Le futur des vaccinations

Pr Odile Launay
Hôpital Cochin, Paris

Cours approfondi de chimiothérapie infectieuse de vaccinologie

Veyrier du Lac, 18 novembre 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

Table 1. Outline of the development of human vaccines

Live attenuated	Killed whole organisms	Purified proteins or polysaccharides	Genetically engineered
18th Century			
Smallpox (1798)			
19th Century			
Rabies (1885)	Typhoid (1896)		
	Cholera (1896)		
	Plague (1897)		
Early 20th Century, first half			
Tuberculosis (bacille Calmette–Guérin) (1927)	Pertussis (1926)	Diphtheria toxoid (1923)	
Yellow fever (1935)	Influenza (1936)	Tetanus toxoid (1926)	
	Rickettsia (1938)		
20th Century, second half			
Polio (oral) (1963)	Polio (injected) (1955)	Anthrax secreted proteins (1970)	Hepatitis B surface antigen recombinant (1986)
Measles (1963)	Rabies (cell culture) (1980)	Meningococcus polysaccharide (1974)	Lyme OspA (1998)
Mumps (1967)	Japanese encephalitis (mouse brain) (1992)	Pneumococcus polysaccharide (1977)	Cholera (recombinant toxin B) (1993)
Rubella (1969)	Tick-borne encephalitis (1981)	*Haemophilus influenzae* type B polysaccharide (1985)	
Adenovirus (1980)	Hepatitis A (1996)	*H.influenzae* type b conjugate (1987)	
Typhoid (*Salmonella* TY21a) (1989)	Cholera (WC-rBS) (1991)	Typhoid (Vi) polysaccharide (1994)	
Varicella (1995)	Meningococcal conjugate (group C) (1999)	Acellular pertussis (1996)	
Rotavirus reassortants (1999)		Hepatitis B (plasma derived) (1981)	
Cholera (attenuated) (1994)			
Cold-adapted influenza (1999)			
21st Century			
Rotavirus (attenuated and new reassortants) (2006)	Japanese encephalitis (2009) (Vero cell)	Pneumococcal conjugates* (heptavalent) (2000)	Human papillomavirus recombinant (quadrivalent) (2006)
Zoster (2006)	Cholera (WC only) (2009)	Meningococcal conjugates* (quadrivalent) (2005)	Human papillomavirus recombinant (bivalent) (2009)
		Pneumococcal conjugates* (13-valent) (2010)	Meningococcal group B proteins (2013)

Choléra, grippe Chikungunya

PCV15, PCV 20, PCV21

HPV9, zona, grippe (HA) VRS, Covid-19, Chikungunya

100 Years 1915-2015

SPECIAL FEATURE: PERSPECTIVE

History of vaccination

Stanley Plotkin[1]

Department of Pediatrics, University of Pennsylvania, Philadelphia, PA 19104

PNAS | **August 26, 2014** | vol. 111 | no. 34 | **12283–12287**

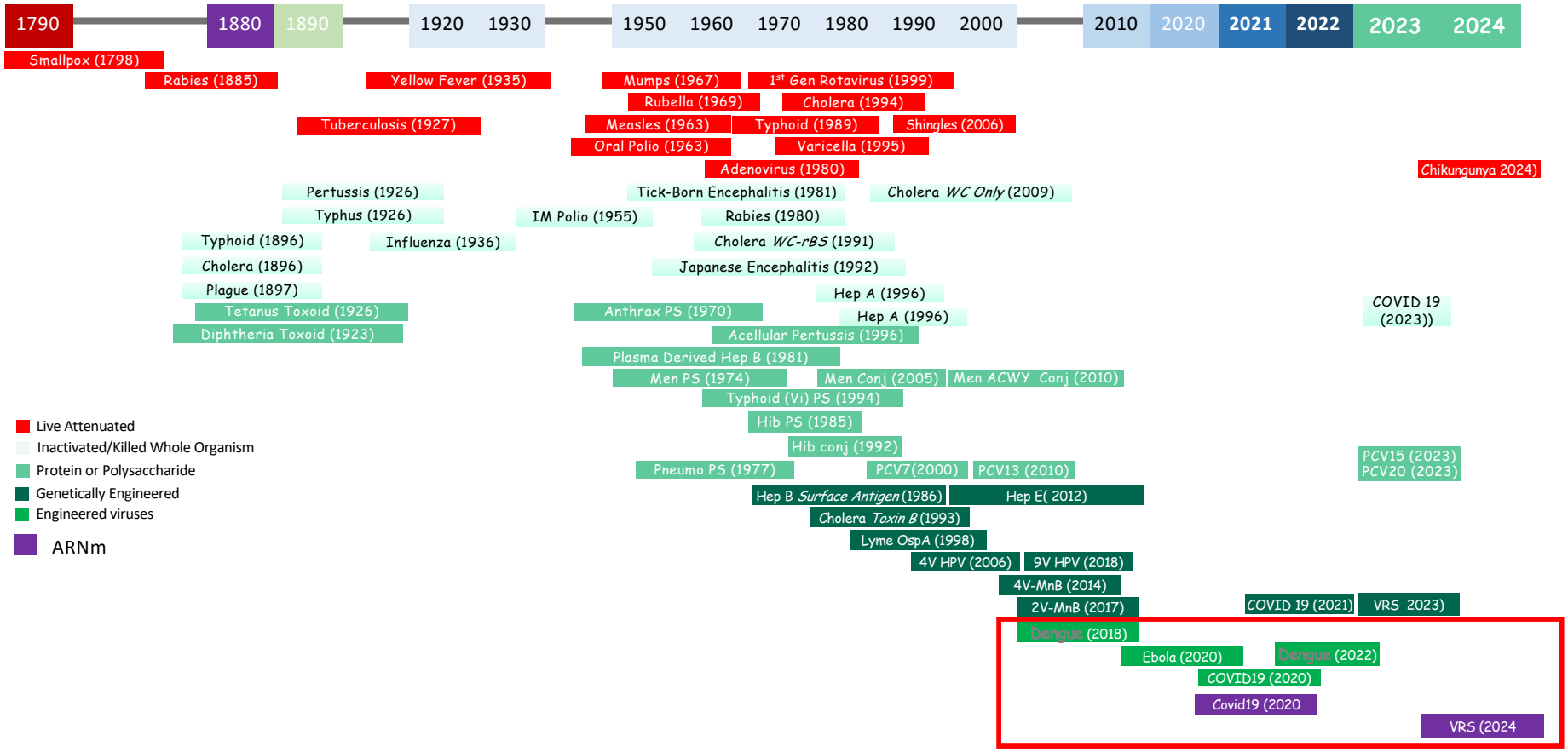
Vaccins vectorisés :

- 2018: Dengue (vaccin chimérique YFV)
- 2020 : Ebola
- 2021: Covid-19
- 2022: Dengue (vaccin chimérique, serotype 2 atténué)

Vaccins ARNm

- 2020: Covid 19
- 2024: VRS

Vaccins disponibles et évolution des technologies vaccinales



Grippe, Covid-19 et autres virus respiratoires

Les vaccins grippaux

- Existent depuis 1944-45 (J Salk)

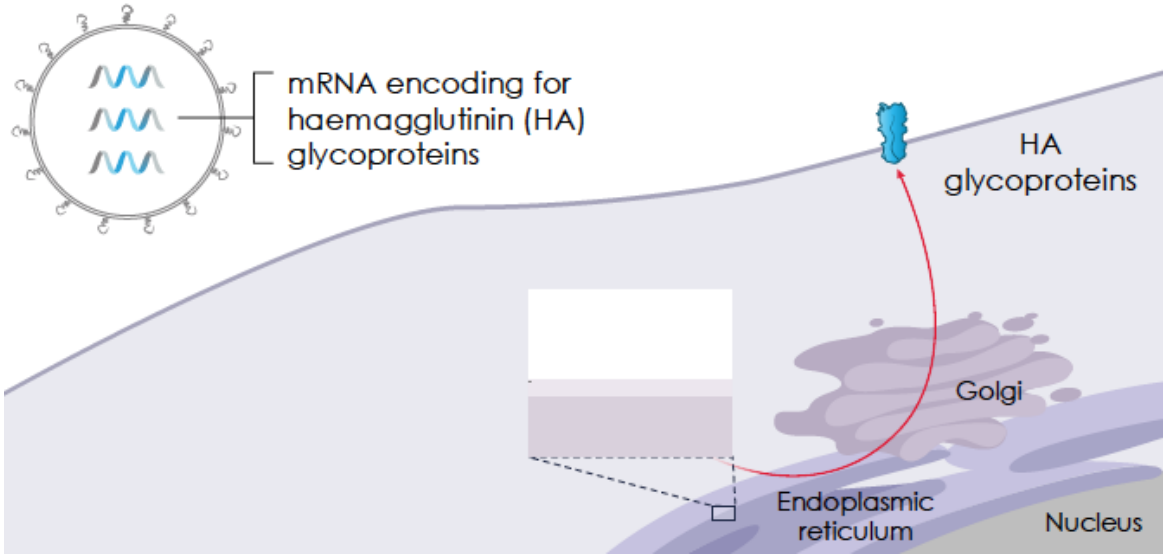
- **Les vaccins disponibles en France sont des vaccins inactivés** préparés à partir de virus cultivés sur œufs de poule embryonnés ou sur cultures cellulaires,
  - **Trivalents** : 2 souches de sous types A (H1N1 et H3N2) et 1 souches de lignés B (B/Victoria)
  - Vaccins standard dose, AMM à partir de l'âge de 6 mois : Influvac (Viatris), Vaxigrip (Sanofi), Flucelvax (CSL Sequirus)
  - **Des vaccins dits 'augmentés', remboursables à partir de l'âge de 65 ans** :
    - vaccin 'haute dose' (4 fois plus dosé) **Efluelda** (Sanofi): AMM chez les personnes de 60 ans et plus,
    - vaccin adjuvanté (MF59), **Fluad** (CSL Sequirus): AMM chez les personnes de 50 ans et plus.

- **Autres vaccins grippaux autorisés en Europe mais non disponibles pour la campagne 2025-2026 :**
  - **Vaccin vivant atténué** : **Fluenz** (Astra Zeneca), AMM chez l'enfant à partir de 2 ans et jusqu'à 18 ans
  - **Vaccin à base de protéine recombinante** (HA) 3 fois plus dosée : **Flublok ou Supemtek** (Sanofi)

Vaccin grippe ARNm

- ARN codant pour les HA des 3 virus grippaux recommandés

- Intérêt potentiel de l'ARNm pour la vaccination grippe:
  - rapidité de production
  - moins de risque de mismatch
  - bonne réponse immunitaire chez les sujets agés



Vaccin grippe ARNm (Moderna): mRNA-1010

Moderna Seasonal Influenza (mRNA-1010) Program Updates

Study Name	Phase	Purpose	Comparator	Recruitment Status (Number of Participants)	Safety Follow-Up Period	NCT
mRNA-1010						
1010 P101	Phase 1/2	Dose finding (immunogenicity) and safety in adults 18+ years (SH)	Placebo Afluria	**Study Completed** (885)	6 months	NCT04956575
1010 P301	Phase 3	Safety and immunogenicity in adults 18+ years	Fluarix	**Study Completed** (6000)	1 year	NCT05415462
1010 P302	Phase 3	Safety and efficacy in preventing seasonal influenza in adults 50+ years	Fluarix	**6-mo Follow up Completed, 1-yr Follow up Completed** (22,502)	1 year	NCT05566639
1010 P303	Phase 3	Safety and humoral immunogenicity relative to active comparator in adults 18+ years	Fluarix / Fluzone HD	**Recruitment Completed, Follow up Completed** (8422)	6 months	NCT05827978
1010 P304	Phase 3	Safety, efficacy and immunogenicity in preventing seasonal influenza in adults 50+ years	Fluarix	**Recruitment ongoing (56,000)**	6 months / End of Flu season	NCT06602024

mRNA-1010 is an investigational product and has not been approved or authorized by any country for any use.

moderna

Vaccin grippe ARNm (mRNA-1010) *vs* vaccin SD : immunogénicité

Vaccine 50 (2025) 126847

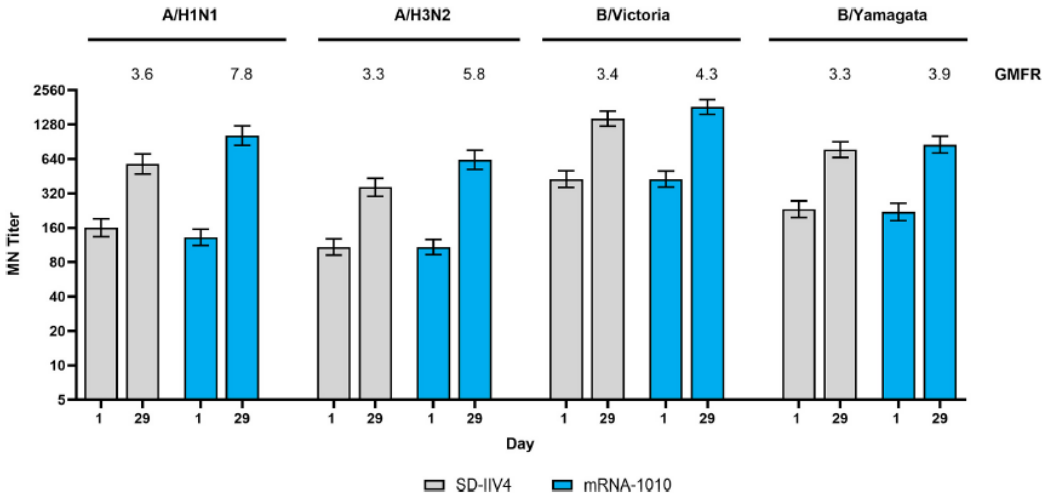
Contents lists available at ScienceDirect

Vaccine

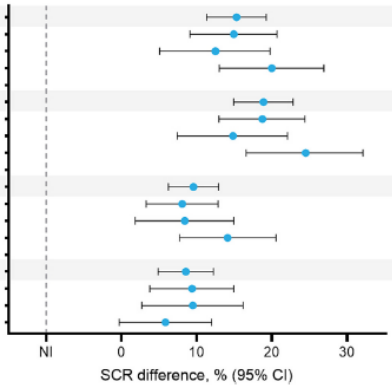
journal homepage: www.elsevier.com/locate/vaccine

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 grippe ARNm (mRNA-1010) *vs* vaccin SD : réactogénicité

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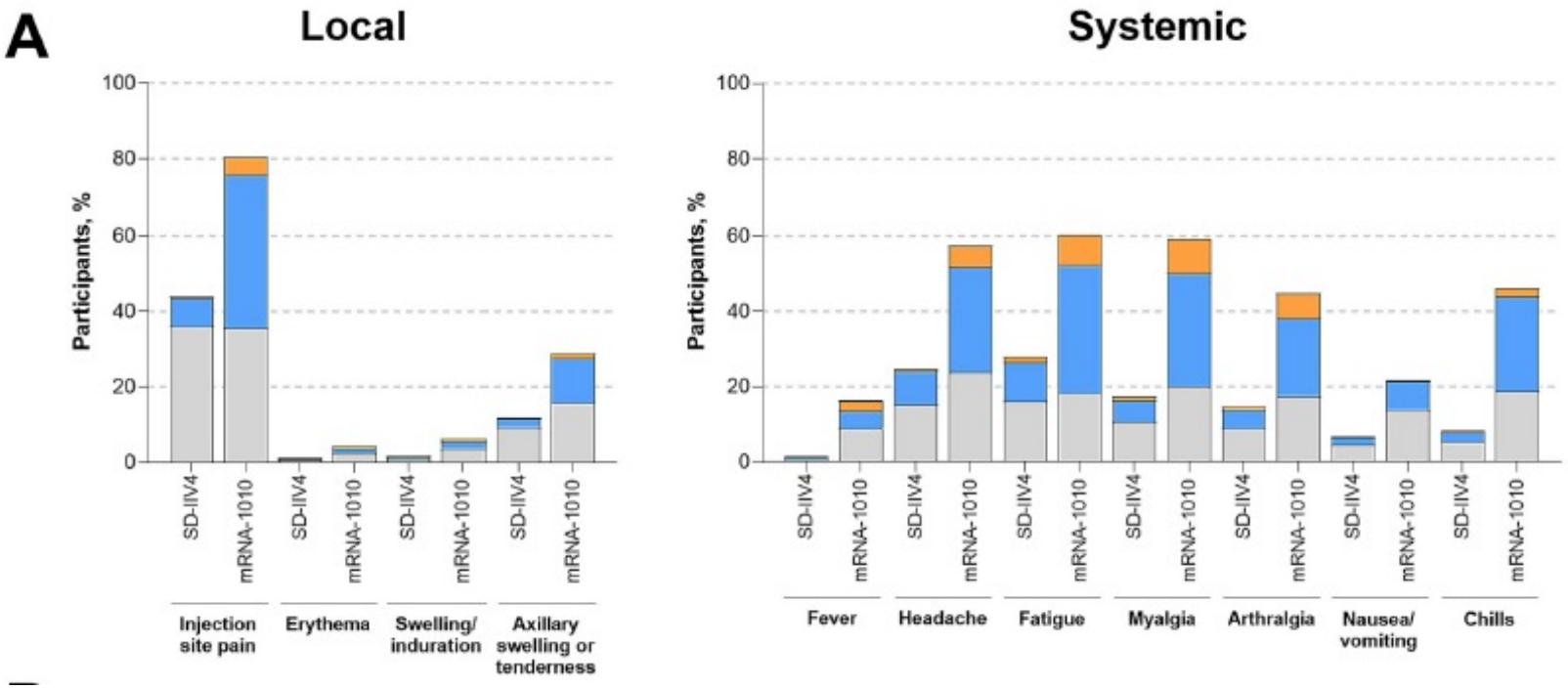
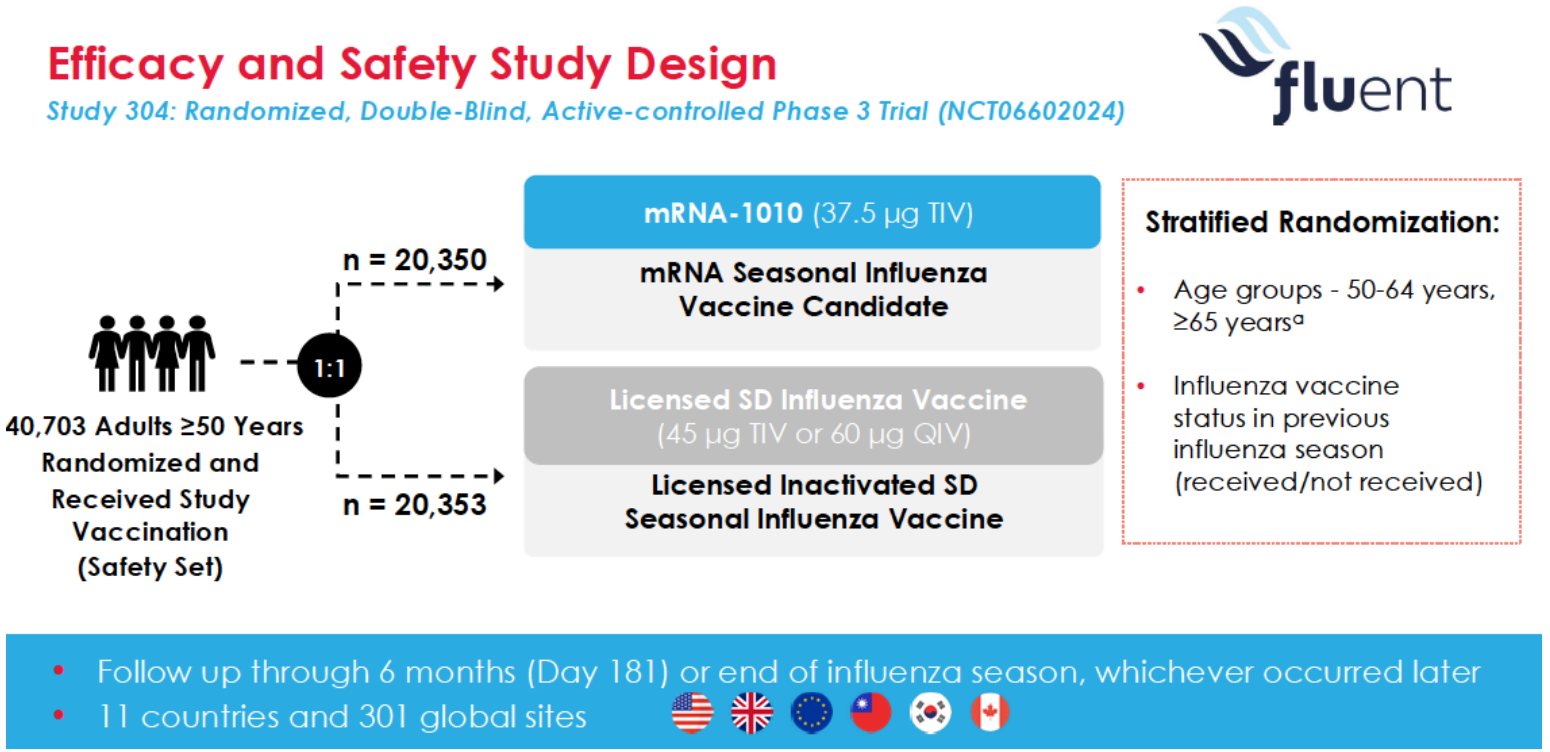


Vaccin grippe ARNm (mRNA-1010) *vs* vaccin SD : efficacité clinique



LB IDweek 2025

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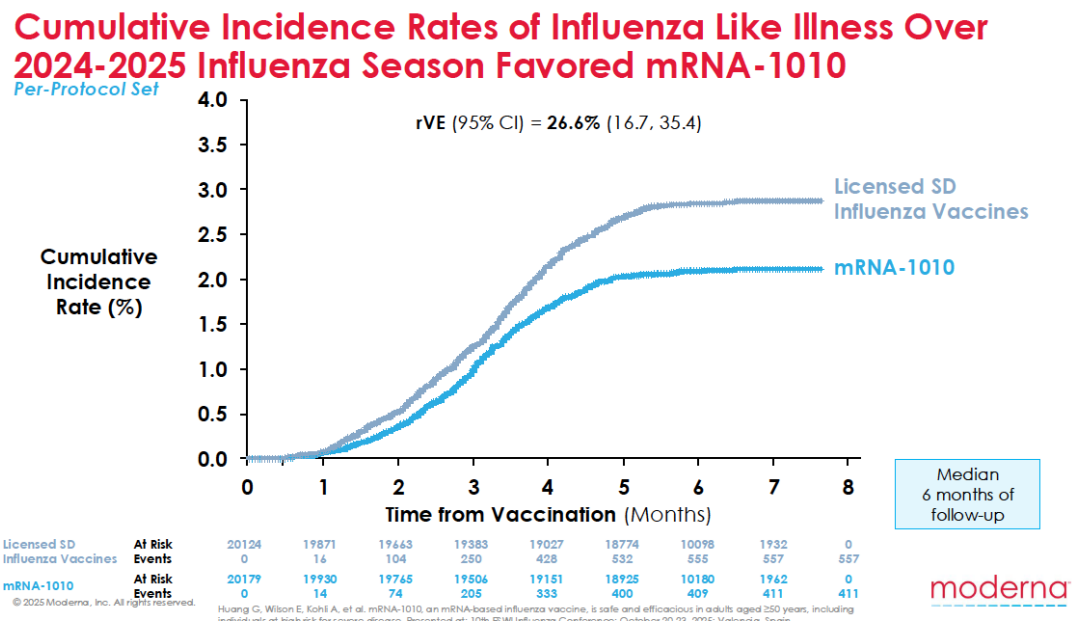

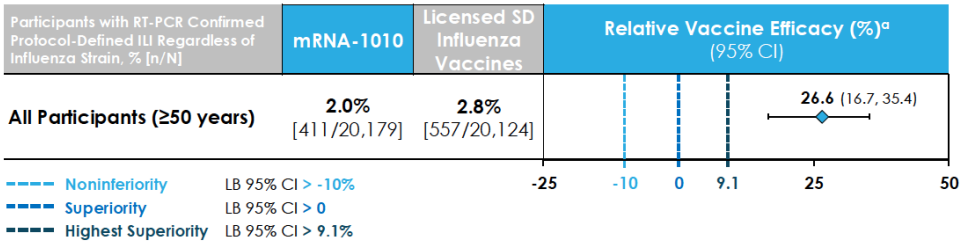

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Vaccin grippe ARNm (mRNA-1010) *vs* vaccin SD : efficacité clinique

Participants With ILI[a] by Age, % [n/N]	mRNA-1010	Licensed SD Influenza Vaccines	Relative Vaccine Efficacy, (%)[b] (95% CI)
50-64 Years	**2.2%** [229/10,542]	**2.9%** [307/10,501]	**26.1** (12.3, 37.7)
≥65 Years	**1.9%** [182/9637]	**2.6%** [250/9623]	**27.4** (12.1, 40.0)
65-74 Years	**1.9%** [138/7307]	**2.6%** [191/7289]	**28.0** (10.4, 42.2)
≥75 Years	**1.9%** [44/2330]	**2.5%** [59/2334]	**25.3** (-10.4, 49.5)

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Participants With ILI[a] by Influenza Strain,% [n/N]	mRNA-1010	Influenza Vaccines	Relative Vaccine Efficacy (%)[b] (95% CI)
Influenza A H1N1	**1.1%** [223/20,179]	**1.6%** [315/20,124]	**29.6** (16.4, 40.7)
Influenza A H3N2	**0.8%** [158/20,179]	**1.0%** [202/20,124]	**22.2** (4.3, 36.9)
Influenza B Victoria	**0.1%** [25/20,179]	**0.2%** [35/20,124]	**29.1** (-18.5, 57.5)

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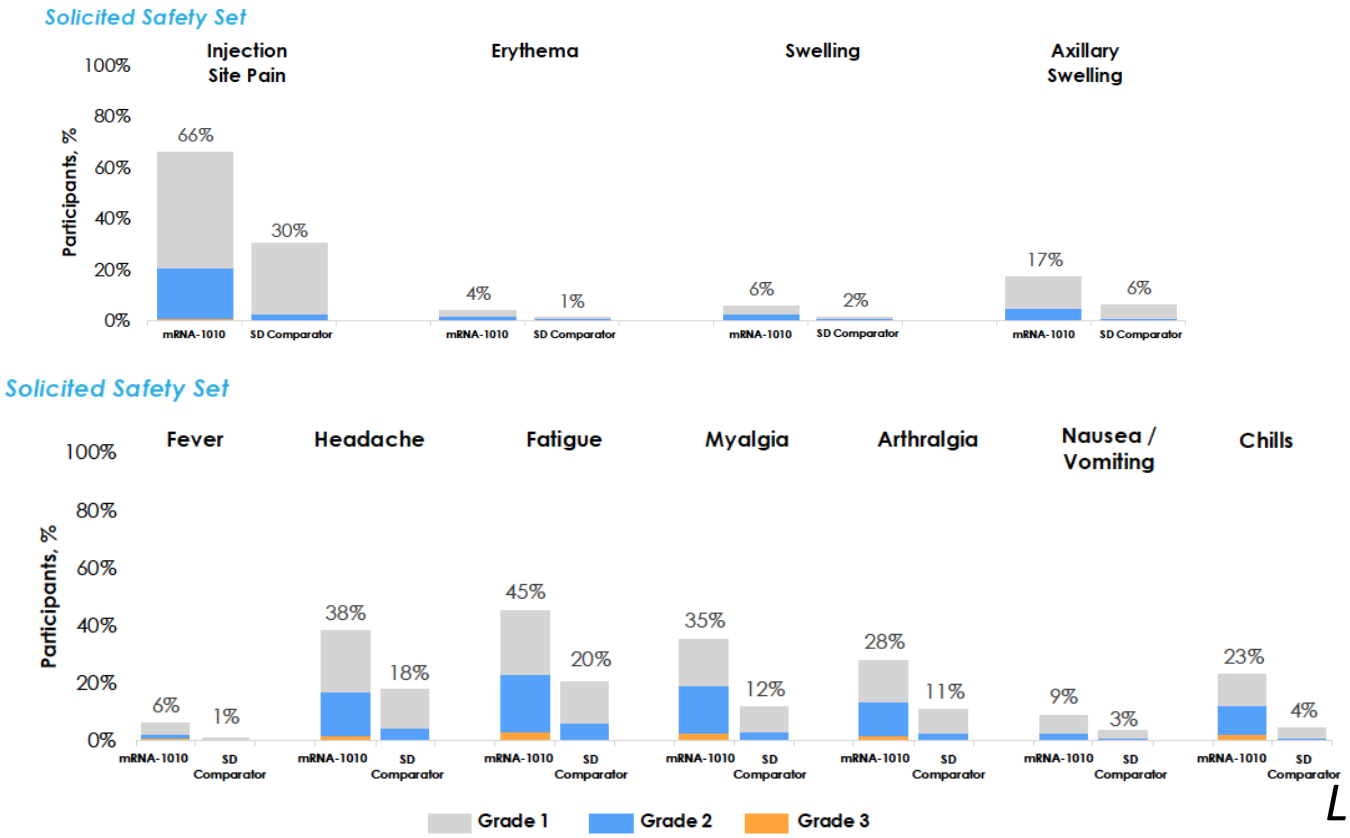
Vaccin grippe ARNm (mRNA-1010) *vs* vaccin SD : réactogénicité



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Vaccin grippe universel?

- Candidat vaccin français (Osivax)
- Composé de la nucléoprotéine (protéine conservée indispensable à la réplication du virus grippal) auto assemblée sur l'oligoDOM OVX313

vaccines MDPI

Article

Evaluation of Safety, Immunogenicity and Cross-Reactive Immunity of OVX836, a Nucleoprotein-Based Universal Influenza Vaccine, in Older Adults

Bart Jacobs [1], Isabel Leroux-Roels [1], Jacques Bruhwyler [2,*], Nicola Groth [2], Gwenn Waerlop [1], Yorick Janssens [1], Jessika Tourneur [2], Fien De Boever [1], Azhar Alhatemi [1], Philippe Moris [2], Alexandre Le Vert [2], Geert Leroux-Roels [1] and Florence Nicolas [2]

Vaccines **2024**, *12*, 1391. https://doi.org/10.3390/vaccines12121391

Vaccin grippe universel?

- Candidat vaccin français (Osivax)
- Composé de la nucléoprotéine (protéine conservée indispensable à la réplication du virus grippal) auto assemblée sur l'oligoDOM OVX313
- Induit une forte réponse humorale et cellulaire dirigée contre la nucléoprotéine
- 1ere données d'efficacité (*Lancet Inf Dis 2023*)
- Essai de phase 2b en cours
- Pourrait être utilisé en association avec un vaccin classique

vaccines MDPI

Article

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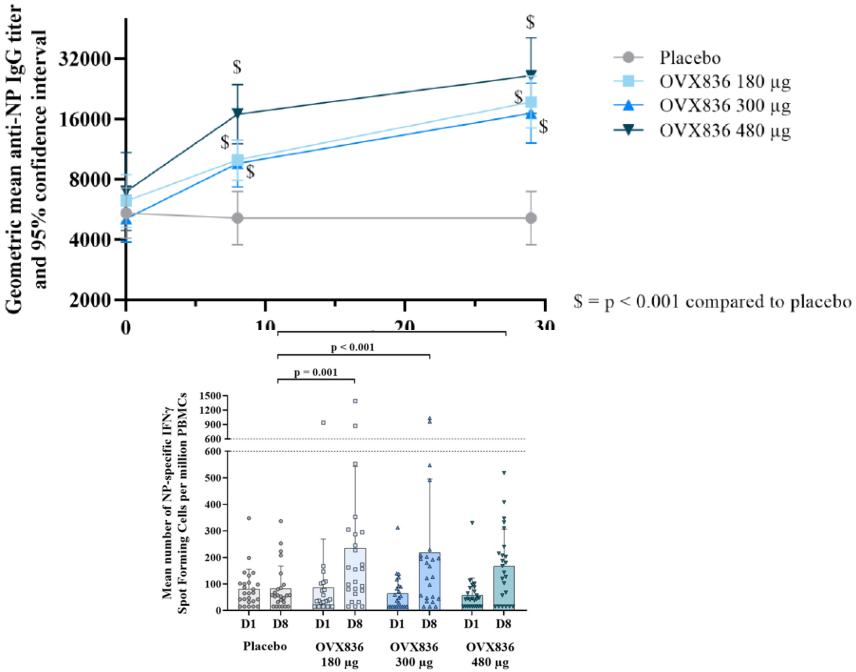


Figure 2. Number of nucleoprotein (NP)-specific IFNγ spot-forming cells (SFCs) per million peripheral blood mononuclear cells (PBMCs) after a single intramuscular administration of OVX836 (180 µg, 300 µg or 480 µg) or placebo. Data are mean (standard deviation) and individual values on Day 1

CD388: un traitement préventif prometteur

- *Formulation injectable à longue demi-vie*
- *Zanamivir conjugué au fragment Fc IgG1 modifié*

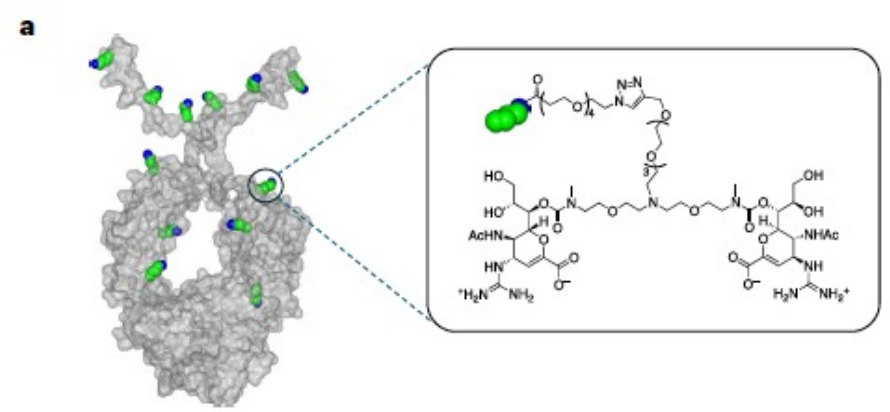
nature microbiology

Article

https://doi.org/10.1038/s41564-025-01955-3

Drug–Fc conjugate CD388 targets influenza virus neuraminidase and is broadly protective in mice

Nature Microbiology | Volume 10 | April 2025 | 912–926



CD388: un traitement préventif prometteur

- *Formulation injectable à longue demi-vie*
- *Zanamivir conjugué au fragment Fc IgG1 modifié*
- *Activité à large spectre sur virus grippaux in vitro et in vivo chez la souris*
- ***Intérêt en prévention en complément du vaccin en particulier en cas d'immunodépresssion***

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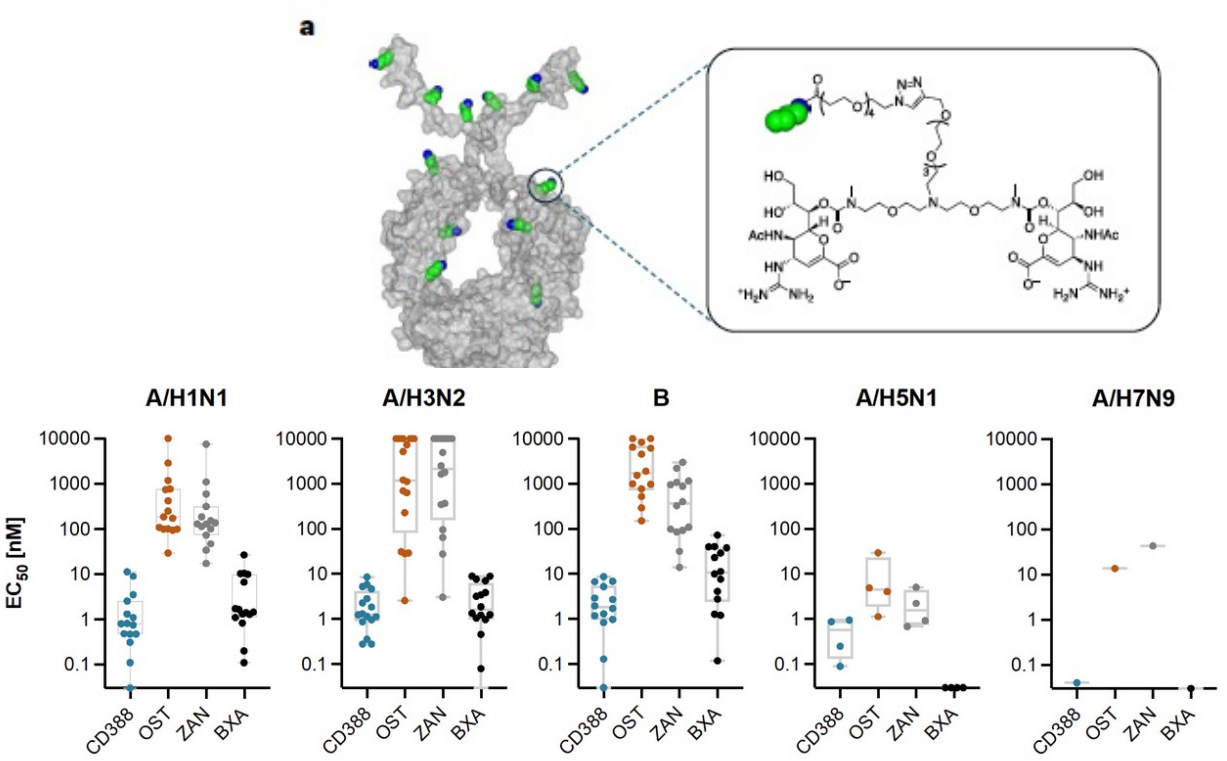


CD388 chez l'homme : résultats de l'essai de phase 2b

- Essai randomisé prospectif vs placebo (USA,UK)
- Une injection
- 4726 adultes 18-50 ans
- Efficacité sur les grippes confirmées virologiquement
- Phase 3 en cours

Primary Efficacy Analysis:

		150 mg N= 1175[3] n (%)	300 mg N = 1192[3] n (%)	450 mg N = 1187[3] n (%)	Placebo N = 1172[3] n (%)
Primary Endpoint[1]	Number of Participants Protocol-Defined ILI[2]	14 (1.2%)	13 (1.1%)	8 (0.7%)	33 (2.8%)
	Prevention Efficacy	57.7%	61.3%	76.1%	–
	95% CI (%)	21.1, 78.9	27.0, 81.2	49.3, 89.9	–
	p-value	0.0050	0.0024	<0.0001	–

ILI, influenza like illness; CI, confidence interval

1. Statistical significance for grouped 300mg + 450mg dose groups was met (PE = 68.6%, p<0.0001), allowing testing of individual dose groups.
2. ILI event defined as central laboratory-confirmed RT-PCR+ influenza infection (nasopharyngeal swab), new onset of fever (oral temperature ≥38.0°C), and new onset of ≥2 respiratory symptoms (nasal congestion, sore throat, cough) or ≥1 respiratory symptom and ≥1 systemic symptom (headache, feeling feverish, body aches/pains, fatigue).
3. Sample size (N) indicates evaluable population at time of primary analysis data cut (April 30, 2025).

Vaccins Covid-19

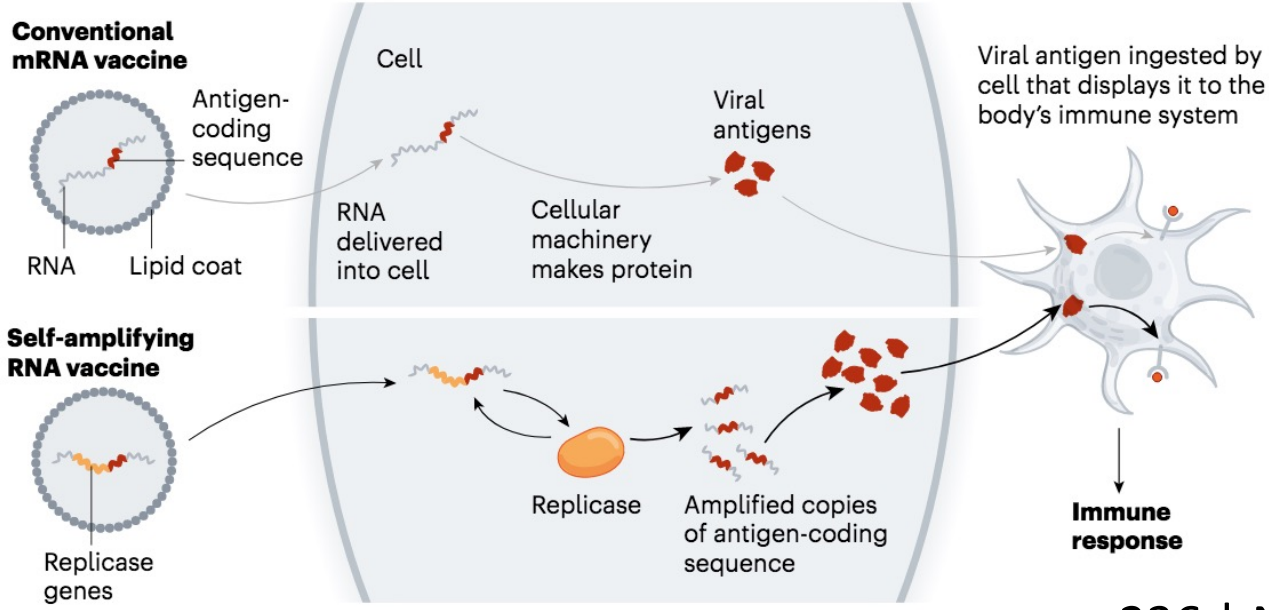
Vaccins ARNm ‘auto-amplifiant’

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

Vaccin COVID-19 ARNm ‘auto-amplifiant’: zapomeran Kostaive

- Essai randomisé prospectif boost vs vaccin Pfizer
- Une injection
- Meilleure immunogéncité
- Persistence prolongée
- Autorisation EMA en février 2025

HUMAN VACCINES & IMMUNOTHERAPEUTICS
2025, VOL. 21, NO. 1, 2530291
https://doi.org/10.1080/21645515.2025.2530291

Taylor & Francis
Taylor & Francis Group

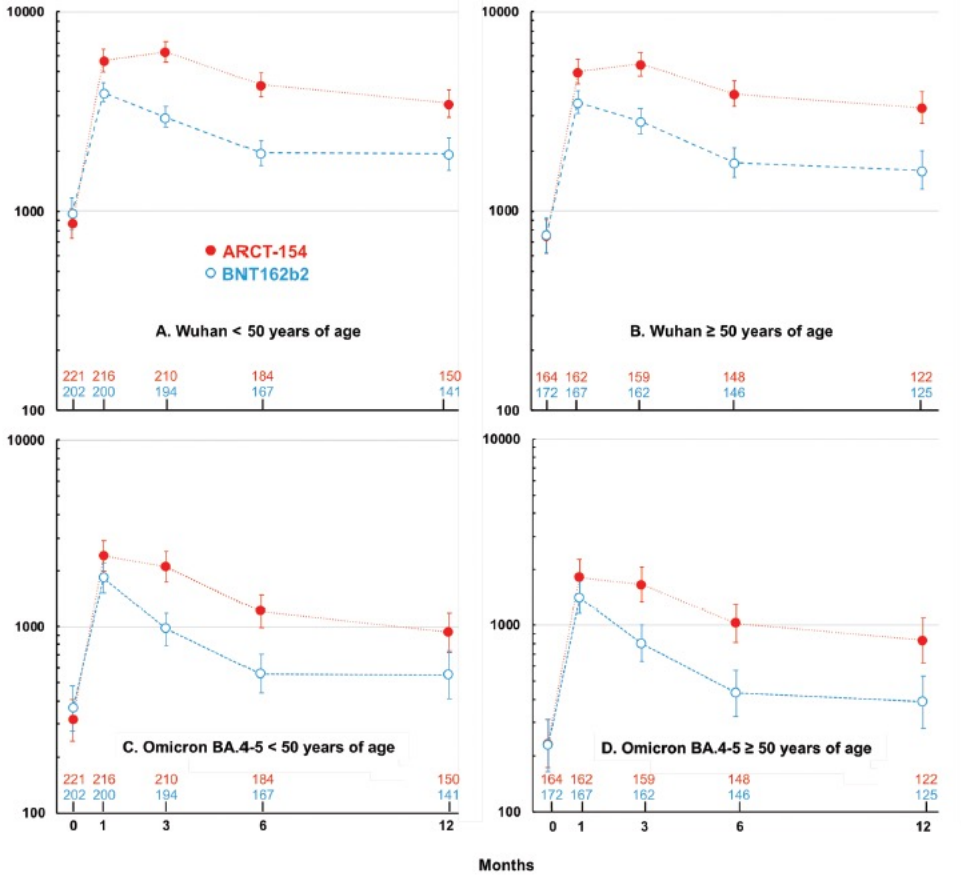
MINI-REVIEW

OPEN ACCESS Check for updates

A second-generation, self-amplifying COVID-19 Vaccine: World’s first approval and distribution in the Japanese market with vaccine hesitancy

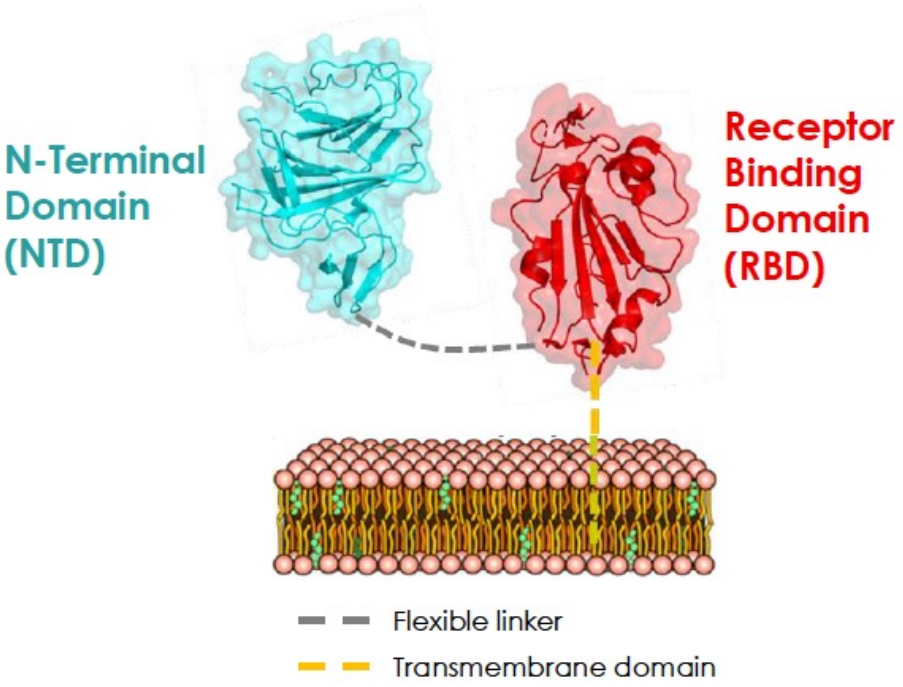
Toshio Naito

Department of General Medicine, Faculty of Medicine, Juntendo University, Tokyo, Japan



Lancet Infect Dis. 2024;24(4):341–343.

Vaccin COVID-19 Moderna ARNm de ‘seconde génération’: mRNA 1283



- mRNA-1283 focuses immune responses to the domains of the SARS-CoV-2 spike protein that are critical for neutralizing antibody and T-cell responses[1-3]
- Significantly shorter mRNA sequence and lower mRNA dose (10 µg mRNA-1283, which is 1/5th the dose of mRNA-1273 [50 µg])

ESCMID 2025

Vaccin COVID-19 Moderna ARNm de ‘seconde génération’: mRNA 1283 vs mRNA1273

Efficacy, immunogenicity, and safety of a next-generation mRNA-1283 COVID-19 vaccine compared with the mRNA-1273 vaccine (NextCOVE): results from a phase 3, randomised, observer-blind, active-controlled trial

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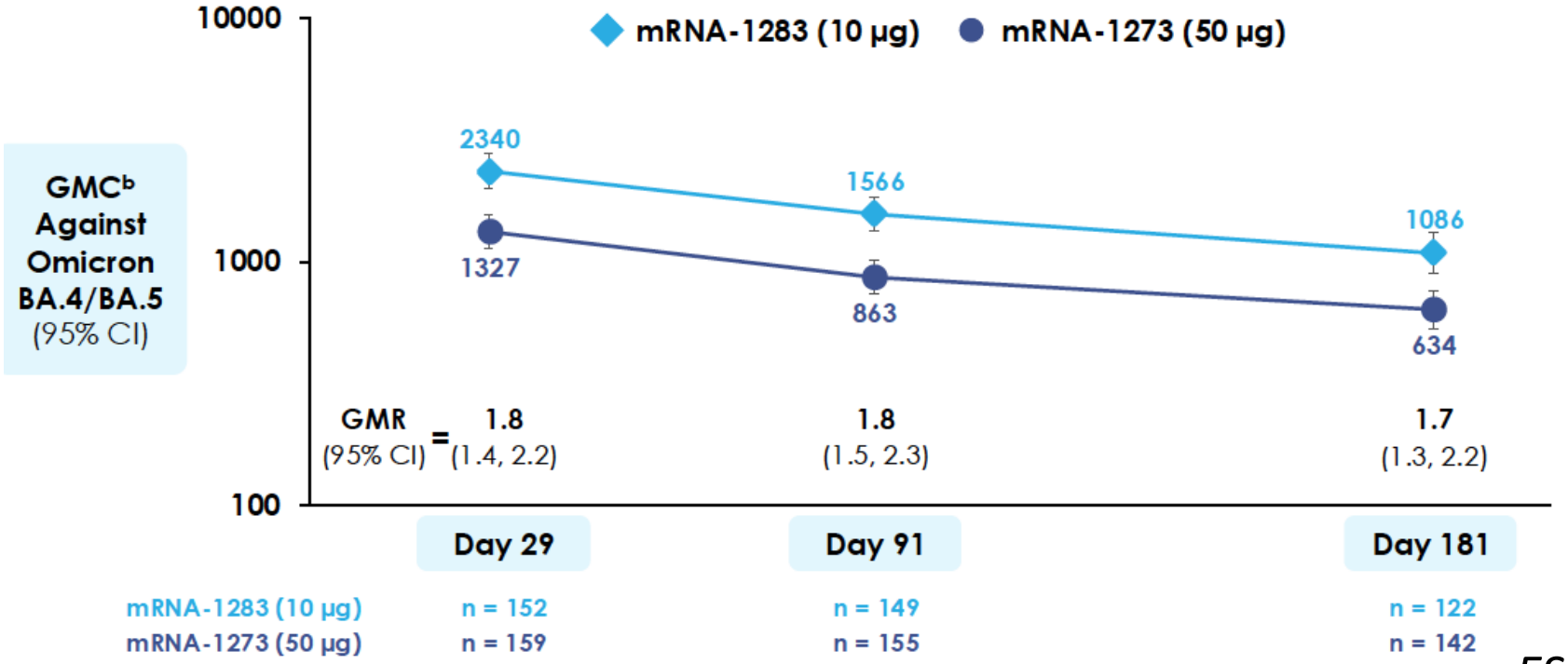
Lancet Infect Dis 2025;
25: 1230–42



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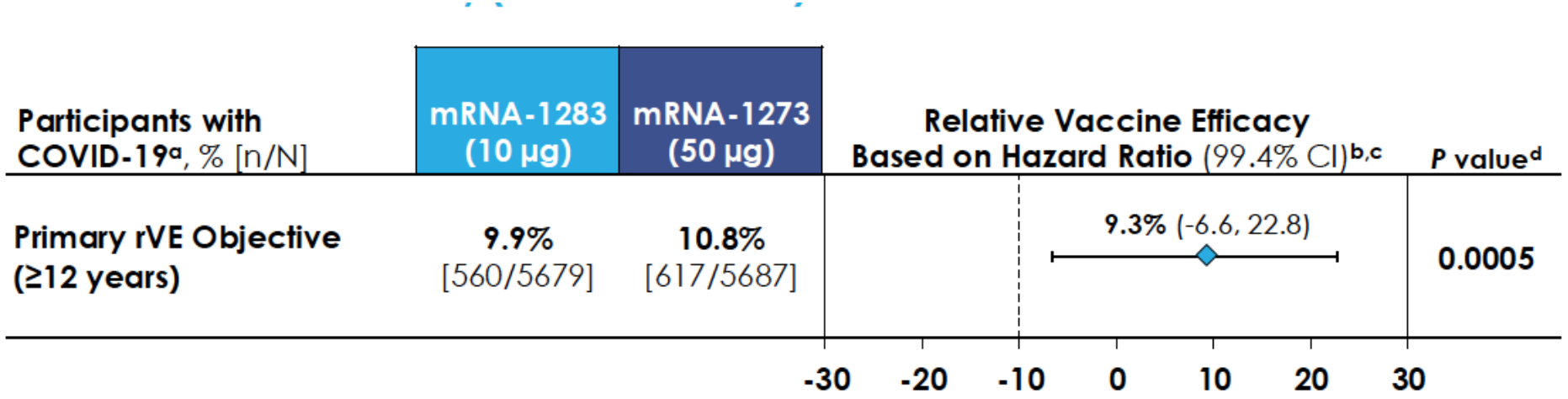
Lancet Infect Dis 2025; 25: 1230–42



- Pas de différence en termes de réactogenicité avec le mRNA 1273
- Autorisé par la FDA en juillet 2025 à partir de l’âge de 65 ans et entre 12 et 65 ans en cas de co morbidités : mNEXSPIKE

ESCMID 2025

Vaccination COVID 19 par voie nasale

- **Vaccination nasale:**

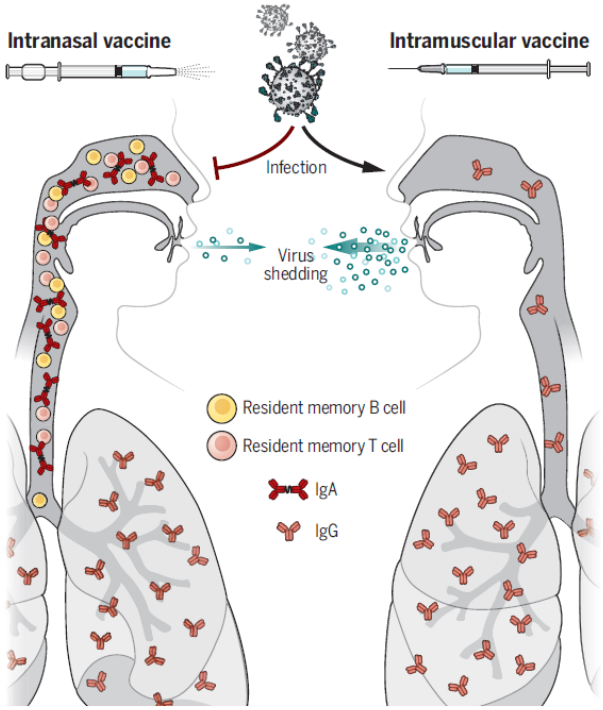
Ig A et cellules T et B mémoires dans le nez et les voies aériennes supérieures

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

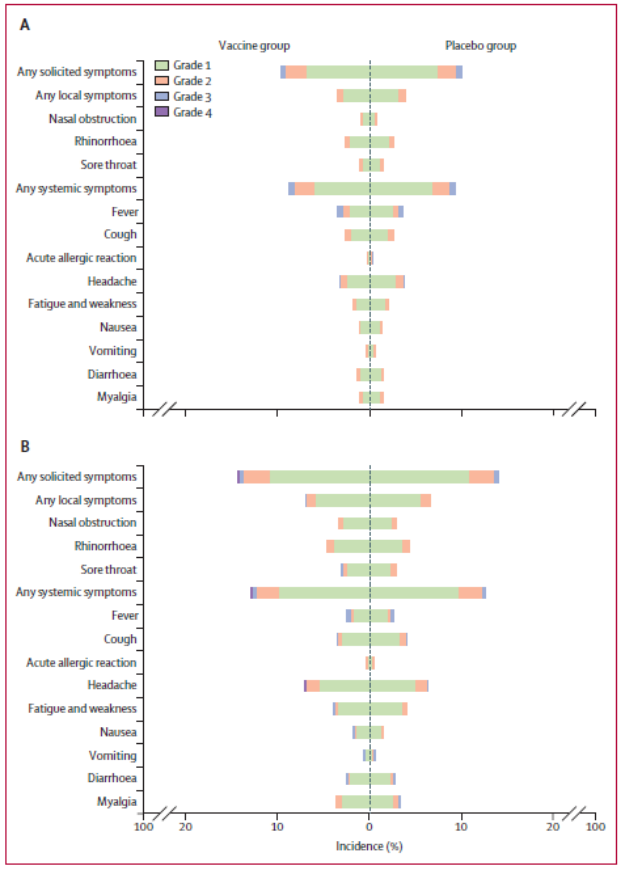


Figure 2: Solicited local and systemic adverse reactions that occurred within 7 days after any dose in the safety population*

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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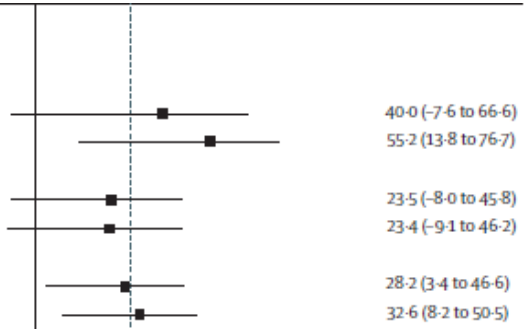
Lancet Respir Med 2023; 11: 1075–88

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)



Vaccin ARNm combiné grippe/Covid-19 (mRNA-1083)

nature medicine

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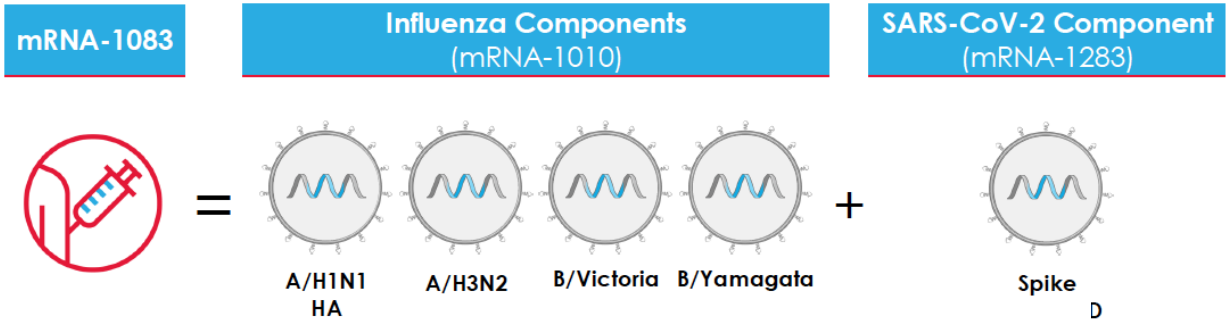
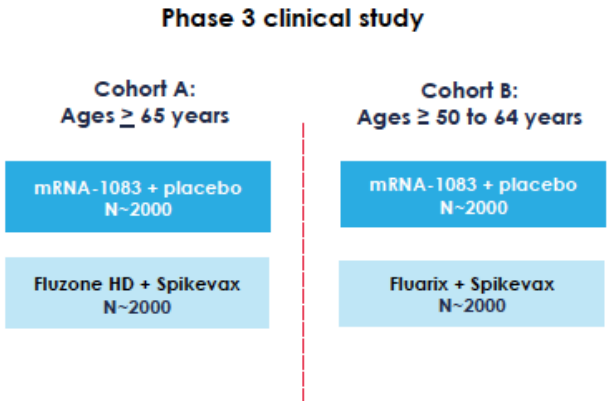
Article | Published: 18 March 2025

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,





Research

JAMA | Original Investigation

Immunogenicity and Safety of Influenza and COVID-19 Multicomponent Vaccine in Adults ≥50 Years
A Randomized Clinical Trial

Amanda K. Rudman Spergel, MD; Iris Wu, PhD; Weiping Deng, PhD; Jose Cardona, MD; Kimball Johnson, MD; Ivette Espinosa-Fernandez, MD; Melissa Sinkiewicz, DO; Veronica Urdaneta, MD, MPH; Lizbeth Carmona, BA; Kristin Schaefers, BS; Bethany Girard, PhD; Yamuna D. Palla, PhD; Darshan Mehta, PhD; Benoit Callendret, PhD; Lusine Kostanyan, MD; Jintanat Ananworanich, MD, PhD; Jacqueline Miller, MD; Rituparna Das, MD, PhD; Christine A. Shaw, PhD

JAMA. 2025;333(22):1977-1987. doi:10.1001/jama.2025.5646
Published online May 7, 2025.

Vaccin ARNm combiné grippe/Covid-19 (mRNA-1083): immunogénicité

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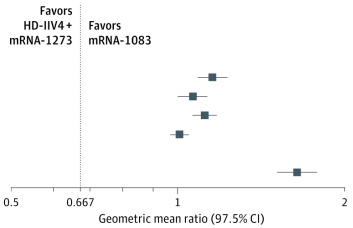
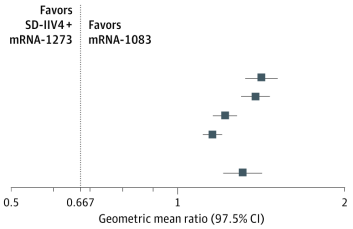
A Antibody levels in adults ≥65 y

Strain	Antibody levels, geometric mean: mRNA-1083 (n = 1886)	Antibody levels, geometric mean: HD-IIV4 + mRNA-1273 (n = 1883)	Primary noninferiority analysis: Geometric mean ratio (97.5% CI)	Secondary superiority analysis: 95% CI
Influenza strain	n = 1885	n = 1883		
A/H1N1	120.5	104.3	1.155 (1.086 to 1.229)	1.094 to 1.220
A/H3N2	114.7	107.9	1.063 (0.999 to 1.130)	1.007 to 1.122
B/Victoria	245.3	219.4	1.118 (1.063 to 1.175)	1.070 to 1.167
B/Yamagata	93.3	92.6	1.007 (0.969 to 1.047)	0.973 to 1.042
SARS-CoV-2 strain	n = 1849	n = 1859		
Omicron XBB.1.5	1396.7	851.1	1.641 (1.510 to 1.783)	1.526 to 1.765



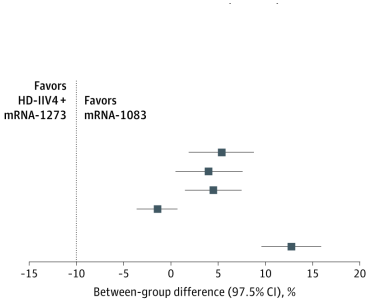
B Antibody levels in adults aged 50-64 y

Strain	Antibody levels, geometric mean: mRNA-1083 (n = 1890)	Antibody levels, geometric mean: SD-IIV4 + mRNA-1273 (n = 1884)	Primary noninferiority analysis: Geometric mean ratio (97.5% CI)	Secondary superiority analysis: 95% CI
Influenza	n = 1889			
A/H1N1	137.7	97.3 (n = 1883)	1.414 (1.322 to 1.513)	1.333 to 1.500
A/H3N2	111.5	80.8 (n = 1882)	1.380 (1.300 to 1.465)	1.310 to 1.454
B/Victoria	224.9	185.0 (n = 1883)	1.216 (1.156 to 1.278)	1.163 to 1.270
B/Yamagata	101.7	88.1 (n = 1882)	1.154 (1.109 to 1.201)	1.115 to 1.195
SARS-CoV-2	n = 1854	n = 1848		
Omicron XBB.1.5	1551.6	1186.1	1.308 (1.207 to 1.418)	1.219 to 1.404



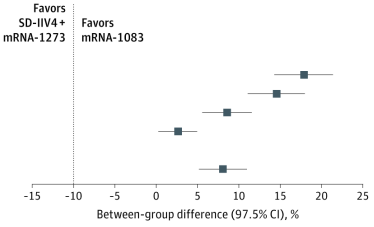
C Seroconversion/seroresponse rate in adults ≥65 y

Strain	Participants, %: mRNA-1083 (n = 1886)	Participants, %: HD-IIV4 + mRNA-1273 (n = 1883)	Primary noninferiority analysis: Between-group difference (97.5% CI), %	Secondary superiority analysis: 95% CI
Influenza	n = 1885	n = 1883		
A/H1N1	36.4	31.1	5.4 (1.9 to 8.8)	2.4 to 8.4
A/H3N2	38.7	34.6	4.0 (0.5 to 7.6)	1.0 to 7.1
B/Victoria	23.9	19.4	4.5 (1.5 to 7.5)	1.9 to 7.2
B/Yamagata	8.8	10.2	-1.4 (-3.6 to 0.7)	-3.3 to 0.4
SARS-CoV-2	n = 1852	n = 1854		
Omicron XBB.1.5	82.3	69.9	12.8 (9.6 to 15.9)	10.0 to 15.5



D Seroconversion/seroresponse rates in adults aged 50-64 y

Strain	Participants, %: mRNA-1083 (n = 1890)	Participants, %: SD-IIV4 + mRNA-1273 (n = 1884)	Primary noninferiority analysis: Between-group difference (97.5% CI), %	Secondary superiority analysis: 95% CI
Influenza	n = 1888			
A/H1N1	50.6	32.7 (n = 1882)	17.9 (14.3 to 21.4)	14.8 to 21.0
A/H3N2	41.9	27.4 (n = 1881)	14.6 (11.1 to 18.0)	11.6 to 17.6
B/Victoria	25.8	17.2 (n = 1882)	8.6 (5.6 to 11.6)	6.0 to 11.2
B/Yamagata	13.0	10.3 (n = 1881)	2.7 (0.3 to 5.0)	0.6 to 4.7
SARS-CoV-2	n = 1852	n = 1846		
Omicron XBB.1.5	84.6	76.5	8.1 (5.2 to 11.0)	5.5 to 10.6



Vaccin ARNm combiné grippe/Covid-19 (mRNA-1083): réactogénicité

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JAMA | Original Investigation

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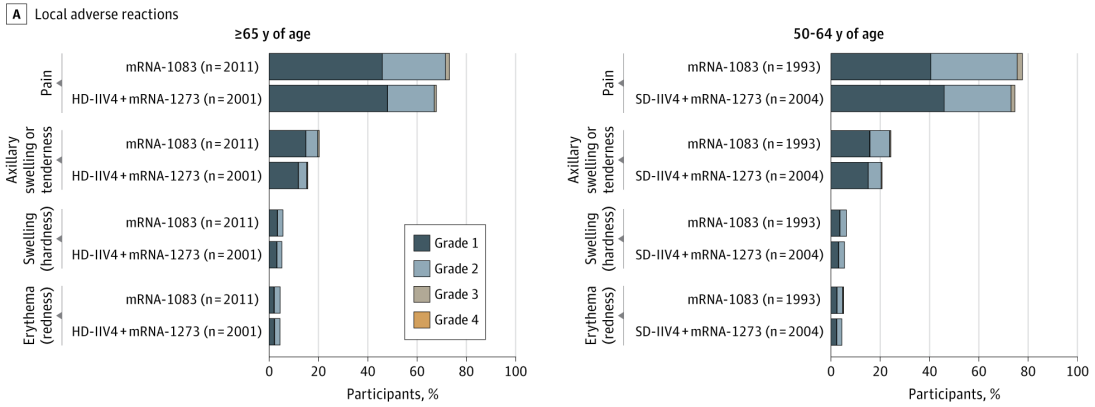
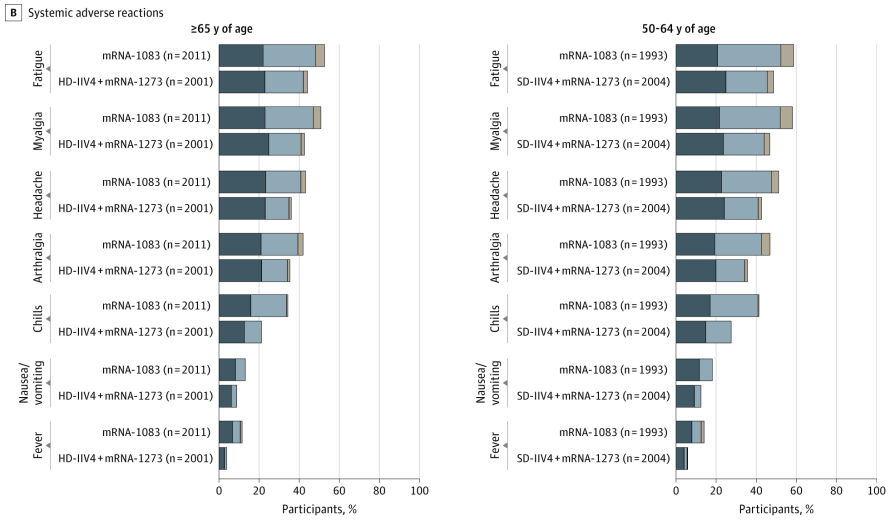
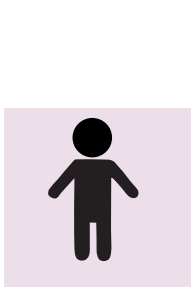




Infections à VRS

Prévention des infections à VRS: indications actuelles



Pédiatrique

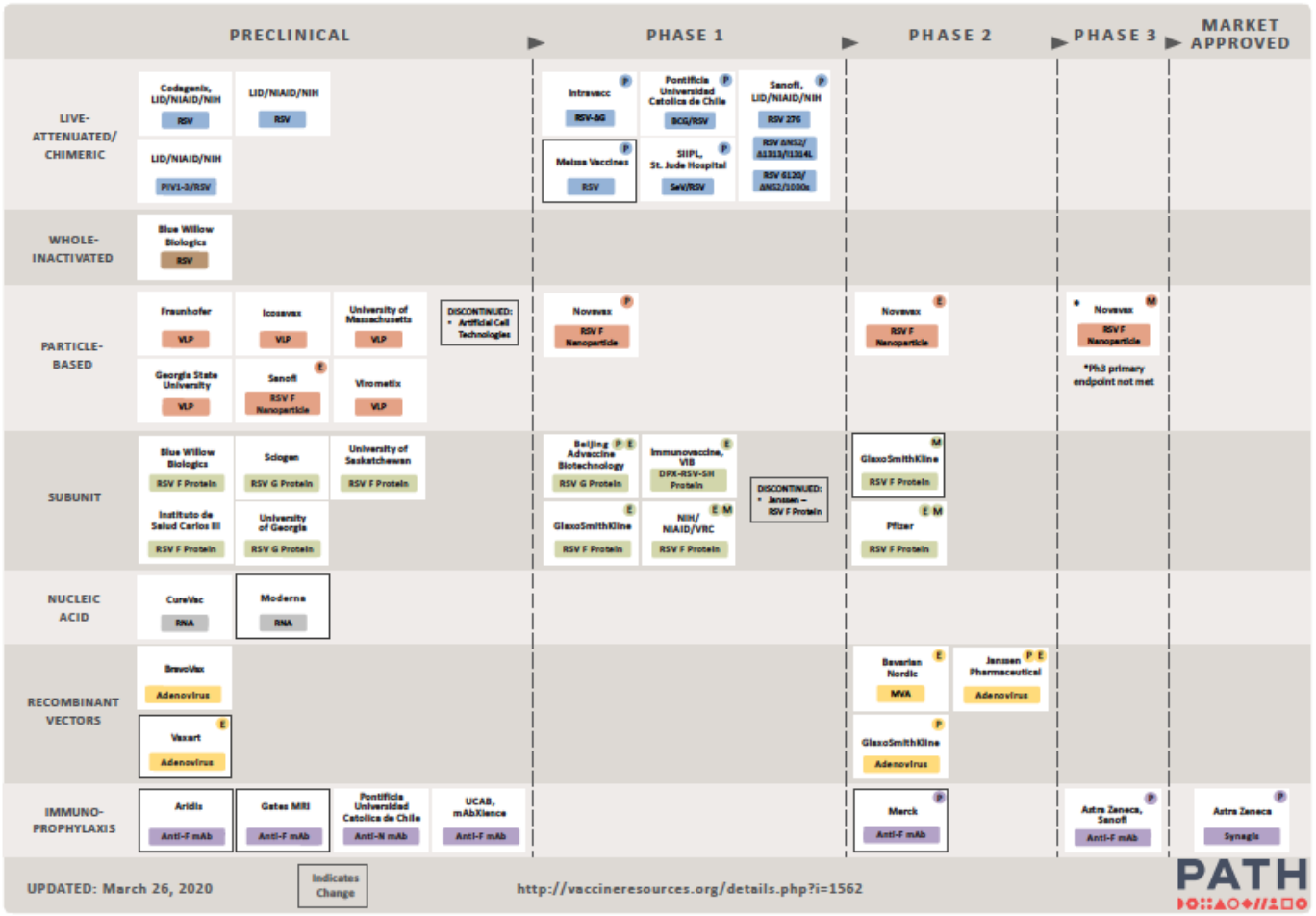
Maternel

Adultes âgés

(> 50/60 ans)

2020

RSV Vaccine and mAb Snapshot

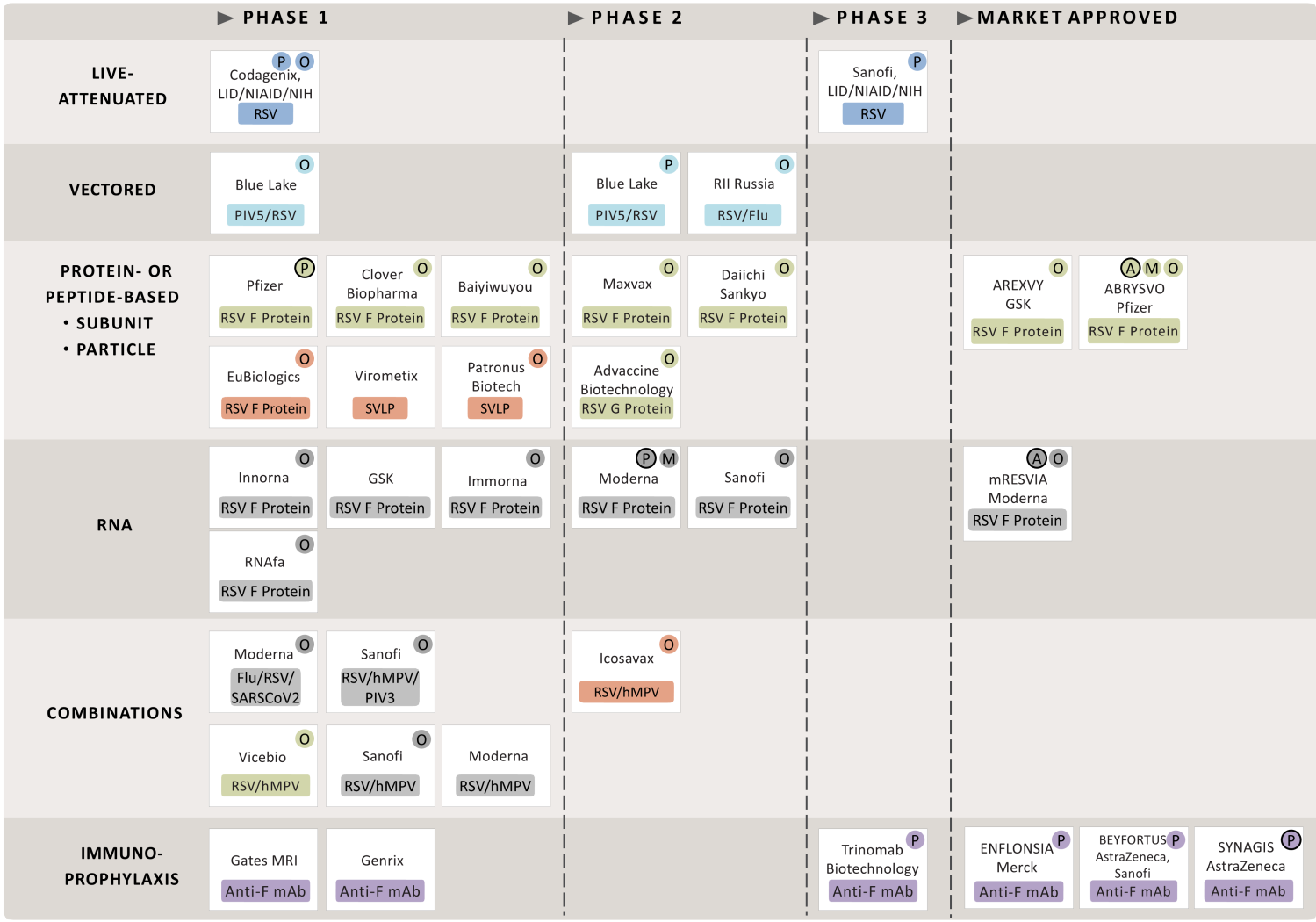


RSV Vaccine and mAb Snapshot

2025

P =PEDIATRIC M =MATERNAL ◯ =LIMITED TO INCREASED RISK
A =ADULT O =OLDER ADULT

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



*SVLP = Synthetic virus-like particle

UPDATED: June 17, 2025

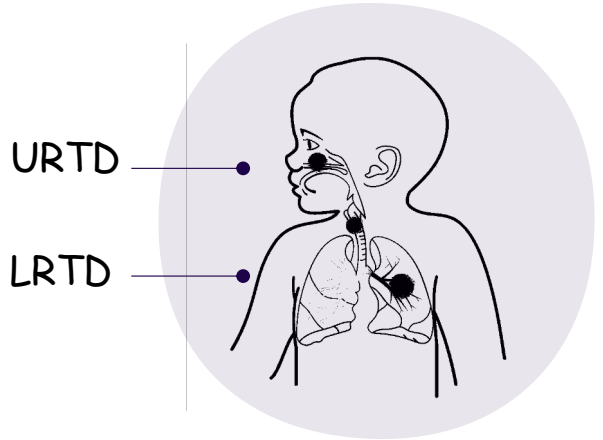
https://www.path.org/resources/rsv-vaccine-and-mab-snapshot/

PATH

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

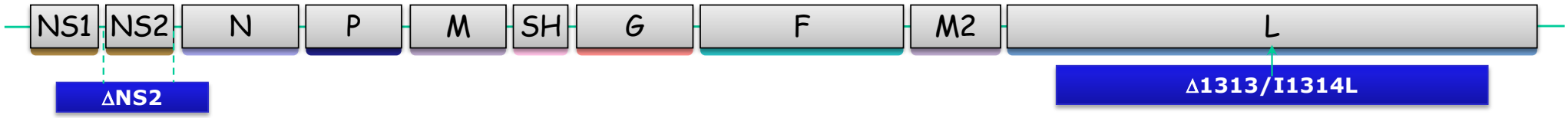
Administration par voie nasale

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



Vaccin vivant atténué
Trois modifications génétiques (OGM)

Génome du VRS



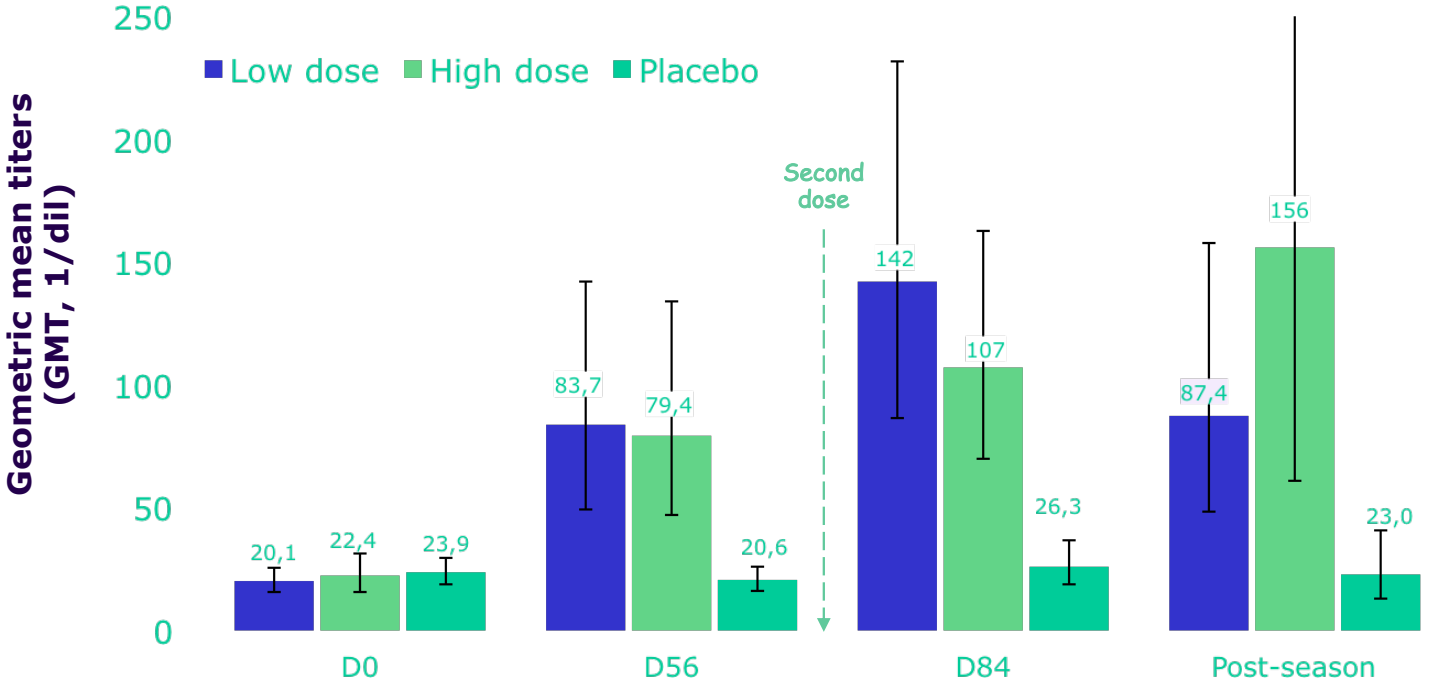
Genetic alteration	*Deletion of NS2 gene (ΔNS2)*[2–7]	*Codon deletion in L gene (Δ1313)*[5–9]	*Missense mutation in L gene (I1314L)*[5–9]
Protein role	Interferon antagonist	RSV polymerase	RSV polymerase
Impact of alteration	Removes risk of NS2-mediated airway obstruction, attenuates RSV, and improves 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



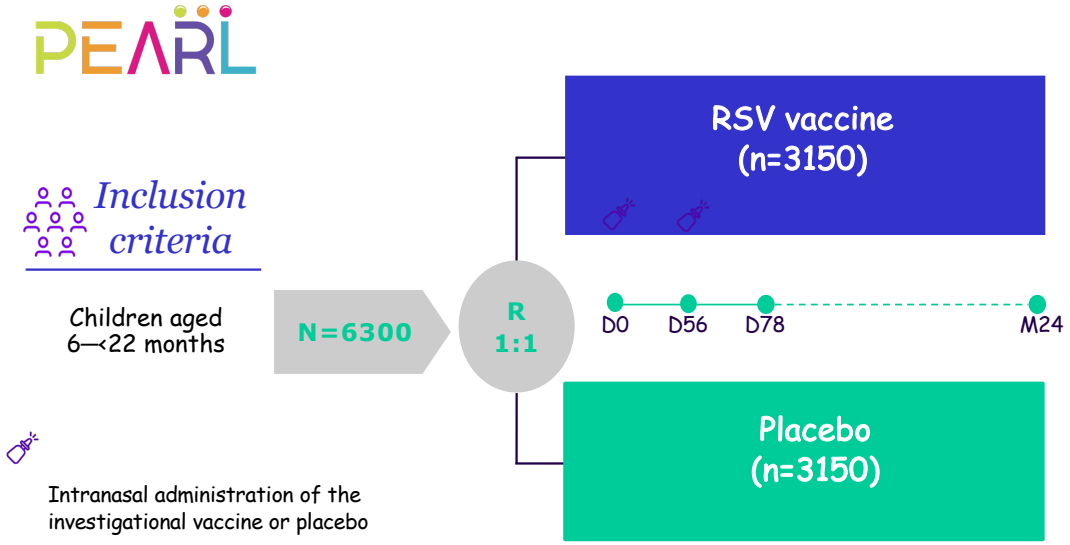
Robust immune responses: Elicited with two administrations of low or high doses of vaccine, which **persist up to 5 months after second injection**

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

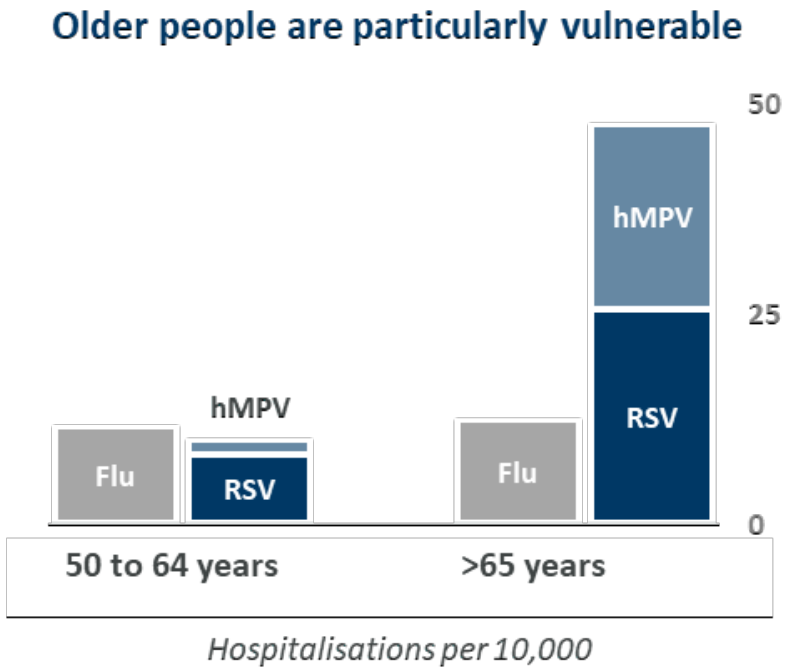
Estimated primary completion date

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 ARNm RSV- humanMetapneumovirus

- Vaccin développé par Sanofi
- Essai pivot prévu 2026-2027
- Essai randomisé vs placebo
- 26 000 participants >60 ans



Autres vaccins

Vaccin contre le CMV

60+ years of CMV vaccine development, yet we still await an approved vaccine

Vaccine Platform	Phase	Efficacy
Live attenuated	Phase I,II	Reduction of disease in renal tx
Live viral vectors	Phase I	-
gB subunit	Phase I,II	**50%**
eVLP	Phase I	-
Single round DISC vectors	Phase I,II	**42%**
gB + PC subunit/MVA	Phase I	-
DNA	Phase I,II	ongoing
mRNA (gB + PC)	Phase I,II,III	ongoing

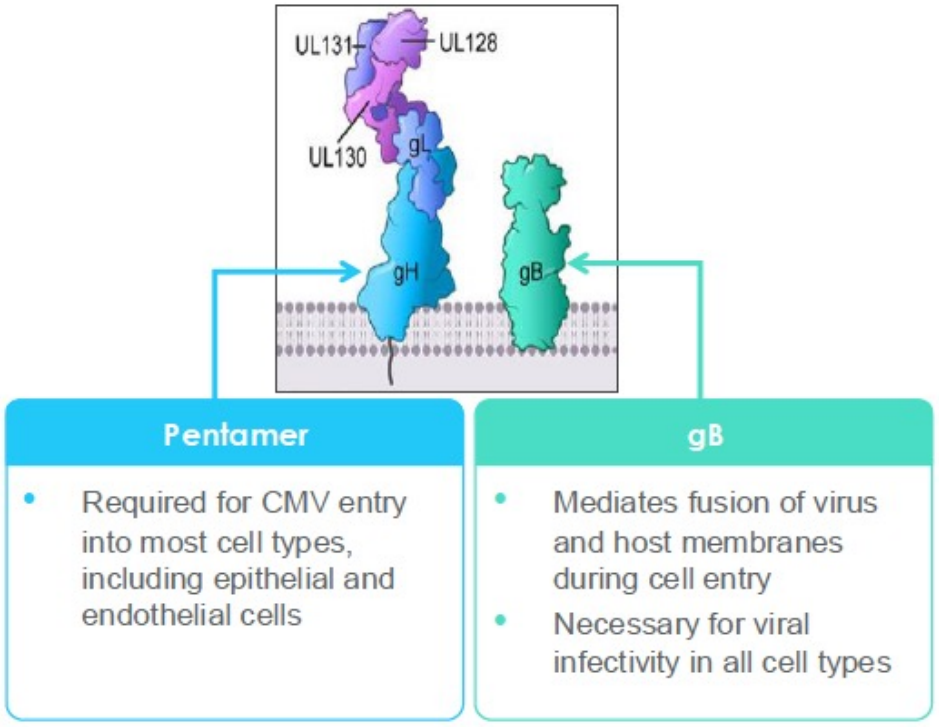
Weill Cornell Medicine Pediatrics

Modified from Schleiss et al, 2017

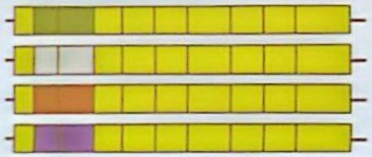
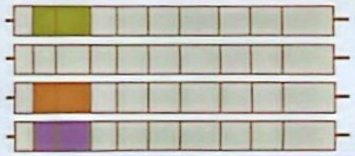
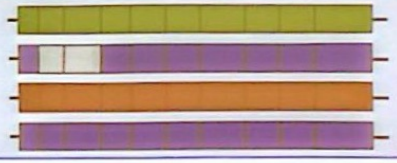
Children's Hospital of New York

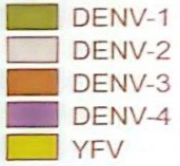
Candidat vaccin CMV ARNm (Moderna): mRNA1647

- contient 6 séquences mRNA :
  - –5 codant pour les sous unités du pentamer GH nécessaire pour l'enttrée du virus dans la cellule
  - –1 codant pour la glycoprotéine B (gB) qui permet la fusion du virus avec avec les membranes cellulaires (infectivité)
- Essai de phase 3,
- 7500 femmes 16-40 ans
- 3 vaccinations (M0, M1, M6)
- **Echec : poursuite du développement pour les patients greffes de moelle**



Vaccination contre la dengue

	Dengvaxia™ (Sanofi Pasteur)	QDenga (TAK-003 - Takeda)	TV003 (multiple manufacturers)
Status	Licensed	Licensed	Phase 3 (Instituto Butantan)
# Doses	**3 doses** over 12 months (0, 6, 12)	**2 doses** (0, 3 months)	**Single dose**
Indicated age	6 – 16 (US), 9-45 (WHO)	Phase 3 (age 4 – 16)	Phase 3 age 2 - 59
Other	**Documented previous DENV infection**	≥ 6 in areas of high DENV endemicity	?
Construct			
Dengue proteins	8	16	32



Vaccin dengue: Dengvaxia®

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Efficacy and Long-Term Safety of a Dengue Vaccine in Regions of Endemic Disease

Sri Rezeki Hadinegoro, M.D., Ph.D., Jose Luis Arredondo-García, M.D., Maria Rosario Capeding, M.D., Carmen Deseda, M.D., Tawee Chotpitayasunondh, M.D., Reynaldo Dietze, M.D., H.I. Hj Muhammad Ismail, M.B., B.S., Humberto Reynales, M.D., Ph.D., Kriengsak Limkittikul, M.D., Doris Maribel Rivera-Medina, M.D., Huu Ngoc Tran, M.D., Ph.D., Alain Bouckenooghe, M.D., et al., for the CYD-TDV Dengue Vaccine Working Group*

- Suivi à 3 ans: 40 hospitalisations

n=27 groupe vacciné,
13 groupe contrôle

- Excès d'hospitalisation: chez les enfants 2-5 ans

Table 1. Annual Incidence of Hospitalization for Virologically Confirmed Dengue, According to Trial, Age Group, and Study Period.*

Trial, Age Group, and Study Period	Vaccine Group			Control Group			Relative Risk (95% CI)
	Cases of Dengue	Total Participants†	Annual Incidence Rate‡	Cases of Dengue	Total Participants†	Annual Incidence Rate‡	
		no.	*% (95% CI)*		*no.*	*% (95% CI)*	
CYD14							
All participants§	27	6,778	0.4 (0.3–0.6)	13	3387	0.4 (0.2–0.7)	1.04 (0.52–2.19)
2–5 yr	15	1,636	1.0 (0.6–1.6)	1	813	0.1 (0.0–0.7)	7.45 (1.15–313.80
6–11 yr	10	3,598	0.3 (0.1–0.6)	8	1806	0.5 (0.2–1.0)	0.63 (0.22–1.83)
12–14 yr	2	1,544	0.1 (0.0; 0.5)	4	768	0.6 (0.2–1.4)	0.25 (0.02–1.74)
<9 yr	19	3,493	0.6 (0.4–0.9)	6	1741	0.4 (0.1–0.8)	1.58 (0.61–4.83)
≥9 yr	8	3,285	0.3 (0.1–0.5)	7	1646	0.5 (0.2–1.0)	0.57 (0.18–1.86)

Le vaccin Dengvaxia® n'est plus commercialisé depuis mars 2024 du fait d'un profil de tolérance défavorable chez les sujets sans antécédent de dengue

N Engl J Med. 2015 Sep 24;373(13):1195-206.

Vaccin Qdenga® (Takeda): efficacité

- Efficacité globale :
  - contre les dengues confirmées virologiquement : 61·2% (95% CI 56·0–65·8)
  - contre les dengues hospitalisées: 84·1% (77·8–88·6)
  - Efficacité moindre chez sujets séronégatifs: 53·5% (41·6–62·9) and 79·3% (63·5–88·2) respectivement
- Efficacité conservée pour tous les sérotypes chez individus séropositifs
- En attente de données d'effectiveness

Long-term efficacy and safety of a tetravalent dengue vaccine (TAK-003): 4·5-year results from a phase 3, randomised, double-blind, placebo-controlled trial

Vianney Tricou, Delia Yu*, Humberto Reynales, Shibadas Biswal, Xavier Saez-Llorens, Chukiat Sirivichayakul, Pio Lopez, Charissa Borja-Tabora, Lulu Bravo, Pope Kosalaraksa, Luis Martinez Vargas, Maria Theresa Alera, Luis Rivera, Veerachai Watanaveeradej, Reynaldo Dietze, LakKumar Fernando, V Pujitha Wickramasinghe, Edson Duarte Moreira Jr, Asvini D Fernando, Dulanie Gunasekera, Kleber Luz, Ana Lucia Oliveira, Suely Tuboi, Ian Escudero, Yanee Hutagalung, Eric Lloyd, Martina Rauscher, Olaf Zent, Nicolas Folschweiller, Inge LeFevre, Felix Espinoza†, Derek Wallace†*

Tricou et al. Lancet Global Health. Feb 2024

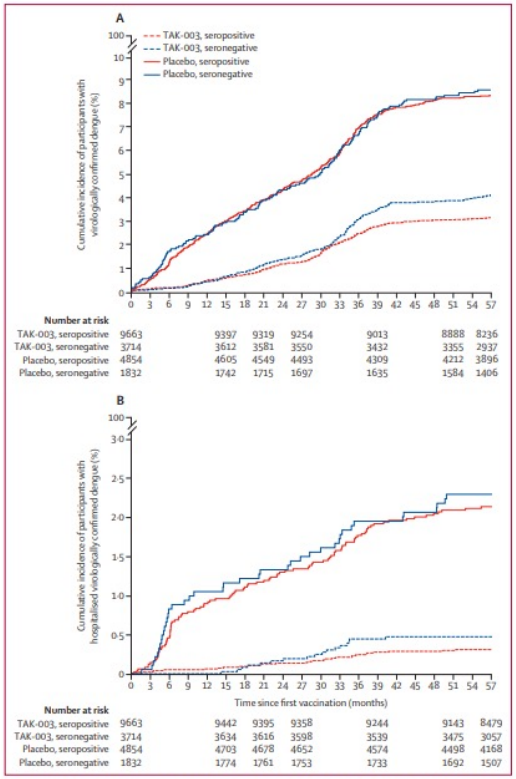


Figure 3: Cumulative incidence of virologically confirmed dengue (A) and hospitalised virologically confirmed dengue (B)

Butantan-Dengue Vaccine

ORIGINAL ARTICLE

Live, Attenuated, Tetravalent Butantan–Dengue Vaccine in Children and Adults

Esper G. Kallás, M.D., Ph.D., Monica A.T. Cintra, M.D., Ph.D., José A. Moreira, M.D., Ph.D., Elizabeth G. Patiño, Ph.D., Patricia Emilia Braga, Ph.D., Juliana C.V. Tenório, Ph.D., Vanessa Infante, M.D., Ricardo Palacios, M.D., Ph.D., Marcus Vínicius Guimarães de Lacerda, M.D., Ph.D., Dhelio Batista Pereira, M.D., Ph.D., Allex Jardim da Fonseca, M.D., Ph.D., Ricardo Queiroz Gurgel. Ph.D.. et al.

The NEW ENGLAND JOURNAL of MEDICINE

N Engl J Med 2024;390:397-4

- Vaccin développé par le NIH, license accordé au Butantan, MSD, et SII
- Essai contrôlé randomisé en double aveugle, conduit au Brésil 16 235 participants

- À 2 ans:
  - 79.6% (95% confidence interval [CI], 70.0 to 86.3)
  - 89.5% (95% CI, 78.7 to 95.0) sur DENV-1
  - **69.6% (95% CI, 50.8 to 81.5) sur DENV-2**

  - 73.6% (95% CI, 57.6 to 83.7) chez les séronégatifs
  - 89.2% (95% CI, 77.6 to 95.6) chez les séropositifs

- Uniquement des cas de DENV 1 et 2

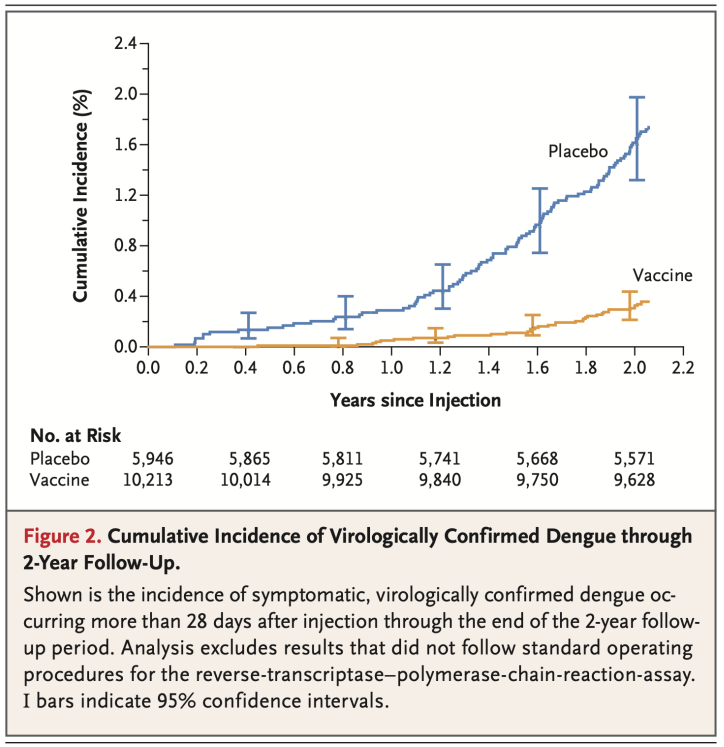


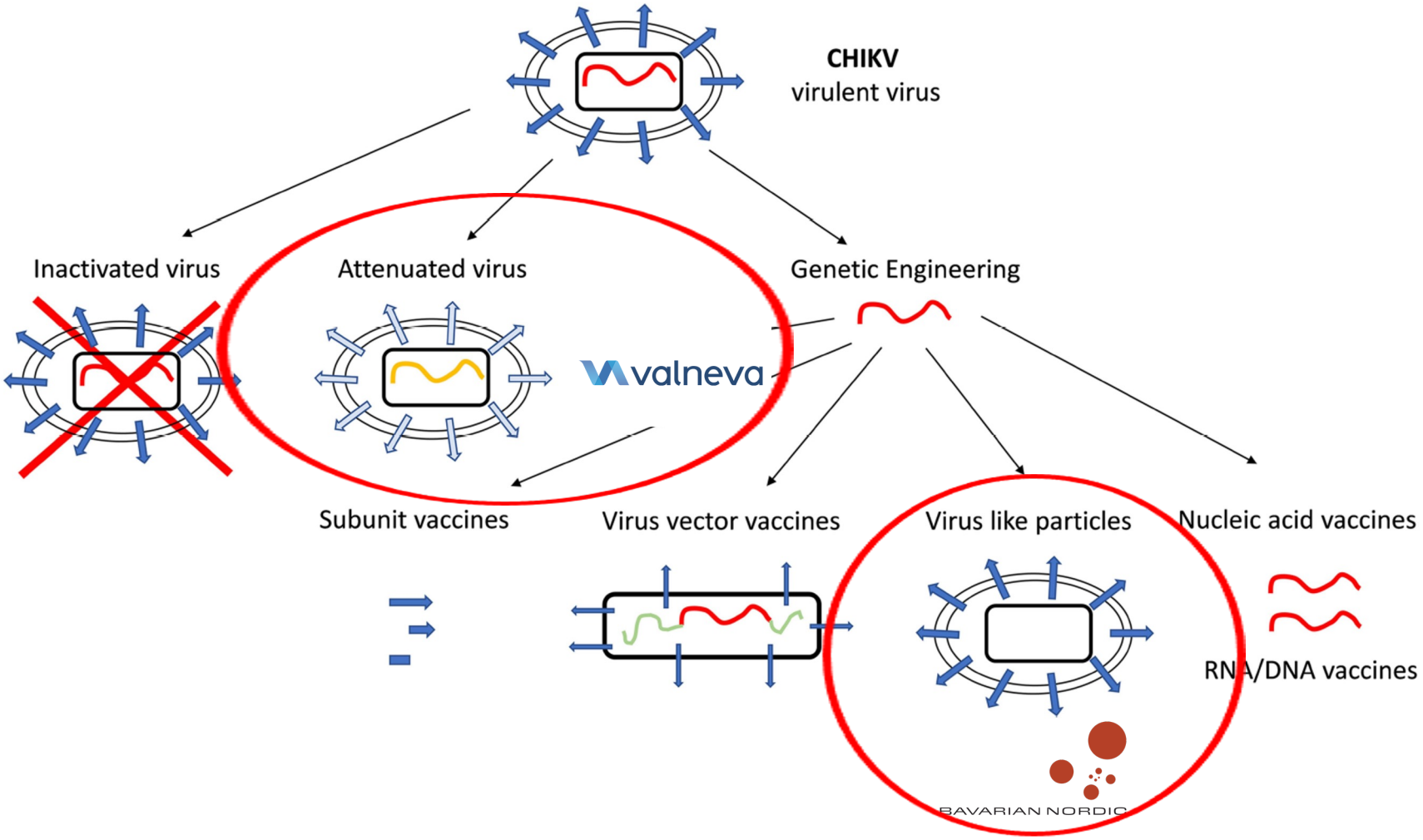
Figure 2. Cumulative Incidence of Virologically Confirmed Dengue through 2-Year Follow-Up.

Shown is the incidence of symptomatic, virologically confirmed dengue occurring more than 28 days after injection through the end of the 2-year follow-up period. Analysis excludes results that did not follow standard operating procedures for the reverse-transcriptase–polymerase-chain-reaction-assay. I bars indicate 95% confidence intervals.

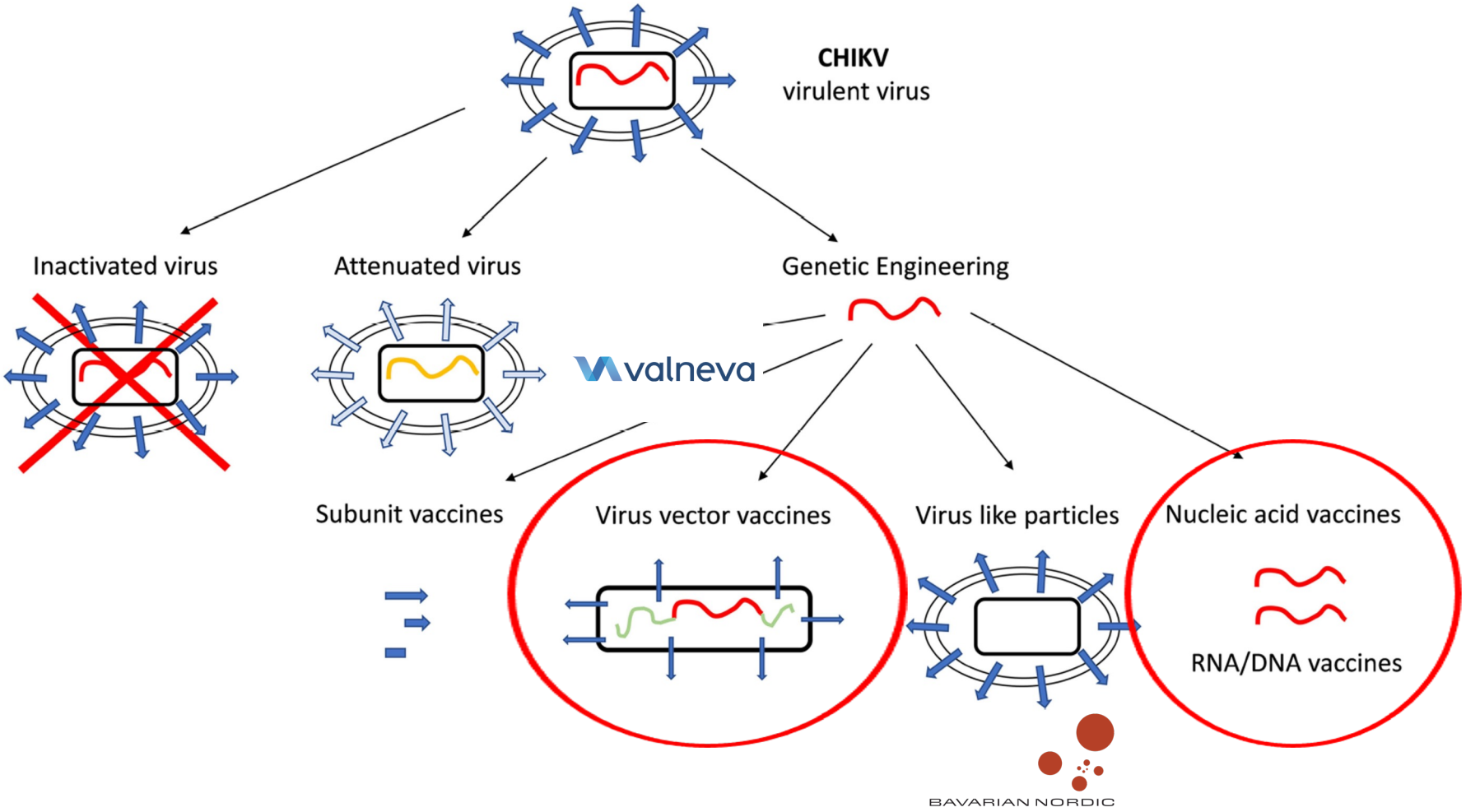
Vaccin fièvre jaune : perspectives

- Doses fractionnées
- Vaccin produit sur cellules Véro (Sanofi)

Deux vaccins Chikungunya ont obtenu une autorisation



Vaccination Chikungunya: perspectives



Vaccin Zika

- Nombreux challenges pour la mise au point d'un vaccin:
  - Epidémies imprévisibles
  - Vaccination femmes enceintes
- Nombreuses phases 1
- Phases 2 en cours

Zika Virus: Research Priorities for Preparedness and Response 2

Zika virus vaccines and monoclonal antibodies: a priority agenda for research and development

Julia T Ostrowsky, Leah C Katzelnick, Nigel Bourne, Alan D T Barrett, Stephen J Thomas, Michael S Diamond, David W

Lancet Infect Dis 2025; 25: e402–15
Published Online February 27, 2025
https://doi.org/10.1016/S1473-3099(24)00750-3

	Antigen, adjuvant	Developer	Phase 1	
Inactivated purified Zika virus				
ZPIV[64-68]	Inactivated virion, alum adjuvanted	Walter Reed Army Institute of Research	NCT03008122; NCT02963909; NCT02952833; NCT02937233	..
TAK-426[69-72]	Inactivated virion, alum adjuvanted	Takeda	NCT03343626	NCT05469802 (withdrawn)
VLA1601-102[73]	Inactivated virion, alum adjuvanted	Valneva	NCT06334393; NCT03425149	..
BBV121[74]	Inactivated virion, alum adjuvanted	Bharat Biotech	NCT04478656	..
Live-attenuated Zika virus-based				
rZIKV/D4Δ30-713[25,26]	prM-E	NIAID	NCT03611946	..
mRNA				
mRNA-1893[27-29]	prM-E	Moderna	NCT04064905	NCT04917861
mRNA-1325	prM-E	Moderna	NCT03014089	..
DNA				
GLS-5700[30]	prM-E	GeneOne	NCT02809443; NCT02887482	..
VRC5283[31-34]	prM-E	NIAID	NCT02996461	NCT03110770
VRC5288[21]	prM-E, ZIKV-JEV chimera	NIAID	NCT02840487	..
Virus-vectored				
MV-ZIKA-RSP	prM-E	Themis (Merck)	NCT04033068	..
MV-ZIKA	prM-E	Themis (Merck)	NCT02996890	..
Zika001 (ChAdOX1)[35,36]	prM-E	Oxford	NCT04015648; NCT04440774	..
Ad26. ZIKV.001[37]	M-E	Janssen	NCT03356561	..
MVAZIKB	..	University of Liverpool	ISRCTN13726895	..
Recombinant peptides				
AGS-v PLUS[38,39]	*Anopheles gambiae* mosquito salivary peptides; ISA-51 adjuvanted	NIAID; PepTcell	NCT03055000	..

M-E=membrane-envelope protein. NIAID=National Institute of Allergy and Infectious Diseases. prM-E=pre-membrane-envelope protein. ZIKV-JEV=Zika virus-Japanese encephalitis virus. ZPIV=Zika purified inactivated virus.

Table 1: **Zika virus vaccine candidates in clinical evaluation as of April, 2024**

Perspectives

- Très nombreux développements vaccinaux en cours
- Investissements parfois risqués
- Mais
  - plus souvent pour les pays à haut niveau de revenu
  - inégalité d'accès (prix)
  - question de l'acceptabilité:

    un vaccin contre l'hésitation vaccinale ?