PUBLICATION CARD

# Immunogenicity and safety of a purified vero rabies vaccine – serum free, compared with two licensed vaccines, in a simulated rabies post-exposure regimen in healthy adults in France: A randomized controlled phase III trial

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## INTRODUCTION

Vaccines are highly prophylactic when administered as pre-exposure prophylaxis (PrEP) in high-risk individuals or as post-exposure prophylaxis (PEP) in individuals exposed to rabid animals, in some cases in conjunction with rabies immunoglobulin.

PVRV-NG (Sanofi), a next-generation rabies vaccine is a serum- and antibiotic-free, highly purified Vero cell rabies vaccine, developed using the same Pitman–Moore viral strain as the licensed HDCV (human diploid cell vaccine) and PVRV (purified Vero cell rabies vaccine) vaccines.

Two PVRV-NG formulations (PVRV-NG and PVRV-NG2) have been developed with a reduced residual DNA content (<100 pg/dose) and is free of raw material derived from animal/human origin.

## OBJECTIVE

This phase III study evaluated non-inferiority of the immune response elicited by PVRV-NG2 versus standard-of-care vaccines (PVRV and HDCV), when co-administered with human rabies immunoglobulin (HRIG) as simulated PEP in healthy adults. Further, the safety and immunogenicity of PVRV-NG2 as a standalone vaccine was also assessed.

## METHODS

### STUDY DESIGN

Phase III, dual-center, modified, double-blind, controlled, randomized study (NCT03965962)

### VACCINES AND HRIG

- PVRV-NG2+HRIG, PVRV+HRIG, HDCV+HRIG, or PVRV-NG2 alone: 3:1:1:1
- Administered and as single doses on D0, D3, D7, D14 D28, with HRIG on D0

### PARTICIPANTS

Healthy adults (N=640)

**Age:** ≥18 years old (mean age: 46.2 years)

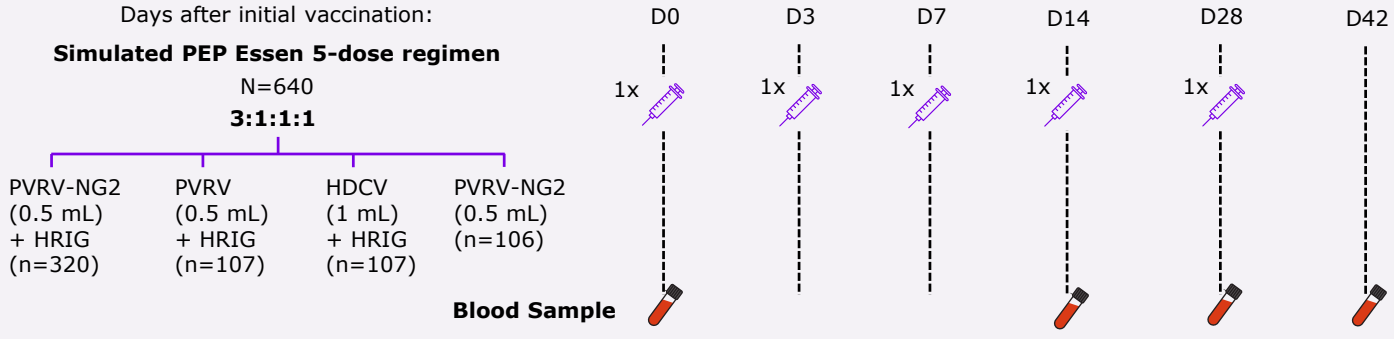
**Exclusion criteria:** High risk of rabies exposure and any prior vaccination with any vaccine, within 4 weeks

### LOCATION AND PERIOD

**Location:** France

**Period:** July 2019 – January 2021

**Figure 1: Study design**




**Immunogenicity assessment:**

- Blood samples at D0 (baseline titer), D14, D28, and D42 to measure RVNA using the RFFIT (rapid fluorescent focus inhibition test)

**Safety assessment:**

- Solicited injection site reactions were recorded for 7 days after each vaccination.
- Solicited systemic reactions were recorded up to 7 days following each vaccination.
- Unsolicited injection site reactions were recorded for 28 days after each vaccination.
- Unsolicited systemic adverse events (AEs) were recorded between each vaccination and for 28 days following the last vaccination.
- Serious AEs (SAEs), AEs of special interest (AESIs), and cases of pregnancy were recorded throughout the study period for up to 6 months after the last vaccination.

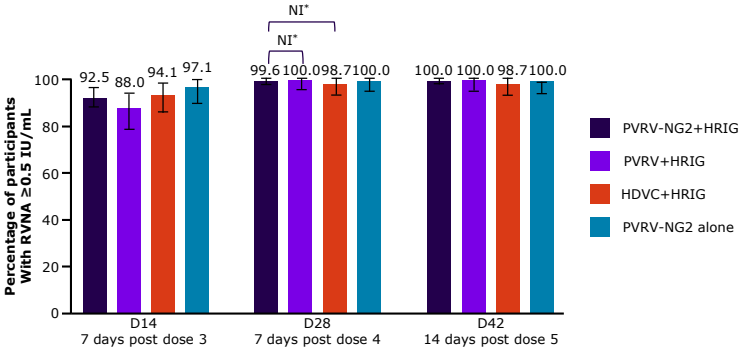
## RESULTS

- A total of 640 healthy participants were enrolled and randomized. Most (95.6%) of them were Caucasian; 59.7% were female
- Baseline characteristics were similar across study groups

### Immunogenicity objectives

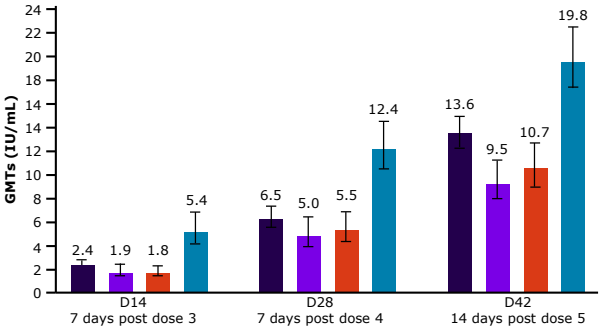
- *Non-inferiority of PVRV-NG2+HRIG* compared with PVRV+HRIG (difference, −0.42%, 95% CI: −2.33%, 4.35%) and HDCV+HRIG (difference, 0.86%, 95% CI: −1.32%, 6.50%) was *demonstrated at D28* **(Figure 2)**
- At D28, almost all participants (99.6%, PVRV-NG2+HRIG; 100%, PVRV+HRIG; 98.7%, HDCV+HRIG; 100%, PVRV-NG2 alone) achieved RVNA titers ≥0.5 IU/mL by PPAS vaccination group **(Figure 2)**
- *Sufficiency was demonstrated* in the PVRV-NG2+HRIG group, with 99.6% (95% CI *97.7%*, 100.0%) of participants achieving an RVNA titer ≥0.5 UI/mL at D28 (lower limit of 95% CI of the percentage of participants ≥95%)
- RVNA GMTs were similar across groups with concomitant HRIG administration, but higher in the PVRV-NG2 alone group, than the other groups, at all given time points **(Figure 3)**

**Figure 2: % of participants achieving RVNA titers ≥0.5 IU/mL at D14, D28, and D42, by vaccination group (PPAS)**




*NI: Non-inferiority demonstrated if lower limit of 95% CI of the difference of % between PVRV-NG2+HRIG and comparators was ≥5% at D28

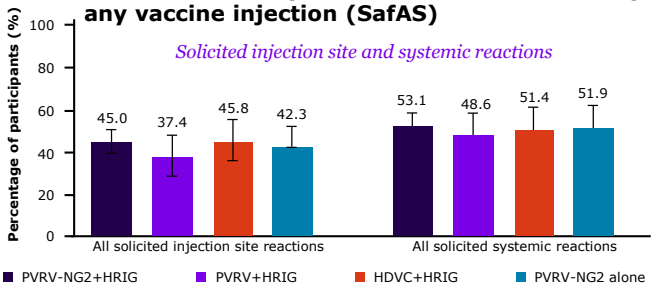
**Figure 3: RVNA GMTs at D14, D28, and D42, by vaccination group (PPAS)**




### Safety objectives

- No major vaccine-related safety concerns were observed; frequency and severity of AEs were similar between PVRV-NG2 and comparator vaccine groups
- The proportion of participants who reported solicited reactions decreased after each subsequent vaccination
- Grade 3 reactions were reported (1 participant with solicited injection site reaction and 8 with systemic reactions (SafAS) **(Figure 4)**
- 12 SAEs reported in 11 participants, 2 of them (dyskinesia and general physical health deterioration) considered as related to vaccine by the investigator but not the sponsor

**Figure 4: % of participants experiencing an injection site reaction or systemic reaction within 7 days after any vaccine injection (SafAS)**




## STUDY LIMITATIONS

- Since the study was conducted in healthy adults, it did not reflect real-life practice for co-administration of HRIG around the wound site, as per WHO recommendations
- There was lack of persistence data, which will be included in a companion study (NCT04127786)

**Footnote:** Figures 1–4 are created based on manuscript text/table.

**Glossary:** AE, adverse event; CI, confidence interval; D, day; DNA, deoxyribonucleic acid; GMT, geometric mean titer; HDCV, human diploid cell vaccine (Imovax Rabies®, Sanofi); HRIG, human rabies immunoglobulin; PEP, post-exposure prophylaxis; PPAS, per-protocol analysis set; PVRV, purified Vero cell vaccine (Verorab®, Sanofi); PVRV-NG, purified Vero cell vaccine-next generation; RFFIT, rapid fluorescent focus inhibition test; RVNA, rabies virus neutralizing antibody; SAE, serious adverse events; SOC, standard-of-care; SafAS, safety analysis set; WHO, World Health Organization

**References:** Pineda-Peña, AC. et. al. Immunogenicity and safety of a purified vero rabies vaccine - serum free, compared with two licensed vaccines, in a simulated rabies post-exposure regimen in healthy adults in France: a randomized controlled phase III trial. *Clin Infect Dis*. 2024 Mar; https://doi.org/10.1093/cid/ciae137

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