Clinical trial results:
A Multi-center, Randomized, Double-blind, Placebo-controlled Phase 3 Efficacy Study of a Heterologous Vaccine Regimen of Ad26.Mos4.HIV and Adjuvanted Clade C gp140 and Mosaic gp140 to Prevent HIV-1 Infection Among Cis-gender Men and Transgender Individuals who Have Sex with Cis-gender Men and/or Transgender Individuals

Summary

EudraCT number	2018-003666-13
Trial protocol	ES PL IT
Global end of trial date	10 August 2023

Results information

Result version number	v1 (current)
This version publication date	20 July 2024
First version publication date	20 July 2024

Trial information

Trial identification

Sponsor protocol code	VAC89220HPX3002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03964415
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Vaccines & Prevention B.V.
Sponsor organisation address	Archimedesweg 4-6, CN Leiden, Netherlands, 2333
Public contact	Clinical Registry Group, Janssen Vaccines & Prevention B.V., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Vaccines & Prevention B.V., ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 August 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 August 2023
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main objective of trial was to evaluate the vaccine efficacy (VE) of a heterologous vaccine regimen utilizing adenovirus serotype 26.Mosaic 4.human immunodeficiency virus (Ad26.Mos4.HIV) and aluminum phosphate-adjuvanted Clade C glycoprotein (gp) 140 and Mosaic gp 140 for the prevention of HIV-1 infection in HIV-1 seronegative cis-gender men and transgender individuals having sex with cis-gender men and/or transgender individuals.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practice (GCP) and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 November 2019
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	Argentina: 405
Country: Number of subjects enrolled	Brazil: 851
Country: Number of subjects enrolled	Italy: 90
Country: Number of subjects enrolled	Mexico: 347
Country: Number of subjects enrolled	Peru: 1620
Country: Number of subjects enrolled	Poland: 117
Country: Number of subjects enrolled	Puerto Rico: 10
Country: Number of subjects enrolled	Spain: 258
Country: Number of subjects enrolled	United States: 189
Worldwide total number of subjects	3887
EEA total number of subjects	465

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	3887
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 3900 subjects were enrolled and randomised in this study, out of which 3887 subjects received at least one treatment. Only 198 subjects completed the study.

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140

Arm description:

Subjects received adenovirus serotype 26.Mosaic 4.human immunodeficiency virus (Ad26.Mos4.HIV) 5*10^10 viral particles (vp) intramuscular (IM) injection into the deltoid muscle as a monotherapy at Months 0 (Day 1) and 3 (Day 84) (preferably the deltoid of the non-dominant upper arm) along with adjuvanted protein formulation consisting of Clade C protein 80 micrograms (mcg), Mosaic protein 75 mcg and adjuvanted aluminum phosphate 425 mcg, into the deltoid muscle at Months 6 (Day 168) and 12 (Day 364) (different deltoid for each injection).

Arm type	Experimental
Investigational medicinal product name	Clade C + Mosaic + aluminum phosphate adjuvanted co-formulation
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Clade C protein 80 mcg, Mosaic protein 75 mcg and adjuvanted aluminum phosphate 425 mcg was administered as IM injection into the deltoid muscle at Months 6 and 12.

Investigational medicinal product name	Ad26.Mos4.HIV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Ad26.Mos4.HIV 5*10^10 vp was administered as IM injection into the deltoid muscle on Months 0 (Day 1), 3, 6, and 12.

Arm title	Group 2: Placebo

Arm description:

Subjects received placebo into the deltoid muscle at Months 0 (Day 1), 3 (Day 84; 1 injection), 6 (Day 168) and 12 (Day 364; 2 injections).

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Injection
Routes of administration	Intramuscular use

Dosage and administration details:

Placebo (0.9% saline) was administered into the deltoid muscle as single IM injection on Months 0 (Day 1) and 3 and 2 IM injections on Months 6 and 12.

Number of subjects in period 1	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic	Group 2: Placebo
Started	1942	1945
Completed	95	103
Not completed	1847	1842
Sponsor's decision	1563	1528
Adverse event, serious fatal	4	6
Consent withdrawn by subject	68	72
Physician decision	34	48
Adverse event, non-fatal	1	-
Adverse event, serious non fatal	2	-
Unspecified	35	38
Lost to follow-up	139	146
Protocol deviation	1	4

Baseline characteristics

Reporting groups	
Reporting group title	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140
Reporting group description:	
Subjects received adenovirus serotype 26.Mosaic 4.human immunodeficiency virus (Ad26.Mos4.HIV) 5*10^10 viral particles (vp) intramuscular (IM) injection into the deltoid muscle as a monotherapy at Months 0 (Day 1) and 3 (Day 84) (preferably the deltoid of the non-dominant upper arm) along with adjuvanted protein formulation consisting of Clade C protein 80 micrograms (mcg), Mosaic protein 75 mcg and adjuvanted aluminum phosphate 425 mcg, into the deltoid muscle at Months 6 (Day 168) and 12 (Day 364) (different deltoid for each injection).	
Reporting group title	Group 2: Placebo
Reporting group description:	
Subjects received placebo into the deltoid muscle at Months 0 (Day 1), 3 (Day 84; 1 injection), 6 (Day 168) and 12 (Day 364; 2 injections).	

Reporting group values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic	Group 2: Placebo	Total
Number of subjects	1942	1945	3887
Title for AgeCategorical Units: subjects			
18-20	198	213	411
21-24	384	355	739
25-29	518	520	1038
30-34	371	376	747
35-44	342	327	669
>=45	129	154	283
Title for AgeContinuous Units: years			
arithmetic mean	29.7	29.9	
standard deviation	± 8.28	± 8.58	-
Title for Gender Units: subjects			
Female (at birth)	9	7	16
Male (at birth)	1933	1937	3870
Undifferentiated (at birth)	0	1	1

End points

End points reporting groups

Reporting group title	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140

Reporting group description:

Subjects received adenovirus serotype 26.Mosaic 4.human immunodeficiency virus (Ad26.Mos4.HIV) 5*10^10 viral particles (vp) intramuscular (IM) injection into the deltoid muscle as a monotherapy at Months 0 (Day 1) and 3 (Day 84) (preferably the deltoid of the non-dominant upper arm) along with adjuvanted protein formulation consisting of Clade C protein 80 micrograms (mcg), Mosaic protein 75 mcg and adjuvanted aluminum phosphate 425 mcg, into the deltoid muscle at Months 6 (Day 168) and 12 (Day 364) (different deltoid for each injection).

Reporting group title	Group 2: Placebo

Reporting group description:

Subjects received placebo into the deltoid muscle at Months 0 (Day 1), 3 (Day 84; 1 injection), 6 (Day 168) and 12 (Day 364; 2 injections).

Primary: Number of Subjects With Confirmed Human Immunodeficiency Virus (HIV)-1 Infections Diagnosed Between the Month 7 and Month 24 Visits (Per-protocol [PP] Set)

End point title	Number of Subjects With Confirmed Human Immunodeficiency Virus (HIV)-1 Infections Diagnosed Between the Month 7 and Month 24 Visits (Per-protocol [PP] Set)[1]

End point description:

Number of subjects with a confirmed HIV-1 infections diagnosed between the Month 7 and Month 24 visits (PP set) was reported. The data represents the cumulative incidence of HIV-1 infections. The PP set included all subjects in the full analysis set (FAS; all randomised subjects who received at least one vaccine administration) population who had a negative HIV test 4 weeks post 3rd vaccination visit (that is, at the Month 7 Visit) and who received all planned vaccinations at the first three vaccination visits within the respective visit windows.

End point type	Primary

End point timeframe:

From Month 7 up to Month 24

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: No inferential statistics were planned for this endpoint. Descriptive statistics were only reported.

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1525	1494		
Units: Subjects	65	58		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Confirmed Human Immunodeficiency Virus (HIV)-1 Infections Diagnosed Between the Month 7 and Month 30 Visits (PP Set)

End point title	Number of Subjects With Confirmed Human Immunodeficiency Virus (HIV)-1 Infections Diagnosed Between the Month 7 and Month 30 Visits (PP Set)[2]

End point description:

Number of subjects with confirmed HIV-1 infections diagnosed between the Month 7 and Month 30 visits (PP set) was reported. The data represents the cumulative incidence of HIV-1 infections. The PP set included all subjects in the FAS population who had a negative HIV test 4 weeks post third vaccination visit (that is, at the Month 7 Visit) and who received all planned vaccinations at the first three vaccination visits within the respective visit windows.

End point type	Primary

End point timeframe:

From Month 7 up to Month 30

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: No inferential statistics were planned for this endpoint. Descriptive statistics were only reported.

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1525	1494		
Units: Subjects	71	67		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Solicited Local Adverse Events (AEs)

End point title	Number of Subjects With Solicited Local Adverse Events (AEs)

End point description:

Number of subjects with solicited local AEs were reported. An AE is any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Solicited local AEs that included injection site pain/tenderness, erythema and swelling at the study vaccine injection site, are used to assess the reactogenicity of the study vaccine and are pre-defined local (injection site) and which were noted by subjects in their subject diary for 7 days post vaccination (day of vaccination and the subsequent 7 days). The FAS set included all randomised subjects who received at least one vaccine administration. Here, 'n' (number analysed) is defined as subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Up to 7 days post each vaccination (dose) on Days 1 (up to Day 8), 84 (up to Day 91), 168 (up to Day 175), and 364 (up to Day 371)

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1942	1945		
Units: Subjects				
Up to 7 days post dose on Day 1 (n=1942,1945)	1225	329		
Up to 7 days post dose on Day 84 (n=1888,1877)	905	239		
Up to 7 days post dose on Day 168 (n=1841,1816)	1010	319		
Up to 7 days post dose on Day 364 (n=1724,1715)	917	252		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Number of subjects with solicited systemic AEs were reported. An AE is any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Solicited systemic events included events such as fatigue, headache, nausea, and myalgia, for which subjects were specifically questioned and which were noted by subjects in their subject diary for 7 days post vaccination (day of vaccination and the subsequent 7 days). The FAS set included all randomised subjects who received at least one vaccine administration. Here, 'n' (number analysed) is defined as subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Up to 7 days after each vaccination (dose) on Days 1 (up to Day 8), 84 (up to Day 91), 168 (up to Day 175), and 364 (up to 371)

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1942	1945		
Units: Subjects				
Up to 7 days post dose on Day 1 (n=1942,1945)	1313	860		
Up to 7 days post dose on Day 84 (n=1888,1877)	891	572		
Up to 7 days post dose on Day 168 (n=1841,1816)	856	535		
Up to 7 days post dose on Day 371 (n=1724,1715)	759	432		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Adverse Events of Special Interest (AESIs)

End point title	Number of Subjects With Adverse Events of Special Interest (AESIs)

End point description:

Number of subjects with AESIs were reported. An AE is any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Thrombotic events and/or thrombocytopenia (defined as platelet count below the lower limit of normal [LLN] range for the testing lab) were considered to be potential AESIs. The FAS set included all randomised subjects who received at least one vaccine administration.

End point type	Secondary

End point timeframe:

Up to 6 months after the last vaccination (up to Month 18)

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1942	1945		
Units: Subjects	4	2		

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

Number of subjects with unsolicited AEs were reported. An AE is any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. Unsolicited AEs are all AEs for which the subjects were not specifically questioned in the subject's diary. The FAS set included all randomised subjects who received at least one vaccine administration. Here, 'n' (number analysed) is defined as subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Up to 28 days after each vaccination (dose) on Days 1 (up to Day 29), 84 (up to Day 112), 168 (up to Day 196), and 364 (up to 392)

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1942	1945		
Units: Subjects				
Up to 28 days post dose on Day 1 (n=1942,1945)	253	245		
Up to 28 days post dose on Day 84 (n=1888,1877)	190	191		
Up to 28 days post dose on Day 168 (n=1841,1816)	298	293		
Up to 28 days post dose on Day 364 (n=1724,1715)	249	297		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Serious Adverse Events (SAEs)

End point title	Number of Subjects With Serious Adverse Events (SAEs)

End point description:

Number of subjects with SAEs were reported. An AE is any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. An SAE is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalisation; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly/birth defect; suspected transmission of any infectious agent via a medicinal product or medically important. The FAS set included all randomised subjects who received at least one vaccine administration.

End point type	Secondary

End point timeframe:

From Day 1 up to Month 40

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1942	1945		
Units: Subjects	82	77		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Confirmed HIV-1 Infections Diagnosed Over Time (Modified Intent-to-Treat [mITT] Set)

End point title	Number of Subjects With Confirmed HIV-1 Infections Diagnosed Over Time (Modified Intent-to-Treat [mITT] Set)

End point description:

Number of subjects with confirmed HIV-1 infections diagnosed over time (mITT set) were reported. The data represents the cumulative incidence of HIV-1 infections. The mITT efficacy population included subjects in the FAS who were HIV-1 uninfected at the date of the first vaccination.

End point type	Secondary

End point timeframe:

Month 0-24, Month 0-30, Month 0-40

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1940	1938		
Units: Subjects				
Month 0-24	124	123		
Month 0-30	130	132		
Month 0-40	130	133		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects Who Discontinued the Study or Study Intervention Due to Adverse Events (AEs)

End point title	Number of Subjects Who Discontinued the Study or Study Intervention Due to Adverse Events (AEs)

End point description:

Number of subjects who discontinued the study or study intervention due to AEs were reported. An AE is any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. The FAS set included all randomised subjects who received at least one vaccine administration.

End point type	Secondary

End point timeframe:

From Day 1 up to Month 40

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1942	1945		
Units: Subjects	11	16		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Medically-attended Adverse Events (MAAEs)

End point title	Number of Subjects With Medically-attended Adverse Events (MAAEs)

End point description:

Number of subjects with MAAEs were reported. An AE is any untoward medical occurrence in a subject participating in a clinical study that does not necessarily have a causal relationship with the pharmaceutical/biological agent under study. MAAEs are defined as AEs with medically-attended visits including hospital, emergency room, urgent care clinic, or other visits to or from medical personnel for any reason. The FAS set included all randomised subjects who received at least one vaccine administration.

End point type	Secondary

End point timeframe:

From Day 1 up to Month 40

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1942	1945		
Units: Subjects	999	1002		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Confirmed HIV-1 Infections Diagnosed Over Time (Modified Intent-to-Treat-2 [mITT-2] Set)

End point title	Number of Subjects With Confirmed HIV-1 Infections Diagnosed Over Time (Modified Intent-to-Treat-2 [mITT-2] Set)

End point description:

Number of subjects with confirmed HIV-1 infections diagnosed over time (mITT-2 set) were reported. The data represents the cumulative incidence of HIV-1 infections. The mITT-2 efficacy population included subjects in the FAS who had a negative HIV test 4 weeks post third vaccination visit (that is, at the Month 7 Visit).

End point type	Secondary

End point timeframe:

Month 7-24, Month 7-30, Month 7-40

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1812	1796		
Units: Subjects				
Month 7-24	75	71		
Month 7-30	81	80		
Month 7-40	81	81		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Confirmed HIV-1 Infections Diagnosed Over Time (Modified Intent-to-Treat-3 [mITT-3] Set)

End point title	Number of Subjects With Confirmed HIV-1 Infections Diagnosed Over Time (Modified Intent-to-Treat-3 [mITT-3] Set)

End point description:

Number of subjects with confirmed HIV-1 infections diagnosed over time (mITT-3 set) were reported. The data represents the cumulative incidence of HIV-1 infections. The mITT-3 efficacy population included subjects in the FAS who had a negative HIV test 4 weeks post third vaccination visit (that is, at Month 7 Visit) and who received all planned vaccinations at the first three vaccination visits regardless of the fact if the vaccinations were within the visit windows.

End point type	Secondary

End point timeframe:

Month 7-24, Month 7-30, Month 7-40

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1793	1775		
Units: Subjects				
Month 7-24	75	71		
Month 7-30	81	80		
Month 7-40	81	81		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Confirmed HIV-1 Infections Diagnosed Over Time (Full Immunization Analysis Set [FIS])

End point title	Number of Subjects With Confirmed HIV-1 Infections Diagnosed Over Time (Full Immunization Analysis Set [FIS])

End point description:

Number of subjects with confirmed HIV-1 infections diagnosed over time (FIS set) were reported. The data represents the cumulative incidence of HIV-1 infections. The FIS included participants in the FAS who were HIV-1 uninfected 4 weeks after the fourth vaccination visit (that is, at the Month 13 Visit) and who received all planned vaccinations within the respective visit windows

End point type	Secondary

End point timeframe:

Month 13-24, Month 13-30, Month 13-40

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1383	1376		
Units: Subjects				
Month 13-24	22	22		
Month 13-30	28	31		
Month 13-40	28	32		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With a Confirmed Human Immunodeficiency Virus (HIV)-1 Infection as Assessed by Demographic Characteristics: Age Groups

End point title	Number of Subjects With a Confirmed Human Immunodeficiency Virus (HIV)-1 Infection as Assessed by Demographic Characteristics: Age Groups

End point description:

Number of subjects with confirmed HIV-1 infection as assessed by demographic characteristics: age groups was reported. Age groups included 18-20, 21-24, 25-29, 30-34, 35-44, and greater than or equal to (>=) 45 years. The data represents the cumulative incidence of HIV-1 infections. The PP set included all subjects in the FAS population who had a negative HIV test 4 weeks post third vaccination visit (that is, at the Month 7 Visit) and who received all planned vaccinations at the first three vaccination visits within the respective visit windows. Here, 'n' (number analysed) indicated defined as subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Month 7-24, Month 7-30, Month 7-40

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1525	1494		
Units: Subjects				
Month 7-24 (Age Group: 18-20 years) (n=140,138)	8	7		
Month 7-24 (Age Group: 21-24 years) (n=298,275)	15	17		
Month 7-24 (Age Group: 25-29 years) (n=406,414)	21	17		
Month 7-24 (Age Group: 30-34 years) (n=296,288)	7	7		
Month 7-24 (Age Group: 35-44 years) (n=274,256)	12	6		
Month 7-24 (Age Group: >=45 years) (n=111,123)	2	4		
Month 7-30 (Age Group: 18-20 years) (n=140,138)	9	10		
Month 7-30 (Age Group: 21-24 years) (n=298,275)	18	17		
Month 7-30 (Age Group: 25-29 years) (n=406,414)	22	21		
Month 7-30 (Age Group: 30-34 years) (n=296,288)	8	8		
Month 7-30 (Age Group: 35-44 years) (n=274,256)	12	7		
Month 7-30 (Age Group: >=45 years) (n=111,123)	2	4		
Month 7-40 (Age Group: 18-20 years) (n=140,138)	9	10		
Month 7-40 (Age Group: 21-24 years) (n=298,275)	18	17		
Month 7-40 (Age Group: 25-29 years) (n=406,414)	22	22		
Month 7-40 (Age Group: 30-34 years) (n=296,288)	8	8		
Month 7-40 (Age Group: 35-44 years) (n=274,256)	12	7		
Month 7-40 (Age Group: >=45 years) (n=111,123)	2	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Confirmed HIV-1 Infections Based on Demographic Characteristics: Region-Wise Enrollment

End point title	Number of Subjects With Confirmed HIV-1 Infections Based on Demographic Characteristics: Region-Wise Enrollment

End point description:

Number of subjects with confirmed HIV-1 infections based on demographic characteristics: region-wise enrollment was reported. Regions were Latin-America (Argentina, Brazil, Mexico, and Peru), North America (Puerto Rico and United States of America), and Europe (Italy, Poland, and Spain). The data represents the cumulative incidence of HIV-1 infections. The PP set included all subjects in the FAS population who had a negative HIV test 4 weeks post third vaccination visit (that is, at the Month 7 Visit) and who received all planned vaccinations at the first three vaccination visits within the respective visit windows. Here, 'n' (number analysed) indicated defined as subjects analysed at specified timepoints.

End point type	Secondary

End point timeframe:

Month 7-24, Month 7-30, Month 7-40

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1525	1494		
Units: Subjects				
Month 7-24: Latin America (n=1244, 1214)	63	54		
Month 7-24: North America (n=74, 71)	0	1		
Month 7-24: Europe (n=207, 209)	2	3		
Month 7-30: Latin America (n=1244, 1214)	68	63		
Month 7-30: North America (n=74, 71)	0	1		
Month 7-30: Europe (n=207, 209)	3	3		
Month 7-40: Latin America (n=1244, 1214)	68	64		
Month 7-40: North America (n=74, 71)	0	1		
Month 7-40: Europe (n=207, 209)	3	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With HIV-1 Infection by Adenovirus Serotype 26 (Ad26) at Baseline

End point title	Number of Subjects With HIV-1 Infection by Adenovirus Serotype 26 (Ad26) at Baseline

End point description:

Number of subjects with HIV-1 infection by Ad26 at baseline were reported. The immunogenicity analysis set included subjects who acquired HIV-1 (case) and HIV-1 test negative (controls) that were selected for the analysis. Here, 'N' (number of subjects analysed) indicates number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Baseline (Day 1)

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	23		
Units: Subjects	204	10		

Statistical analyses

No statistical analyses for this end point

Secondary: Geometric Mean Antibody Titers For Adenovirus Serotype 26 (Ad26) as Determined by Vector Neutralization Assay (VNA)

End point title	Geometric Mean Antibody Titers For Adenovirus Serotype 26 (Ad26) as Determined by Vector Neutralization Assay (VNA)

End point description:

Geometric mean antibody titers for Ad26 as determined by VNA were reported. The immunogenicity analysis set included subjects who acquired HIV-1 (case) and HIV-1 test negative (controls) that were selected for the analysis. Here, 'N' (number of subjects analysed) indicates number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Up to Month 40

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	364	23		
Units: Titers				
geometric mean (confidence interval 95%)	66.6 (54.1 to 82.0)	41.3 (16.1 to 106.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With HIV-1 Infection by Pre/Post-exposure Prophylaxis (P[r]EP) Use

End point title	Number of Subjects With HIV-1 Infection by Pre/Post-exposure Prophylaxis (P[r]EP) Use

End point description:

Number of subjects with HIV-1 infection by P(r)EP use were reported. P(r)EP was assessed with a 4 item survey. Each item was measured on a scale ranging from 1 (strongly disagree) to 5 (strongly agree). Higher scores indicating higher levels of self-efficacy. If subject showed any evidence of PrEP or PEP use during the period based on questionnaire responses, concomitant medications or dried blood spot analysis, the response was "yes". The data represents the cumulative incidence of HIV-1 infections. The PP set included all subjects in the full analysis set (FAS; all randomised subjects who received at least one vaccine administration) population who had a negative HIV test 4 weeks post 3rd vaccination visit (that is, at the Month 7 Visit) and who received all planned vaccinations at the first three vaccination visits within the respective visit windows. Here, 'n' (number analysed) indicates subjects analysed for specified timepoints.

End point type	Secondary

End point timeframe:

Month 7-24, Month 7-30, Month 7-40

End point values	Group 1: Ad26.Mos4.HIV + Clade C and Mosaic gp140	Group 2: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1525	1494		
Units: Subjects				
Month 7-24: P(r)EP Use=Y (n=335, 359)	5	3		
Month 7-24: P(r)EP Use=N (n=1190, 1135)	60	55		
Month 7-30: P(r)EP Use=Y (n=355, 371)	5	5		
Month 7-30: P(r)EP Use=N (n=1170, 1123)	66	62		
Month 7-40: P(r)EP Use=Y (n=355, 372)	5	5		
Month 7-40: P(r)EP Use=N (n=1170, 1122)	66	63		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Unsolicited AEs: 28 days after each vaccination (up to Day 392); Solicited AEs: 7 days after each vaccination (up to Day 371); All-cause mortality and SAE: From Day 1 up to Month 40

Adverse event reporting additional description:

The full analysis set (FAS) set included all randomised subjects who received at least one vaccine administration.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	Group 2: Placebo

Reporting group description:

Subjects received placebo into the deltoid muscle at Months 0 (Day 1), 3 (Day 84; 1 injection), 6 (Day 168) and 12 (Day 364; 2 injections).

Reporting group title	Experimental: Group 1

Reporting group description:

Subjects received adenovirus serotype 26.Mosaic 4.human immunodeficiency virus (Ad26.Mos4.HIV) 5*10^10 viral particles (vp) intramuscular (IM) injection into the deltoid muscle as a monotherapy at Months 0 (Day 1) and 3 (Day 84) (preferably the deltoid of the non-dominant upper arm) along with adjuvanted protein formulation consisting of Clade C protein 80 micrograms (mcg), Mosaic protein 75 mcg and adjuvanted aluminum phosphate 425 mcg, into the deltoid muscle at Months 6 (Day 168) and 12 (Day 364) (different deltoid for each injection).

Serious adverse events	Group 2: Placebo	Experimental: Group 1	
Total subjects affected by serious adverse events			
subjects affected / exposed	77 / 1945 (3.96%)	82 / 1942 (4.22%)	
number of deaths (all causes)	6	4	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Testicular Seminoma (Pure)			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone Neoplasm			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			

subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head and Neck Cancer			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-Hodgkin's Lymphoma			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
T-Cell Type Acute Leukaemia			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral Venous Disease			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Nasal Septal Operation			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Death			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Pneumothorax Spontaneous			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Embolism			
subjects affected / exposed	0 / 1945 (0.00%)	2 / 1942 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute Respiratory Failure			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asphyxia			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nasal Septum Deviation			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural Effusion			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Bipolar Disorder			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Behaviour Disorder			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol Withdrawal Syndrome			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed Suicide			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Generalised Anxiety Disorder			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug Use Disorder			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug Abuse			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression Suicidal			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			

subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional Self-Injury			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental Disorder			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal Ideation			
subjects affected / exposed	1 / 1945 (0.05%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide Attempt			
subjects affected / exposed	6 / 1945 (0.31%)	4 / 1942 (0.21%)	
occurrences causally related to treatment / all	0 / 7	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Patient-Device Incompatibility			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
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			
Clavicle Fracture			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral Injury			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial Bones Fracture			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur Fracture			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot Fracture			
subjects affected / exposed	2 / 1945 (0.10%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand Fracture			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus Fracture			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Dislocation			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint Injury			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament Rupture			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Limb Fracture			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Injuries			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax Traumatic			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post-Traumatic Pain			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius Fracture			

subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal Burn			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist Fracture			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic Lung Injury			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Traumatic Intracranial Haemorrhage			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic Fracture			
subjects affected / exposed	0 / 1945 (0.00%)	2 / 1942 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to Various Agents			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac Arrest			

subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myocardial Ischaemia			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial Infarction			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Syncope			
subjects affected / exposed	1 / 1945 (0.05%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve Compression			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral Haemorrhage			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coagulopathy			

subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenitis			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Inguinal Hernia			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Perforation			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intussusception			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedematous Pancreatitis			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated Umbilical Hernia			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileal Perforation			

subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 1945 (0.05%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Fistula			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholic Pancreatitis			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis Acute			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	1 / 1945 (0.05%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			

subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Cellulite			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus Urinary			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 1945 (0.05%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Failure			
subjects affected / exposed	2 / 1945 (0.10%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Obstruction			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Facial Asymmetry			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Intervertebral Disc Protrusion			
subjects affected / exposed	0 / 1945 (0.00%)	3 / 1942 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular Weakness			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 1945 (0.00%)	2 / 1942 (0.10%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Acute Hepatitis C			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute HIV Infection			
subjects affected / exposed	1 / 1945 (0.05%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess Limb			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess Jaw			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Sepsis			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			

subjects affected / exposed	11 / 1945 (0.57%)	8 / 1942 (0.41%)	
occurrences causally related to treatment / all	0 / 11	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Helicobacter Sepsis			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 1945 (0.00%)	3 / 1942 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fournier's Gangrene			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue Fever			
subjects affected / exposed	2 / 1945 (0.10%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated Appendicitis			

subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 1945 (0.05%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19 Pneumonia			
subjects affected / exposed	0 / 1945 (0.00%)	2 / 1942 (0.10%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
COVID-19			
subjects affected / exposed	2 / 1945 (0.10%)	5 / 1942 (0.26%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bacterial Colitis			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis Tuberculous			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monkeypox			
subjects affected / exposed	1 / 1945 (0.05%)	2 / 1942 (0.10%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurosyphilis			
subjects affected / exposed	0 / 1945 (0.00%)	3 / 1942 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary Tract Infection			

subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous Abscess			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft Tissue Infection			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic Shock			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pyelonephritis Acute			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 1945 (0.05%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Tuberculosis			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary Sepsis			

subjects affected / exposed	0 / 1945 (0.00%)	3 / 1942 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 1945 (0.10%)	3 / 1942 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar Abscess			
subjects affected / exposed	2 / 1945 (0.10%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis Chronic			
subjects affected / exposed	1 / 1945 (0.05%)	0 / 1942 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis Viral			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetic Metabolic Decompensation			
subjects affected / exposed	0 / 1945 (0.00%)	1 / 1942 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Group 2: Placebo	Experimental: Group 1	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1348 / 1945 (69.31%)	1687 / 1942 (86.87%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	24 / 1945 (1.23%)	17 / 1942 (0.88%)	
occurrences (all)	25	18	

Nervous system disorders			
Headache (Solicited)			
subjects affected / exposed	863 / 1945 (44.37%)	1181 / 1942 (60.81%)	
occurrences (all)	1834	2550	
General disorders and administration site conditions			
Chills (Solicited)			
subjects affected / exposed	342 / 1945 (17.58%)	857 / 1942 (44.13%)	
occurrences (all)	533	1405	
Fatigue (Solicited)			
subjects affected / exposed	928 / 1945 (47.71%)	1323 / 1942 (68.13%)	
occurrences (all)	2018	3376	
Vaccination Site Pain (Solicited)			
subjects affected / exposed	695 / 1945 (35.73%)	1519 / 1942 (78.22%)	
occurrences (all)	1521	5543	
Vaccination Site Erythema (Solicited)			
subjects affected / exposed	7 / 1945 (0.36%)	47 / 1942 (2.42%)	
occurrences (all)	7	66	
Pyrexia (Solicited)			
subjects affected / exposed	137 / 1945 (7.04%)	400 / 1942 (20.60%)	
occurrences (all)	174	508	
Vaccination Site Swelling (Solicited)			
subjects affected / exposed	9 / 1945 (0.46%)	89 / 1942 (4.58%)	
occurrences (all)	10	144	
Gastrointestinal disorders			
Vomiting (Solicited)			
subjects affected / exposed	85 / 1945 (4.37%)	128 / 1942 (6.59%)	
occurrences (all)	115	154	
Nausea (Solicited)			
subjects affected / exposed	361 / 1945 (18.56%)	520 / 1942 (26.78%)	
occurrences (all)	552	758	
Diarrhoea			
subjects affected / exposed	54 / 1945 (2.78%)	51 / 1942 (2.63%)	
occurrences (all)	61	60	
Musculoskeletal and connective tissue disorders			

Arthralgia (Solicited)			
subjects affected / exposed	380 / 1945 (19.54%)	806 / 1942 (41.50%)	
occurrences (all)	639	1503	
Myalgia (Solicited)			
subjects affected / exposed	563 / 1945 (28.95%)	1124 / 1942 (57.88%)	
occurrences (all)	991	2333	
Infections and infestations			
Upper Respiratory Tract Infection			
subjects affected / exposed	27 / 1945 (1.39%)	29 / 1942 (1.49%)	
occurrences (all)	28	31	
Syphilis			
subjects affected / exposed	40 / 1945 (2.06%)	24 / 1942 (1.24%)	
occurrences (all)	41	25	
Proctitis Gonococcal			
subjects affected / exposed	32 / 1945 (1.65%)	33 / 1942 (1.70%)	
occurrences (all)	33	33	
Pharyngitis			
subjects affected / exposed	20 / 1945 (1.03%)	20 / 1942 (1.03%)	
occurrences (all)	21	22	
Oropharyngeal Gonococcal Infection			
subjects affected / exposed	40 / 1945 (2.06%)	27 / 1942 (1.39%)	
occurrences (all)	43	28	
Nasopharyngitis			
subjects affected / exposed	28 / 1945 (1.44%)	25 / 1942 (1.29%)	
occurrences (all)	29	25	
Influenza			
subjects affected / exposed	34 / 1945 (1.75%)	34 / 1942 (1.75%)	
occurrences (all)	38	35	
COVID-19			
subjects affected / exposed	79 / 1945 (4.06%)	75 / 1942 (3.86%)	
occurrences (all)	81	76	
Anal Chlamydia Infection			
subjects affected / exposed	39 / 1945 (2.01%)	22 / 1942 (1.13%)	
occurrences (all)	39	22	
Gastroenteritis			

subjects affected / exposed occurrences (all)	23 / 1945 (1.18%) 23	16 / 1942 (0.82%) 16	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 May 2019	The amendment was written in response to the feedback received from Health Authorities, partners and the community.
20 June 2019	The amendment was written to remove questionnaires from the protocol, to allow for clarifications to be added, and for minor inconsistencies and errors to be corrected.
02 July 2020	The amendment was written to address comments from Health Authorities, to allow for clarifications to be added, and for minor inconsistencies and errors to be corrected. An appendix was included to outline temporary measures while access to the sites was restricted during public health crises such as for example, coronavirus disease 2019 (COVID-19) outbreak and to provide investigators with flexibility to conduct study assessments while ensuring the safety and well-being of participants and site staff during the pandemic. These measures were not described in the body of the protocol but rather outlined in Appendix 18.
03 March 2023	Decision was made to terminate the Mosaico study (VAC89220HPX3002/HVTN 706) prematurely by meeting the stopping rules for non-efficacy. Based on the non-efficacy results of the Mosaico study as well as the outcome of immune correlates analysis in the Imbokodo study (VAC89220HPX2008/HVTN 705), the immunogenicity analyses as specified in the secondary endpoint of the Mosaico study were no longer relevant. The sponsor continued to evaluate immunogenicity as described under the exploratory endpoints.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported