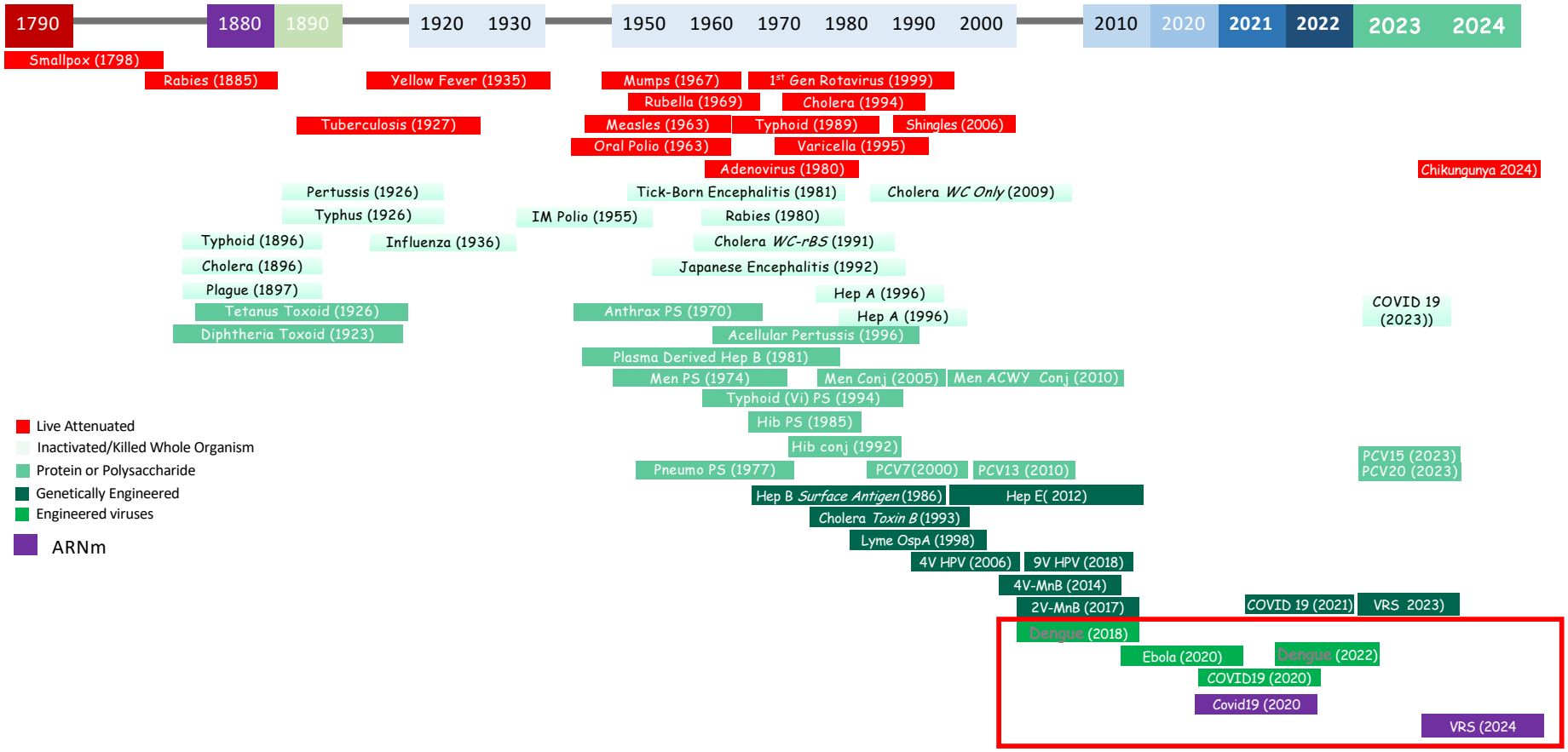


Figure 1. Histoire des découvertes et des grands noms de la vaccination.

Vaccins disponibles et évolution des technologies vaccinales



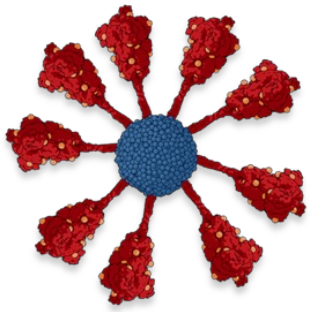
Perspectives vaccinales à court terme

Vaccination Covid-19

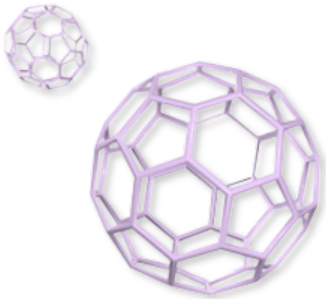
Campagne de vaccination Covid-19 2024/2025

- La saison conjointe grippe-Covid a débuté le 15 octobre
- Sujets éligibles au vaccin Covid:
  - Automne: adultes de 65 ans et plus, et personnes à risque de forme grave
  - Printemps: une dose supplémentaire pour les >80 ans, ainsi que les immunodéprimés & personnes à risque de forme grave
- DGS-Urgent du 17/09/2024
  - Santé publique France proposera gratuitement à la commande le ARNm JN.1 du laboratoire Pfizer disponible en stock d'Etat.
  - Le vaccin ARNm JN.1 (Pfizer) est le seul vaccin à ARNm distribué durant cette campagne hivernale.
  - Deux autres vaccins, mRNA-1273 (Moderna) et NVX-CoV2373 (Novavax) , ont été évaluées par la HAS mais ne sont pas disponibles en droit commun pour cette campagne.

Vaccin COVID-19 protéine recombinant, adjuvantée avec Matrix-M™



Nanoparticule de protéine recombinante



Matrix-M™

Vaccin à base de protéine recombinante : technologie similaire à celle d'autres vaccins tels que ceux contre la grippe et l'hépatite B.

5 µg de protéine de spicule Spike recombinante et 50 µg d'adjuvant Matrix-M

Adjuvant qui améliore la réponse immunitaire des cellules B et T et pourrait renforcer la durabilité de la protection. [2]

1. Cox MMJ. Recombinant protein vaccines produced in insect cells. *Vaccine*. 2012;30(10):1759-1766. 2. Stertman L, et al. Hum Vaccin Immunother.2023;19(1):2189885.

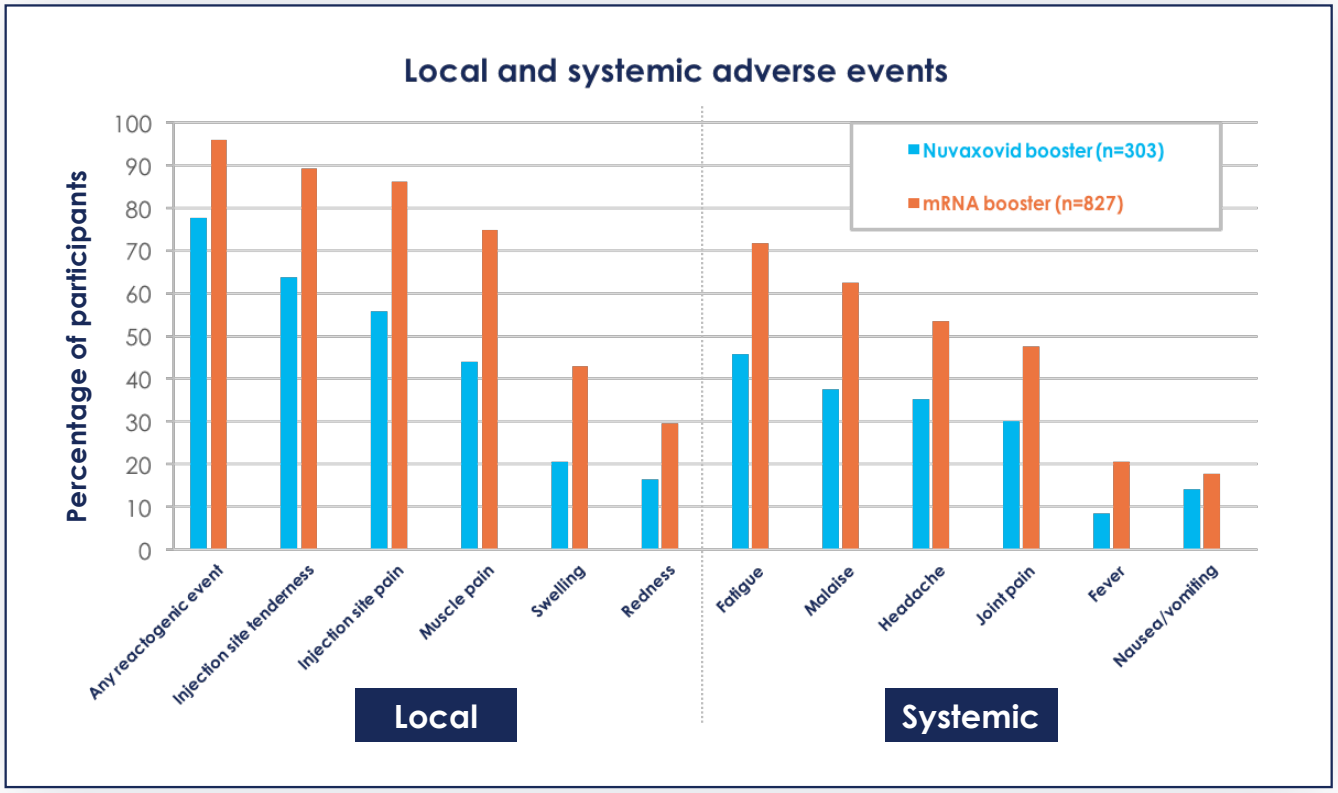
Efficacité à travers essais de phase 3 (vaccins de première génération)

	UK Phase 3[1] N=15,203	**PREVENT-19 (US/Mexico)[2]** N=29,960	**BNT-162b2 (Pfizer)[3]** N=43,548	**mRNA-1273 (Moderna)[4]** N=30,420
Efficacité	89.7% (95% CI 80.2 to 94.6)	90.4% (95% CI 82.9 to 94.6)	95% (95% CI 90.3 to 97.6)	94.1% (95% CI 89.3 to 96.8)
Efficacité contre les souches similaires	96.4% (95% CI 73.8 to 99.4)	100% (95% CI 85.8 to 100)	95% (95% CI 90.3 to 97.6)	94.1% (95% CI 89.3 to 96.8)
Efficacité contre les variants	86.3% (95% CI 71.3 to 93.5) Alpha (B.1.1.7)	93.6% (95% CI 81.7 to 97.8) Alpha (B.1.1.7)	NA	NA
Efficacité contre formes sévères*	NA (les 5 formes sévères ont eu lieu dans le groupe plaecebo)	100% (95% CI 34.6 to 100)	75% (95% CI -152.6 to 99.5)	100% (95% CI not estimated)

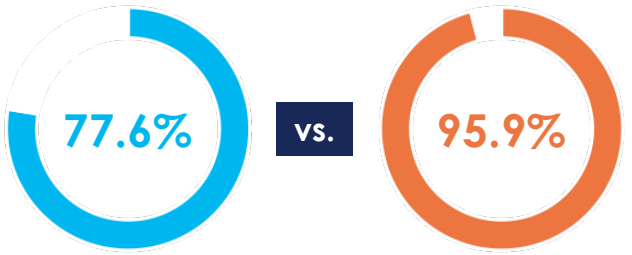
*Maladie grave : tachypnée, tachycardie ou hypoxie cliniquement significatives ; besoin de soutien respiratoire intensif ; dysfonctionnement majeur d'un ou plusieurs systèmes organiques ; admission en unité de soins intensifs ; ou décès. Basé sur les critères de la FDA.

1. Heath PT, et al. N Engl J Med. 2021;385(13):1172-1183. 2. Dunkle LM, et al. N Engl J Med. 2022;386(6):531-543. 3. Polack FP, et al. N Engl J Med. 2020;383(27):2603-2615 4. Baden LR, et al. N Engl J Med. 2021;384(5):403-416. 5.FDA, « Development and Licensure of Vaccines to Prevent COVID-19; Guidance for Industry », October 2023.

Moindre réactogénicité du vaccin protéique : étude en vie réelle



Les résultats ont démontré que le pourcentage global de bénéficiaires (adultes âgés entre ≥18 et ≤65 ans) du rappel Novavax contre la COVID-19 ayant subi un événement de réactogénicité (77.6%) était inférieur à celui des doses d'ARNm (95.9%).



Results are based on participant diaries collected over 6 days post-vaccination in a prospective observational study of reactogenicity and associated impairments in adults in the United States and Canada who received an approved/authorized COVID-19 vaccine.
Rousculp MD et al. Vaccines (Basel) 2024;12:83.

Vaccination COVID 19 par voie nasale

- **Vaccination nasale:**

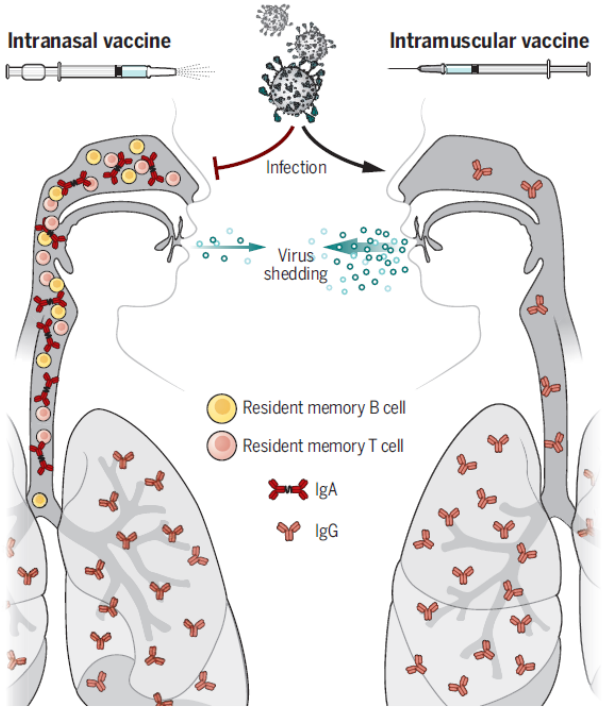
Ig A et cellules T et B mémoires dans le nez et les voies aériennes supérieures

Prévention de l'infection et réduction de l'excrétion virale

- **Vaccination IM:**

IgG sériques,

protection infection pulmonaire par transsudation au niveau pulmonaire mais n'empêche pas l'infection nasale et l'excrétion virale



VIEWPOINT: COVID-19

Scent of a vaccine

Intranasal vaccination should block SARS-CoV-2 transmission at the source

By **Frances E. Lund**[1] *and* **Troy D. Randall**[2]

Scent of a vaccine

Frances E. Lund and Troy D. Randall

Science **373** (6553), 397-399.
DOI: 10.1126/science.abg9857

> 15 candidats vaccins en essais cliniques (vaccins vectorisés, sous unitaires, vivants atténues, inactivés)

Résultats d'un essai de phase 3 vs placebo

- Vaccin vectorisé (virus grippal atténué)
- 2 doses administrées en intranasale à 14 jours d'intervalle vs placebo
- Résultats:
  - Pas de problème de sécurité

Safety and efficacy of the intranasal spray SARS-CoV-2 vaccine dNS1-RBD: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial

Fengcai Zhu, Shoujie Huang*, Xiaohui Liu*, Qi Chen*, Chunlan Zhuang*, Hui Zhao*, Jinle Han*, Anjuli May Jaen, Thai Hung Do, Jonathan Grant Peter, Alexander Gonzalez Dorado, Louie S Tirador, Gelza Mae A Zabat, Ralph Elvi M Villalobos, Gemalyn Pineda Gueco, Lauren Livia Greta Botha, Shirley Patricia Iglesias Pertuz, Jiaxiang Tan, Kongxin Zhu, Jiali Quan, Hongyan Lin, Yue Huang, Jizong Jia, Xiafei Chu, Junyu Chen, Yixin Chen, Tianying Zhang†, Yingying Su†, Changqui Li†, Xiangzhong Ye†, Ting Wu†, Jun Zhang†, Ningshao Xia†, for the*

Lancet Respir Med 2023; 11: 1075–88
Published Online November 15, 2023
https://doi.org/10.1016/S2213-2600(23)00349-1

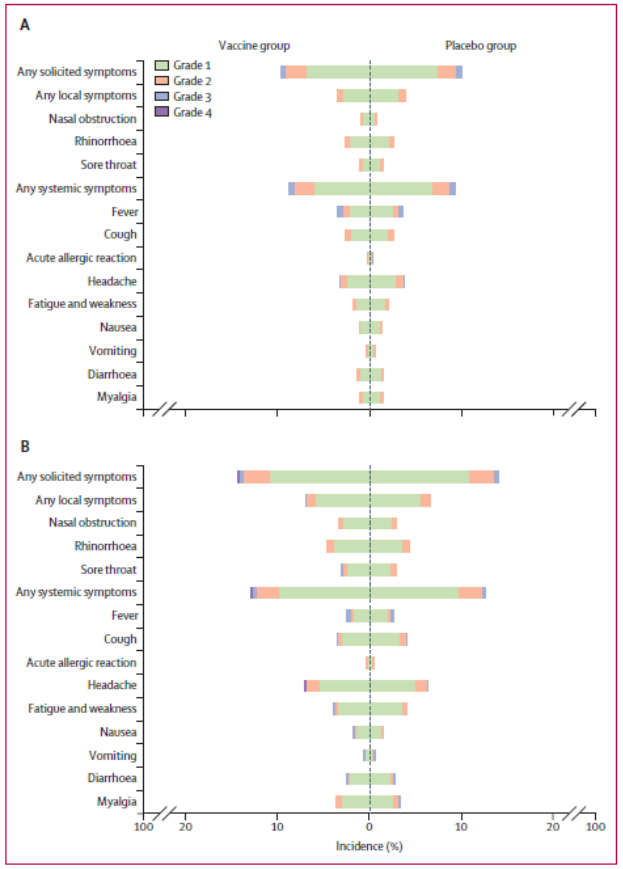


Figure 2: Solicited local and systemic adverse reactions that occurred within 7 days after any dose in the safety population*

Résultats d'un essai de phase 3 vs placebo

Safety and efficacy of the intranasal spray SARS-CoV-2 vaccine dNS1-RBD: a multicentre, randomised, double-blind, placebo-controlled, phase 3 trial

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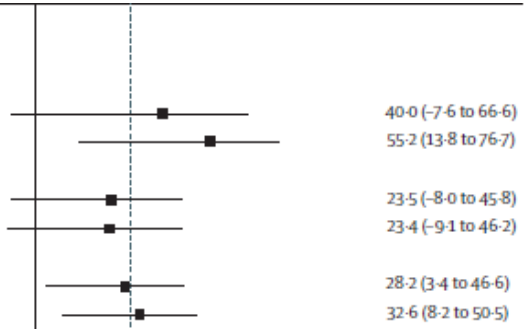
Lancet Respir Med 2023; 11: 1075–88

Published Online November 15, 2023 https://doi.org/10.1016/S2213-2600(23)00349-1

- Vaccin vectorisé (virus grippal atténué)
- 2 doses administrées en intranasale à 14 jours d'intervalle vs placebo
- Résultats:
  - Pas de problème de sécurité
- Efficacité 28,2% (IC95: 3,4-46,6)

Primary analysis: symptomatic SARS-CoV-2 infection						
Per-protocol population						
Participants without a history of SARS-CoV-2 vaccination						
≥15 days	48	6508 (2800)	0·6%	6517 (2794)	1·1%	40·0 (−7·6 to 66·6)
15–90 days	42	6508 (1347)	1·0%	6517 (1346)	2·2%	55·2 (13·8 to 76·7)
Participants with a history of SARS-CoV-2 vaccination						
≥15 days	132	6332 (1847)	3·1%	6385 (1852)	4·1%	23·5 (−8·0 to 45·8)
15–90 days	125	6332 (1212)	4·5%	6385 (1218)	5·8%	23·4 (−9·1 to 46·2)
Overall						
≥15 days	180	12 840 (4647)	1·6%	12 902 (4646)	2·3%	28·2 (3·4 to 46·6)
15–90 days	167	12 840 (2559)	2·6%	12 902 (2565)	3·9%	32·6 (8·2 to 50·5)



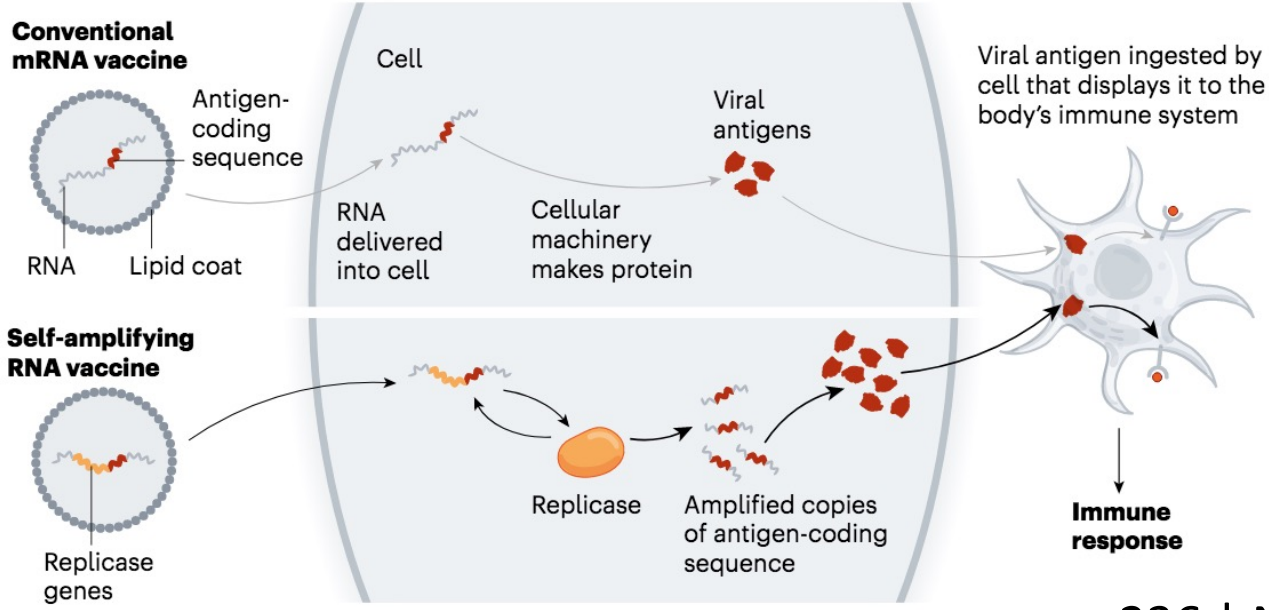
Vaccins ARNm ‘auto-amplifiant’

News in focus

SELF-COPYING RNA VACCINE WINS APPROVAL: WHAT’S NEXT?

SELF-AMPLIFYING RNA

Presented with an RNA vaccine, the body’s cells produce antigens — protein sequences normally encoded by the virus the vaccine is targeting — from a set of RNA instructions to prompt an immune response. If these instructions include the recipe for a replicase enzyme, that enzyme, once created, can make more copies of the antigen’s RNA sequence. This might mean that a vaccine made using this strategy can be given in smaller doses yet elicit a similar response to conventional RNA vaccines.



236 | Nature | Vol 624 | 14 December 2023

Vaccination grippe

Vaccin ARNm grippe

Vaccine 50 (2025) 126847

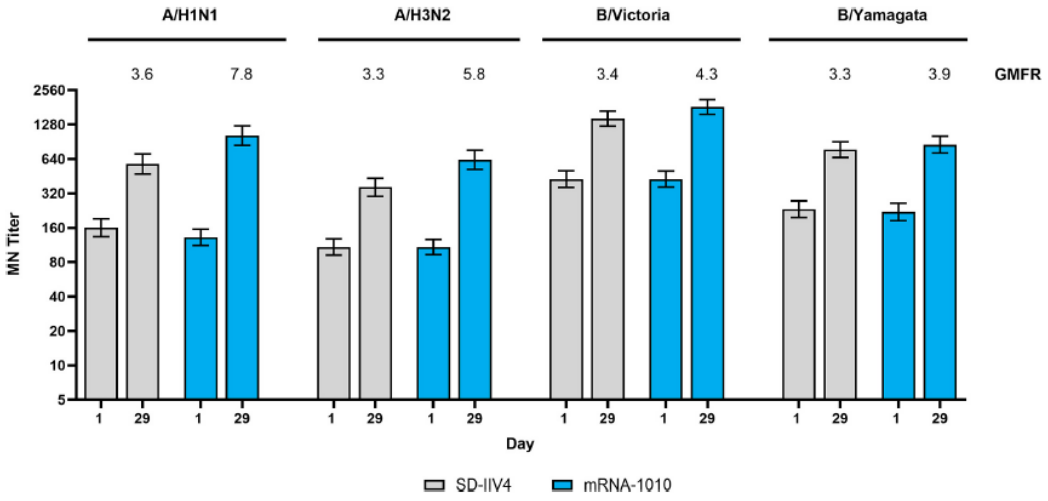
Contents lists available at ScienceDirect

Vaccine

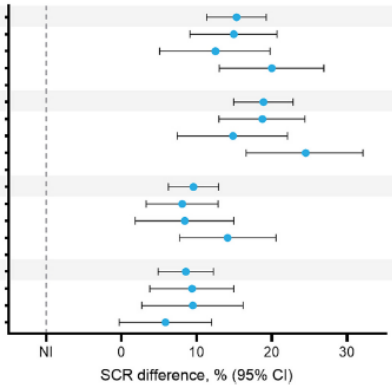
journal homepage: www.elsevier.com/locate/vaccine

A phase 3 randomized safety and immunogenicity trial of mRNA-1010 seasonal influenza vaccine in adults

Mieke Soens [a,*], Jintanat Ananworanich [a,1], Bryony Hicks [b], Kathryn Jean Lucas [c],



Influenza strain	Group	mRNA-1010, n	SD-IIV4, n	SCR difference, % (95% CI)
A/H1N1	≥18 years	1185	1135	15.32 (11.32, 19.27)
	18-49 years	568	550	14.94 (9.11, 20.68)
	50-64 years	349	328	12.50 (5.09, 19.78)
	≥65 years	268	257	20.00 (12.99, 26.93)
A/H3N2	≥18 years	1185	1135	18.90 (14.93, 22.80)
	18-49 years	568	550	18.75 (12.96, 24.41)
	50-64 years	349	328	14.85 (7.44, 22.09)
	≥65 years	268	257	24.51 (16.61, 32.13)
B/Victoria	≥18 years	1185	1135	9.58 (6.24, 12.91)
	18-49 years	568	550	8.08 (3.29, 12.85)
	50-64 years	349	328	8.44 (1.84, 14.97)
	≥65 years	268	257	14.12 (7.73, 20.57)
B/Yamagata	≥18 years	1185	1135	8.58 (4.90, 12.24)
	18-49 years	568	550	9.39 (3.76, 14.96)
	50-64 years	349	328	9.49 (2.73, 16.17)
	≥65 years	268	257	5.85 (-0.28, 12.01)



Vaccin ARNm grippe

Vaccine 50 (2025) 126847

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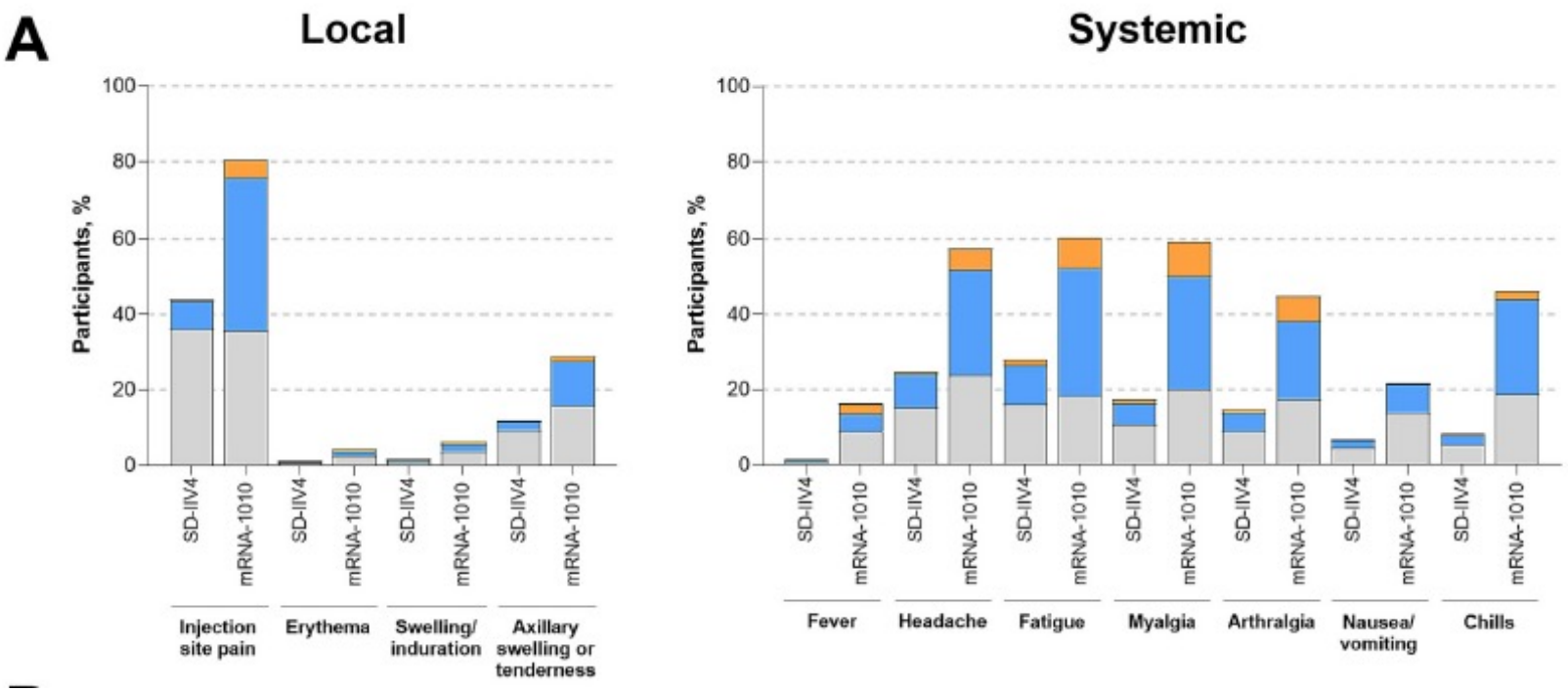

Vaccin ARNm grippe/Covid-19

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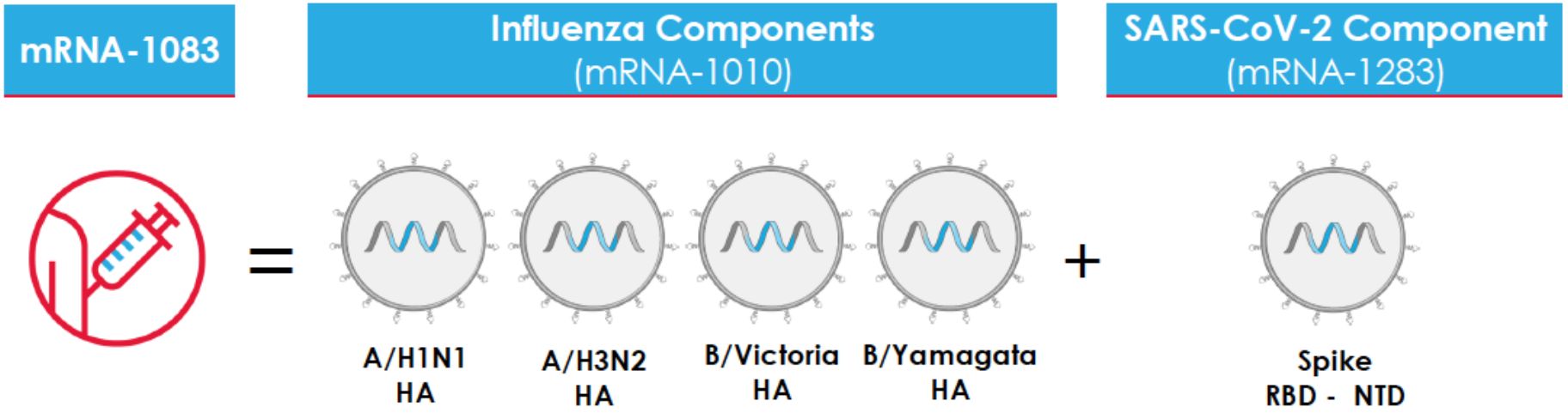
Article | Published: 18 March 2025

mRNA-based seasonal influenza and SARS-CoV-2 multicomponent vaccine in healthy adults: a phase 1/2 trial

Amanda K. Rudman Spergel, Jintanat Ananworanich, Ruiting Guo, Weiping Deng, Lizbeth Carmona,



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mRNA-based seasonal influenza and SARS-CoV-2 multicomponent vaccine in healthy adults: a phase 1/2 trial

voranich, Ruiting Guo, Weiping Deng, Lizbeth Carmona,

mRNA-1083-P301 Phase 3 study; presenting data charts today

Study was designed to test the immunogenicity and safety of mRNA-1083

Design
Randomized, observer-blind, active control study

Participants
~8,000 adults ≥ 50 years of age

Vaccination schedule
2 injections on Day 1 (mRNA-1083 + placebo or licensed influenza vaccine + COVID-19 vaccine)

Duration: 6 months
Participants followed up for 6 months

Site locations
Northern hemisphere (United States)

Phase 3 clinical study

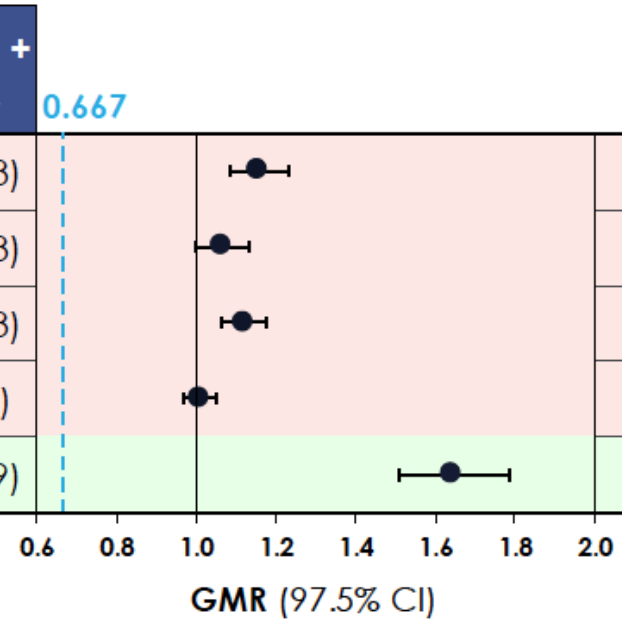
Cohort A: Ages ≥ 65 years	Cohort B: Ages ≥ 50 to 64 years
mRNA-1083 + placebo N~2000	mRNA-1083 + placebo N~2000
Fluzone HD + Spikevax N~2000	Fluarix + Spikevax N~2000

Vaccin ARNm grippe/Covid-19

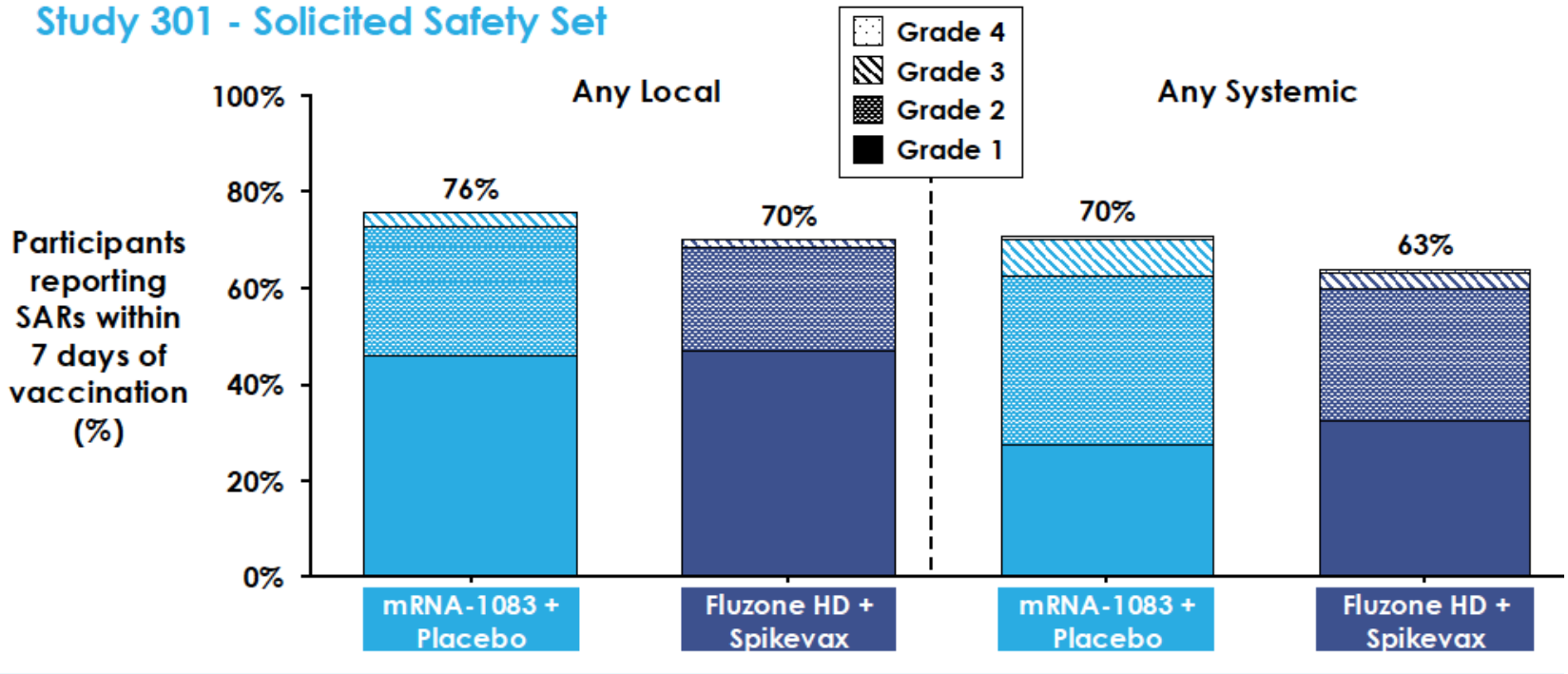
Geometric Mean Ratio (GMR) of mRNA-1083 versus Separate Vaccines in Adults ≥65 Years at Day 29

Study 301, Cohort A – Per Protocol Set for Immunogenicity*

GMT (N)	mRNA-1083 + Saline Placebo	Fluzone HD + Spikevax	GMR (97.5% CI)
Influenza A/H1N1	**120.5** (1885)	**104.3** (1883)	**1.20** (1.09, 1.23)
Influenza A/H3N2	**114.7** (1885)	**107.9** (1883)	**1.06** (1.00, 1.13)
Influenza B/Victoria	**245.3** (1885)	**219.4** (1883)	**1.12** (1.06, 1.18)
Influenza B/Yamagata	**93.3** (1885)	**92.6** (1883)	**1.01** (0.97, 1.05)
SARS-CoV-2 Omicron XBB.1.5	**1396.7** (1849)	**851.1** (1859)	**1.64** (1.51, 1.78)

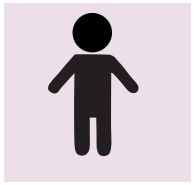


Vaccin ARNm grippe/Covid-19



Infections à VRS

Vaccins VRS: indications actuelles



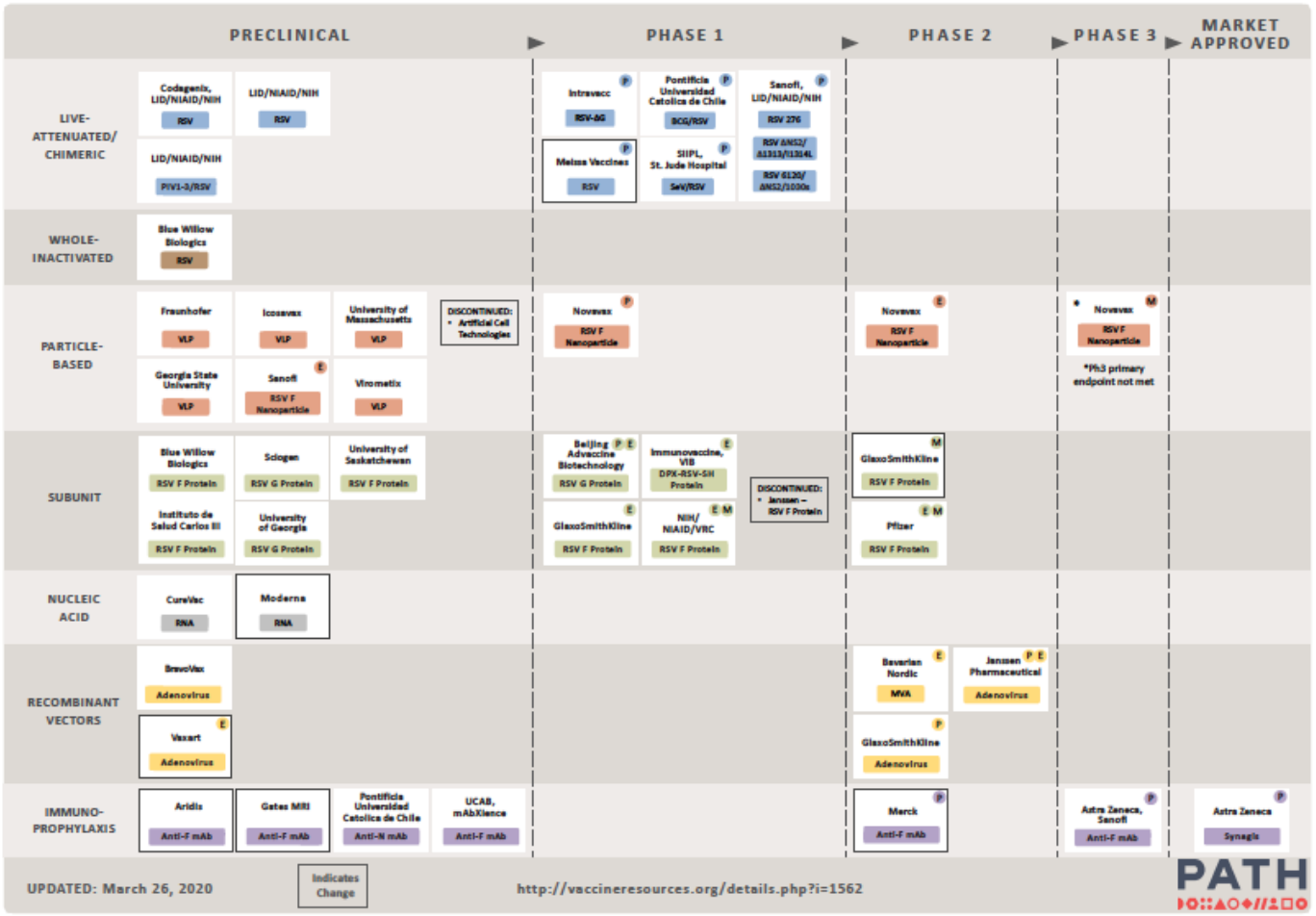
Pédiatrique

Maternel

Adultes âgés
(50/60 ans)

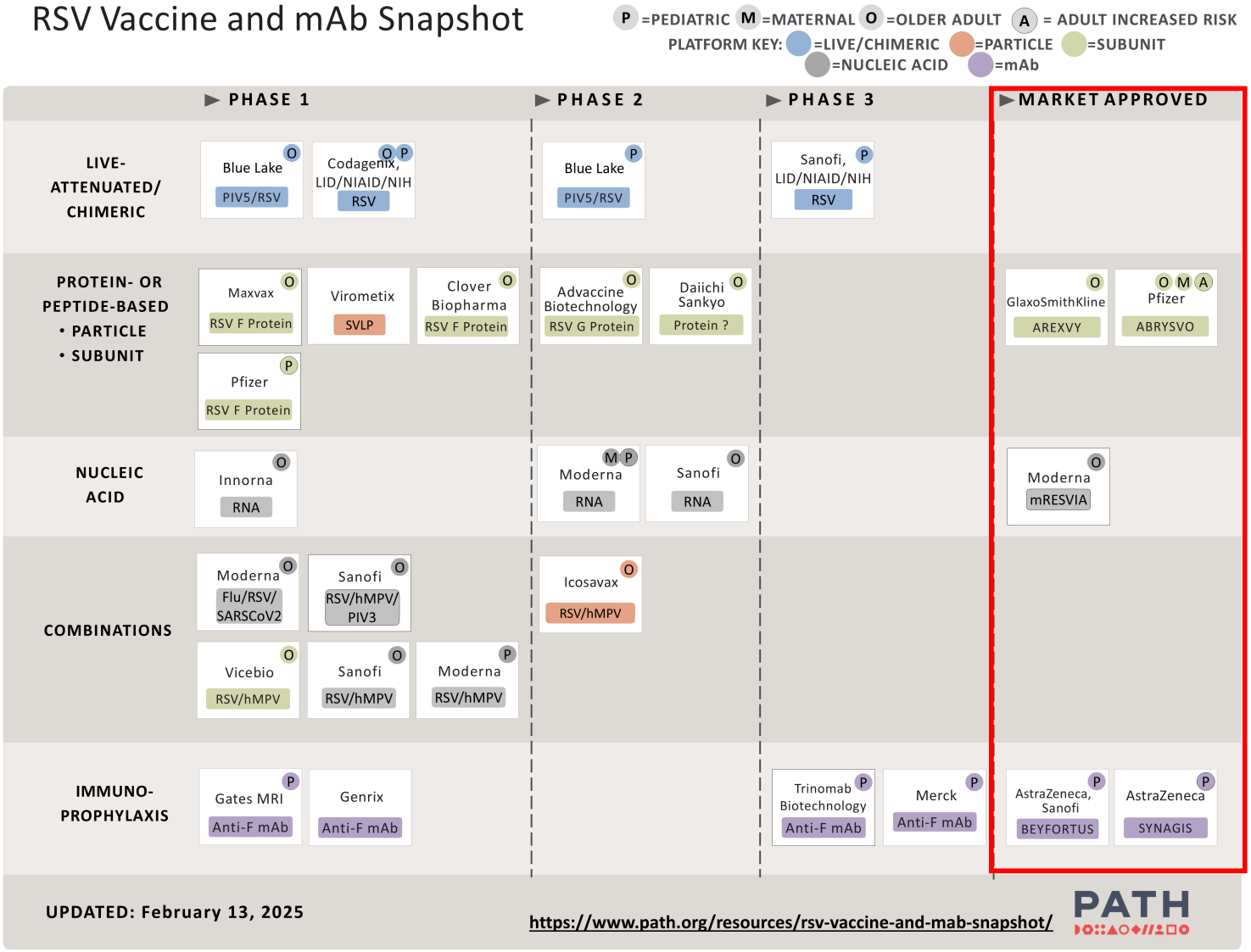
2020

RSV Vaccine and mAb Snapshot



RSV Vaccine and mAb Snapshot

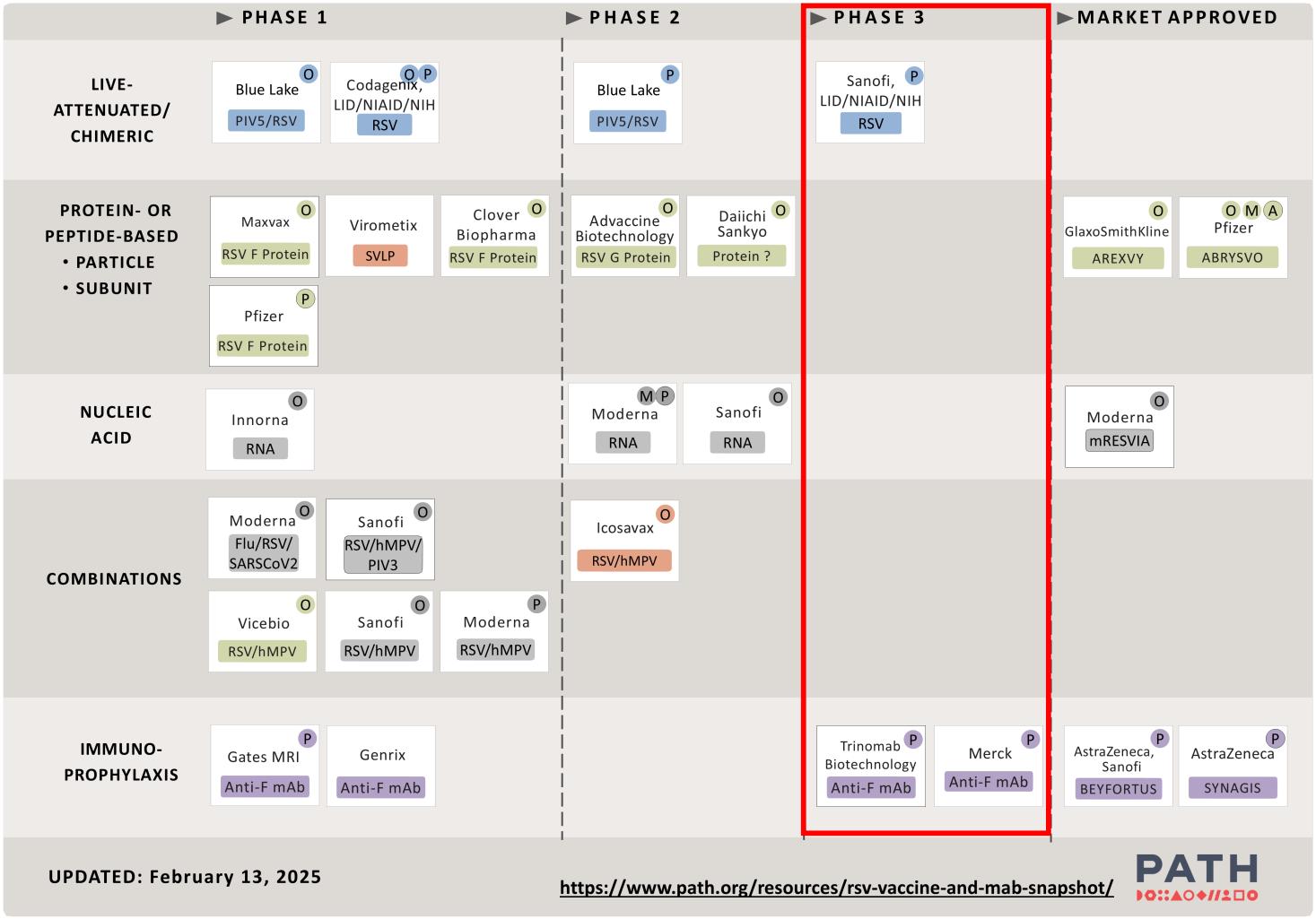
2025



RSV Vaccine and mAb Snapshot

P =PEDIATRIC M =MATERNAL O =OLDER ADULT A = ADULT INCREASED RISK

PLATFORM KEY: =LIVE/CHIMERIC =PARTICLE =SUBUNIT =NUCLEIC ACID =mAb



UPDATED: February 13, 2025

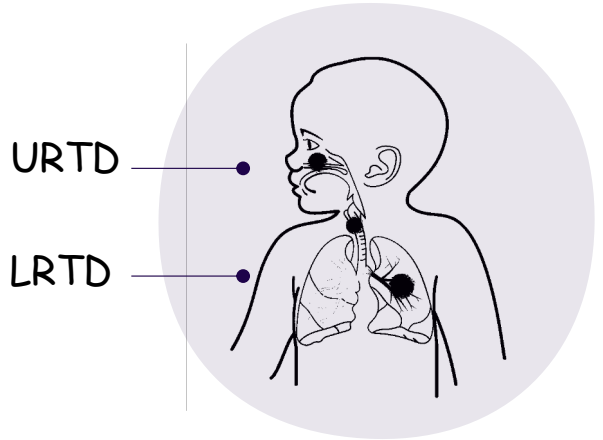
https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/

PATH

Candidat vaccin développé pour la protection des nourrissons au cours de la seconde saison VRS

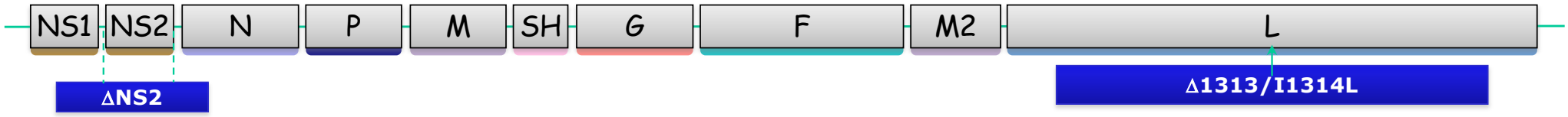
Administration par voie nasale

- Immunité au site d'infection
- Protection contre les infections respiratoires hautes et basses



Vaccin vivant atténué
Trois modifications génétiques (OGM)

Génome du VRS



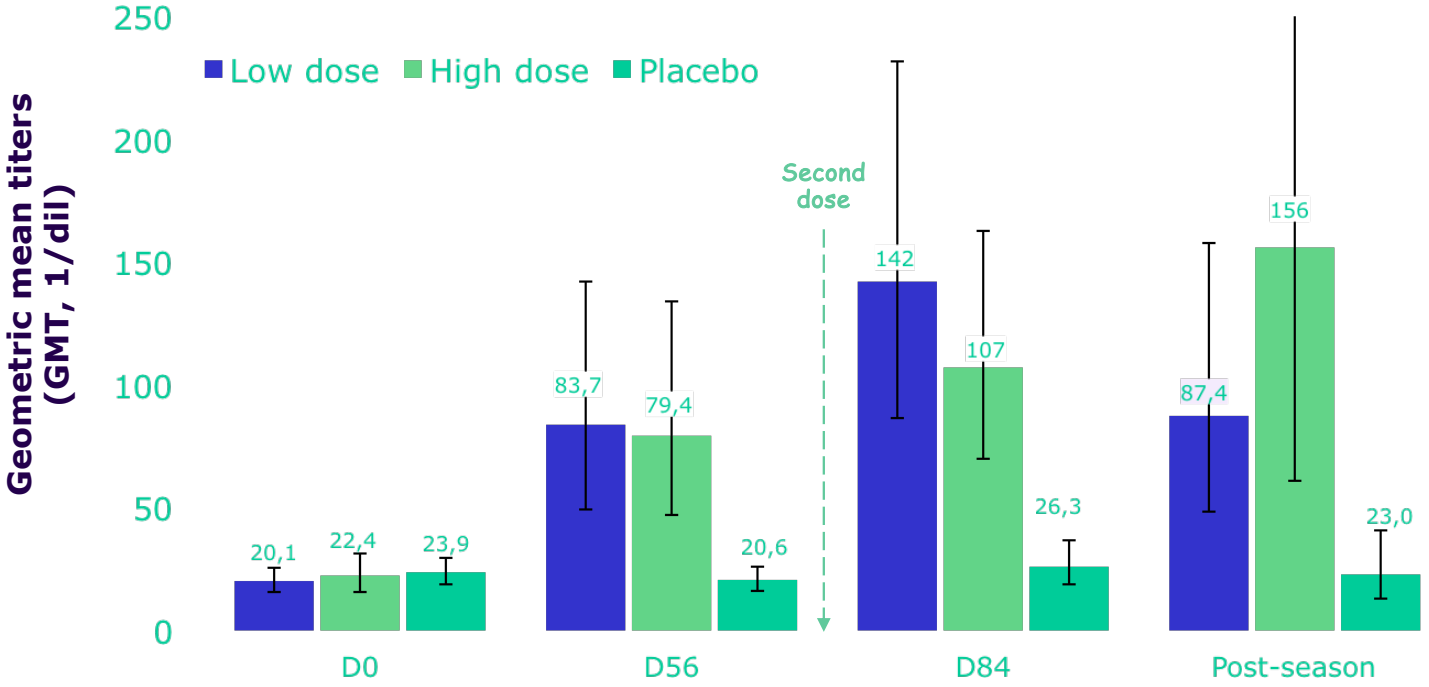
Genetic alteration	*Deletion of NS2 gene (ΔNS2)*[2–7]	*Codon deletion in L gene (Δ1313)*[5–9]	*Missense mutation in L gene (I1314L)*[5–9]
Protein role	Interferon antagonist	RSV polymerase	RSV polymerase
Impact of alteration	Removes risk of NS2-mediated airway obstruction, attenuates RSV, and improves immunogenicity for effective viral clearance	Confers moderate temperature sensitive phenotype; replication restricted to the cooler URT (shutoff at 38–39ºC)	Stabilizes the Δ1313 deletion

Attenuating *Stabilizing*

F, fusion; G, attachment; L, large polymerase subunit; M, matrix; N, nucleoprotein; NS, nonstructural; P, phosphoprotein polymerase cofactor; RSV, respiratory syncytial virus; SH, small hydrophobic; URT, upper respiratory tract. 1. Battles MB, et al. Nat Rev Micro 2019;17:33–245; 2. Ramaswamy M, et al. Virology 2006;344:328–39; 3. Lo MS, et al. J Virol 2005;79:9315–9; 4. Valarcher JF, et al. J Virol 2003;77:8426–39; 5. Karron RA, et al. J Inf Dis 2020;222:82–9; 6. Cunningham CK, et al. J Inf Dis 2022;226:2069–78; 7. Alamares-Sapuay J et al. PloS one 2024;19:e0301773; 8. Liesman RM, et al. J Clin Invest 2014;124:2219–33; 9. Luongo C, et al. J Vir 2013;87:1985–96.

Données des essais de Phase I/II : immunogénicité

Titres d'anticorps sériques anti-VRS A avant et après la deuxième administration du vaccin par voie intranasale



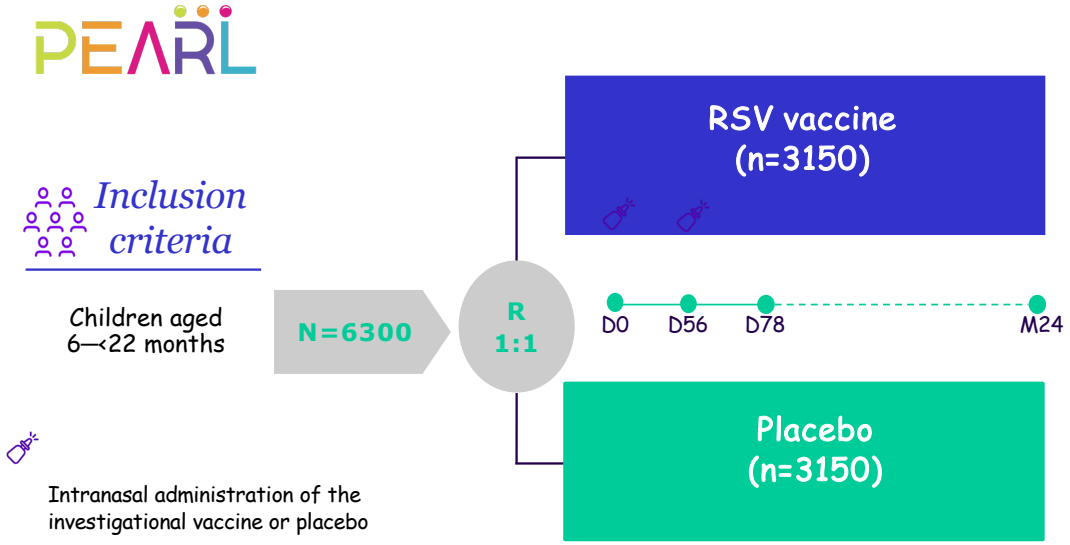
Robust immune responses: Elicited with two administrations of low or high doses of vaccine, which **persist up to 5 months after second injection**

No safety signals: **Rhinorrhea and nasal congestion** are slightly more common in vaccine recipients than in placebo recipients

D, day; dil, dilution; GMT, geometric mean titer; RSV, respiratory syncytial virus. D0, baseline; D56, before 2nd vaccine administration; D84, 28 days after 2nd vaccination; Post-season, end of RSV season or 5 months after last vaccination. 1Olubukola T, et al. 8th ReSViNET Conference. February 2024, Mumbai, India. Abstract booklet available at: Abstract-Booklet-06May24.pdf (resvinet.org) (accessed May 2024); 2. Olubukola T, et al. 34th Congress of ESCMID, April 2024, Barcelona, Spain.

Essai de phase 3 en cours (debut 2024)

PEARL is a phase III, randomized, observer-blind, placebo-controlled, multi-center, multinational study to evaluate the efficacy, immunogenicity, and safety of the RSV vaccine candidate in infants and toddlers



Primary objective

To demonstrate the clinical efficacy of the investigational vaccine for the prevention of
RT-PCR-confirmed RSV lower respiratory tract disease, over the first RSV season post-vaccination

Investigational Sites

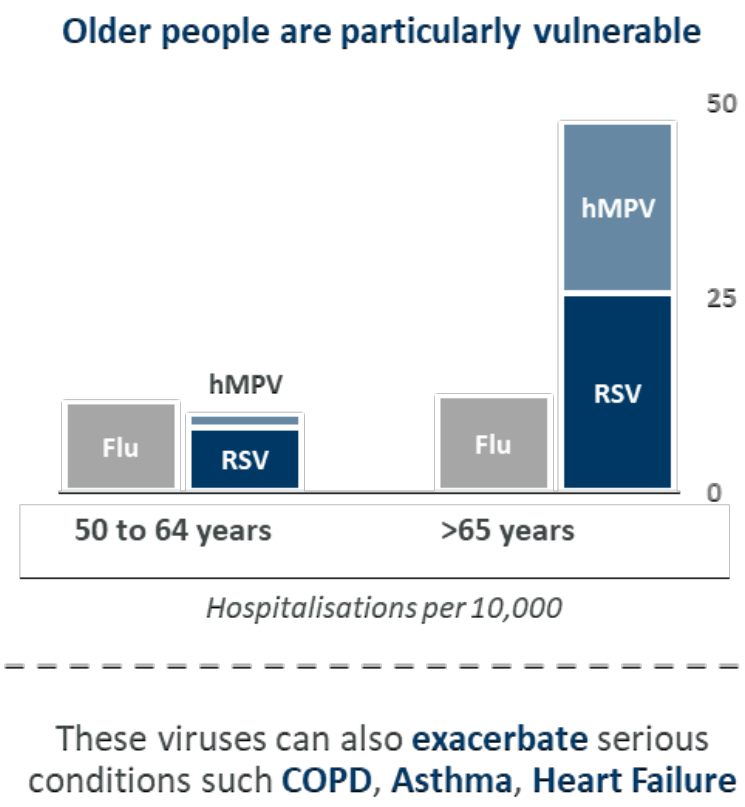
- North America
- Africa
- Latin America
- Asia
- Europe

Estimated primary completion date

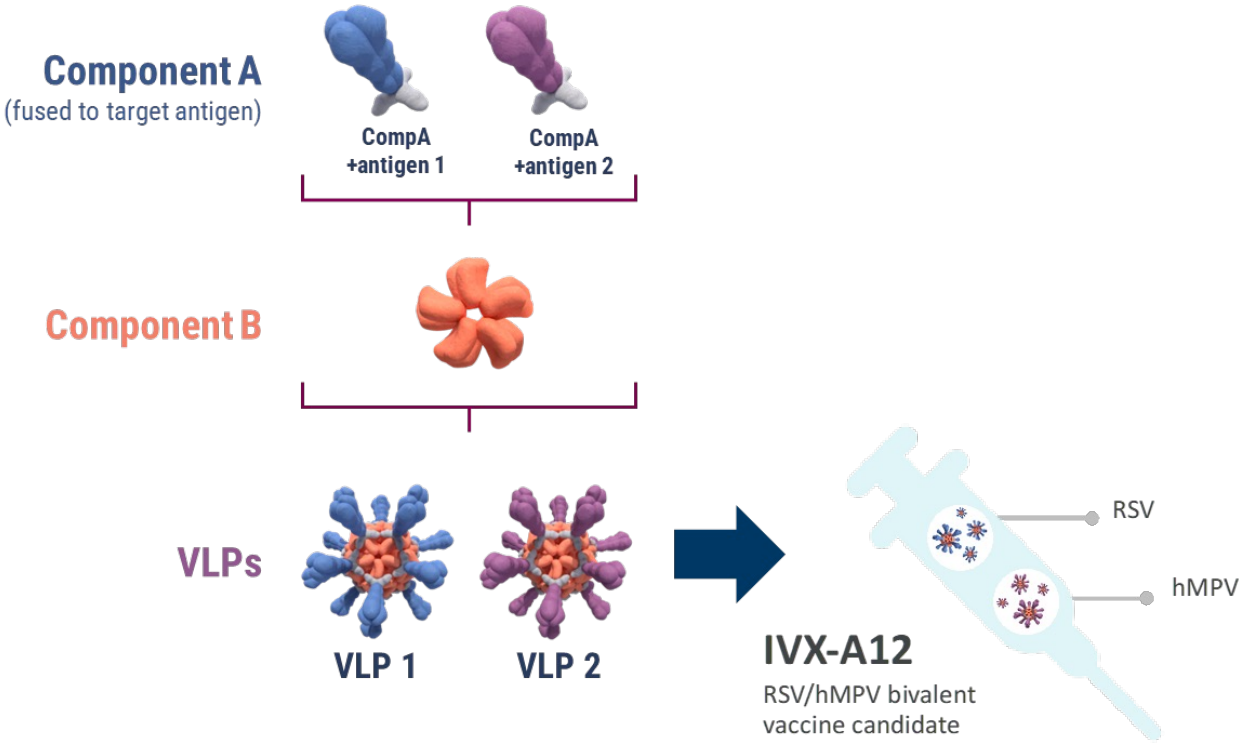
May 2026 (final data collection)

D, day; M, month; Q, quarter; R, randomization; RSV, respiratory syncytial virus; RT-PCR, reverse transcription polymerase chain reaction.
ClinicalTrials.gov. Efficacy, Immunogenicity, and Safety Study of a Respiratory Syncytial Virus Vaccine in Infants and Toddlers (PEARL). Available at: https://classic.clinicaltrials.gov/ct2/show/NCT06252285 (accessed May 2024). Non-contractual: final dates and values may vary.

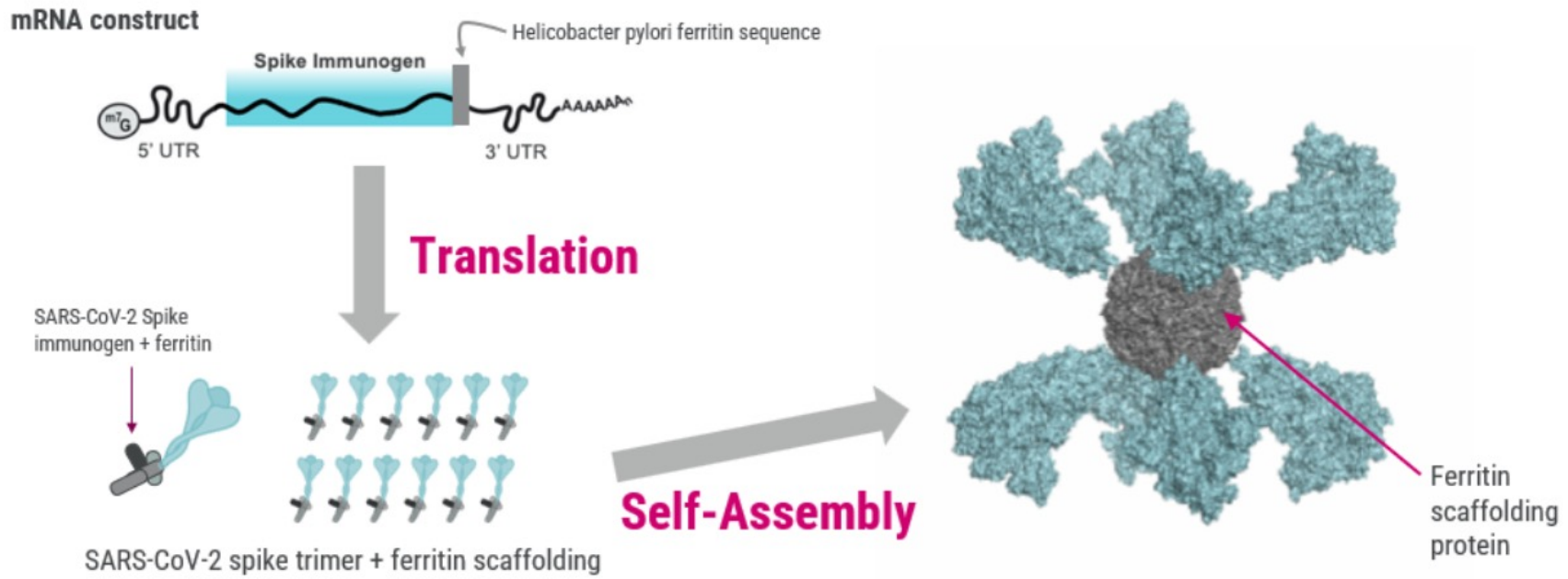
Vaccin combiné RSV-metapneumovirus



These viruses can also **exacerbate** serious conditions such **COPD**, **Asthma**, **Heart Failure**



Vaccin ARNm VLP (Isocavax/AZ)



Ferritin self-assembly concept can be used for other infectious diseases vaccines (e.g., influenza, RSV).

Vaccination contre les infections à pneumocoque de l'adulte

Vaccins pneumocoque

- Vaccins **polyosidiques** développés à partir de la capsule de *S. pneumoniae*
- Contiennent des **sérotypes "choisis"** en fonction**:**
  - de leur fréquence dans les IIP, chez les enfants et les adultes
  - de leur virulence
  - de leur résistance aux antibiotiques, certains sérotypes étant classiquement associés à une sensibilité diminuée aux β-lactamines
- En 2023, 3 vaccins sont disponibles en France :
  - vaccin non conjugué 23 valent (Pneumovax)
  - vaccin conjugué 15 valent (Vaxneuvance) :
    - **AMM européenne le 13 décembre 2021 chez l'adulte,**
    - **extension le 21 octobre 2022 de 6 semaines à moins de 18 ans** : prévention des maladies invasives causées par le *Streptococcus pneumoniae* sérotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 22F, 23F et 33F
  - vaccin conjugué 20 valent (Prevenar 20):
    - **AMM européenne Avril 2022 chez l'adulte**: prévention des maladies invasives et de la pneumonie causés par le *Streptococcus pneumoniae* 13 sérotypes du Prevenar 13 plus 7 sérotypes : 8, 10A, 11A, 12F, 15B, 22F, 33F
    - E**xtension chez l'enfant à partir de 6 semaines le 13 mars 2024**

VPC21 V116 Capvaxive®

AMM USA : 17 juin 2024,
AMM européenne : 24 mars 2025

→ Immunisation active pour la prévention des infections invasives et des pneumonies causées par les sérotypes 3, 6A, 7F, 8, 9N, 10A, 11A, 12F, 15A, deOAc15B*, 16F, 17F, 19A, 20A, 22F, 23A, 23B, 24F, 31, 33F et 35B de *Streptococcus pneumoniae* **chez les personnes âgées de 18 ans et plus**

→ Protéine vectrice CRM_{197}; non adjuvanté

→ Une dose administrée par injection intramusculaire uniquement (seringue préremplie unidose)

→ Co-administration possible avec le vaccin le vaccin quadrivalent contre la grippe (inactivé, à virion fragmenté)

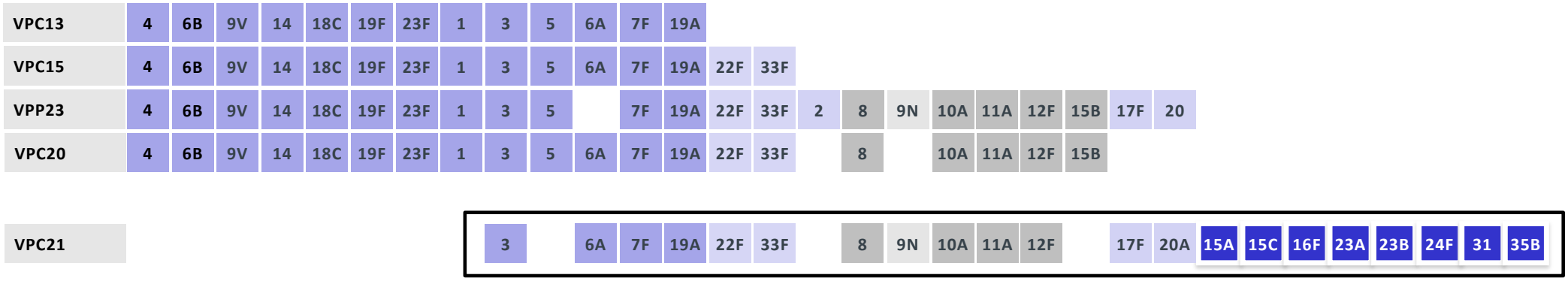
Demande en cours : dépôt dossier VPC21 (V116) HAS en avril 2024

Vaccins pneumocoque et couverture sérotypique

Composition sérotypique

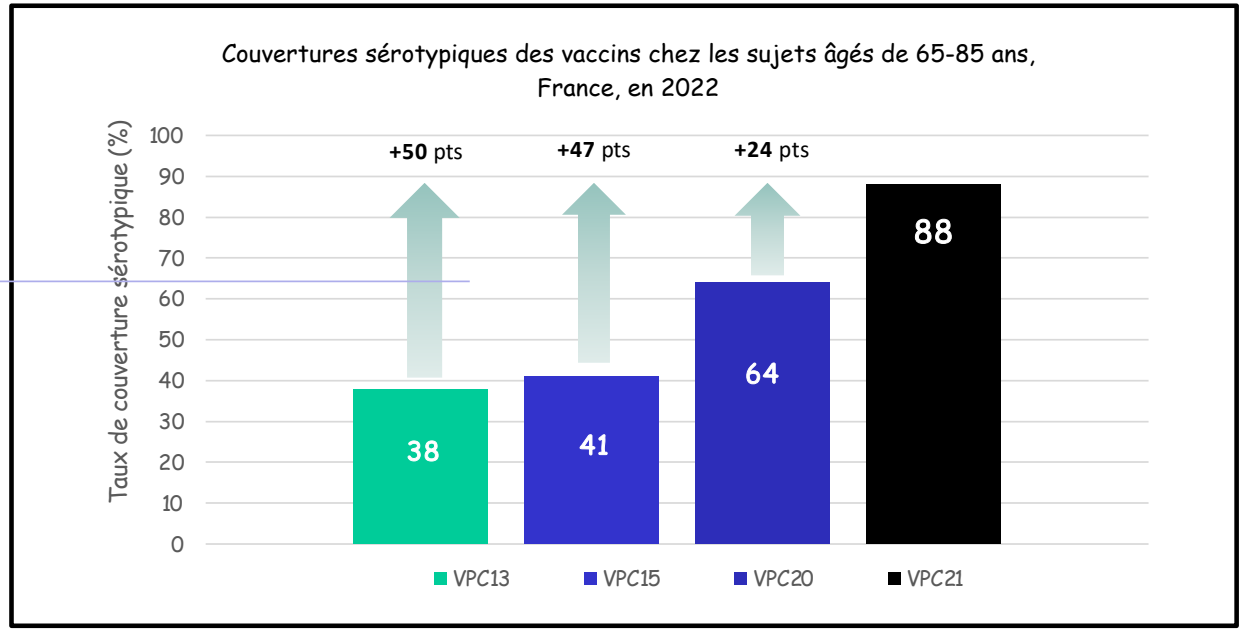
10 sérotypes communs entre VPC21 et VPC20

11 sérotypes spécifiques au VPC21



Vaccins pneumocoque et couverture sérotypique

11 sérotypes spécifiques permettant une couverture d'environ 9 IIP sur 10 de l'adulte



Couverture sérotypique des différents vaccins pour les IIP (méningites et bactériémies) chez les adultes* en 2022 (*R. Cohen, et al. Immunisation contre les Pneumocoques : Quoi de neuf en 2023)*

Vaccination pneumocoque de l'adulte en mars 2025

- Simplification de la vaccination avec le PCV20 (HAS 27 juillet 2023, Stratégie de vaccination contre les infections à pneumocoque)

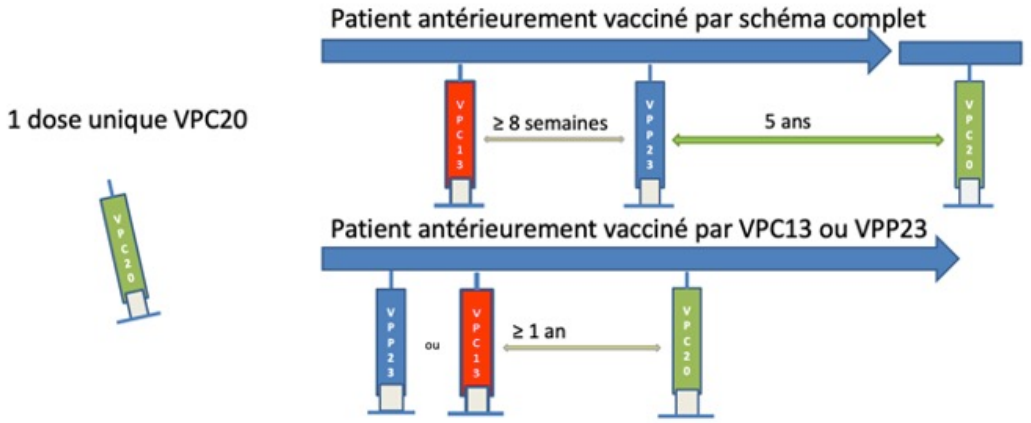


Figure 1 : Schéma vaccinal en fonction de la vaccination antérieure

- Fin 2024:
  - vaccination basée sur l'âge (comme pour la grippe, Covid-19 et zona) à partir de l'âge de 65 ans
  - maintien des recommandations chez les sujets de moins de 65 ans à risque

Autres vaccins

Vaccin ARNm CMV

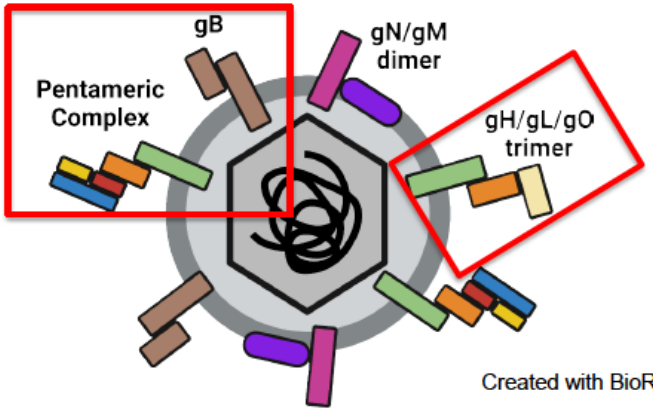
Entry glycoproteins: Glycoprotein B (gB) and pentameric complex (PC) are targets of current generation CMV vaccines

HCMV Glycoprotein complexes:

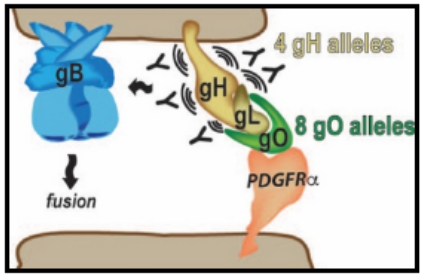
- gB
  - Required for entry into all cells
  - Primarily non-neutralizing Abs
  - Potent neutralization against AD2 site 1

- Pentameric complex (PC)
  - Epithelial/endothelial cell entry/tropism
  - Target of potent neutralizing Abs (primarily to UL128-131)

- gH/gL/gO
  - Part of entry/fusion "complex"
  - Target of neutralizing Abs (gH vs gO?)
  - Susceptible to allelic diversity

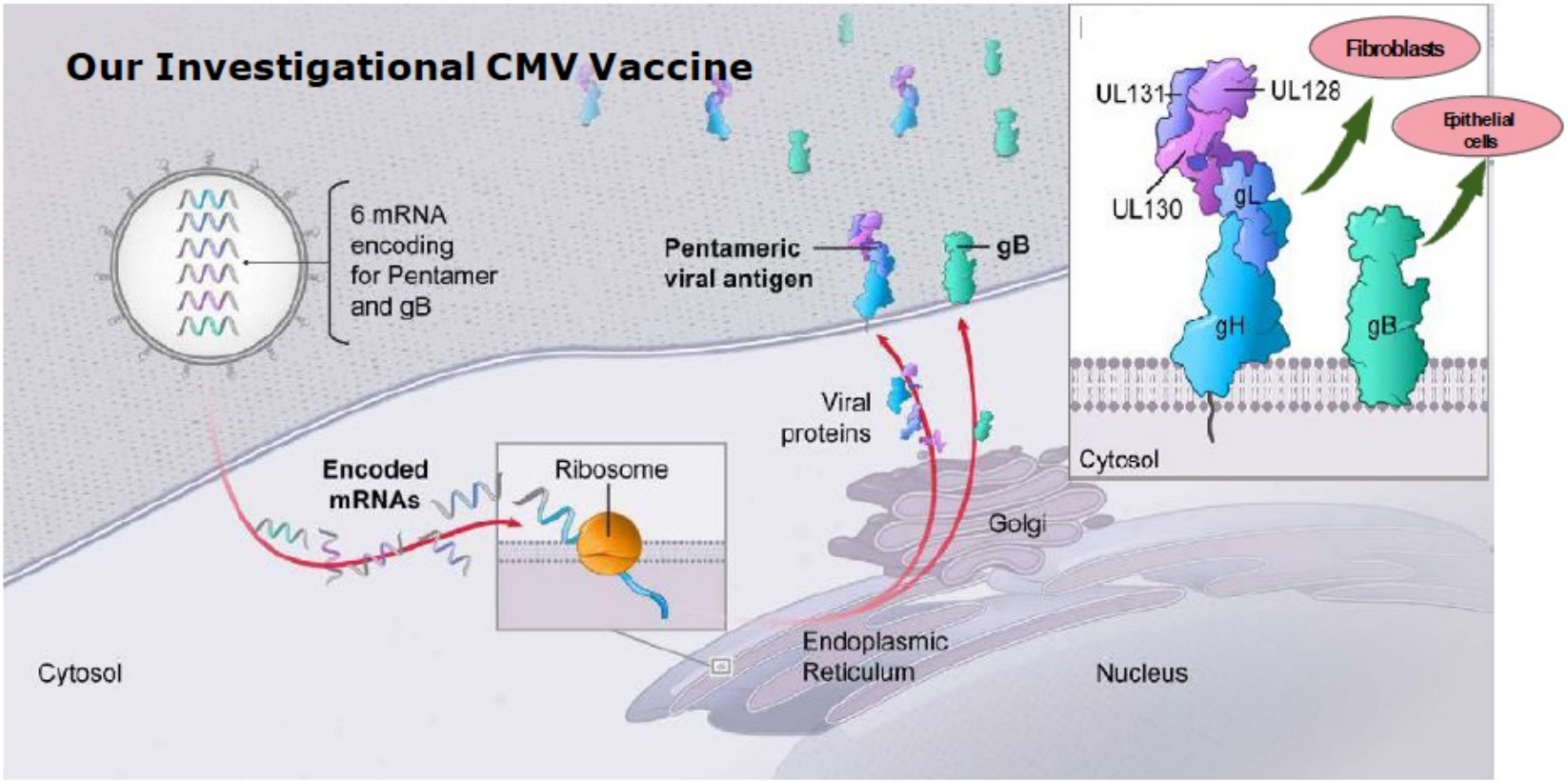


Created with BioRender.com



Brent Rychman

Vaccin ARNm CMV



Vaccin CMV (mRNA-1647) : Essai clinique de Phase 3

- Designed to evaluate the efficacy, safety and immunogenicity of mRNA-1647 in healthy females aged 16–40 years

Design
Randomized, observer-blind, placebo-controlled study

Participants
Healthy females aged 16–40 years who are not pregnant or planning to become pregnant within the next 9 months

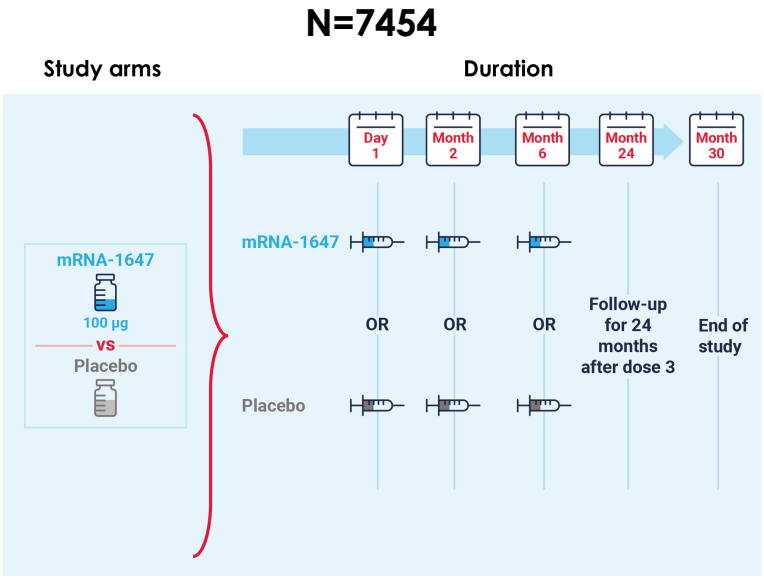
Participants aged ≥20 years who have or anticipate having direct exposure to ≥1 child aged ≤5 years

Vaccination schedule
Three doses of mRNA-1647 or placebo (Day 1, 57 and 169)

Primary efficacy endpoint
Seroconversion in CMV-seronegative women

Duration
24-month follow-up after dose 3
Estimated study completion: April 2026

Site location
296 sites globally



This Phase 3 pivotal registration study will provide comprehensive data on efficacy and safety required to support marketing authorization applications by regulatory authorities

Vaccins contre le Chikungunya

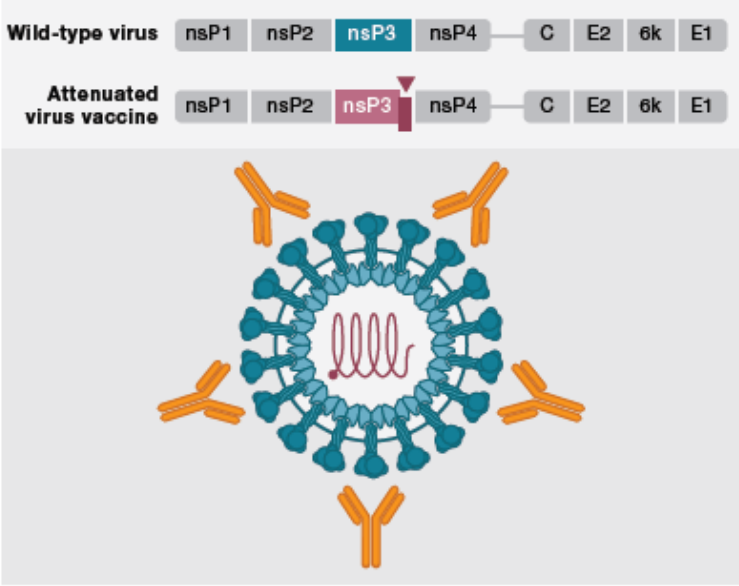
Vaccin
Chikungunya
IXCHIQ

Cell
Leading Edge
Bench to Bedside

CellPress

Live-attenuated chikungunya virus vaccine

Lisa F.P. Ng[1] and Laurent Rénia[1,2]
[1]A*STAR Infectious Diseases Labs (ID Labs), A*STAR, Singapore, Singapore; [2]Lee Kong Chian School of Medicine, Nanyang Technological University,



Ixchiq is the first licensed vaccine for prevention of chikungunya virus (CHIKV) infection. The vaccine is a live-attenuated virus with a large deletion of 60 amino acids in the nSP3 protein, which is part of the virus replication complex, and thus replicates less efficiently than wild-type CHIKV. Delivered as a single 0.5 mL dose, it induces high levels of neutralizing antibodies in humans against CHIKV.

Vaccin Chikungunya : IXCHIQ

- Vaccin vivant atténué
- Essai de phase 3 conduit aux USA
- 4128 adultes randomisés 3:1 vaccin placebo
- Objectif principal: immunogenicité : % de participants ayant développé des Ac neutralisants 28 jours après vaccination

Safety and immunogenicity of a single-shot live-attenuated chikungunya vaccine: a double-blind, multicentre, randomised, placebo-controlled, phase 3 trial

Martina Schneider, Marivic Narciso-Abraham, Sandra Hadl, Robert McMahon, Sebastian Toepfer, Ulrike Fuchs, Romana Hochreiter, Annegret Bitzer, Karin Kosulin, Julian Larcher-Senn, Robert Mader, Katrin Dubischar, Oliver Zoihsl, Juan-Carlos Jaramillo, Susanne Eder-Lingelbach, Vera Buerger, Nina Wressnigg

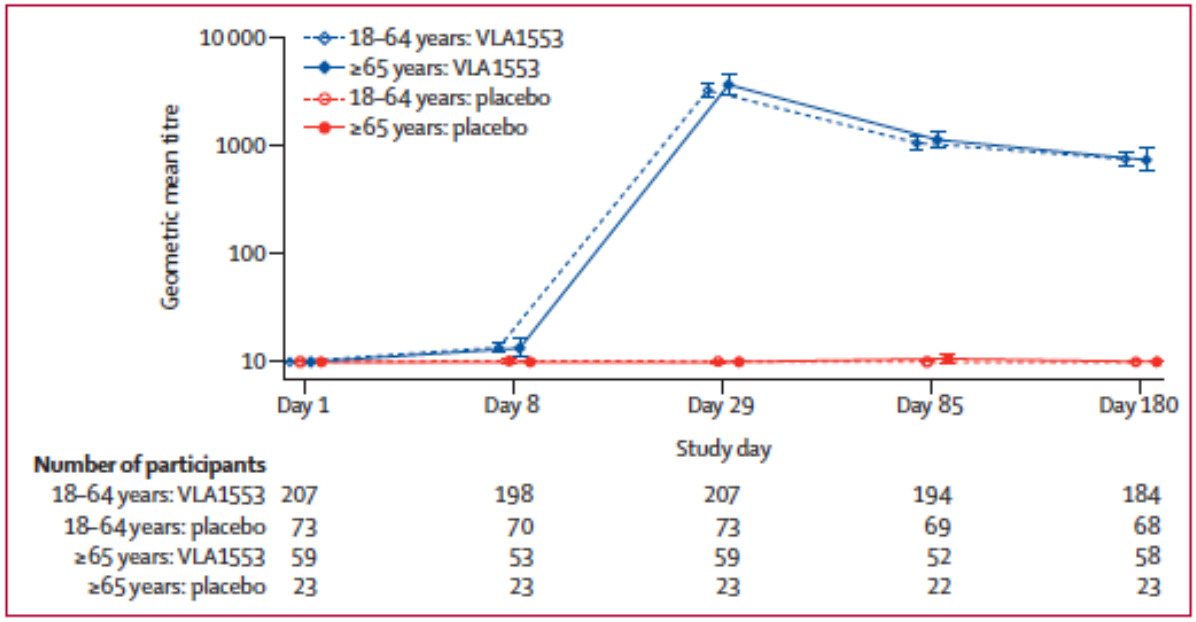


Figure 2: **Assessment of neutralising antibodies after vaccination**

After a single vaccination, VLA1553 induced seroprotective chikungunya virus neutralising antibody levels in 263 (98·9%) of 266 participants in the VLA1553 group (95% CI 96·7–99·8; p<0·0001) 28 days post-vaccination, independent of age. VLA1553 was generally safe with an adverse event profile similar to other licensed vaccines and

cet 2023; 401: 2138–47
Published Online June 12, 2023 https://doi.org/10.1016/0140-6736(23)00641-4

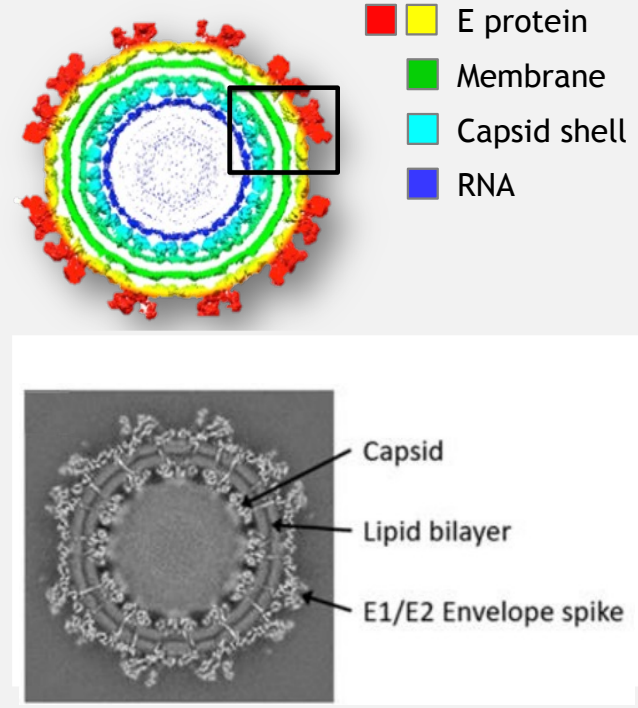
CHIKV VLP VIMKUNYA

Recombinant VLP vaccine comprising three CHIKV structural proteins:

- **Capsid**
- **Envelope 1** – a class II fusion glycoprotein that mediates membrane fusion during viral infection of cells
- **Envelope 2** – a type I transmembrane glycoprotein responsible for receptor binding to cells during viral replication

- Intramuscular route of administration
- Single 40 µg VLP dose (0.8 mL) in a prefilled syringe

CHIKV VLP vaccine is **adjuvanted with aluminium hydroxide**



CHIKV VLP vaccine

Cryo-electron microscopy reconstruction of CHIKV VLP[2]

Safety and immunogenicity of an adjuvanted chikungunya virus virus-like particle (CHIKV VLP) vaccine in previous recipients of other alphavirus vaccines versus alphavirus vaccine-naive controls: an open-label, parallel-group, age-matched, sex-matched, phase 2 randomised controlled study

Melinda J Hamer*, James M McCarty*, Benjamin C Pierson, Jason A Regules, Jason Mendy, Aaron D Sanborn, Christina L Gardner, Melissa K Gregory, Dani L Liggett, Pamela J Glass, Neha Ghosh, Sarah Royalty Tredo, Kelly L Warfield, Crystal W Burke, Christine I Lisa Bedell, Jason S Richardson

Lancet Microbe 2025; 6: 101000

Published Online February 12, 2025

https://doi.org/10.1016/j.lanmic.2024.101000

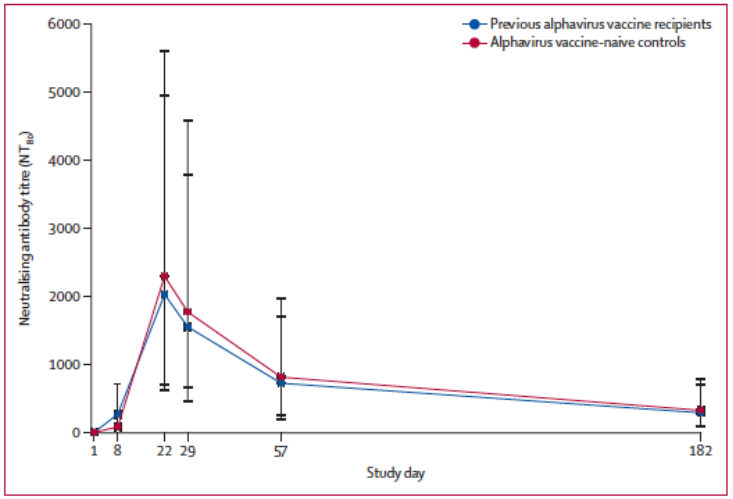
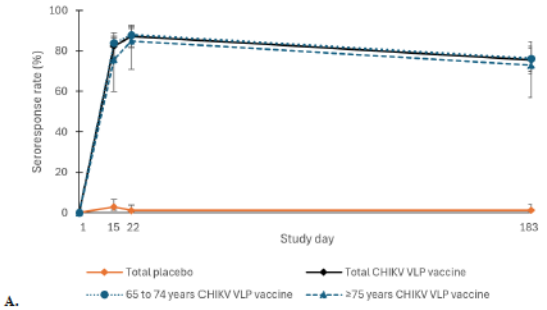


Figure 1: Geometric mean anti-chikungunya virus neutralising antibody titres (immunogenicity evaluable population)
Error bars show 95% CIs.

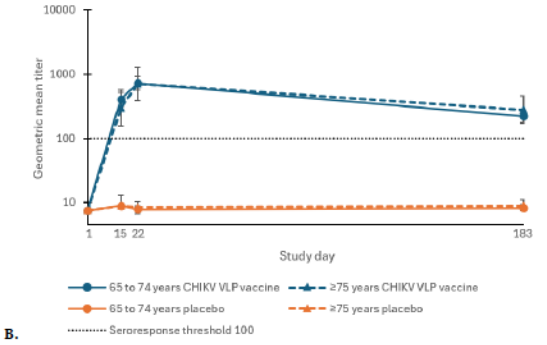
Chikungunya Virus VLP Vaccine: Phase 3 Trial in Adults ≥65 Years of Age

Lauren C. Tindale, PhD[1], Jason S. Richardson, PhD[1], Debbie M. Anderson, MS[1], Jason Mendy, MS[2], Sufia Muhammad, MD[2], Tobi Loreth, BA[1], Sarah Royalty Tredo, MBA[3], Roshan Ramanathan, MD, MPH[3], Victoria A. Jenkins, PhD[4], Lisa Bedell, MA[2], Patrick Ajiboye, MD[2], for the EBSI-CV-317-005 Study Group*

[1] Bavarian Nordic Canada Inc., Toronto, Ontario, Canada
[2] Bavarian Nordic Inc., San Diego, California, USA
[3] Emergent BioSolutions, Gaithersburg, Maryland, USA
[4] Bavarian Nordic Belgium, Brussels, Belgium



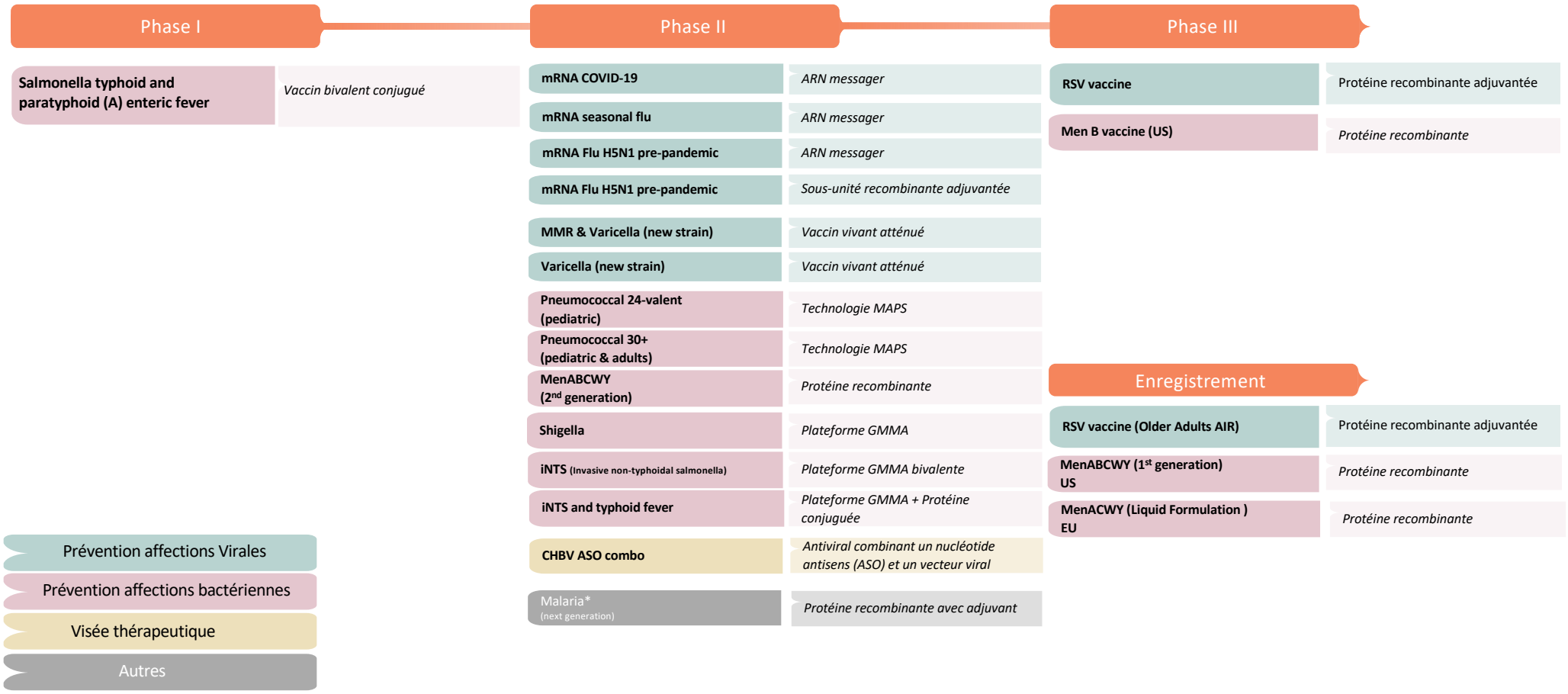
A.



B.

AMM > 12 ans
FDA: février 2024
EMA: 23 mars 2025

Candidats Vaccins GSK en cours de développement



*Use of a delayed fractional dose regimen

AIR: At Increased Risk; ASO, antisense oligonucleotide; CHBV, chronic hepatitis B virus; CMV, cytomegalovirus; COVID-19, coronavirus disease 2019; GMMA, generalized modules for membrane antigens; HBV, hepatitis B virus; HPV, human papillomavirus; HSV, herpes simplex virus; iNTS, invasive non-typhoidal salmonella; MAPS, Multiple Antigen Presenting System; MenABCWY, meningococcal A, B, C, W, and Y strains; MenB, meningococcal B strain; MMRV, measles, mumps, rubella, and varicella; RSV, respiratory syncytial virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2;

GSK, 2024. https://www.gsk.com/en-gb/innovation/pipeline/?infectious-diseases (URL accessed June 2024)