

April 2026 *Authors:* Emmanuel Feroldi, Mark J. Mulligan, Kawsar R. Ilaal, Chen Sabrina Tan, Kristopher Paolino, Sriatha Edupuganti, Matthew H. Collins, Sarah L. George, Matthew Davis, Brandon Essink, Robert Jeanfreau, James Peterson, David Fried, Ada-Maria Minutello, Sandrine Orlando, Joanna Korejwo, Andrey Rojas, Marine Dufournet, Tiffany Macchabert, Louis Devlin, and Carina Frago, for the vYF Vaccine Study Team
Journal: The New England Journal of Medicine. DOI: 10.1056/NEJMoa2505665

yVF (Sanofi) is a next-generation live-attenuated yellow fever vaccine derived from the YF-17D 204 substrain, produced in Vero cells to improve supply scalability⁵. A phase 1 clinical trial showed that yVF had safety and immunogenicity similar to that of YF-VAX⁶.



RESULTS

- Baseline characteristics were similar between the two vaccine groups in both the randomized population and the per-protocol analysis population
- Most participants were female (61.6%) and White (65.1%), with a mean age of 39.7 ± 11.9 years
- Most participants had no prior history of infection with or vaccination for orthoflaviviruses, including yellow fever, at baseline
- For the per-protocol population used in the noninferiority analysis, 329 participants from the vYF group and 156 participants from the YF-VAX group were included, representing 485 participants in total

IMMUNOGENICITY OUTCOMES

- Among participants with no prior history of yellow fever infection or vaccination, seroconversion by day 29 (28 days post-vaccination) was achieved in 328 (99.7%) in the vYF group and 155 participants (99.4%) in the YF-VAX group, meeting the criterion for noninferiority (Table 1)

Table 1. Non-inferiority¹ of the percentage of YF-naïve participants achieving SC[§] 28 days after 1 dose^{||} of YF vaccine (PPAS)[#]

vYF (n=370)			YF-VAX (n=183)			vYF – YF-VAX		
n/N	SC [§] rate (%)	95% CI (2-sided)	n/N	SC [§] rate (%)	95% CI (2-sided)	Difference (%)	95% CI (2-sided)	Non-inferiority ¹
328/329	99.7	(98.3, 100)	155/156	99.4	(96.5, 100)	0.3	(-1.2, 3.2)	Yes

- Seroconversion (titers $\geq 1:10$) was achieved in 99.4% of participants with no history of yellow fever infection or vaccination, by day 29 in both vaccine groups, with $\geq 97\%$ maintaining protective titers through month 6 and year 1 (Figure 2)
- At day 11, 38% (21/56) of vYF recipients and 61% (19/31) of YF-VAX recipients achieved neutralizing antibody titers meeting the likely protective threshold (Figure 2)
- Both vYF and YF-VAX vaccine groups showed identical baseline GMTs (1:5) in participants with no prior yellow fever exposure, and comparable GMTs in those with prior exposure (1:67 vs. 1:56) (Figure 3)
- In both vaccine groups, GMTs increased from baseline to day 29, then decreased slightly through year 1 but remained above seroprotection level ($\geq 1:10$) regardless of prior yellow fever history (Figure 3)
- Participants without prior yellow fever exposure showed stronger GMT responses at day 29 compared to those with previous infection or vaccination history (Figure 3)

Figure 2. Seroprotection among participants with no history of yellow fever infection or vaccination (full analysis population)

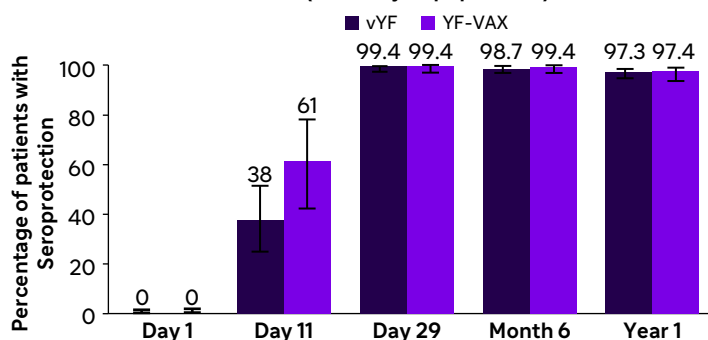
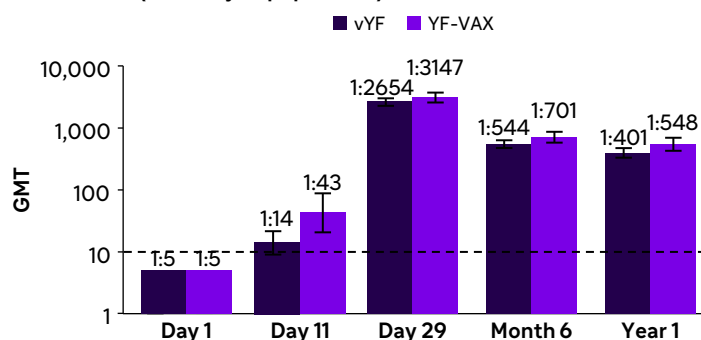


Figure 3. GMTs in participants with no history of yellow fever infection or vaccination (full analysis population)



SAFETY

- No major safety concerns were observed
- Similar rates of solicited and unsolicited AEs, including grade 3 reactions among the 2 vaccine groups
- No participants discontinued the trial owing to an AE, and no vaccine-related SAEs or AESIs were reported up to 1 year after vaccination
- 2 participants (1.1%) in the YF-VAX group reported at least one SAE within 28 days after vaccination (blood loss anemia in 1 participant and appendicitis in 1 participant)



LIMITATIONS

- Trial participants were limited to healthy adults aged 18–60 years, restricting generalizability to vulnerable populations including children, pregnant women, older adults, and immunocompromised individuals
- Non-endemic setting (US only) population representative of travelers, not endemic-area residents
- The trial was not powered to demonstrate noninferiority with respect to early immune response; therefore, early immunogenicity results should be interpreted with caution

SUMMARY

- In healthy adults aged 18–60 years with no prior yellow fever exposure, the vYF vaccine was shown to be non-inferior to YF-VAX in inducing seroconversion at 28 days post-vaccination. Neutralizing antibody titers were maintained for a minimum of one year, with long-term immune persistence continuing to be evaluated
- vYF demonstrated a comparable safety profile to YF-VAX

*The agent discussed herein is investigational and has not been approved by the U.S. Food and Drug Administration (FDA) or any other regulatory authority worldwide. Therefore, no conclusions should be drawn regarding its safety or efficacy.

¹Non-inferiority demonstrated if the lower limit of the 2-sided 95% CI is $\geq 5\%$; [§]SC defined as a 4-fold increase in neutralizing antibody titers vs the pre-vaccination value; ^{||}i.e., on Day 29; [#]Per protocol population defined as a subset of the full analysis population where no protocol deviations occurred. AE, adverse event; AESI, adverse event of special interest; CI, confidence interval; GMT, geometric mean titer; MAAE, medically attended adverse events; N, number of participants with available data; n, number of participants with seroconversion; NCT, National Clinical Trial; PPAS, per-protocol analysis set; R, randomized; SAE, serious adverse event; SC, seroconversion; WHO, World Health Organization; vYF, next-generation live-attenuated yellow fever vaccine; YF-VAX, yellow fever vaccine, adsorbed

References: 1. Lindsey NP, et al. *NPJ Vaccines*. 2022;7:137; 2. Shearer FM, et al. *Lancet Infect Dis*. 2017;17:1209–1217; 3. Gaythorpe KAM, et al. *Elife*. 2021;10:e64670–e64670; 4. WHO. Vaccines and vaccination against yellow fever. WHO position paper — June 2013. *Wkly Epidemiol Rec* 2013;88:269–283; 5. Sanchez-Felipe L, et al. *Eur J Immunol*. 2024; 54(5): e2250133; 6. Modjarrad K, et al. *Lancet Infect Dis*. 2024;24: 1393–402



Scan the QR