Clinical trial results:
Immunogenicity and Safety of a Purified Vero Rabies Vaccine– Serum Free (VRVg) Assessed with the Institut Pasteur du Cambodge (IPC: 2-2-2-0-0) and the Thai Red Cross (TRC: 2-2-2-0-2) Intradermal Regimens as Simulated Rabies Post-exposure Prophylaxis in Healthy Subjects in Thailand

Summary

EudraCT number	2019-004008-36
Trial protocol	Outside EU/EEA
Global end of trial date	21 July 2022

Results information

Result version number	v1 (current)
This version publication date	01 February 2023
First version publication date	01 February 2023

Trial information

Trial identification

Sponsor protocol code	VRV09

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04478084
WHO universal trial number (UTN)	U1111-1227-4143

Notes:

Sponsors

Sponsor organisation name	Sanofi Pasteur
Sponsor organisation address	14 Espace Henry Vallée, Lyon, France, 69007
Public contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi Pasteur, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002234-PIP01-17
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 July 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To describe the immune response induced by purified vero rabies vaccine - serum free vaccine formulation 2 (VRVg-2) and Verorab vaccine at Day 14 (to assess the immune response after 3 doses [2-2-2]) and Day 42 (to assess the immune response after 4 doses [2-2-2-0-2]) when administered as standalone in healthy pediatric population or co-administered with human rabies immunoglobulins (HRIG) (Group 5 and Group 6) at Day 0 in healthy adults.

Protection of trial subjects:

Vaccinations were performed by qualified and trained study personnel. Subjects with allergy to any of the vaccine components were not vaccinated. After vaccination, subjects were also kept under clinical observation for 30 minutes to ensure their safety. Appropriate medical equipment were also available on site in case of any immediate allergic reactions.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 August 2020
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Thailand: 402
Worldwide total number of subjects	402
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	3
Children (2-11 years)	81
Adolescents (12-17 years)	84
Adults (18-64 years)	229
From 65 to 84 years	5

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 3 active sites in Thailand between 04 August 2020 and 21 July 2022.

Pre-assignment

Screening details:

A total of 402 subjects were enrolled and randomised in the study. Subjects received vaccination during the active phase of the study on Days 0, 3, 7 and 28 and were followed-up for safety 6-months post-vaccination.

Period 1

Period 1 title	Overall study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: VRVg-2

Arm description:

Pediatric subjects aged 1 year to less than (<) 18 years received 8 injections (1 vaccination on each arm) of 0.5 millilitres (mL) of VRVg-2 intradermally on Days 0, 3, 7 and 28.

Arm type	Experimental
Investigational medicinal product name	Purified vero rabies vaccine - serum free
Investigational medicinal product code	
Other name	VRVg-2
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

8 injections (1 vaccination on each arm) intradermally at Days 0, 3, 7, and 28.

Arm title	Group 2: Verorab®

Arm description:

Pediatric subjects aged 1 year to <18 years received 8 injections (1 vaccination on each arm) of 0.5 mL purified inactivated rabies vaccine prepared on Vero cell line (Verorab®) intradermally on Days 0, 3, 7 and 28.

Arm type	Active comparator
Investigational medicinal product name	Purified inactivated rabies vaccine
Investigational medicinal product code	
Other name	Verorab®
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

8 injections (1 vaccination on each arm) intradermally at Days 0, 3, 7, and 28.

Arm title	Group 3: VRVg-2 + ERIG

Arm description:

Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3 and 7 along with Equine rabies immunoglobulins (ERIG) intramuscular (IM) injection at Day 0.

Arm type	Experimental

Investigational medicinal product name	Purified vero rabies vaccine - serum free
Investigational medicinal product code	
Other name	VRVg-2
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

6 injections (1 vaccination on each arm) intradermally at Days 0, 3 and 7.

Investigational medicinal product name	Equine rabies immunoglobulins
Investigational medicinal product code	
Other name	ERIG
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intramuscular use

Dosage and administration details:

Single 0.5 mL IM injection at Day 0.

Arm title	Group 4: Verorab® + ERIG

Arm description:

Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3 and 7 along with ERIG IM injection at Day 0.

Arm type	Active comparator
Investigational medicinal product name	Purified inactivated rabies vaccine
Investigational medicinal product code	
Other name	Verorab®
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

6 injections (1 vaccination on each arm) intradermally at Days 0, 3 and 7.

Investigational medicinal product name	Equine rabies immunoglobulins
Investigational medicinal product code	
Other name	ERIG
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intramuscular use

Dosage and administration details:

Single 0.5 mL IM injection at Day 0.

Arm title	Group 5: VRVg-2 + HRIG

Arm description:

Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.

Arm type	Experimental
Investigational medicinal product name	Purified vero rabies vaccine - serum free
Investigational medicinal product code	
Other name	VRVg-2
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

8 injections (1 vaccination on each arm) intradermally at Days 0, 3, 7, and 28.

Investigational medicinal product name	Human rabies immunoglobulins
Investigational medicinal product code	
Other name	IMOGAM® Rabies-HT, HRIG
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intramuscular use

Dosage and administration details:

Single 0.5 mL IM injection at Day 0.

Arm title	Group 6: Verorab + HRIG

Arm description:

Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.

Arm type	Active comparator
Investigational medicinal product name	Purified inactivated rabies vaccine
Investigational medicinal product code	
Other name	Verorab®
Pharmaceutical forms	Powder for solution for injection
Routes of administration	Intradermal use

Dosage and administration details:

8 injections (1 vaccination on each arm) intradermally at Days 0, 3, 7, and 28.

Investigational medicinal product name	Human rabies immunoglobulins
Investigational medicinal product code	
Other name	IMOGAM® Rabies-HT, HRIG
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intramuscular use

Dosage and administration details:

Single 0.5 mL IM injection at Day 0.

Number of subjects in period 1	Group 1: VRVg-2	Group 2: Verorab®	Group 3: VRVg-2 + ERIG
Started	112	56	26
Vaccination 1 (Day 0)	112	56	26
Vaccination 2 (Day 3)	112	56	23
Vaccination 3 (Day 7)	112	56	21
Vaccination 4 (Day 28)	112	56	0
Completed	112	56	0
Not completed	0	0	26
Adverse event	-	-	6
Protocol deviation	-	-	20

Number of subjects in period 1	Group 4: Verorab® + ERIG	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG
Started	14	129	65
Vaccination 1 (Day 0)	14	129	65
Vaccination 2 (Day 3)	14	129	65
Vaccination 3 (Day 7)	12	129	65
Vaccination 4 (Day 28)	0	127	64
Completed	0	114	54
Not completed	14	15	11
Adverse event	2	-	-
Protocol deviation	12	15	11

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: VRVg-2
Reporting group description:	
Pediatric subjects aged 1 year to less than (<) 18 years received 8 injections (1 vaccination on each arm) of 0.5 mililitres (mL) of VRVg-2 intradermally on Days 0, 3, 7 and 28.	
Reporting group title	Group 2: Verorab®
Reporting group description:	
Pediatric subjects aged 1 year to <18 years received 8 injections (1 vaccination on each arm) of 0.5 mL purified inactivated rabies vaccine prepared on Vero cell line (Verorab®) intradermally on Days 0, 3, 7 and 28.	
Reporting group title	Group 3: VRVg-2 + ERIG
Reporting group description:	
Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3 and 7 along with Equine rabies immunoglobulins (ERIG) intramuscular (IM) injection at Day 0.	
Reporting group title	Group 4: Verorab® + ERIG
Reporting group description:	
Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3 and 7 along with ERIG IM injection at Day 0.	
Reporting group title	Group 5: VRVg-2 + HRIG
Reporting group description:	
Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.	
Reporting group title	Group 6: Verorab + HRIG
Reporting group description:	
Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.	

Reporting group values	Group 1: VRVg-2	Group 2: Verorab®	Group 3: VRVg-2 + ERIG
Number of subjects	112	56	26
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	10.1	10.8	36.2
standard deviation	± 4.3	± 3.8	± 10.4
Gender categorical			
Units: Subjects			
Female	54	24	18
Male	58	32	8

Reporting group values	Group 4: Verorab® + ERIG	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG
Number of subjects	14	129	65
Age categorical			
Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	37.3 ± 11.1	40.2 ± 11.1	39.2 ± 10.9
Gender categorical Units: Subjects			
Female	9	78	39
Male	5	51	26

Reporting group values	Total		
Number of subjects	402		
Age categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	- -		
Gender categorical Units: Subjects			
Female	222		
Male	180		

End points

End points reporting groups

Reporting group title	Group 1: VRVg-2
Reporting group description:	
Pediatric subjects aged 1 year to less than (<) 18 years received 8 injections (1 vaccination on each arm) of 0.5 millilitres (mL) of VRVg-2 intradermally on Days 0, 3, 7 and 28.	
Reporting group title	Group 2: Verorab®
Reporting group description:	
Pediatric subjects aged 1 year to <18 years received 8 injections (1 vaccination on each arm) of 0.5 mL purified inactivated rabies vaccine prepared on Vero cell line (Verorab®) intradermally on Days 0, 3, 7 and 28.	
Reporting group title	Group 3: VRVg-2 + ERIG
Reporting group description:	
Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3 and 7 along with Equine rabies immunoglobulins (ERIG) intramuscular (IM) injection at Day 0.	
Reporting group title	Group 4: Verorab® + ERIG
Reporting group description:	
Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3 and 7 along with ERIG IM injection at Day 0.	
Reporting group title	Group 5: VRVg-2 + HRIG
Reporting group description:	
Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.	
Reporting group title	Group 6: Verorab + HRIG
Reporting group description:	
Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.	

Primary: Percentage of Subjects With Rabies Virus Neutralising Antibody (RVNA) Titer Greater Than or Equal to (>=) 0.5 International Units per Millilitres (IU/mL)

End point title	Percentage of Subjects With Rabies Virus Neutralising Antibody (RVNA) Titer Greater Than or Equal to (>=) 0.5 International Units per Millilitres (IU/mL)[1][2]
End point description:	
RVNA titer against rabies virus was assessed using the Rapid Fluorescent Focus Inhibition test (RFFIT) assay method. Analysis was performed on the per-protocol analysis set (PPAS) that included all subjects who received at least 1 dose of the study vaccine. The subjects who presented protocol deviations and met PPAS exclusion criteria were excluded from PPAS. Here, 'n' = subjects with available data for each specified category.	
End point type	Primary
End point timeframe:	
Day 0 (pre-vaccination), Day 14 and Day 42 (post-vaccination)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was reported for the endpoint.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for applicable arms in the study.

End point values	Group 1: VRVg-2	Group 2: Verorab®	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	98	52	78	37
Units: percentage of subjects				
number (confidence interval 95%)				
Day 0 (n=98,52,78,37)	0.0 (0.0 to 3.7)	0.0 (0.0 to 6.8)	0.0 (0.0 to 4.6)	0.0 (0.0 to 9.5)
Day 14 (n=97,49,74,36)	100 (96.3 to 100)	98.0 (89.1 to 99.9)	59.5 (47.4 to 70.7)	52.8 (35.5 to 69.6)
Day 42 (n=98,52,78,37)	100 (96.3 to 100)	100 (93.2 to 100)	96.2 (89.2 to 99.2)	100 (90.5 to 100)

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of Subjects With RVNA Titer >=0.2 IU/mL (Lower Limit of Quantification [LLOQ])

End point title	Percentage of Subjects With RVNA Titer >=0.2 IU/mL (Lower Limit of Quantification [LLOQ])[3][4]

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. LLOQ for the RFFIT assay was 0.2 IU/mL. Analysis was performed on PPAS population. Here 'n'= subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination), Day 14 and Day 42 (post-vaccination)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was reported for the endpoint.

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for applicable arms in the study.

End point values	Group 1: VRVg-2	Group 2: Verorab®	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	98	52	78	37
Units: percentage of subjects				
number (confidence interval 95%)				
Day 0 (n=98,52,78,37)	0.0 (0.0 to 3.7)	0.0 (0.0 to 6.8)	0.0 (0.0 to 4.6)	0.0 (0.0 to 9.5)
Day 14 (n=97,49,74,36)	100 (96.3 to 100)	100 (92.7 to 100)	85.1 (75.0 to 92.3)	83.3 (67.2 to 93.6)
Day 42 (n=98,52,78,37)	100 (96.3 to 100)	100 (93.2 to 100)	98.7 (93.1 to 100)	100 (90.5 to 100)

Statistical analyses

No statistical analyses for this end point

Primary: Geometric Mean Titer Ratios (GMTRs) of Individual RVNA Titers

End point title	Geometric Mean Titer Ratios (GMTRs) of Individual RVNA

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. GMTRs were calculated as the ratio of GMTs post-vaccination (i.e., on Day 14 and Day 42) and pre-vaccination on Day 0. Analysis was performed on PPAS population. Here, 'n' = subjects with available data for each specified category.

End point type	Primary

End point timeframe:

Day 0 (pre-vaccination), Day 14 and Day 42 (post-vaccination)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Only descriptive statistical analysis was reported for the endpoint.

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for applicable arms in the study.

End point values	Group 1: VRVg-2	Group 2: Verorab®	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	98	52	78	37
Units: ratio				
geometric mean (confidence interval 95%)				
Day 14/ Day 0 (n=97,49,74,36)	29.4 (24.8 to 34.9)	25.3 (19.7 to 32.6)	6.77 (5.21 to 8.79)	5.39 (3.65 to 7.96)
Day 42/Day 0 (n=98,52,78,37)	114 (96.4 to 134)	96.2 (79.5 to 116)	31.3 (24.9 to 39.2)	44.1 (33.1 to 58.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With RVNA Titer >= 0.5 IU/mL: Group 3 and Group 4

End point title	Percentage of Subjects With RVNA Titer >= 0.5 IU/mL: Group 3 and Group 4[7]

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. Analysis was performed on PPAS population.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 14 (post-vaccination)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for applicable arms in the study.

End point values	Group 3: VRVg-2 + ERIG	Group 4: Verorab® + ERIG		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	9		
Units: percentage of subjects				
number (confidence interval 95%)				
Day 0	0.0 (0.0 to 20.6)	0.0 (0.0 to 33.6)		
Day 14	75.0 (47.6 to 92.7)	55.6 (21.2 to 86.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With RVNA Titer >= 0.2 IU/mL (LLOQ): Group 3 and Group 4

End point title	Percentage of Subjects With RVNA Titer >= 0.2 IU/mL (LLOQ): Group 3 and Group 4[8]

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. LLOQ for the RFFIT assay was 0.2 IU/mL. Analysis was performed on PPAS population.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 14 (post-vaccination)

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for applicable arms in the study.

End point values	Group 3: VRVg-2 + ERIG	Group 4: Verorab® + ERIG		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	9		
Units: percentage of subjects				
number (confidence interval 95%)				
Day 0	0.0 (0.0 to 20.6)	0.0 (0.0 to 33.6)		
Day 14	100 (79.4 to 100)	77.8 (40.0 to 97.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: GMTRs of Individual RVNA Titers: Group 3 and Group 4

End point title	GMTRs of Individual RVNA Titers: Group 3 and Group 4[9]

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. GMTRs were calculated as the ratio of GMTs post-vaccination (i.e., on Day 14) and pre-vaccination on Day 0. Analysis was performed on PPAS population.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day 14 (post-vaccination)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for applicable arms in the study.

End point values	Group 3: VRVg-2 + ERIG	Group 4: Verorab® + ERIG		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	16	9		
Units: ratio				
geometric mean (confidence interval 95%)				
Day 14/Day 0	10.1 (6.17 to 16.4)	13.6 (1.98 to 92.9)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With RVNA Titer >= 0.5 IU/mL: Groups 1, 2, 5 and 6

End point title	Percentage of Subjects With RVNA Titer >= 0.5 IU/mL: Groups 1, 2, 5 and 6[10]

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. Analysis was performed on PPAS population. Here, 'number analysed' = subjects with available data for this endpoint. Data for this endpoint was not planned to be collected and analysed for Groups 3 and 4.

End point type	Secondary

End point timeframe:

Day 90 (post-vaccination)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for applicable arms in the study.

End point values	Group 1: VRVg-2	Group 2: Verorab®	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	52	76	37
Units: percentage of subjects				
number (confidence interval 95%)	99.0 (94.4 to 100)	98.1 (89.7 to 100)	75.0 (63.7 to 84.2)	78.4 (61.8 to 90.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With RVNA Titer >= 0.2 IU/mL (LLOQ): Groups 1, 2, 5 and 6

End point title	Percentage of Subjects With RVNA Titer >= 0.2 IU/mL (LLOQ): Groups 1, 2, 5 and 6[11]

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. LLOQ for the RFFIT assay was 0.2 IU/mL. Analysis was performed on PPAS population. Here, 'number analysed' = subjects with available data for this endpoint. Data for this endpoint was not planned to be collected and analysed for Groups 3 and 4.

End point type	Secondary

End point timeframe:

Day 90 (post-vaccination)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint is reporting data for applicable arms in the study.

End point values	Group 1: VRVg-2	Group 2: Verorab®	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	52	76	37
Units: percentage of subjects				
number (confidence interval 95%)	100 (96.3 to 100)	100 (93.2 to 100)	88.2 (78.7 to 94.4)	94.6 (81.8 to 99.3)

Statistical analyses

No statistical analyses for this end point

Secondary: GMTRs of Individual RVNA Titers: Groups 1, 2, 5 and 6

End point title	GMTRs of Individual RVNA Titers: Groups 1, 2, 5 and 6[12]

End point description:

RVNA titer against rabies virus was assessed using the RFFIT assay method. GMTRs were calculated as the ratio of GMTs post vaccination (i.e., on Day 90) and pre-vaccination on Day 0. Analysis was performed on PPAS population. Here, 'number analysed' = subjects with available data for this endpoint. Data for this endpoint was not planned to be collected and analysed for Groups 3 and 4.

End point type	Secondary

End point timeframe:

Day 0 (pre-vaccination) and Day (90 post-vaccination)

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Endpoint is reporting data for applicable arms in the study.

End point values	Group 1: VRVg-2	Group 2: Verorab®	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	97	52	76	37
Units: ratio				
geometric mean (confidence interval 95%)				
Day 90/Day 0	30.3 (25.6 to 36.0)	22.3 (18.5 to 26.7)	7.70 (6.08 to 9.73)	9.58 (6.92 to 13.2)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Immediate Unsolicited Systemic Adverse Events (AEs)

End point title	Number of Subjects With Immediate Unsolicited Systemic Adverse Events (AEs)

End point description:

An AE was defined as any untoward medical occurrence in a subject who received study vaccine and does not necessarily had to have a causal relationship with treatment. An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the case report book (CRB) in terms of diagnosis and/or onset post-vaccination. All subjects were observed for 30 minutes after any vaccination, and any unsolicited AEs occurred during that time were recorded as immediate unsolicited AEs in the CRB. Analysis was performed on the safety analysis set (SafAS) that included subjects who had received at least one dose of the study vaccine and were analysed according to the actual study vaccine they received and after any dose according to the study vaccine received at the first dose. Reported AEs were presented for each arm as pre-specified in the protocol.

End point type	Secondary

End point timeframe:

Within 30 minutes post-any vaccination

End point values	Group 1: VRVg-2	Group 2: Verorab®	Group 3: VRVg-2 + ERIG	Group 4: Verorab® + ERIG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	56	26	14
Units: subjects	0	0	0	0

End point values	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	65		
Units: subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Solicited Injection Site Reactions

End point title	Number of Subjects With Solicited Injection Site Reactions

End point description:

A solicited reaction (SR) was an expected adverse reaction (AR) observed and reported under conditions (nature and onset) prelisted (i.e., solicited) in the protocol and CRB and considered as related to vaccination (vacc). An AR was all noxious and unintended responses to a medicinal product related to any dose. Solicited injection site reactions included pain, erythema and swelling at and around the injection site. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category. Here, "99999" is used as a space filler and denotes that no subjects were available for analysis for the specified category at each specified timepoint. Reported AEs were presented for each arm as pre-specified in the protocol.

End point type	Secondary

End point timeframe:

Within 7 days post any and each vaccination (Vaccination 1 [Day 0], 2 [Day 3], 3 [Day 7] and 4 [Day 28])

End point values	Group 1: VRVg-2	Group 2: Verorab®	Group 3: VRVg-2 + ERIG	Group 4: Verorab® + ERIG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	56	26	14
Units: subjects				
Pain Post-any vacc. (n=112,56,26,14,129,65)	44	23	14	5
Pain Post-vacc. 1 (n=112,56,26,14,129,65)	30	19	13	4
Pain Post-vacc. 2 (n=112,56,23,14,129,65)	33	16	4	1
Pain Post-vacc. 3 (n=112,56,21,12,129,65)	23	6	2	2
Pain Post-vacc. 4 (n=112,56,0,0,127,64)	18	8	99999	99999
Erythema Post-any vacc. (n=112,56,26,14,129,65)	40	15	0	0
Erythema Post-vacc. 1 (n=112,56,26,14,129,65)	20	8	0	0
Erythema Post-vacc. 2 (n=112,56,23,14,129,65)	22	10	0	0
Erythema Post-vacc. 3 (n=112,56,21,12,129,65)	23	11	0	0
Erythema Post-vacc. 4 (n=112,56,0,0,127,64)	31	12	99999	99999
Swelling Post-any vacc. (n=112,56,26,14,129,65)	53	27	0	0

Swelling Post-vacc. 1 (n=112,56,26,14,129,65)	28	10	0	0
Swelling Post-vacc. 2 (n=112,56,23,14,129,65)	32	18	0	0
Swelling Post-vacc. 3 (n=112,56,21,12,129,65)	41	20	0	0
Swelling Post-vacc. 4 (n=112,56,0,0,127,64)	46	21	99999	99999

End point values	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	65		
Units: subjects				
Pain Post-any vacc. (n=112,56,26,14,129,65)	57	30		
Pain Post-vacc. 1 (n=112,56,26,14,129,65)	35	20		
Pain Post-vacc. 2 (n=112,56,23,14,129,65)	25	11		
Pain Post-vacc. 3 (n=112,56,21,12,129,65)	31	13		
Pain Post-vacc. 4 (n=112,56,0,0,127,64)	24	12		
Erythema Post-any vacc. (n=112,56,26,14,129,65)	0	2		
Erythema Post-vacc. 1 (n=112,56,26,14,129,65)	0	0		
Erythema Post-vacc. 2 (n=112,56,23,14,129,65)	0	1		
Erythema Post-vacc. 3 (n=112,56,21,12,129,65)	0	0		
Erythema Post-vacc. 4 (n=112,56,0,0,127,64)	0	1		
Swelling Post-any vacc. (n=112,56,26,14,129,65)	0	0		
Swelling Post-vacc. 1 (n=112,56,26,14,129,65)	0	0		
Swelling Post-vacc. 2 (n=112,56,23,14,129,65)	0	0		
Swelling Post-vacc. 3 (n=112,56,21,12,129,65)	0	0		
Swelling Post-vacc. 4 (n=112,56,0,0,127,64)	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Solicited Systemic Reactions

End point title	Number of Subjects With Solicited Systemic Reactions

End point description:

SR: expected AR observed and reported under conditions (nature and onset) prelisted (i.e., solicited) in protocol and CRB and considered as related to vaccination. Solicited reactions were collected for different age groups: fever, vomiting, crying abnormal, drowsiness, appetite lost and irritability were collected for subjects aged 12 to 23 months and fever, headache, malaise and myalgia were collected for subjects aged >= 2 years. Solicited systemic reactions were analysed between each vaccination if vaccinations are separated less than 7 days, and up to 7 days after each vaccination if vaccinations were separated by 7 days or more. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category. Here, "99999" is used as a space filler and denotes that no subjects were available for analysis for the specified category at each specified timepoint. Reported AEs were presented for each arm as pre-specified in protocol.

End point type	Secondary

End point timeframe:

Within 7 days post any and each vaccination (Vaccination 1 [Day 0], 2 [Day 3], 3 [Day 7] and 4 [Day 28])

End point values	Group 1: VRVg-2	Group 2: Verorab®	Group 3: VRVg-2 + ERIG	Group 4: Verorab® + ERIG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	56	26	14
Units: subjects				
Fever Post-any Vacc. (n=112,56,26,14,129,65)	1	0	2	0
Fever Post-vacc. 1 (n=112,56,26,14,129,65)	0	0	0	0
Fever Post-vacc. 2 (n=112,56,23,14,129,65)	1	0	0	0
Fever Post-vacc. 3 (n=112,56,21,12,129,65)	0	0	2	0
Fever Post-vacc. 4 (n=112,56,0,0,127,64)	0	0	99999	99999
Vomiting Post-any Vacc. (n=2,1,0,0,0,0)	0	0	99999	99999
Vomiting Post-vacc. 1 (n=2,1,0,0,0,0)	0	0	99999	99999
Vomiting Post-vacc. 2 (n=2,1,0,0,0,0)	0	0	99999	99999
Vomiting Post-vacc. 3 (n=2,1,0,0,0,0)	0	0	99999	99999
Vomiting Post-vacc. 4 (n=2,1,0,0,0,0)	0	0	99999	99999
Crying abnormal Post-any Vacc. (n=2,1,0,0,0,0)	1	0	99999	99999
Crying abnormal Post-vacc. 1 (n=2,1,0,0,0,0)	1	0	99999	99999
Crying abnormal Post-vacc. 2 (n=2,1,0,0,0,0)	1	0	99999	99999
Crying abnormal Post-vacc. 3 (n=2,1,0,0,0,0)	1	0	99999	99999
Crying abnormal Post-vacc. 4 (n=2,1,0,0,0,0)	1	0	99999	99999
Drowsiness Post-any Vacc. (n=2,1,0,0,0,0)	0	0	99999	99999
Drowsiness Post-vacc. 1 (n=2,1,0,0,0,0)	0	0	99999	99999
Drowsiness Post-vacc. 2 (n=2,1,0,0,0,0)	0	0	99999	99999
Drowsiness Post-vacc. 3 (n=2,1,0,0,0,0)	0	0	99999	99999
Drowsiness Post-vacc. 4 (n=2,1,0,0,0,0)	0	0	99999	99999
Appetite lost Post-any Vacc. (n=2,1,0,0,0,0)	0	0	99999	99999

Appetite lost Post-vacc. 1 (n=2,1,0,0,0,0)	0	0	99999	99999
Appetite lost Post-vacc. 2 (n=2,1,0,0,0,0)	0	0	99999	99999
Appetite lost Post-vacc. 3 (n=2,1,0,0,0,0)	0	0	99999	99999
Appetite lost Post-vacc. 4 (n=2,1,0,0,0,0)	0	0	99999	99999
Irritability Post-any Vacc. (n=2,1,0,0,0,0)	1	0	99999	99999
Irritability Post-vacc. 1 (n=2,1,0,0,0,0)	0	0	99999	99999
Irritability Post-vacc. 2 (n=2,1,0,0,0,0)	0	0	99999	99999
Irritability Post-vacc. 3 (n=2,1,0,0,0,0)	0	0	99999	99999
Irritability Post-vacc. 4 (n=2,1,0,0,0,0)	1	0	99999	99999
Headache Post-any Vacc. (n=110,55,26,14,129,65)	20	10	5	3
Headache Post-vacc. 1 (n=110,55,26,14,129,65)	11	7	4	1
Headache Post-vacc. 2 (n=109,55,23,14,129,65)	8	3	3	2
Headache Post-vacc. 3 (n=110,55,21,12,129,65)	7	4	0	2
Headache Post-vacc. 4 (n=110,55,0,0,127,64)	6	1	99999	99999
Malaise Post-any Vacc. (n=110,55,26,14,129,65)	18	9	6	5
Malaise Post-vacc. 1 (n=110,55,26,14,129,65)	13	6	5	4
Malaise Post-vacc. 2 (n=108,55,23,14,128,65)	8	4	2	1
Malaise Post-vacc. 3 (n=109,55,21,12,129,65)	3	2	1	1
Malaise Post-vacc. 4 (n=110,55,0,0,127,64)	6	2	99999	99999
Myalgia Post-any Vacc. (n=110,55,26,14,129,65)	26	10	11	8
Myalgia Post-vacc. 1 (n=110,55,26,14,129,65)	13	6	11	6
Myalgia Post-vacc. 2 (n=109,55,23,14,129,65)	16	6	3	0
Myalgia Post-vacc. 3 (n=108,55,21,12,129,65)	5	4	1	2
Myalgia Post-vacc. 4 (n=110,55,0,0,127,64)	7	4	99999	99999

End point values	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	65		
Units: subjects				
Fever Post-any Vacc. (n=112,56,26,14,129,65)	2	2		
Fever Post-vacc. 1 (n=112,56,26,14,129,65)	0	0		
Fever Post-vacc. 2 (n=112,56,23,14,129,65)	0	0		

Fever Post-vacc. 3 (n=112,56,21,12,129,65)	0	0		
Fever Post-vacc. 4 (n=112,56,0,0,127,64)	2	2		
Vomiting Post-any Vacc. (n=2,1,0,0,0,0)	99999	99999		
Vomiting Post-vacc. 1 (n=2,1,0,0,0,0)	99999	99999		
Vomiting Post-vacc. 2 (n=2,1,0,0,0,0)	99999	99999		
Vomiting Post-vacc. 3 (n=2,1,0,0,0,0)	99999	99999		
Vomiting Post-vacc. 4 (n=2,1,0,0,0,0)	99999	99999		
Crying abnormal Post-any Vacc. (n=2,1,0,0,0,0)	99999	99999		
Crying abnormal Post-vacc. 1 (n=2,1,0,0,0,0)	99999	99999		
Crying abnormal Post-vacc. 2 (n=2,1,0,0,0,0)	99999	99999		
Crying abnormal Post-vacc. 3 (n=2,1,0,0,0,0)	99999	99999		
Crying abnormal Post-vacc. 4 (n=2,1,0,0,0,0)	99999	99999		
Drowsiness Post-any Vacc. (n=2,1,0,0,0,0)	99999	99999		
Drowsiness Post-vacc. 1 (n=2,1,0,0,0,0)	99999	99999		
Drowsiness Post-vacc. 2 (n=2,1,0,0,0,0)	99999	99999		
Drowsiness Post-vacc. 3 (n=2,1,0,0,0,0)	99999	99999		
Drowsiness Post-vacc. 4 (n=2,1,0,0,0,0)	99999	99999		
Appetite lost Post-any Vacc. (n=2,1,0,0,0,0)	99999	99999		
Appetite lost Post-vacc. 1 (n=2,1,0,0,0,0)	99999	99999		
Appetite lost Post-vacc. 2 (n=2,1,0,0,0,0)	99999	99999		
Appetite lost Post-vacc. 3 (n=2,1,0,0,0,0)	99999	99999		
Appetite lost Post-vacc. 4 (n=2,1,0,0,0,0)	99999	99999		
Irritability Post-any Vacc. (n=2,1,0,0,0,0)	99999	99999		
Irritability Post-vacc. 1 (n=2,1,0,0,0,0)	99999	99999		
Irritability Post-vacc. 2 (n=2,1,0,0,0,0)	99999	99999		
Irritability Post-vacc. 3 (n=2,1,0,0,0,0)	99999	99999		
Irritability Post-vacc. 4 (n=2,1,0,0,0,0)	99999	99999		
Headache Post-any Vacc. (n=110,55,26,14,129,65)	31	11		
Headache Post-vacc. 1 (n=110,55,26,14,129,65)	19	7		
Headache Post-vacc. 2 (n=109,55,23,14,129,65)	10	2		
Headache Post-vacc. 3 (n=110,55,21,12,129,65)	10	3		
Headache Post-vacc. 4 (n=110,55,0,0,127,64)	8	2		
Malaise Post-any Vacc. (n=110,55,26,14,129,65)	39	13		
Malaise Post-vacc. 1 (n=110,55,26,14,129,65)	26	5		
Malaise Post-vacc. 2 (n=108,55,23,14,128,65)	17	3		
Malaise Post-vacc. 3 (n=109,55,21,12,129,65)	17	5		

Malaise Post-vacc. 4 (n=110,55,0,0,127,64)	12	5		
Myalgia Post-any Vacc. (n=110,55,26,14,129,65)	61	25		
Myalgia Post-vacc. 1 (n=110,55,26,14,129,65)	44	21		
Myalgia Post-vacc. 2 (n=109,55,23,14,129,65)	25	11		
Myalgia Post-vacc. 3 (n=108,55,21,12,129,65)	21	8		
Myalgia Post-vacc. 4 (n=110,55,0,0,127,64)	20	6		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Unsolicited AEs

End point title	Number of Subjects With Unsolicited AEs

End point description:

An AE was defined as any untoward medical occurrence in a subject who received study vaccine and does not necessary had to have a causal relationship with treatment. An unsolicited AE was an observed AE that did not fulfill the conditions prelisted in the CRB in terms of diagnosis and/or onset window post-vaccination. Analysis was performed on SafAS. Here, 'n' = subjects with available data for each specified category. Here, "99999" is used as a space filler and denotes that no subjects were available for analysis for the specified category at each specified timepoint. Reported AEs were presented for each arm as pre-specified in the protocol.

End point type	Secondary

End point timeframe:

Within 28 days post any and each vaccination (Vaccination 1 [Day 0], 2 [Day 3], 3 [Day 7] and 4 [Day 28])

End point values	Group 1: VRVg-2	Group 2: Verorab®	Group 3: VRVg-2 + ERIG	Group 4: Verorab® + ERIG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	56	26	14
Units: subjects				
Post-any Vacc. (n=112,56,26,14,129,65)	22	12	26	12
Post Vacc. 1 (n=112,56,26,14,129,65)	1	1	25	12
Post Vacc. 2 (n=112,56,23,14,129,65)	4	0	3	1
Post Vacc. 3 (n=112,56,21,12,129,65)	12	5	5	2
Post Vacc. 4 (n=112,56,0,0,127,64)	7	7	99999	99999

End point values	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	65		
Units: subjects				
Post-any Vacc. (n=112,56,26,14,129,65)	4	2		
Post Vacc. 1 (n=112,56,26,14,129,65)	3	0		
Post Vacc. 2 (n=112,56,23,14,129,65)	0	1		
Post Vacc. 3 (n=112,56,21,12,129,65)	0	0		
Post Vacc. 4 (n=112,56,0,0,127,64)	1	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious Adverse Events (SAEs) and Adverse Event of Special Interest (AESIs)

End point title	Number of Subjects With Serious Adverse Events (SAEs) and Adverse Event of Special Interest (AESIs)

End point description:

An SAE was any untoward medical occurrence that at any dose resulted in death, was life-threatening, required initial or prolonged inpatient hospitalisation, resulted in persistent or significant disability/incapacity, congenital anomaly/birth defect or was a medically important event. An AESI was defined as one of scientific and medical concern specific to the Sponsor’s product or program, for which ongoing monitoring and rapid communication by the Investigator to the Sponsor was appropriate. Relatedness to study vaccine was based on Investigator's discretion. Analysis was performed on SafAS. Reported AEs were presented for each arm as pre-specified in the protocol.

End point type	Secondary

End point timeframe:

From Day 0 up to 6 months after last vaccination (i.e., up to Month 7)

End point values	Group 1: VRVg-2	Group 2: Verorab®	Group 3: VRVg-2 + ERIG	Group 4: Verorab® + ERIG
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	112	56	26	14
Units: subjects				
SAEs	0	0	1	2
AESIs	0	0	0	0

End point values	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	129	65		
Units: subjects				
SAEs	5	3		
AESIs	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited AEs were collected from Day 0 up to 28 days post any and each vaccination. SR data were collected up to 7 days post any and each vaccination. SAE data were collected from Day 0 up to 6 months post last vaccination (i.e., up to Month 7)

Adverse event reporting additional description:

SR: expected AR observed & reported under conditions (nature and onset) prelisted (i.e., solicited) in protocol & CRB & considered as related vaccination. Unsolicited AE: AE that did not fulfill conditions prelisted (i.e., solicited) in CRB in terms of diagnosis & onset window post-vaccination. SafAS. In AE section, SR fever is reported as pyrexia.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.0

Reporting groups

Reporting group title	Group 1: VRVg-2

Reporting group description:

Pediatric subjects aged 1 year to < 18 years received 8 injections (1 vaccination on each arm) of 0.5 mL of VRVg-2 intradermally on Days 0, 3, 7 and 28.

Reporting group title	Group 2: Verorab

Reporting group description:

Pediatric subjects aged 1 year to <18 years received 8 injections (1 vaccination on each arm) of 0.5 mL purified inactivated rabies vaccine prepared on Vero cell line (Verorab®) intradermally on Days 0, 3, 7 and 28.

Reporting group title	Group 3: VRVg-2 + ERIG

Reporting group description:

Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3 and 7 along with ERIG IM injection at Day 0.

Reporting group title	Group 4: Verorab + ERIG

Reporting group description:

Adult subjects aged 18 year and above received 6 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3 and 7 along with ERIG IM injection at Day 0.

Reporting group title	Group 5: VRVg-2 + HRIG

Reporting group description:

Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL VRVg-2 intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.

Reporting group title	Group 6: Verorab + HRIG

Reporting group description:

Adult subjects aged 18 year and above received 8 injections (1 vaccination on each arm) of 0.5 mL Verorab® intradermally on Days 0, 3, 7, and 28 along with HRIG IM injection at Day 0.

Serious adverse events	Group 1: VRVg-2	Group 2: Verorab	Group 3: VRVg-2 + ERIG
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	1 / 26 (3.85%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

Injury, poisoning and procedural complications			
Limb Traumatic Amputation			
subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Mammoplasty			
subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	1 / 26 (3.85%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Lower Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity Vasculitis			
subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis Perforated			
subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19			

subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	0 / 26 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 4: Verorab + ERIG	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 14 (14.29%)	5 / 129 (3.88%)	3 / 65 (4.62%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Limb Traumatic Amputation			
subjects affected / exposed	0 / 14 (0.00%)	1 / 129 (0.78%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Mammoplasty			
subjects affected / exposed	0 / 14 (0.00%)	0 / 129 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 14 (0.00%)	0 / 129 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Lower Gastrointestinal Haemorrhage			
subjects affected / exposed	0 / 14 (0.00%)	0 / 129 (0.00%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 14 (7.14%)	0 / 129 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypersensitivity Vasculitis			

subjects affected / exposed	1 / 14 (7.14%)	0 / 129 (0.00%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis Perforated			
subjects affected / exposed	0 / 14 (0.00%)	1 / 129 (0.78%)	0 / 65 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19			
subjects affected / exposed	0 / 14 (0.00%)	3 / 129 (2.33%)	1 / 65 (1.54%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Group 1: VRVg-2	Group 2: Verorab	Group 3: VRVg-2 + ERIG
Total subjects affected by non-serious adverse events			
subjects affected / exposed	85 / 112 (75.89%)	42 / 56 (75.00%)	26 / 26 (100.00%)
Nervous system disorders			
Headache	Additional description: Headache events that occurred after 7 days post-vaccination were considered as unsolicited AE.		
subjects affected / exposed	20 / 112 (17.86%)	11 / 56 (19.64%)	5 / 26 (19.23%)
occurrences (all)	34	16	7
General disorders and administration site conditions			
Application Site Pain			
subjects affected / exposed	0 / 112 (0.00%)	0 / 56 (0.00%)	7 / 26 (26.92%)
occurrences (all)	0	0	7
Injection Site Erythema			
subjects affected / exposed	40 / 112 (35.71%)	15 / 56 (26.79%)	0 / 26 (0.00%)
occurrences (all)	168	76	0
Injection Site Pain			
subjects affected / exposed	44 / 112 (39.29%)	23 / 56 (41.07%)	14 / 26 (53.85%)
occurrences (all)	177	81	37
Injection Site Swelling			

subjects affected / exposed	53 / 112 (47.32%)	27 / 56 (48.21%)	0 / 26 (0.00%)
occurrences (all)	243	116	0
Malaise			
subjects affected / exposed	18 / 112 (16.07%)	9 / 56 (16.07%)	6 / 26 (23.08%)
occurrences (all)	30	14	8
Pyrexia	Additional description: Pyrexia/Fever events that occurred after 7 days post-vaccination were considered as unsolicited AE.		
subjects affected / exposed	1 / 112 (0.89%)	1 / 56 (1.79%)	2 / 26 (7.69%)
occurrences (all)	1	1	2
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	1 / 112 (0.89%)	0 / 56 (0.00%)	7 / 26 (26.92%)
occurrences (all)	1	0	7
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: Myalgia events that occurred after 7 days post-vaccination were considered as unsolicited AE.		
subjects affected / exposed	26 / 112 (23.21%)	10 / 56 (17.86%)	19 / 26 (73.08%)
occurrences (all)	41	20	33
Infections and infestations			
Upper Respiratory Tract Infection			
subjects affected / exposed	10 / 112 (8.93%)	7 / 56 (12.50%)	0 / 26 (0.00%)
occurrences (all)	10	7	0

Non-serious adverse events	Group 4: Verorab + ERIG	Group 5: VRVg-2 + HRIG	Group 6: Verorab + HRIG
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 14 (100.00%)	80 / 129 (62.02%)	38 / 65 (58.46%)
Nervous system disorders			
Headache	Additional description: Headache events that occurred after 7 days post-vaccination were considered as unsolicited AE.		
subjects affected / exposed	3 / 14 (21.43%)	31 / 129 (24.03%)	11 / 65 (16.92%)
occurrences (all)	5	47	14
General disorders and administration site conditions			
Application Site Pain			
subjects affected / exposed	2 / 14 (14.29%)	0 / 129 (0.00%)	0 / 65 (0.00%)
occurrences (all)	2	0	0
Injection Site Erythema			
subjects affected / exposed	0 / 14 (0.00%)	0 / 129 (0.00%)	2 / 65 (3.08%)
occurrences (all)	0	0	2
Injection Site Pain			

subjects affected / exposed	5 / 14 (35.71%)	57 / 129 (44.19%)	30 / 65 (46.15%)
occurrences (all)	11	200	102
Injection Site Swelling			
subjects affected / exposed	0 / 14 (0.00%)	0 / 129 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0
Malaise			
subjects affected / exposed	5 / 14 (35.71%)	39 / 129 (30.23%)	13 / 65 (20.00%)
occurrences (all)	6	72	18
Pyrexia	Additional description: Pyrexia/Fever events that occurred after 7 days post-vaccination were considered as unsolicited AE.		
subjects affected / exposed	0 / 14 (0.00%)	2 / 129 (1.55%)	2 / 65 (3.08%)
occurrences (all)	0	2	2
Skin and subcutaneous tissue disorders			
Urticaria			
subjects affected / exposed	2 / 14 (14.29%)	0 / 129 (0.00%)	0 / 65 (0.00%)
occurrences (all)	2	0	0
Musculoskeletal and connective tissue disorders			
Myalgia	Additional description: Myalgia events that occurred after 7 days post-vaccination were considered as unsolicited AE.		
subjects affected / exposed	12 / 14 (85.71%)	61 / 129 (47.29%)	25 / 65 (38.46%)
occurrences (all)	18	113	46
Infections and infestations			
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 14 (0.00%)	0 / 129 (0.00%)	0 / 65 (0.00%)
occurrences (all)	0	0	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 November 2019	Protocol amended for update of Principal investigator.
22 November 2021	Following changes were made: Deleted virus complete or incomplete neutralisation endpoint at 1/5 dilution. Wording changed to clarify new sample size calculated. Adult study arm receiving vaccines + ERIG was temporary halt by Sponsor for safety reasons after enrolling 40 subjects, following receipt of cluster of 3 SAEs of hypersensitivity assessed as related to both ERIG and study vaccine by investigator, & assessed as unrelated to study vaccine but related to ERIG by sponsor. Therefore, ERIG administration on Day (D) 0 in adult subjects (Groups 3 and 4) was discontinued and HRIG was then co-administrated on D0 in Groups 5 and 6. Wording changed to clarify: ERIG administration was applied for Groups 3 & 4 & HRIG administration was applied for Groups 5 & 6. Primary immunogenicity objective modified. Additional immunogenicity secondary objective added: Included immunogenicity data analysis for adult subjects in Groups 3 & 4 to evaluate immune response induced by VRVg-2 & Verorab vaccine at D14. Secondary immunogenicity objective on D90 was applied only for adult subjects in Groups 5 and 6 since no immunogenicity data was available at D90 for Groups 3 & 4. Informed that safety profile was described for all groups. Wording changed to clarify the statistical analysis for the new sample size calculated. Wording changed to clarify that ERIG administration was applied only for Groups 3 & 4 & to provide ERIG batch number used until study halt. Deleted "optional, based on Investigator's judgement" since TRC Society ERIG recommended doing positive skin test prior administration. However, it was agreed with the investigators to do the test in all subjects as additional precautionary safety measure. Missing Diary Cards numbers added. Wording changed since the assessment of immediate unsolicited systemic events was recorded in V01, V02, V03 and V05 only. Footnote removed to clarify event reporting at D0. Injection site reaction and systemic AE/AR recorded daily (from V01 to V07).
24 June 2022	Following changes were made: Modified GSO representative contact details. Modified justification of study design to clarify that after the discontinuation of ERIG, the 40 subjects were withdrawn and excluded from the PPAS for D42 because unable to complete the 4-dose vaccination schedule, and part of the 40 subjects were also excluded from the PPAS for D14 because unable to complete the first 3 doses of the vaccination schedule. Paragraph added to explain the rationale for developing amendment 3. Re-inserted Amendment 1 to provide history of protocol amendments. Per-protocol analysis set for D42 - paragraph modified to clarify PPAS for D42 definition and notably to remove blood sample 2 at D14 from the list of exclusion criteria.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported