Clinical trial results:
A Phase 3 Safety, Immunogenicity, and Lot-Consistency Trial of the VLP-Based Chikungunya Vaccine PXVX0317 in Healthy Adults and Adolescents

Summary

EudraCT number	2023-001124-42
Trial protocol	Outside EU/EEA
Global end of trial date	03 April 2023

Results information

Result version number	v1 (current)
This version publication date	19 April 2024
First version publication date	19 April 2024

Trial information

Trial identification

Sponsor protocol code	EBSICV317004

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05072080
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bavarian Nordic A/S
Sponsor organisation address	Philip Heymans Alle 3, Hellerup, Denmark, 2900
Public contact	Medical Information, Bavarian Nordic A/S, medical.information_eu@bavarian-nordic.com
Scientific contact	Medical Information, Bavarian Nordic A/S, medical.information_eu@bavarian-nordic.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-002656-PIP01-19
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	02 February 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 April 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Coprimary Objectives:
1. To evaluate the safety of PXVX0317 (CHIKV VLP vaccine) in healthy adult and adolescent participants 12 to <65 years of age.
2. To compare the anti-CHIKV serum neutralising antibody (SNA) response to PXVX0317 (CHIKV VLP vaccine) and placebo at Day 22, as measured by geometric mean titre (GMT) and clinically relevant difference in seroresponse rate (PXVX0317 minus placebo).
3. To demonstrate the consistency of the anti-CHIKV SNA response across three consecutively manufactured lots of PXVX0317 (CHIKV VLP vaccine) at Day 22 as measured by GMT.

Protection of trial subjects:

Study documents and participant facing documents including recruiting materials were reviewed and approved by an Institutional Review Board (IRB) before enrolment of participants in the study and prior to implementation.
All study participants were required to read and sign an Informed Consent Form. Assent was also obtained from the study participant where required.
Participants were monitored by study staff for signs of an acute adverse reaction(s) for 30 minutes after injection of IP. Vital signs were taken before and after study vaccine administration.
Reactogenicity/solicited adverse events were collected from Day 1 (administration of IP) through Day 8. Unsolicited AEs were collected from Day 1 through Day 29. Serious adverse events, adverse events of special interest (defined as the occurrence of new onset or worsening arthralgia that was medically attended), and medically attended adverse events (defined as medically attended visits and included hospital, emergency room, urgent care clinic, or other visits to or from medical personnel) were collected from Day 1 through the Day 183 EOS.
A planned independent Safety Monitoring Committee (SMC) blinded safety data review was conducted after the first 300 participants completed the Day 29 Visit and a second blinded SMC safety data review was conducted after the last participant completed the Day 29 visit.

Background therapy:

N/A

Evidence for comparator:

N/A - Placebo

Actual start date of recruitment	29 September 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 3258
Worldwide total number of subjects	3258
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)	0
Children (2-11 years)	0
Adolescents (12-17 years)	254
Adults (18-64 years)	3004
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This was a multicenter study conducted in the United States, using 47 sites. Healthy participants were enroled in this study. Recruitment Period was from 29Sep2021 to 06Oct2022.

Pre-assignment

Screening details:

A total of 4215 participants were screened. Screening window was no greater than 30 days prior to Day 1. Rescreening was permissible. Eligibility data was collected including medical history, concomitant therapy, viral screening, vital signs, physical exams, and urine pregnancy tests. Informed consent or informed consent with assent was obtained.

Period 1

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

Blinding implementation details:

Use of a standardised pre-filled syringe and injection volume for all injections. All syringes had a semi-transparent barrel cover to mask any difference in appearance between placebo and CHIKV VLP vaccine. No sponsor personnel had access to the randomisation schedule. No site personnel had access to treatment assignments. Assays were run in a blinded manner. The assay titre results were not delivered to the sponsor data management and analysis team until after database lock.

Arms

Are arms mutually exclusive?	No
Arm title	Group 1 - PXVX0317 Lot 104

Arm description:

Biological/Vaccine: CHIKV VLP/adjuvant - Lot 104
CHIKV VLP vaccine is comprised of chikungunya virus virus-like particles (CHIKV VLP), adsorbed on aluminum hydroxide adjuvant 2%

Arm type	Experimental
Investigational medicinal product name	CHIKV VLP Vaccine
Investigational medicinal product code	PXVX0317
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

CHIKV VLP vaccine (PXVX0317) is comprised of CHIKV VLP 40 µg with 300 µg aluminum hydroxide 2%. Participants received CHIKV VLP vaccine on Day 1 by intramuscular injection in the deltoid muscle. The CHIKV VLP vaccine was supplied as a single dose 0.8 mL pre-filled syringe. The injection was to be administered within 2 hours of removal of the pre-filled syringe from 2 to 8°C storage.

Arm title	Group 2 - PXVX0317 Lot 105

Arm description:

Biological/Vaccine: CHIKV VLP/adjuvant - Lot 105
CHIKV VLP vaccine is comprised of chikungunya virus virus-like particles (CHIKV VLP), adsorbed on aluminum hydroxide adjuvant 2%

Arm type	Experimental
Investigational medicinal product name	CHIKV VLP Vaccine
Investigational medicinal product code	PXVX0317
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

CHIKV VLP vaccine (PXVX0317) is comprised of CHIKV VLP 40 µg with 300 µg aluminum hydroxide 2%. Participants received CHIKV VLP vaccine on Day 1 by intramuscular injection in the deltoid muscle. The CHIKV VLP vaccine was supplied as a single dose 0.8 mL pre-filled syringe. The injection was to be administered within 2 hours of removal of the pre-filled syringe from 2 to 8°C storage.

Arm title	Group 3 - PXVX0317 Lot 106

Arm description:

Biological/Vaccine: CHIKV VLP/adjuvant - Lot 106
CHIKV VLP vaccine is comprised of chikungunya virus virus-like particles (CHIKV VLP), adsorbed on aluminum hydroxide adjuvant 2%

Arm type	Experimental
Investigational medicinal product name	CHIKV VLP Vaccine
Investigational medicinal product code	PXVX0317
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

CHIKV VLP vaccine (PXVX0317) is comprised of CHIKV VLP 40 µg with 300 µg aluminum hydroxide 2%. Participants received CHIKV VLP vaccine on Day 1 by intramuscular injection in the deltoid muscle. The CHIKV VLP vaccine was supplied as a single dose 0.8 mL pre-filled syringe. The injection was to be administered within 2 hours of removal of the pre-filled syringe from 2 to 8°C storage.

Arm title	Group 4 - Placebo

Arm description:

Biological/Vaccine: Placebo
Placebo is comprised of formulation buffer

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Placebo is a sterile aqueous solution with the same excipient composition as the drug product without CHIKV VLP and aluminum hydroxide adjuvant. Participants received placebo on Day 1 by intramuscular injection in the deltoid muscle. Placebo was supplied as a single dose 0.8 mL pre-filled syringe. The injection was to be administered within 2 hours of removal of the pre-filled syringe from 2 to 8°C storage.

Arm title	Pooled PXVX0317

Arm description:

Arm created for reporting results purposes only.

Includes all participants in Group 1 (PXVX0317 Lot 104) + Group 2 (PXVX0317 Lot 105) + Group 3 (PXVX0317 Lot 106).

Arm type	Experimental
Investigational medicinal product name	CHIKV VLP Vaccine
Investigational medicinal product code	PXVX0317
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

CHIKV VLP vaccine (PXVX0317) is comprised of CHIKV VLP 40 µg with 300 µg aluminum hydroxide 2%. Participants received CHIKV VLP vaccine on Day 1 by intramuscular injection in the deltoid muscle. The CHIKV VLP vaccine was supplied as a single dose 0.8 mL pre-filled syringe. The injection was to be administered within 2 hours of removal of the pre-filled syringe from 2 to 8°C storage.

Number of subjects in period 1	Group 1 - PXVX0317 Lot 104	Group 2 - PXVX0317 Lot 105	Group 3 - PXVX0317 Lot 106
Started	919	948	927
Completed	803	837	832
Not completed	116	111	95
Withdrawal by parent	-	-	1
Consent withdrawn by subject	45	30	27
Physician decision	2	1	1
Subject incarcerated	-	1	-
Subject missed last visit (Day 183)	3	1	1
Subject left site without receiving dose	-	1	-
Death	-	-	1
Noncompliance (protocol, visits, ediary, etc	-	2	1
Subject was deployed	-	1	-
Subject moved	1	3	5
Lost to follow-up	65	70	58
Sponsor decision	-	1	-

Number of subjects in period 1	Group 4 - Placebo	Pooled PXVX0317
Started	464	2794
Completed	430	2472
Not completed	34	322
Withdrawal by parent	-	1
Consent withdrawn by subject	7	102
Physician decision	-	4
Subject incarcerated	1	1
Subject missed last visit (Day 183)	-	5
Subject left site without receiving dose	-	1
Death	-	1
Noncompliance (protocol, visits, ediary, etc	1	3
Subject was deployed	-	1
Subject moved	2	9
Lost to follow-up	23	193
Sponsor decision	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Group 1 - PXVX0317 Lot 104
Reporting group description:	
Biological/Vaccine: CHIKV VLP/adjuvant - Lot 104 CHIKV VLP vaccine is comprised of chikungunya virus virus-like particles (CHIKV VLP), adsorbed on aluminum hydroxide adjuvant 2%	
Reporting group title	Group 2 - PXVX0317 Lot 105
Reporting group description:	
Biological/Vaccine: CHIKV VLP/adjuvant - Lot 105 CHIKV VLP vaccine is comprised of chikungunya virus virus-like particles (CHIKV VLP), adsorbed on aluminum hydroxide adjuvant 2%	
Reporting group title	Group 3 - PXVX0317 Lot 106
Reporting group description:	
Biological/Vaccine: CHIKV VLP/adjuvant - Lot 106 CHIKV VLP vaccine is comprised of chikungunya virus virus-like particles (CHIKV VLP), adsorbed on aluminum hydroxide adjuvant 2%	
Reporting group title	Group 4 - Placebo
Reporting group description:	
Biological/Vaccine: Placebo Placebo is comprised of formulation buffer	
Reporting group title	Pooled PXVX0317
Reporting group description:	
Arm created for reporting results purposes only. Includes all participants in Group 1 (PXVX0317 Lot 104) + Group 2 (PXVX0317 Lot 105) + Group 3 (PXVX0317 Lot 106).	

Reporting group values	Group 1 - PXVX0317 Lot 104	Group 2 - PXVX0317 Lot 105	Group 3 - PXVX0317 Lot 106
Number of subjects	919	948	927
Age categorical Units: Subjects			
Adolescents (12-17 years)	67	76	74
Adults (18-64 years)	852	872	853
Age continuous Units: years			
arithmetic mean	39	38	39
standard deviation	± 14.4	± 14.3	± 14.0
Gender categorical Units: Subjects			
Female	452	506	478
Male	467	442	449
Ethnicity Units: Subjects			
Hispanic or Latino	165	166	175
Not Hispanic or Latino	735	760	731
Not Reported	18	22	21
Unknown	1	0	0
Race (NIH/OMB) Units: Subjects			

American Indian or Alaska Native	11	6	13
Asian	26	30	23
Native Hawaiian or Other Pacific Islander	2	4	0
Black or African American	190	175	169
White	663	693	687
More than one race	23	32	23
Unknown or Not Reported	4	8	12
Baseline Anti-CHIKV SNA Serostatus			
LLOQ = lower limit of quantitation.			
Units: Subjects			
Negative (<LLOQ)	894	925	906
Positive (>=LLOQ)	24	18	21
Missing	1	5	0
Height			
Units: cm			
arithmetic mean	171.4	170.4	170.7
standard deviation	± 10.03	± 9.55	± 10.02
Weight			
Units: kg			
arithmetic mean	78.5	78.4	78.3
standard deviation	± 16.50	± 16.08	± 16.42
Body mass index (BMI)			
Units: kg/m^2			
arithmetic mean	26.63	26.89	26.73
standard deviation	± 4.579	± 4.480	± 4.499

Reporting group values	Group 4 - Placebo	Pooled PXVX0317	Total
Number of subjects	464	2794	3258
Age categorical			
Units: Subjects			
Adolescents (12-17 years)	37	217	254
Adults (18-64 years)	427	2577	3004
Age continuous			
Units: years			
arithmetic mean	39	39	
standard deviation	± 14.4	± 14.3	-
Gender categorical			
Units: Subjects			
Female	231	1436	1667
Male	233	1358	1591
Ethnicity			
Units: Subjects			
Hispanic or Latino	71	506	577
Not Hispanic or Latino	379	2226	2605
Not Reported	14	61	75
Unknown	0	1	1
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	2	30	32
Asian	16	79	95

Native Hawaiian or Other Pacific Islander	4	6	10
Black or African American	89	534	623
White	341	2043	2384
More than one race	8	78	86
Unknown or Not Reported	4	24	28
Baseline Anti-CHIKV SNA Serostatus			
LLOQ = lower limit of quantitation.			
Units: Subjects			
Negative (<LLOQ)	458	2725	3183
Positive (>=LLOQ)	6	63	69
Missing	0	6	6
Height			
Units: cm			
arithmetic mean	171.2	170.8	
standard deviation	± 9.97	± 9.87	-
Weight			
Units: kg			
arithmetic mean	77.6	78.4	
standard deviation	± 16.42	± 16.33	-
Body mass index (BMI)			
Units: kg/m^2			
arithmetic mean	26.38	26.75	
standard deviation	± 4.570	± 4.519	-

End points

End points reporting groups

Reporting group title	Group 1 - PXVX0317 Lot 104
Reporting group description:	
Biological/Vaccine: CHIKV VLP/adjuvant - Lot 104 CHIKV VLP vaccine is comprised of chikungunya virus virus-like particles (CHIKV VLP), adsorbed on aluminum hydroxide adjuvant 2%	
Reporting group title	Group 2 - PXVX0317 Lot 105
Reporting group description:	
Biological/Vaccine: CHIKV VLP/adjuvant - Lot 105 CHIKV VLP vaccine is comprised of chikungunya virus virus-like particles (CHIKV VLP), adsorbed on aluminum hydroxide adjuvant 2%	
Reporting group title	Group 3 - PXVX0317 Lot 106
Reporting group description:	
Biological/Vaccine: CHIKV VLP/adjuvant - Lot 106 CHIKV VLP vaccine is comprised of chikungunya virus virus-like particles (CHIKV VLP), adsorbed on aluminum hydroxide adjuvant 2%	
Reporting group title	Group 4 - Placebo
Reporting group description:	
Biological/Vaccine: Placebo Placebo is comprised of formulation buffer	
Reporting group title	Pooled PXVX0317
Reporting group description:	
Arm created for reporting results purposes only. Includes all participants in Group 1 (PXVX0317 Lot 104) + Group 2 (PXVX0317 Lot 105) + Group 3 (PXVX0317 Lot 106).	

Primary: Incidence of solicited Adverse Events (AE)

End point title	Incidence of solicited Adverse Events (AE)[1]
End point description:	
Incidence of solicited AEs through Day 8 for PXVX0317 (CHIKV VLP Vaccine) and placebo for all age strata combined (safety population). Number of subjects analysed is number of safety population participants who completed a memory aid following the vaccination.	
End point type	Primary
End point timeframe:	
7 days 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: Statistical analyses does not apply to this endpoint. Endpoint is reporting a count of subjects that reported a solicited adverse event.

End point values	Group 1 - PXVX0317 Lot 104	Group 2 - PXVX0317 Lot 105	Group 3 - PXVX0317 Lot 106	Group 4 - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	906	939	920	458
Units: Subjects	319	373	366	124

End point values	Pooled PXVX0317			
Subject group type	Reporting group			
Number of subjects analysed	2765			
Units: Subjects	1058			

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of unsolicited AEs

End point title	Incidence of unsolicited AEs[2]

End point description:

Incidence of unsolicited AEs through Day 29 for PXVX0317 (CHIKV VLP Vaccine) and placebo for all age strata combined (safety population).

Analysis population: Safety Population (vaccinated participants who provided safety assessment data), all ages pooled

End point type	Primary

End point timeframe:

28 days post-vaccination

Notes:

[2] - 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: Statistical analyses does not apply to this endpoint. Endpoint is reporting a count of subjects that reported an unsolicited adverse event.

End point values	Group 1 - PXVX0317 Lot 104	Group 2 - PXVX0317 Lot 105	Group 3 - PXVX0317 Lot 106	Group 4 - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	918	945	927	464
Units: Subjects	139	146	155	62

End point values	Pooled PXVX0317			
Subject group type	Reporting group			
Number of subjects analysed	2790			
Units: Subjects	440			

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Adverse Events of Special Interest (AESI)

End point title	Incidence of Adverse Events of Special Interest (AESI)[3]

End point description:

Incidence of AESIs, through Day 183 for PXVX0317 (CHIKV VLP Vaccine) and placebo for all age strata combined (safety population).

Adverse events of special interest (AESI) were defined as the occurrence of new onset or worsening arthralgia that was medically attended.

Analysis population: Safety Population (vaccinated participants who provided safety assessment data), all ages pooled

End point type	Primary

End point timeframe:

182 days 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: Statistical analyses does not apply to this endpoint. Endpoint is reporting a count of subjects that reported an adverse event of special interest (AESI).

End point values	Group 1 - PXVX0317 Lot 104	Group 2 - PXVX0317 Lot 105	Group 3 - PXVX0317 Lot 106	Group 4 - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	918	945	927	464
Units: Subjects	3	2	1	1

End point values	Pooled PXVX0317			
Subject group type	Reporting group			
Number of subjects analysed	2790			
Units: Subjects	6			

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Medically Attended Adverse Event (MAAE)

End point title	Incidence of Medically Attended Adverse Event (MAAE)[4]

End point description:

Incidence of MAAEs through Day 183 for PXVX0317 (CHIKV VLP vaccine) and placebo for all age strata combined (safety population).

Medically attended adverse events (MAAE) were defined as medically attended visits and included hospital, emergency room, urgent care clinic, or other visits to or from medical personnel.

Analysis population: Safety Population (vaccinated participants who provided safety assessment data), all ages pooled.

End point type	Primary

End point timeframe:

182 days post-vaccination

Notes:

[4] - 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: Statistical analyses does not apply to this endpoint. Endpoint is reporting a count of subjects that reported a medically attended adverse event (MAAE).

End point values	Group 1 - PXVX0317 Lot 104	Group 2 - PXVX0317 Lot 105	Group 3 - PXVX0317 Lot 106	Group 4 - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	918	945	927	464
Units: Subjects	81	83	85	42

End point values	Pooled PXVX0317			
Subject group type	Reporting group			
Number of subjects analysed	2790			
Units: Subjects	249			

Statistical analyses

No statistical analyses for this end point

Primary: Incidence of Serious Adverse Event (SAE)

End point title	Incidence of Serious Adverse Event (SAE)[5]

End point description:

Incidence of SAEs through Day 183 for PXVX0317 (CHIKV VLP vaccine) and placebo for all age strata combined (safety population).

Analysis population: Safety Population (vaccinated participants who provided safety assessment data), all ages pooled.

End point type	Primary

End point timeframe:

182 days 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: Statistical analyses does not apply to this endpoint. Endpoint is reporting a count of subjects that reported a serious adverse event.

End point values	Group 1 - PXVX0317 Lot 104	Group 2 - PXVX0317 Lot 105	Group 3 - PXVX0317 Lot 106	Group 4 - Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	918	945	927	464
Units: Subjects	10	7	6	1

End point values	Pooled PXVX0317			
Subject group type	Reporting group			
Number of subjects analysed	2790			
Units: Subjects	23			

Statistical analyses

No statistical analyses for this end point

Primary: Anti-CHIKV serum neutralising antibody (SNA) seroresponse rates at Day 22

End point title	Anti-CHIKV serum neutralising antibody (SNA) seroresponse rates at Day 22[6]

End point description:

Anti-CHIKV SNA seroresponse rates for PXVX0317 (CHIKV VLP vaccine) and placebo, difference (PXVX0317 minus placebo), and associated 95% confidence interval (CI) at Day 22 for the immunogenicity evaluable population (IEP), all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

End point type	Primary

End point timeframe:

21 days post-vaccination

Notes:

[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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	424	2559		
Units: percentage of participants				
number (confidence interval 95%)	1.2 (0.5 to 2.7)	97.8 (97.2 to 98.3)		

Statistical analyses

Statistical analysis title	Anti-CHIKV SNA seroresponse rates at Day 22

Statistical analysis description:

Anti-CHIKV serum neutralising antibody (SNA) seroresponse rates at Day 22.

Seroresponse rate difference is (PXVX0317 minus placebo).

All 3 coprimary endpoints were required to be met for success, so no multiple comparisons were performed.

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2983
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	96.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	95
upper limit	97.5

Notes:

[7] - p-value is from a two-sided chi-square test of equality of seroresponse percentages between groups.

Primary: Anti-CHIKV SNA geometric mean titres (GMT) at Day 22

End point title	Anti-CHIKV SNA geometric mean titres (GMT) at Day 22[8]

End point description:

Anti-CHIKV SNA GMTs and associated 95% CIs at Day 22 for PXVX0317 (CHIKV VLP vaccine) and placebo for the IEP, all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

End point type	Primary

End point timeframe:

21 days 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	424	2559		
Units: Titre				
geometric mean (confidence interval 95%)	8 (7 to 9)	1618 (1522 to 1720)		

Statistical analyses

Statistical analysis title	Anti-CHIKV SNA Geometric Mean Titres at Day 22

Statistical analysis description:

Anti-CHIKV SNA Geometric Mean Titres (GMT) at Day 22.
All 3 coprimary endpoints were required to be met for success, so no multiple comparisons were performed. Ratio of GMTs is (PXVX0317:placebo).

Comparison groups	Pooled PXVX0317 v Group 4 - Placebo
Number of subjects included in analysis	2983
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [9]
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	206
Confidence interval	
level	95 %
sides	2-sided
lower limit	183
upper limit	232

Notes:

[9] - ANOVA model includes site and treatment group as fixed effects, assuming normality of log titres. P-value tests equivalence of group GMTs on log scale.

Primary: Anti-CHIKV SNA GMT ratios between pairs of PXVX0317 (CHIKV VLP vaccine) lots at Day 22

End point title	Anti-CHIKV SNA GMT ratios between pairs of PXVX0317 (CHIKV VLP vaccine) lots at Day 22[10]

End point description:

Anti-CHIKV SNA GMT ratios and associated 95% CIs between all three pairs of PXVX0317 (CHIKV VLP vaccine) lots (104:105, 104:106, 105:106) in adults 18 to <46 years of age in the IEP at Day 22.

Analysis population was adults 18 to <46 years in the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

End point type	Primary

End point timeframe:

21 days 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 does not apply to all arms in the study. Endpoint only applies to Group 1, Group 2, and Group 3, as these are the arms in which participants received one of the three consecutively manufactured lots of CHIKV-VLP vaccine. Endpoint is reporting ratios between pairs of these CHIKV-VLP vaccine lots (Group 1:Group 2, Group 1:Group 3, and Group 2:Group 3).

End point values	Group 1 - PXVX0317 Lot 104	Group 2 - PXVX0317 Lot 105	Group 3 - PXVX0317 Lot 106	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	488	498	494	
Units: Titre				
geometric mean (confidence interval 95%)	1857 (1641 to 2101)	1887 (1672 to 2130)	1950 (1724 to 2207)	

Statistical analyses

Statistical analysis title	SNA GMT Ratios at Day 22 (Lot 104:Lot 105)

Statistical analysis description:

Anti-CHIKV SNA GMT ratios between pairs of PXVX0317 (CHIKV VLP vaccine) Lots at Day 22. Group 1 (Lot 104) and Group 2 (Lot 105).

Success criterion was pairwise GMT ratios (104:105, 105:106, 104:106) each with a two-sided 95% CI within [0.667; 1.5].
All 3 coprimary endpoints were required to be met for success, so no multiple comparisons were performed.
GMT estimates and 95% CIs derived from an ANOVA model that includes site and product lot as fixed effects assuming normality of log titres.

Comparison groups	Group 1 - PXVX0317 Lot 104 v Group 2 - PXVX0317 Lot 105
Number of subjects included in analysis	986
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	GMT Ratio
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.14

Statistical analysis title	SNA GMT Ratios at Day 22 (Lot 105:Lot 106)

Statistical analysis description:

Anti-CHIKV SNA GMT ratios between pairs of PXVX0317 (CHIKV VLP vaccine) Lots at Day 22. Group 2 (Lot 105) and Group 3 (Lot 106).

Success criterion was pairwise GMT ratios (104:105,105:106,104:106) each with a two-sided 95% CI within [0.667; 1.5].
All 3 coprimary endpoints were required to be met for success, so no multiple comparisons were performed.
GMT estimates and 95% CIs derived from an ANOVA model that includes site and product lot as fixed effects assuming normality of log titres

Comparison groups	Group 2 - PXVX0317 Lot 105 v Group 3 - PXVX0317 Lot 106

Number of subjects included in analysis	992
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	GMT Ratio
Point estimate	0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.84
upper limit	1.12

Statistical analysis title	SNA GMT Ratios at Day 22 (Lot 104:Lot 106)

Statistical analysis description:

Anti-CHIKV SNA GMT ratios between pairs of PXVX0317 (CHIKV VLP vaccine) Lots at Day 22. Group 1 (Lot 104) and Group 3 (Lot 106).

Success criterion was pairwise GMT ratios (104:105, 105:106, 104:106) each with a two-sided 95% CI within [0.667; 1.5].
All 3 coprimary endpoints were required to be met for success, so no multiple comparisons were performed.
GMT estimates and 95% CIs derived from an ANOVA model that includes site and product lot as fixed effects assuming normality of log titres.

Comparison groups	Group 3 - PXVX0317 Lot 106 v Group 1 - PXVX0317 Lot 104
Number of subjects included in analysis	982
Analysis specification	Pre-specified
Analysis type	equivalence
Parameter estimate	GMT Ratio
Point estimate	0.95
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.82
upper limit	1.1

Secondary: Anti-CHIKV SNA seroresponse rates at Days 15

End point title	Anti-CHIKV SNA seroresponse rates at Days 15[11]

End point description:

Anti-CHIKV SNA seroresponse rates for PXVX0317 and placebo, difference (PXVX0317 minus placebo), and associated 95% CIs at Day 15 for the IEP, all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at the indicated visit.

End point type	Secondary

End point timeframe:

14 days 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	395	2434		
Units: percentage of participants				
number (confidence interval 95%)	0.8 (0.3 to 2.2)	96.8 (96.0 to 97.4)		

Statistical analyses

Statistical analysis title	Anti-CHIKV SNA seroresponse rates at Day 15

Statistical analysis description:

Key secondary endpoints were tested hierarchically, such that each was only tested if all 3 coprimary endpoints and prior key secondary endpoints were met, so no multiple comparisons were performed.

Seroresponse rate difference is (PXVX0317 minus placebo).

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2829
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [12]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	96
Confidence interval	
level	95 %
sides	2-sided
lower limit	94.3
upper limit	96.8

Notes:

[12] - p-value is from a two-sided chi-square test of equality of seroresponse percentages between groups.

Secondary: Anti-CHIKV SNA seroresponse rates at Day 183

End point title	Anti-CHIKV SNA seroresponse rates at Day 183[13]

End point description:

Anti-CHIKV SNA seroresponse rates for PXVX0317 (CHIKV VLP vaccine) and placebo, difference (PXVX0317 minus placebo), and associated 95% CIs at Day 183 for the IEP, all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at the indicated visit.

End point type	Secondary

End point timeframe:

182 days post-vaccination

Notes:

[13] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	401	2301		
Units: percentage of participants				
number (confidence interval 95%)	1.5 (0.7 to 3.2)	85.5 (84.0 to 86.9)		

Statistical analyses

Statistical analysis title	Anti-CHIKV SNA seroresponse rates at Day 183

Statistical analysis description:

Key secondary endpoints were tested hierarchically, such that each was only tested if all 3 coprimary endpoints and prior key secondary endpoints were met, so no multiple comparisons were performed.

Seroresponse rate difference is (PXVX0317 minus placebo).

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2702
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [14]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	84
Confidence interval	
level	95 %
sides	2-sided
lower limit	81.7
upper limit	85.6

Notes:

[14] - p-value is from a two-sided chi-square test of equality of seroresponse percentages between groups.

Secondary: Anti-CHIKV SNA seroresponse rates at Day 8

End point title	Anti-CHIKV SNA seroresponse rates at Day 8[15]

End point description:

Anti-CHIKV SNA seroresponse rates for PXVX0317 and placebo, difference (PXVX0317 minus placebo), and associated 95% CIs at Day 8 for the IEP, all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at the indicated visit.

End point type	Secondary

End point timeframe:

7 days post-vaccination

Notes:

[15] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	419	2510		
Units: percentage of participants				
number (confidence interval 95%)	0.5 (0.1 to 1.7)	46.6 (44.6 to 48.5)		

Statistical analyses

Statistical analysis title	Anti-CHIKV SNA seroresponse rates at Day 8

Statistical analysis description:

Key secondary endpoints were tested hierarchically, such that each was only tested if all 3 coprimary endpoints and prior key secondary endpoints were met, so no multiple comparisons were performed.

Seroresponse rate difference is (PXVX0317 minus placebo).

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2929
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [16]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	46.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	43.8
upper limit	48.1

Notes:

[16] - p-value is from a two-sided chi-square test of equality of seroresponse percentages between groups.

Secondary: Anti-CHIKV SNA Geometric Mean Titres (GMTs) at Day 8

End point title	Anti-CHIKV SNA Geometric Mean Titres (GMTs) at Day 8[17]

End point description:

Anti-CHIKV SNA GMTs with associated 95% CIs at Day 8 for PXVX0317 (CHIKV VLP vaccine) and placebo for the IEP, all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at the indicated visit.

End point type	Secondary

End point timeframe:

7 days post-vaccination

Notes:

[17] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	419	2510		
Units: Titre				
geometric mean (confidence interval 95%)	7 (6 to 8)	93 (87 to 100)		

Statistical analyses

Statistical analysis title	Anti-CHIKV SNA Geometric Mean Titres at Day 8

Statistical analysis description:

Ratio of GMTs is (PXVX0317:placebo)

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2929
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [18]
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	13

Confidence interval	
level	95 %
sides	2-sided
lower limit	11
upper limit	14

Notes:

[18] - ANOVA model includes site and treatment group as fixed effects, assuming normality of log titres. P-value tests equivalence of group GMTs on log scale.

Secondary: Anti-CHIKV SNA Geometric Mean Titres (GMTs) at Day 15

End point title	Anti-CHIKV SNA Geometric Mean Titres (GMTs) at Day 15[19]

End point description:

Anti-CHIKV SNA GMTs with associated 95% CIs at Day 15 for PXVX0317 (CHIKV VLP vaccine) and placebo for the IEP, all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at the indicated visit.

End point type	Secondary

End point timeframe:

14 days post-vaccination

Notes:

[19] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	395	2434		
Units: Titre				
geometric mean (confidence interval 95%)	8 (7 to 9)	1096 (1029 to 1167)		

Statistical analyses

Statistical analysis title	Anti-CHIKV SNA Geometric Mean Titres at Day 15

Statistical analysis description:

Ratio of GMTs is (PXVX0317:placebo).

Comparison groups	Group 4 - Placebo v Pooled PXVX0317

Number of subjects included in analysis	2829
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [20]
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	144
Confidence interval	
level	95 %
sides	2-sided
lower limit	128
upper limit	162

Notes:

[20] - ANOVA model includes site and treatment group as fixed effects, assuming normality of log titres. P-value tests equivalence of group GMTs on log scale.

Secondary: Anti-CHIKV SNA Geometric Mean Titres (GMTs) at Day 183

End point title	Anti-CHIKV SNA Geometric Mean Titres (GMTs) at Day 183[21]

End point description:

Anti-CHIKV SNA GMTs with associated 95% CIs at Day 183 for PXVX0317 (CHIKV VLP vaccine) and placebo for the IEP, all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at the indicated visit.

End point type	Secondary

End point timeframe:

182 days post-vaccination

Notes:

[21] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	401	2301		
Units: Titre				
geometric mean (confidence interval 95%)	8 (7 to 9)	338 (318 to 358)		

Statistical analyses

Statistical analysis title	Anti-CHIKV SNA Geometric Mean Titres at Day 183

Statistical analysis description:

Ratio of GMTs is (PXVX0317:placebo).

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2702
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [22]
Method	ANOVA
Parameter estimate	GMT Ratio
Point estimate	41
Confidence interval	
level	95 %
sides	2-sided
lower limit	37
upper limit	46

Notes:

[22] - ANOVA model includes site and treatment group as fixed effects, assuming normality of log titres. P-value tests equivalence of group GMTs on log scale.

Secondary: Geometric Mean Fold Increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 8

End point title	Geometric Mean Fold Increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 8[23]

End point description:

Geometric mean fold increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 8 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at both Day 1 and the indicated visit.

End point type	Secondary

End point timeframe:

7 days post-vaccination

Notes:

[23] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	419	2510		
Units: Fold increase in geometric mean titre				
number (confidence interval 95%)	1.0 (0.9 to 1.1)	12.5 (11.6 to		

13.3)

Statistical analyses

Statistical analysis title	GMFI in SNA Titres from Day 1 to Day 8

Statistical analysis description:

Geometric Mean Fold Increase (GMFI) in Anti-CHIKV SNA Titres from Day 1 to Day 8

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2929
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [24]
Method	t-test, 2-sided

Notes:

[24] - GMFI estimates and 95% CIs are based on t-statistics assuming a normal distribution of the log fold increase in titre.
P-value tests equality of log fold increase in titre between groups.

Secondary: Geometric Mean Fold Increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 15

End point title	Geometric Mean Fold Increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 15[25]

End point description:

Geometric mean fold increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 15 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at both Day 1 and the indicated visit.

End point type	Secondary

End point timeframe:

14 days post-vaccination

Notes:

[25] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	395	2434		
Units: Fold increase in geometric mean titre				
number (confidence interval 95%)	1.0 (0.9 to 1.1)	146.1 (137.2 to 155.6)		

Statistical analyses

Statistical analysis title	GMFI in SNA Titres from Day 1 to Day 15

Statistical analysis description:

Geometric Mean Fold Increase (GMFI) in Anti-CHIKV SNA Titres from Day 1 to Day 15

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2829
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [26]
Method	t-test, 2-sided

Notes:

[26] - GMFI estimates and 95% CIs are based on t-statistics assuming a normal distribution of the log fold increase in titre.
P-value tests equality of log fold increase in titre between groups.

Secondary: Geometric Mean Fold Increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 22

End point title	Geometric Mean Fold Increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 22[27]

End point description:

Geometric mean fold increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 22 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at both Day 1 and the indicated visit.

End point type	Secondary

End point timeframe:

21 days post-vaccination

Notes:

[27] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	424	2559		
Units: Fold increase in geometric mean titre				
number (confidence interval 95%)	1.1 (0.9 to 1.2)	215.7 (203.0 to 229.3)		

Statistical analyses

Statistical analysis title	GMFI in SNA Titres from Day 1 to Day 22

Statistical analysis description:

Geometric Mean Fold Increase (GMFI) in Anti-CHIKV SNA Titres from Day 1 to Day 22

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2983
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [28]
Method	t-test, 2-sided

Notes:

[28] - GMFI estimates and 95% CIs are based on t-statistics assuming a normal distribution of the log fold increase in titre.
P-value tests equality of log fold increase in titre between groups.

Secondary: Geometric Mean Fold Increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 183

End point title	Geometric Mean Fold Increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 183[29]

End point description:

Geometric mean fold increase (GMFI) in anti-CHIKV SNA titres from Day 1 to Day 183 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at both Day 1 and the indicated visit.

End point type	Secondary

End point timeframe:

182 days post-vaccination

Notes:

[29] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	401	2301		
Units: Fold increase in geometric mean titre				
number (confidence interval 95%)	1.1 (1.0 to 1.2)	45.0 (42.4 to 47.8)		

Statistical analyses

Statistical analysis title	GMFI in SNA Titres from Day 1 to Day 183
Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2702
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [30]
Method	t-test, 2-sided

Notes:

[30] - GMFI estimates and 95% CIs are based on t-statistics assuming a normal distribution of the log fold increase in titre.
P-value tests equality of log fold increase in titre between groups.

Secondary: Number and Percentage of Participants with Anti-CHIKV SNA Titre ≥15 at Day 8

End point title	Number and Percentage of Participants with Anti-CHIKV SNA Titre ≥15 at Day 8[31]

End point description:

Number and percentage of participants with anti-CHIKV SNA titres ≥15 at Day 8 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at the indicated visit.

End point type	Secondary

End point timeframe:

7 days post-vaccination

Notes:

[31] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	419	2510		
Units: Percentage of participants				
number (confidence interval 95%)	1.2 (0.5 to 2.8)	91.9 (90.7 to 92.9)		

Statistical analyses

Statistical analysis title	SNA Titres ≥15 at Day 8

Statistical analysis description:

Seroresponse rate difference is (PXVX0317 minus placebo)

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2929
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [32]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	90.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	88.7
upper limit	91.9

Notes:

[32] - p-value is from a two-sided chi-square test of equality of seroresponse percentages between groups.

Secondary: Number and Percentage of Participants with Anti-CHIKV SNA Titre ≥15 at Day 15

End point title	Number and Percentage of Participants with Anti-CHIKV SNA Titre ≥15 at Day 15[33]

End point description:

Number and percentage of participants with anti-CHIKV SNA titres ≥15 at Day 15 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at the indicated visit.

End point type	Secondary

End point timeframe:

14 days post-vaccination

Notes:

[33] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled

PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	395	2434		
Units: Percentage of participants				
number (confidence interval 95%)	0.8 (0.3 to 2.2)	99.5 (99.1 to 99.7)		

Statistical analyses

Statistical analysis title	SNA Titres ≥15 at Day 15
Statistical analysis description:	
Seroresponse rate difference is (PXVX0317 minus placebo)	
Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2829
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [34]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	98.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	97.2
upper limit	99.3

Notes:

[34] - p-value is from a two-sided chi-square test of equality of seroresponse percentages between groups.

Secondary: Number and Percentage of Participants with Anti-CHIKV SNA Titre ≥15 at Day 22

End point title	Number and Percentage of Participants with Anti-CHIKV SNA Titre ≥15 at Day 22[35]

End point description:

Number and percentage of participants with anti-CHIKV SNA titres ≥15 at Day 22 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at the indicated visit.

End point type	Secondary

End point timeframe:

21 days post-vaccination

Notes:

[35] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	424	2559		
Units: Percentage of participants				
number (confidence interval 95%)	1.7 (0.8 to 3.4)	99.2 (98.8 to 99.5)		

Statistical analyses

Statistical analysis title	SNA Titres ≥15 at Day 22

Statistical analysis description:

Seroresponse rate difference is (PXVX0317 minus placebo)

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2983
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [36]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	97.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	95.8
upper limit	98.5

Notes:

[36] - p-value is from a two-sided chi-square test of equality of seroresponse percentages between groups.

Secondary: Number and Percentage of Participants with Anti-CHIKV SNA Titre ≥15 at Day 183

End point title	Number and Percentage of Participants with Anti-CHIKV SNA Titre ≥15 at Day 183[37]

End point description:

Number and percentage of participants with anti-CHIKV SNA titres ≥15 at Day 183 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at the indicated visit.

End point type	Secondary

End point timeframe:

182 days post-vaccination

Notes:

[37] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	401	2301		
Units: Percentage of participants				
number (confidence interval 95%)	2.2 (1.2 to 4.2)	99.0 (98.6 to 99.4)		

Statistical analyses

Statistical analysis title	SNA Titres ≥15 at Day 183

Statistical analysis description:

Seroresponse rate difference is (PXVX0317 minus placebo)

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2702
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [38]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	96.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	94.8
upper limit	97.9

Notes:

[38] - p-value is from a two-sided chi-square test of equality of seroresponse percentages between groups.

Secondary: Number and Percentage of Participants with ≥4-fold Rise over Baseline at Day 8

End point title	Number and Percentage of Participants with ≥4-fold Rise over Baseline at Day 8[39]

End point description:

Number and percentage of participants with ≥4-fold rise over baseline at Day 8 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at Day 1 and at the indicated visit.

End point type	Secondary

End point timeframe:

7 days post-vaccination

Notes:

[39] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	419	2510		
Units: Percentage of participants				
number (confidence interval 95%)	0.7 (0.2 to 2.1)	65.5 (63.6 to 67.3)		

Statistical analyses

Statistical analysis title	≥4-fold rise over Baseline at Day 8

Statistical analysis description:

Seroresponse rate difference is (PXVX0317 minus placebo)

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2929
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [40]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	64.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	62.5
upper limit	66.7

Notes:

[40] - p-value is from a two-sided chi-square test of equality of seroresponse percentages between groups.

Secondary: Number and Percentage of Participants with ≥4-fold Rise over Baseline

at Day 15	
End point title	Number and Percentage of Participants with ≥4-fold Rise over Baseline at Day 15[41]

End point description:

Number and percentage of participants with ≥4-fold rise over baseline at Day 15 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at Day 1 and at the indicated visit.

End point type	Secondary

End point timeframe:

14 days post-vaccination

Notes:

[41] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	395	2434		
Units: Percentage of participants				
number (confidence interval 95%)	0.8 (0.3 to 2.2)	98.6 (98.0 to 99.0)		

Statistical analyses

Statistical analysis title	≥4-fold rise over Baseline at Day 15

Statistical analysis description:

Seroresponse rate difference is (PXVX0317 minus placebo)

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2829
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [42]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	97.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	96.3
upper limit	98.4

Notes:

[42] - p-value is from a two-sided chi-square test of equality of seroresponse percentages between groups.

Secondary: Number and Percentage of Participants with ≥4-fold Rise over Baseline at Day 22

End point title	Number and Percentage of Participants with ≥4-fold Rise over Baseline at Day 22[43]

End point description:

Number and percentage of participants with ≥4-fold rise over baseline at Day 22 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at Day 1 and at the indicated visit.

End point type	Secondary

End point timeframe:

21 days post-vaccination

Notes:

[43] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	424	2559		
Units: Percentage of participants				
number (confidence interval 95%)	1.4 (0.7 to 3.1)	98.6 (98.1 to 99.0)		

Statistical analyses

Statistical analysis title	≥4-fold rise over Baseline at Day 22

Statistical analysis description:

Seroresponse rate difference is (PXVX0317 minus placebo)

Comparison groups	Group 4 - Placebo v Pooled PXVX0317
Number of subjects included in analysis	2983
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	97.2

Confidence interval	
level	95 %
sides	2-sided
lower limit	95.5
upper limit	98.1

Secondary: Number and Percentage of Participants with ≥4-fold Rise over Baseline at Day 183

End point title	Number and Percentage of Participants with ≥4-fold Rise over Baseline at Day 183[44]

End point description:

Number and percentage of participants with ≥4-fold rise over baseline at Day 183 for the IEP for all age strata combined.

Analysis population was the Immunogenicity evaluable population (IEP): all randomised and vaccinated participants who provided an evaluable Day 22 anti-CHIKV human SNA sample within the analysis window, had no measurable anti-CHIKV human SNA assay titre at Day 1 (i.e., seronegative at baseline; participants missing a Day 1 titre were excluded from IEP), and had no important protocol deviation deemed exclusionary or other reason to be excluded as defined prior to unblinding.

Number of subjects analysed is number of participants with a sample result available at Day 1 and at the indicated visit.

End point type	Secondary

End point timeframe:

182 days post-vaccination

Notes:

[44] - 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: Study had 4 arms - Group 1, Group 2, Group 3, and Group 4. The additional arm, 'pooled PXVX0317', was created for reporting purposes on EudraCT.

Endpoint is reporting for Group 4 (Placebo) and the 'Pooled PXVX0317' Group (which is inclusive of CHIKV-VLP vaccinated participants in Group 1, Group 2, and Group 3). Therefore, data is being reported for participants from all arms of the study.

End point values	Group 4 - Placebo	Pooled PXVX0317		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	401	2301		
Units: Percentage of participants				
number (confidence interval 95%)	1.5 (0.7 to 3.2)	92.9 (91.8 to 93.9)		

Statistical analyses

Statistical analysis title	≥4-fold rise over Baseline at Day 183

Statistical analysis description:

Seroresponse rate difference is (PXVX0317 minus placebo)

Comparison groups	Group 4 - Placebo v Pooled PXVX0317

Number of subjects included in analysis	2702
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [45]
Method	Chi-squared
Parameter estimate	Mean difference (final values)
Point estimate	91.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	89.4
upper limit	92.7

Notes:

[45] - p-value is from a two-sided chi-square test of equality of seroresponse percentages between groups.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from Day 1 through to the Day 183 end of study visit.

Adverse event reporting additional description:

A solicited AE is a protocol-specified AE which the investigator (or designee) proactively asks the participants during a protocol-specified time period. (Systematic Assessment)
An unsolicited AE is an AE that is spontaneously reported by the participant or discovered by investigator (Non-systematic Assessment).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.1

Reporting groups

Reporting group title	Group 4 - Placebo

Reporting group description:

Biological/Vaccine: Placebo
Placebo is comprised of formulation buffer

Reporting group title	Pooled PXVX0317

Reporting group description:

All participants that received CHIKV VLP vaccine.

Includes all participants in Group 1 (PXVX0317 Lot 104) + Group 2 (PXVX0317 Lot 105) + Group 3 (PXVX0317 Lot 106).

Serious adverse events	Group 4 - Placebo	Pooled PXVX0317	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 464 (0.22%)	23 / 2790 (0.82%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Bipolar disorder			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Craniocerebral injury			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gun shot wound			
alternative assessment type: Non-			

systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Skin laceration			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Arnold-Chiari malformation			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalocele			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Basal ganglia infarction			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Retinal detachment			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Vomiting			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Nephrolithiasis			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 464 (0.22%)	0 / 2790 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubo-ovarian abscess			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
alternative assessment type: Non-systematic			

subjects affected / exposed	0 / 464 (0.00%)	1 / 2790 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
alternative assessment type: Non-systematic			
subjects affected / exposed	0 / 464 (0.00%)	2 / 2790 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Group 4 - Placebo	Pooled PXVX0317	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	127 / 464 (27.37%)	1065 / 2790 (38.17%)	
Nervous system disorders			
Headache			
subjects affected / exposed	78 / 464 (16.81%)	508 / 2790 (18.21%)	
occurrences (all)	78	523	
General disorders and administration site conditions			
Chills			
subjects affected / exposed	15 / 464 (3.23%)	239 / 2790 (8.57%)	
occurrences (all)	15	240	
Fatigue			
subjects affected / exposed	79 / 464 (17.03%)	557 / 2790 (19.96%)	
occurrences (all)	79	564	
Injection site pain			
subjects affected / exposed	49 / 464 (10.56%)	657 / 2790 (23.55%)	
occurrences (all)	49	661	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	31 / 464 (6.68%)	212 / 2790 (7.60%)	
occurrences (all)	31	221	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	34 / 464 (7.33%)	225 / 2790 (8.06%)	
occurrences (all)	36	230	
Myalgia			
subjects affected / exposed	45 / 464 (9.70%)	488 / 2790 (17.49%)	
occurrences (all)	46	492	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 July 2021	The major edit in protocol version 2.0 added the Day 15 visit for a more robust immunogenicity assessment. Hierarchical testing in the statistical section was added to control type I error.
10 November 2021	Minor edits in protocol version 3.0 included updates to the key study contact information related to the medical monitoring team, inclusion criteria, and labeling of the IP.
10 February 2022	Minor edits in protocol version 4.0 updated exclusion criterion 11, added a purpose statement, added HCV RNA testing if HCV antibody was positive, and clarified the definition of medically attended visits.
20 March 2023	Protocol version 5.0 updated the study objectives and endpoints per regulatory (US FDA and EMA) discussions.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported