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# Quels vaccins pour l'Amérique latine ?

Les anciens et les nouveaux

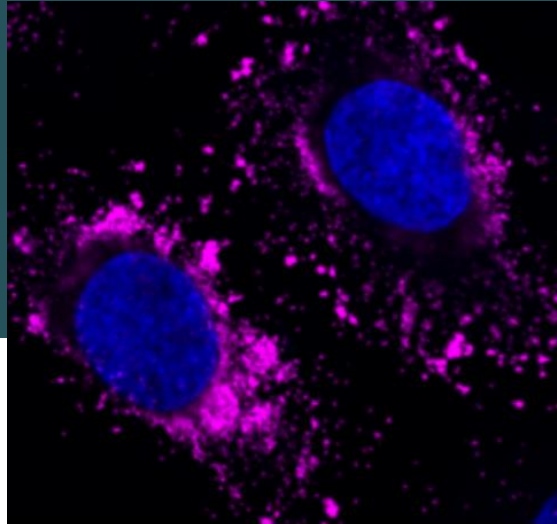


Quels vaccins pour l'Amérique latine ?

## Les anciens

Quels vaccins pour l'Amérique latine ?

# Fièvre jaune



Fièvre jaune

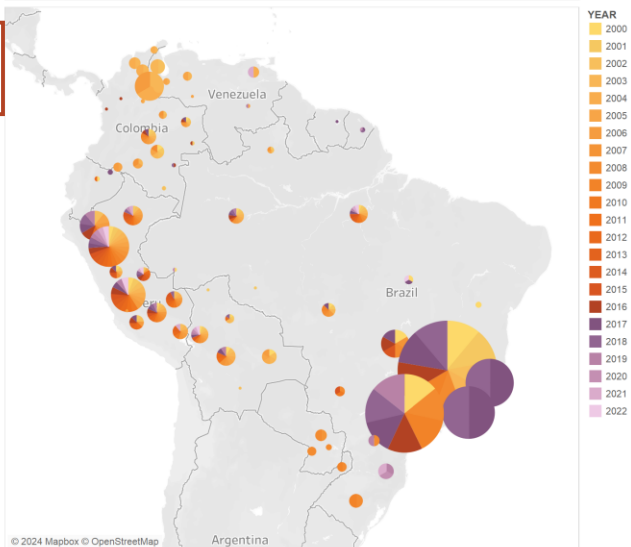
## Epidémiologie

1. Brésil
2. Pérou
3. Colombie
4. Bolivie
5. Venezuela



**YELLOW FEVER: Confirmed cases in the Americas, 2000-2022**  
Number of cases by year and first administrative subdivision.

Totals	
Brazil	2,624
Peru	625
Colombia	228
Bolivia	108
Venezuela	66
Paraguay	28
Argentina	10
Ecuador	6
French Guiana	3
Suriname	1



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Data Sources: PAHO-WHO Member States reports to Health Emergency Information & Risk Assessment Unit (HIM), MOH Epidemiological Bulletins and Brazil OpenDATASUS. Data compilation, analysis and report production: PAHO Health Emergencies Department (PHE)  
NOTE: Totals don't include cases of non-endemic countries.

Fièvre jaune

## Risque d'émergence dans les pays n'ayant pas déclaré de cas récent : l'exemple du Venezuela

Travel Medicine and Infectious Disease 41 (2021) 102025



ELSEVIER

Contents lists available at ScienceDirect

Travel Medicine and Infectious Disease

journal homepage: [www.elsevier.com/locate/tmaid](http://www.elsevier.com/locate/tmaid)

Correspondence

Re-emergence of yellow fever in Venezuela: Report of the first case after 14 years



Fièvre jaune

## Risque de sous-déclaration : l'exemple du Suriname

[Euro Surveill.](#) 2017 Mar 16; 22(11): 30488.doi: [10.2807/1560-7917.ES.2017.22.11.30488](https://doi.org/10.2807/1560-7917.ES.2017.22.11.30488)

PMCID: PMC5356427

PMID: [28333617](https://pubmed.ncbi.nlm.nih.gov/28333617/)

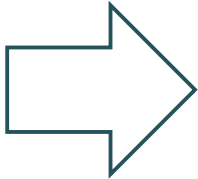
### Yellow fever in a traveller returning from Suriname to the Netherlands, March 2017

[Marjan Wouthuyzen-Bakker](#),<sup>1,2</sup> [Marjolein Knoester](#),<sup>2,3</sup> [Aad P van den Berg](#),<sup>4</sup> [Corine H GeurtsvanKessel](#),<sup>5</sup> [Marion PG Koopmans](#),<sup>5</sup> [Coretta Van Leer-Buter](#),<sup>3</sup> [Bob Oude Velthuis](#),<sup>6</sup> [Suzan D Pas](#),<sup>5</sup> [Wilhelmina LM Ruijs](#),<sup>7</sup> [Jonas Schmidt-Chanasit](#),<sup>8,9</sup> [Stephen GS Vreden](#),<sup>10</sup> [Tjip S van der Werf](#),<sup>1</sup> [Chantal BEM Reusken](#),<sup>5</sup> and [Wouter FW Bierman](#)<sup>1</sup>

Quels vaccins pour l'Amérique latine ?

## Fièvre jaune

- **Obligation administrative pour la Guyane Française / déplacements entre les pays**
- **Indispensable pour le Brésil, Pérou, Colombie, Bolivie et Venezuela**
- **Faible nombre de cas pour les autres pays mais risque d'émergence et de sous-déclaration**



**Indications inchangées**

Quels vaccins pour l'Amérique latine ?

## Hépatite A



Hépatite A

# Epidémiologie

**Endemicity level (AMPI)**  
(N/D: Grey)

- high (<5yo)
- high-intermediate (5–9yo)
- intermediate (10–14yo)
- low-intermediate (15–19yo)
- low (20–29 yo)
- very low (>30yo)

EXPERT REVIEW OF VACCINES  
2020, VOL. 19, NO. 9, 795–805  
<https://doi.org/10.1080/14760584.2020.1813575>

Taylor & Francis  
Taylor & Francis Group

REVIEW

**Hepatitis A epidemiology in Latin American countries: a 2020 view from a systematic literature review**

Anar Andani<sup>a</sup>, Tessa M. van Elten<sup>b</sup>, Eveline M. Bunge<sup>b</sup>, Cinzia Marano<sup>c</sup>, Fernanda Salgado<sup>d</sup> and Kathryn H. Jacobsen<sup>d</sup>

**Table 3.** Nationwide incidence rates of hepatitis A infection per 100,000 inhabitants: the most recent published data that were identified per country are shown.

Country	Time period	Incidence rate per 100,000 inhabitants	Reference
Argentina <sup>a</sup>	2006–2011	7.9	[74]
Belize	1994–1995	26.0	[68]
Brazil <sup>a</sup>	2017	0.72	[19]
Chile	First 39 weeks of 2018	11.6	[38]
Colombia <sup>a</sup>	First 7 weeks of 2019	0.8	[41]
Costa Rica	2012	7.91	[43]
Ecuador	2018	23.82	[69]
El Salvador	First 14 weeks of 2019	4.21	[50]
Guatemala	First 11 weeks of 2018 <sup>b</sup>	2.24	[52]
Honduras	First 14 weeks of 2019	8.84	[53]
Nicaragua	2012	36.9	[70]
Panama <sup>a</sup>	2016	0.82	[58]
Paraguay	2010	0.42	[59]
Uruguay <sup>a</sup>	2010	2.7	[76]
Venezuela	2016	13.88	[65]

<sup>a</sup>Data following introduction of vaccination against hepatitis A virus (HAV) in national immunization program.  
<sup>b</sup>Incidence rate per 100,000 inhabitants for the first 11 weeks of 2019 (see Supplement 6) was higher than 2018 (5.22), implying an outbreak of HAV infection.  
No incidence data were found for 10 countries.

Quels vaccins pour l'Amérique latine ?

## Hépatite A

Indications inchangées

Quels vaccins pour l'Amérique latine ?

# Typhoïde



Typhoïde

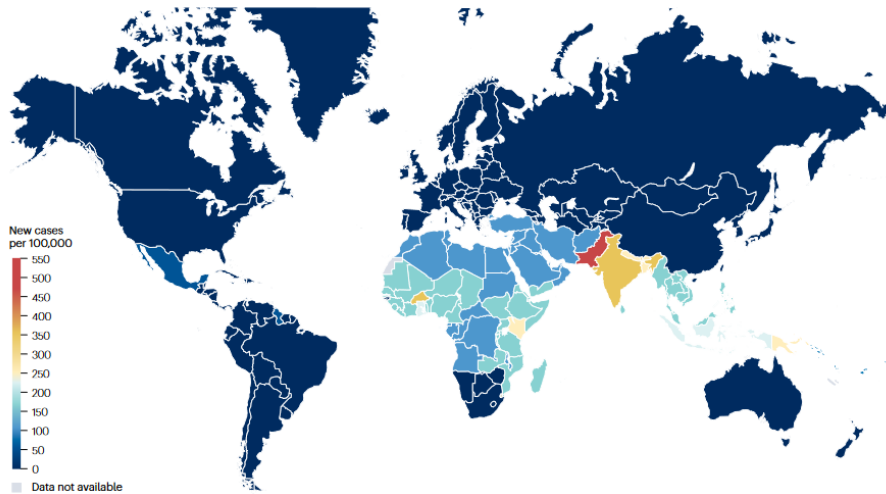
## Epidémiologie

nature reviews disease primers  
Primer

<https://doi.org/10.1038/s41572-023-00480-z>

## Typhoid fever

James E. Meiring<sup>1,2</sup>, Farhana Khanam<sup>3</sup>, Buddha Banerjee<sup>4</sup>, Richelle C. Charles<sup>5</sup>, John A. Crump<sup>6</sup>, Frederic Debellut<sup>7</sup>, Kathryn E. Holt<sup>8</sup>, Samuel Kariuki<sup>9</sup>, Emmanuel Mugisha<sup>10</sup>, Kathleen M. Neuzil<sup>11</sup>, Christopher M. Parry<sup>12</sup>, Virginia E. Pitzer<sup>6</sup>, Andrew J. Pollard<sup>13,14</sup>, Firdausi Qadri<sup>15</sup> & Melita A. Gordon<sup>1,16</sup>



**Fig. 1 | Global incidence of typhoid fever.** Incidence rates per 100,000 person-years of observation for typhoid fever, by country. In 2019. Areas with the highest incidence are shown in red, and areas with the lowest incidence in blue. Reprinted with permission from ref. 31, The Institute for Health Metrics and Evaluation.

Typhoïde

## Epidémiologie

THE LANCET  
Infectious Diseases

ARTICLES | VOLUME 19, ISSUE 4, P369-381, APRIL 2019

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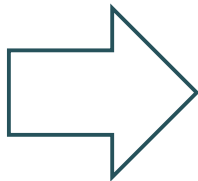
The global burden of typhoid and paratyphoid fevers: a systematic analysis for the Global Burden of Disease Study 2017

GBD 2017 Typhoid and Paratyphoid Collaborators <sup>†</sup> • [Show footnotes](#)

Régions	Incidence (per 100 000)		Percentage change
	1990	2017	
Andean Latin America	2.4 (1.8 to 3.1)	1.5 (1.2 to 2.0)	-35.4% (-40.9 to -29.6)
Caribbean	8.0 (6.7 to 9.5)	5.7 (4.7 to 6.7)	-29.3% (-32.4 to -26.1)
Central Latin America	23.1 (19.2 to 29.0)	8.2 (6.9 to 10.2)	-64.3% (-67.5 to -60.5)
Tropical Latin America	2.8 (2.2 to 3.6)	1.9 (1.5 to 2.4)	-33.2% (-38.2 to -29.4)
Southern Latin America	3.2 (2.7 to 3.8)	0.7 (0.5 to 0.9)	-79.2% (-82.8 to -75.1)
Global	439.2 (376.7 to 507.7)	197.8 (172.0 to 226.2)	-54.9% (-56.5 to -53.4)
South Asia	1506.8 (1308.4 to 1729.6)	549.2 (480.7 to 625.4)	-63.5% (-64.9 to -62.3)
Western sub-Saharan Africa	354.6 (301.7 to 418.3)	161.1 (138.1 to 187.3)	-54.5% (-55.9 to -53.2)
North Africa and Middle East	132.1 (115.2 to 150.6)	39.3 (33.7 to 45.6)	-70.2% (-71.1 to -69.3)
Western Europe	0.4 (0.3 to 0.5)	0.3 (0.2 to 0.4)	-28.8% (-35.2 to -21.4)

Quels vaccins pour l'Amérique latine ?

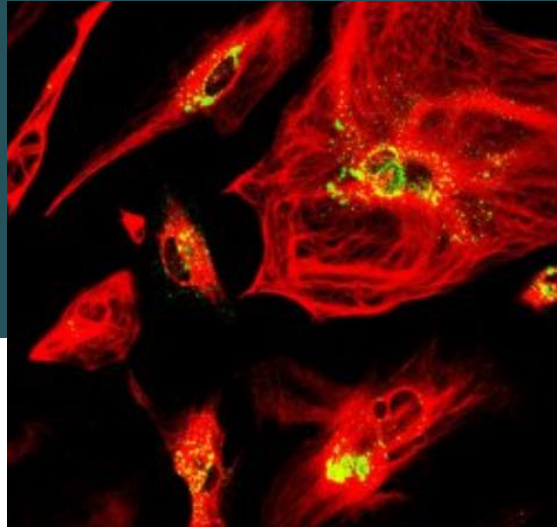
## Typhoïde



Faible niveau d'indication

Quels vaccins pour l'Amérique latine ?

## Rage



R a g e

## Epidémiologie : rage canine

Current Tropical Medicine Reports (2022) 9:28–39  
<https://doi.org/10.1007/s40475-022-00257-6>

EMERGING TROPICAL DISEASES (K BARR, SECTION EDITOR)



### Rabies in the Tropics

Charles E. Rupprecht<sup>1,2</sup> · Reeta S. Mani<sup>3</sup> · Phillip P. Mshelbwala<sup>4,5</sup> · Sergio E. Recuenco<sup>6</sup> · Michael P. Ward<sup>7</sup>

Accepted: 13 February 2022 / Published online: 28 March 2022  
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#### • Amérique centrale

- Mexique : déclaré indemne de rage canine en 2019
- Belize, El Salvador, Honduras, Guatemala et Nicaragua : cas sporadiques

#### • Caraïbes

- Présence de rage canine à Haïti
- Possible sous-déclaration pour Cuba, Grenade, Porto Rico, Trinité et Tobago

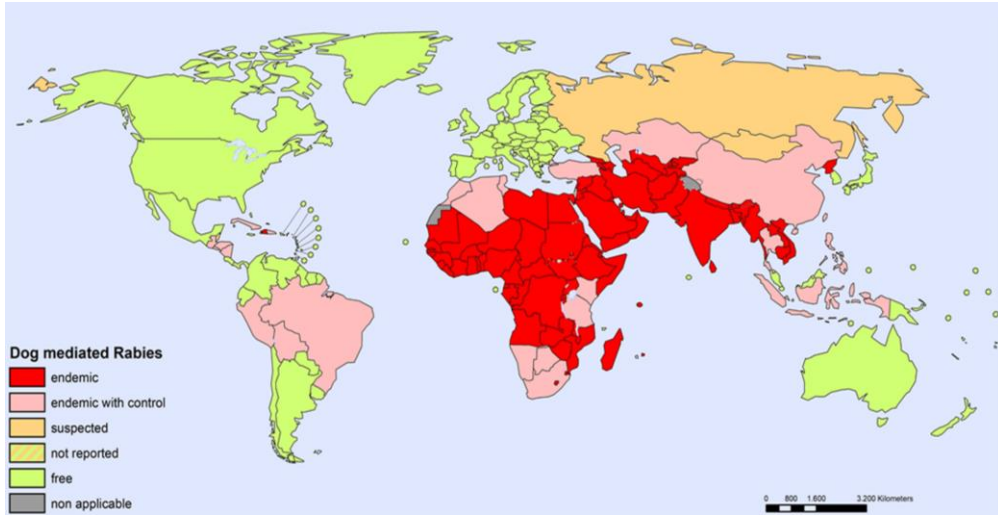
#### • Amérique du Sud

- La plupart du continent est considéré indemne de rage, sauf la Bolivie, le sud du Pérou (Arequipa), certaines régions du Brésil
- Problème d'accès à une prise en charge post-exposition correcte en Bolivie (vaccins sur tissus nerveux)



R a g e

## Epidémiologie : rage canine



Disponible sur <https://www.who-rabies-bulletin.org/>

R a g e

## Epidémiologie : rage des chiroptères



Article

Présence de chauves-souris hémato-phages,

### Evolution of Rabies in South America and Inter-Species Dynamics (2009–2018)

principalement en Amazonie

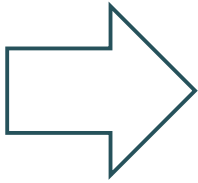
Mauro Meske <sup>1</sup>, Angela Fanelli <sup>2</sup>, Felipe Rocha <sup>3</sup>, Lina Awada <sup>1</sup>, Paula Caceres Soto <sup>1</sup>, Neo Mapitse <sup>1</sup> and Paolo Tizzani <sup>1,\*</sup>

**Table 4.** Number of human cases reported during the period of study, main source of infection in reported cases (aerial or terrestrial) and percentage of administrative divisions reporting rabies cases by country.

Country	Number of Rabies (Cases in Humans)	Predominant Cycle with Regards to the Main Source of Infection (Percentage of Human Cases Due to the Main Reservoir in the Specific Cycle)	Percentage of Administrative Divisions with Human Rabies Cases (Number of Affected Administrative Divisions in Brackets)
Peru	90	Aerial cycle: 93.3% (84) Terrestrial cycle: 6.7% (6)	40% (10)
Brazil	28	Aerial cycle: 76% (21) Terrestrial cycle: 24% (7)	52% (14)
Bolivia	40	Terrestrial cycle: 100% (40)	66% (6)
Ecuador	12	Aerial cycle: 91.6% (11) Terrestrial cycle: 8.3% (1)	8.7% (2)
Colombia	9	Aerial cycle: 100% (9)	15% (5)
Venezuela	2	Terrestrial cycle: 100% (2)	4% (1)
Chile	1	Aerial cycle: 100% (1)	6.6% (1)
<b>Total</b>	<b>192</b>	<b>Aerial cycle: 70% (134) Terrestrial cycle: 30% (58)</b>	<b>16.3% (39)</b>

Quels vaccins pour l'Amérique latine ?

## Rage



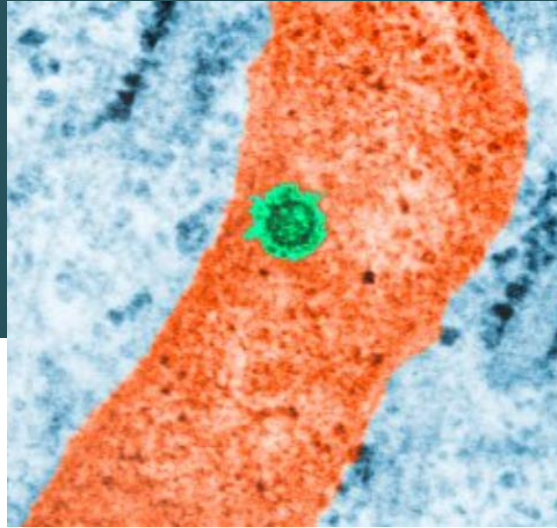
- Intérêt pour la Bolivie : présence de rage canine et prise en charge post-exposition sur place limitée
- Séjours prolongés dans certaines régions du Brésil, du Pérou, de l'Amérique centrale et des caraïbes
- Intérêt pour certains séjours en Amazonie
- Indication limitée pour les autres pays ?

Quels vaccins pour l'Amérique latine ?

## Et les vaccins à venir ?

Quels vaccins pour l'Amérique latine ?

# Dengue



D e n g u e

## Vaccins / candidats

- Tous des vaccins vivants atténués, chimériques recombinants, quadrivalents
- Différence sur la base utilisée

	Dengvaxia (Sanofi Pasteur)	TAK-003 (Takeda)	TV003 (NIH/Butantan/Merck)
Doses	3 doses (0, 6, 12 mois)	2 doses (0, 3 mois)	Une dose
Base			

Arrêt de commercialisation

PHASE 3

- Fièvre jaune
- DENV-1
- DENV-2
- DENV-3
- DENV-4

Dengue

# TAK-003 Essai de phase 3

## 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\*, Della 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 Watanaveerodj, Reynaldo Dietze, Lakshmi Fernando, V Pujitha Wickramasinghe, Edson Duarte Moreira Jr, Asvini D Fernando, Dulanie Gunasekera, Kleber Luz, Ana Lucia Oliveira, Suely Tuboi, Ian Escudero, Yaneer Hutagalung, Eric Lloyd, Martina Rauscher, Olaf Zent, Nicolas Folschweiler, Inge LeFevre, Felix Espinoza†, Derek Wallace†

Lancet Glob Health 2024; 12: e257-70  
See Comment page e179

- Essai randomisé contrôlé en double aveugle, TAK-003 ou placebo 2:1
- Population : Enfants et adolescents de 4 à 16 ans
- 5 pays en Amérique du Sud et 3 en Asie
- 20 071 participants, dont 28% séronégatifs
- Critère de jugement principal : dengue confirmée virologiquement
- Critères de jugement secondaires : hospitalisation, dengue hémorragique, dengue sévère
- Stratification par statut sérologique, sérotype, année et âge

Dengue

## TAK-003 : très bons résultats globaux

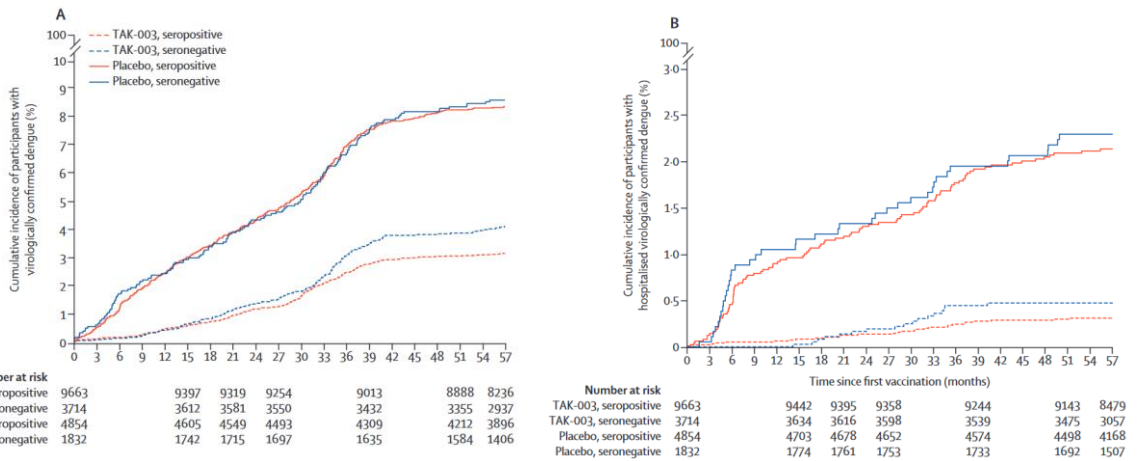


Figure 3: Cumulative incidence of virologically confirmed dengue (A) and hospitalised virologically confirmed dengue (B). Data are for the safety set and are presented from the first dose to up to 4.5 years after the second dose (approximately month 57 after the first dose) and are truncated at month 57.

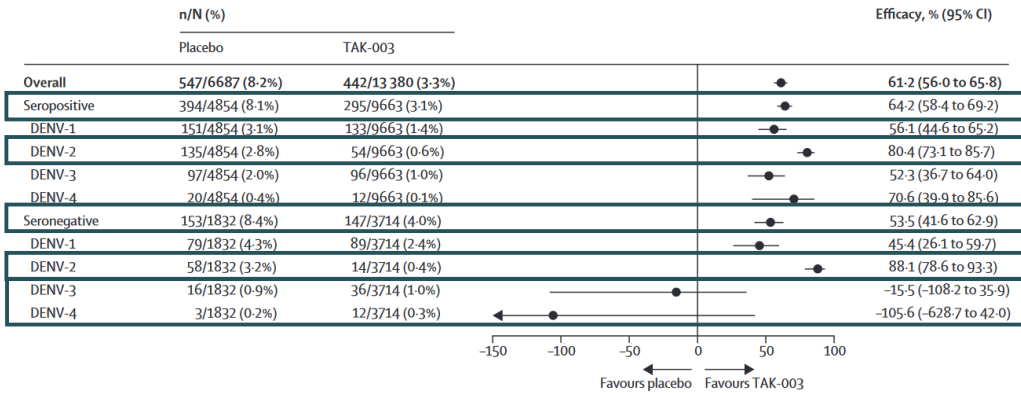
→ Les vaccinés font moins d'infection et sont moins hospitalisés

D e n g u e

## TAK-003 : résultats des sous-groupes (1)

### A Virologically confirmed dengue

Figure 2: Efficacy of TAK-003 in preventing virologically confirmed dengue (A) and hospitalised virologically confirmed dengue, dengue haemorrhagic fever, and DCAE-defined severe dengue (B)



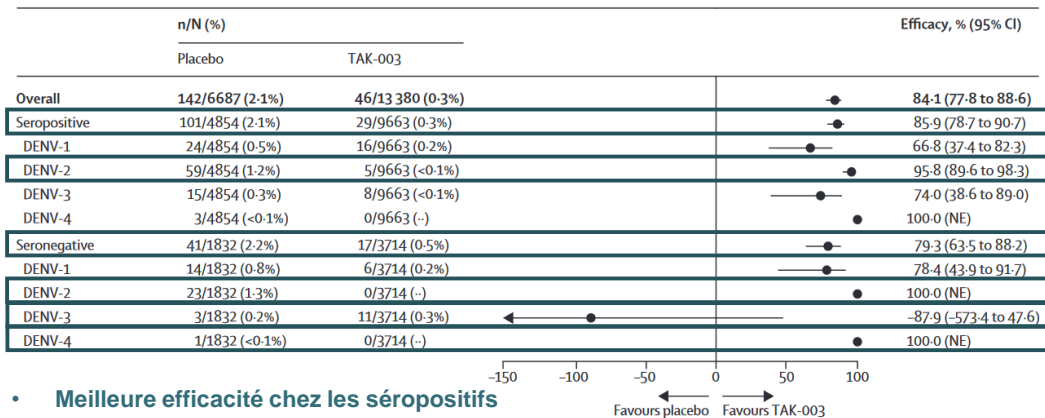
- Meilleure efficacité chez les séropositifs
- Meilleure efficacité pour DENV-2
- Efficacité « négative » pour DENV-3 et DENV-4 chez les séronégatifs mais non significatif

D e n g u e

## TAK-003 : résultats des sous-groupes (2)

### B Hospitalised virologically confirmed dengue

Figure 2: Efficacy of TAK-003 in preventing virologically confirmed dengue (A) and hospitalised virologically confirmed dengue, dengue haemorrhagic fever, and DCAE-defined severe dengue (B)



- Meilleure efficacité chez les séropositifs
- Meilleure efficacité pour DENV-2 chez les séropositifs
- Non significatif pour DENV-3 chez les séronégatifs
- Effectifs trop faibles pour DENV-2 DENV-4 chez les séronégatifs

D e n g u e

## TAK-003 : résultats des sous-groupes (3)

### B Hospitalised virologically confirmed dengue

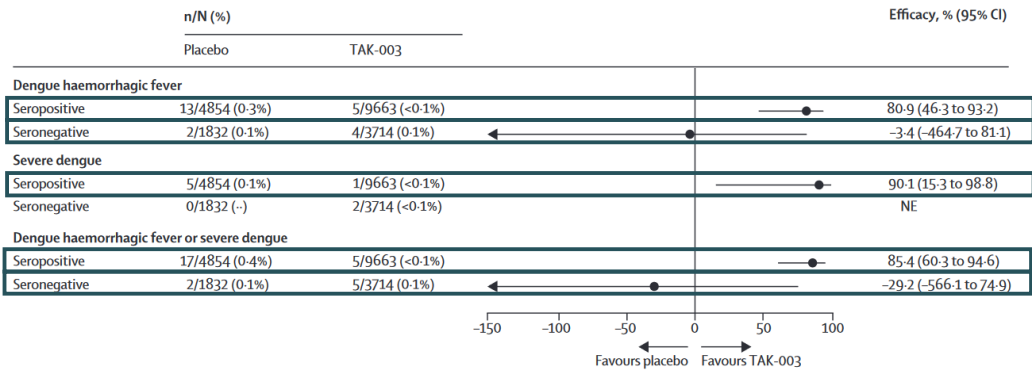
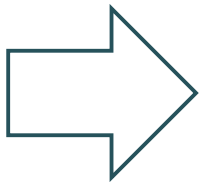


Figure 2: Efficacy of TAK-003 in preventing virologically confirmed dengue (A) and hospitalised virologically confirmed dengue, dengue haemorrhagic fever, and DCAC-defined severe dengue (B)

- Efficacité chez les séropositifs
- Efficacité « négative » chez les séronégatifs mais non significatif

Quels vaccins pour l'Amérique latine ?

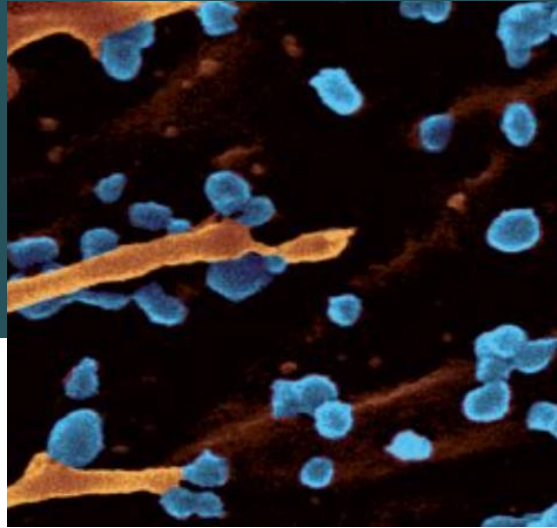
## Dengue



- Surtout efficace pour éviter une hospitalisation
- Plus efficace chez les personnes séropositives et pour le sérotype 2
- Pas d'efficacité prouvée pour prévenir les formes graves chez les séronégatifs
- Pas d'efficacité prouvée +/- possible signal sur la sécurité (mais manque de puissance) pour DENV-3 et DENV-4 chez les séronégatifs

Quels vaccins pour l'Amérique latine ?

## Chikungunya



Chikungunya

### VAL1553 Essai de phase 3

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

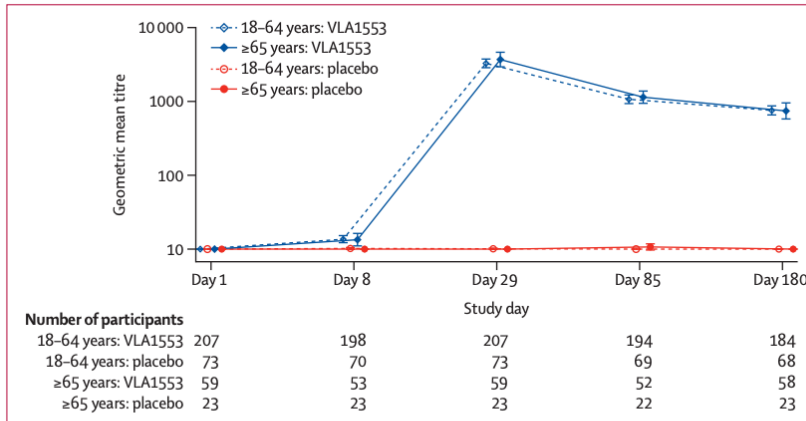
*Martina Schneider, Marivic Narciso-Abraham, Sandra Hadl, Robert McMahon, Sebastian Toepfer, Ulrike Fuchs, Romana Hochreiter, Annegret Blitzer, Karin Kosulin, Julian Larcher-Senn, Robert Mader, Katrin Dubischar, Oliver Zaihsli, Juan-Carlos Jaramillo, Susanne Eder-Lingelbach, Vera Buerger, Nina Wressnigg*

*Lancet* 2023; 401: 2138–47  
Published Online  
June 12, 2023  
[https://doi.org/10.1016/S0140-6736\(23\)00641-4](https://doi.org/10.1016/S0140-6736(23)00641-4)

- Vaccin vivant atténué, une dose
- Essai randomisé contrôlé en double aveugle, VAL1553 ou placebo 3:1
- Population : Adultes  $\geq$  18 ans
- 43 centres aux Etats-Unis
- 4 128 participants
- Critère de jugement principal : présence d'anticorps neutralisants 28 jours après la vaccination
- Critères de jugement secondaires : présence d'anticorps neutralisants 7 jours, 3 mois et 6 mois après la vaccination

Chikungunya

## VAL1553 : anticorps neutralisants post-vaccination



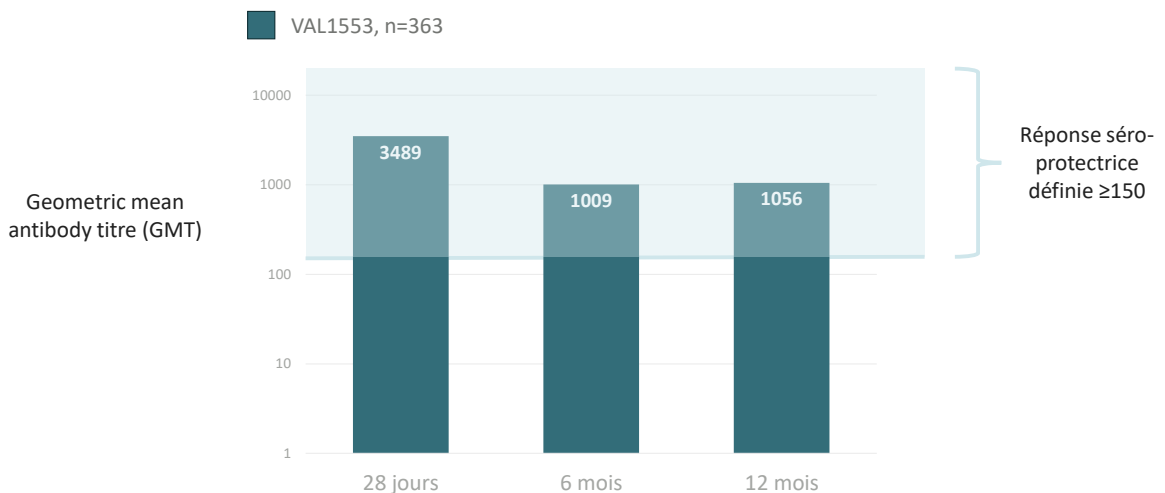
Séroconversion chez 99,2% à J29

Figure 2: Assessment of neutralising antibodies after vaccination

Line plot of chikungunya virus-specific neutralising antibodies geometric mean titres by study day and age stratum. Days shown in the figure refer to study days; day 1=day of vaccination. Error bars indicate 95% CIs. Neutralising antibodies to the vaccine were evaluated from clinical specimen (human serum) using a micro plaque reduction neutralisation test ( $\mu$ PRNT). A  $\mu$ PRNT<sub>50</sub> titre was defined as the dilution with 50% plaque reduction in the  $\mu$ PRNT.

Chikungunya

## VAL1553 : persistance des anticorps à 12 mois



Réponse séro-protectrice définie  $\geq 150$



Chikungunya

**VAL1553 : sécurité**

	VLA1553 (n=3082)	Placebo (n=1033)	Total (n=4115)
Any adverse events	1926 (62.5%, 60.8-64.2) 6415	463 (44.8%, 41.8-47.9) 1071	2389 (58.1%, 56.5-59.6) 7486
Any related adverse events	1575 (51.1%, 49.3-52.9) 4621	322 (31.2%, 28.4-34.1) 647	1897 (46.1%, 44.6-47.6) 5268
Any related severe adverse events	62 (2.0%, 1.5-2.6) 70	1 (0.1%, 0.0-0.5) 3	63 (1.5%, 1.2-2.0) 73
Any serious adverse events	46 (1.5%, 1.1-2.0) 73	8 (0.8%, 0.3-1.5) 10	54 (1.3%, 1.0-1.7) 83
Any related serious adverse events	2 (0.1%, 0.0-0.2) 2	0 (0%, 0.0-0.4) 0	2 (0.0%, 0.0-0.2) 2
Any adverse events of special interest	10 (0.3%, 0.2-0.6) 26	1 (0.1%, 0.0-0.5) 2	11 (0.3%, 0.1-0.5) 28
Any adverse event with a frequency $\geq 10\%$ in at least one study arm			
Headache	986 (32.0%, 30.3-33.7) 1028	160 (15.5%, 13.3-17.8) 178	1146 (27.8%, 26.5-29.2) 1206
Fatigue	886 (28.7%, 27.2-30.4) 893	137 (13.3%, 11.3-15.5) 139	1023 (24.9%, 23.5-26.2) 1032
Myalgia	750 (24.3%, 22.8-25.9) 758	82 (7.9%, 6.4-9.8) 84	832 (20.2%, 19.0-21.5) 842
Arthralgia	554 (18.0%, 16.6-19.4) 589	63 (6.1%, 4.7-7.7) 70	617 (15.0%, 13.9-16.1) 659
Injection site pain	413 (13.4%, 12.2-14.7) 519	101 (9.8%, 8.0-11.8) 122	514 (12.5%, 11.5-13.5) 641
Pyrexia	427 (13.9%, 12.7-15.1) 429	13 (1.3%, 0.7-2.1) 13	440 (10.7%, 9.8-11.7) 442
Nausea	359 (11.6%, 10.5-12.8) 364	63 (6.1%, 4.7-7.7) 64	422 (10.3%, 9.3-11.2) 428
Any serious adverse event with a frequency $\geq 0.2\%$ in at least one study arm by system organ class			
Infections and infestations	9 (0.3%, 0.1-0.6) 9	3 (0.3%, 0.1-0.8) 3	12 (0.3%, 0.2-0.5) 12
Injury, poisoning, and procedural complications	8 (0.3%, 0.1-0.5) 15	1 (0.1%, 0.0-0.5) 1	9 (0.2%, 0.1-0.4) 16
Psychiatric disorders	7 (0.2%, 0.1-0.5) 8	2 (0.2%, 0.0-0.7) 4	9 (0.2%, 0.1-0.4) 12
Cardiac disorders	5 (0.2%, 0.1-0.4) 7	0 (0%, 0.0-0.4) 0	5 (0.1%, 0.0-0.3) 7

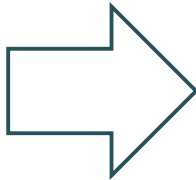
Data are n (%; 95% CI) N. For each category, participants were included only once, even if they experienced multiple events in that category. Related adverse events are those recorded as probably related or possibly related on the eCRF. Adverse events of special interest counts are for the overall event and the adverse event of special interest symptom count includes a count of all symptoms contributing to the event. Two-sided exact Clopper-Pearson 95% CIs are presented. eCRF=electronic case report form. n=number of participants. N=number of events.

**Table 3: Overall summary of adverse events (safety population)**

➔ **Deux effets indésirables « graves » attribués au vaccins :**

- Une patiente de 58 ans hospitalisée pour myalgie
- Un patient de 66 ans hospitalisé pour fièvre prolongée, compliquée de fibrillation atriale et hyponatrémie sévère

Quels vaccins pour l'Amérique latine ?

**Chikungunya**

- Vaccin prometteur
- Indications chez le voyageur ?

## **CONCLUSION :**

### **Quels vaccins pour l'Amérique latine ?**

- **Fièvre jaune et hépatite A : restent fortement indiqués**
- **Typhoïde : faible niveau d'indication**
- **Rage : principalement pour la Bolivie et l'Amazonie**
- **Dengue : indication chez le voyageur à rediscuter**
- **Chikungunya : vaccin prometteur sur les premiers résultats**