Clinical trial results:
A Staged Phase 3 Study, Including a Double-Blinded Controlled Stage to Evaluate the Safety and Immunogenicity of Ad26.ZEBOV and MVA-BN-Filo as Candidate Prophylactic Vaccines for Ebola

Summary

EudraCT number	2019-000691-42
Trial protocol	Outside EU/EEA
Global end of trial date	03 July 2019

Results information

Result version number	v1 (current)
This version publication date	11 January 2020
First version publication date	11 January 2020

Trial information

Trial identification

Sponsor protocol code	VAC52150EBL3001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02509494
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Vaccines & Prevention B.V.
Sponsor organisation address	Archimedesweg 4-6, Leiden, Netherlands, 2333 CN
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-002573-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?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	10 September 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of this study during stage 1 was to evaluate the safety of a 2-dose heterologous vaccination regimen utilizing adenovirus serotype 26 expressing the Ebola virus Mayinga glycoprotein (Ad26.ZEBOV) as dose 1 and Modified Vaccinia Ankara - Bavarian Nordic-multivalent filovirus vector (MVA-BN-Filo) as dose 2, administered at a 56-day interval and during stage 2 was to evaluate the safety of a 2-dose heterologous vaccination regimen utilizing Ad26.ZEBOV as dose 1 and MVA-BN-Filo as dose 2, administered at a 56-day interval, compared to an active control vaccine.

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 Practices and applicable regulatory requirements. Safety evaluations included measurement of vital signs, clinical laboratory tests (Hematology, serum chemistry and urinalysis), physical examinations, assessment of adverse events (AEs).

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 September 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	36 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sierra Leone: 1020
Worldwide total number of subjects	1020
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)	70

Children (2-11 years)	314
Adolescents (12-17 years)	192
Adults (18-64 years)	440
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 1020 subjects were enrolled in the study. Of the 1020 subjects, 443 (adult) subjects were enrolled in Stages 1 and 2 and 577 (adolescents and children) subjects in Stage 2.

Period 1

Period 1 title	REGIMEN (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	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV

Arm description:

Subjects received 0.5 milliliter (mL) of adenovirus serotype 26 expressing the Ebola virus Mayinga glycoprotein (Ad26.ZEBOV) (5*10^10 viral particles [vp]) intramuscular (IM) injection as Dose 1 on Day 1 followed by 0.5 mL of Modified Vaccinia Ankara - Bavarian Nordic-multivalent filovirus vector (MVA-BN-Filo) (1*10^8 infectious units [Inf.U]) IM injection as Dose 2 on Day 57. The booster vaccination of 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection was administered to subjects who consented (2 years [Day 720] post Dose 1).

Arm type	Experimental
Investigational medicinal product name	Ad26.ZEBOV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection.

Investigational medicinal product name	MVA-BN-Filo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection.

Arm title	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo

Arm description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.

Arm type	Experimental
Investigational medicinal product name	Ad26.ZEBOV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection.

Investigational medicinal product name	MVA-BN-Filo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection.

Arm title	Stage 2, Adults: MenACWY, Placebo

Arm description:

Subjects received 0.5 mL of Meningococcal Group A, C, W135 and Y conjugate vaccine (MenACWY) vaccine as Dose 1 on Day 1 and then matching placebo as Dose 2 on Day 57.

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

Dosage and administration details:

Subjects received matching placebo (0.9 percent [%] saline) as IM injection.

Investigational medicinal product name	MenACWY
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL IM injection of MenACWY vaccine as Dose 1.

Arm title	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo

Arm description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.

Arm type	Experimental
Investigational medicinal product name	MVA-BN-Filo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection.

Investigational medicinal product name	Ad26.ZEBOV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection.

Arm title	Stage 2, 12-17 Years: MenACWY, Placebo

Arm description:

Subjects received 0.5 mL of MenACWY vaccine as Dose 1 on Day 1 and then matching placebo as Dose 2 on Day 57.

Arm type	Placebo

Investigational medicinal product name	MenACWY
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL IM injection of MenACWY vaccine as Dose 1.

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

Dosage and administration details:

Subjects received matching placebo (0.9% saline) as IM injection.

Arm title	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo

Arm description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.

Arm type	Experimental
Investigational medicinal product name	MVA-BN-Filo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection.

Investigational medicinal product name	Ad26.ZEBOV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection.

Arm title	Stage 2, 4-11 Years: MenACWY, Placebo

Arm description:

Subjects received 0.5 mL of MenACWY vaccine as Dose 1 on Day 1 and then matching placebo as Dose 2 on Day 57.

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

Dosage and administration details:

Subjects received 0.5 mL IM injection of MenACWY vaccine as Dose 1.

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

Dosage and administration details:

Subjects received matching placebo (0.9% saline) as IM injection.

Arm title	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo

Arm description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57. Children aged less than (<) 2 years at randomization received placebo at 3 months post dose 2.

Arm type	Experimental
Investigational medicinal product name	Ad26.ZEBOV
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection.

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

Dosage and administration details:

Subjects received matching placebo (0.9% saline) as IM injection.

Investigational medicinal product name	MVA-BN-Filo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection.

Arm title	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY

Arm description:

Subjects received MenACWY vaccine as Dose 1 on Day 1 and then placebo as Dose 2 on Day 57. Children aged less than (<) 2 years at randomization received MenACWY at 3 months post dose 2.

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

Dosage and administration details:

Subjects received matching placebo (0.9% saline) as IM injection.

Investigational medicinal product name	MenACWY
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection
Routes of administration	Intramuscular use

Dosage and administration details:

Subjects received 0.5 mL IM injection of MenACWY vaccine as Dose 1.

Number of subjects in period 1[1]	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, Adults: MenACWY, Placebo
Started	43	298	102
Completed	28	217	64
Not completed	15	81	38
Physician decision	2	1	-
Consent withdrawn by subject	4	17	7
Death	-	1	-
Non-compliance with study drug	1	11	7
Unspecified	-	4	5
Lost to follow-up	8	47	19

Number of subjects in period 1[1]	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, 12-17 Years: MenACWY, Placebo	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo
Started	143	48	144
Completed	132	43	133
Not completed	11	5	11
Physician decision	-	-	-
Consent withdrawn by subject	5	-	6
Death	-	1	-
Non-compliance with study drug	-	1	2
Unspecified	-	-	-
Lost to follow-up	6	3	3

Number of subjects in period 1[1]	Stage 2, 4-11 Years: MenACWY, Placebo	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY
Started	48	144	48
Completed	45	137	46
Not completed	3	7	2
Physician decision	-	-	-
Consent withdrawn by subject	1	2	1
Death	-	1	-
Non-compliance with study drug	1	1	-
Unspecified	-	-	-
Lost to follow-up	1	3	1

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Two participants were excluded from the summary tables because one received Ad26.ZEBOV followed by placebo and the other received MVA-BN-Filo as dose 1 (i.e. both sequences not in accordance with the protocol).

Baseline characteristics

Reporting groups	
Reporting group title	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV
Reporting group description:	
Subjects received 0.5 milliliter (mL) of adenovirus serotype 26 expressing the Ebola virus Mayinga glycoprotein (Ad26.ZEBOV) (5*10^10 viral particles [vp]) intramuscular (IM) injection as Dose 1 on Day 1 followed by 0.5 mL of Modified Vaccinia Ankara - Bavarian Nordic-multivalent filovirus vector (MVA-BN-Filo) (1*10^8 infectious units [Inf.U]) IM injection as Dose 2 on Day 57. The booster vaccination of 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection was administered to subjects who consented (2 years [Day 720] post Dose 1).	
Reporting group title	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo
Reporting group description:	
Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.	
Reporting group title	Stage 2, Adults: MenACWY, Placebo
Reporting group description:	
Subjects received 0.5 mL of Meningococcal Group A, C, W135 and Y conjugate vaccine (MenACWY) vaccine as Dose 1 on Day 1 and then matching placebo as Dose 2 on Day 57.	
Reporting group title	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo
Reporting group description:	
Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.	
Reporting group title	Stage 2, 12-17 Years: MenACWY, Placebo
Reporting group description:	
Subjects received 0.5 mL of MenACWY vaccine as Dose 1 on Day 1 and then matching placebo as Dose 2 on Day 57.	
Reporting group title	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo
Reporting group description:	
Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.	
Reporting group title	Stage 2, 4-11 Years: MenACWY, Placebo
Reporting group description:	
Subjects received 0.5 mL of MenACWY vaccine as Dose 1 on Day 1 and then matching placebo as Dose 2 on Day 57.	
Reporting group title	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo
Reporting group description:	
Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57. Children aged less than (<) 2 years at randomization received placebo at 3 months post dose 2.	
Reporting group title	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY
Reporting group description:	
Subjects received MenACWY vaccine as Dose 1 on Day 1 and then placebo as Dose 2 on Day 57. Children aged less than (<) 2 years at randomization received MenACWY at 3 months post dose 2.	

Reporting group values	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, Adults: MenACWY, Placebo
Number of subjects	43	298	102
Title for AgeCategorical Units: subjects			
Children (1-3 years)	0	0	0
Adolescents (12-17 years)	0	0	0

Adults (18-64 years)	43	295	101
From 65 to 84 years	0	3	1
85 years and over	0	0	0
Children (4-11 years)	0	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	26.9	27.5	29.6
standard deviation	± 9.87	± 10.46	± 11.6
Title for Gender			
Units: subjects			
Female	1	50	22
Male	42	248	80

Reporting group values	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, 12-17 Years: MenACWY, Placebo	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo
Number of subjects	143	48	144
Title for AgeCategorical			
Units: subjects			
Children (1-3 years)	0	0	0
Adolescents (12-17 years)	143	48	0
Adults (18-64 years)	0	0	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Children (4-11 years)	0	0	144
Title for AgeContinuous			
Units: years			
arithmetic mean	14.2	14	7.7
standard deviation	± 1.58	± 1.58	± 1.88
Title for Gender			
Units: subjects			
Female	69	21	73
Male	74	27	71

Reporting group values	Stage 2, 4-11 Years: MenACWY, Placebo	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY
Number of subjects	48	144	48
Title for AgeCategorical			
Units: subjects			
Children (1-3 years)	0	144	48
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Children (4-11 years)	48	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	7.9	1.9	1.9
standard deviation	± 1.96	± 0.79	± 0.76
Title for Gender			
Units: subjects			
Female	26	67	21

Male	22	77	27

Reporting group values	Total		
Number of subjects	1018		
Title for AgeCategorical Units: subjects			
Children (1-3 years)	192		
Adolescents (12-17 years)	191		
Adults (18-64 years)	439		
From 65 to 84 years	4		
85 years and over	0		
Children (4-11 years)	192		
Title for AgeContinuous Units: years			
arithmetic mean			
standard deviation	-		
Title for Gender Units: subjects			
Female	350		
Male	668		

End points

End points reporting groups

Reporting group title	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV

Reporting group description:

Subjects received 0.5 milliliter (mL) of adenovirus serotype 26 expressing the Ebola virus Mayinga glycoprotein (Ad26.ZEBOV) (5*10^10 viral particles [vp]) intramuscular (IM) injection as Dose 1 on Day 1 followed by 0.5 mL of Modified Vaccinia Ankara - Bavarian Nordic-multivalent filovirus vector (MVA-BN-Filo) (1*10^8 infectious units [Inf.U]) IM injection as Dose 2 on Day 57. The booster vaccination of 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection was administered to subjects who consented (2 years [Day 720] post Dose 1).

Reporting group title	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo

Reporting group description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.

Reporting group title	Stage 2, Adults: MenACWY, Placebo

Reporting group description:

Subjects received 0.5 mL of Meningococcal Group A, C, W135 and Y conjugate vaccine (MenACWY) vaccine as Dose 1 on Day 1 and then matching placebo as Dose 2 on Day 57.

Reporting group title	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo

Reporting group description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.

Reporting group title	Stage 2, 12-17 Years: MenACWY, Placebo

Reporting group description:

Subjects received 0.5 mL of MenACWY vaccine as Dose 1 on Day 1 and then matching placebo as Dose 2 on Day 57.

Reporting group title	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo

Reporting group description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.

Reporting group title	Stage 2, 4-11 Years: MenACWY, Placebo

Reporting group description:

Subjects received 0.5 mL of MenACWY vaccine as Dose 1 on Day 1 and then matching placebo as Dose 2 on Day 57.

Reporting group title	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo

Reporting group description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57. Children aged less than (<) 2 years at randomization received placebo at 3 months post dose 2.

Reporting group title	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY

Reporting group description:

Subjects received MenACWY vaccine as Dose 1 on Day 1 and then placebo as Dose 2 on Day 57. Children aged less than (<) 2 years at randomization received MenACWY at 3 months post dose 2.

Primary: Stages 1 and 2: Percentage of Subjects with Solicited Local Adverse Events

End point title	Stages 1 and 2: Percentage of Subjects with Solicited Local Adverse Events[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a clinical study subject administered a medicinal product, it does not necessarily have a causal relationship with the treatment. Subjects with solicited local (injection site) adverse events were instructed on how to note occurrences of erythema, induration/swelling (measured using the ruler supplied), pain/tenderness and itching at the injection site in the evening after each study vaccine administration and then daily for the next 7 days in the diary.

Full Analysis set included all subjects who received at least one dose of study vaccine, regardless of the occurrence of protocol deviations. Here 'n' indicates the number of subjects who were analyzed at specified timepoint for each arm and '99999' defines that Dose 3 was not administered in Stage 2 participants hence no data with solicited local AEs is available.

End point type	Primary

End point timeframe:

Until 7 days post each dose (Day 727 for Stage 1 and Day 64 for Stage 2)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, Adults: MenACWY, Placebo	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	298	102	143
Units: Percentage of subjects				
number (not applicable)				
Post-dose 1 (n=43,298,102,143,48,144,48,144,48)	27.9	17.1	16.7	9.8
Post-dose 2 (n=43,246,86,142,46,143,48,143,48)	14.0	23.6	9.3	14.8
Post-dose 3 (n=29,0,0,0,0,0,0,0,0)	17.2	99999	99999	99999

End point values	Stage 2, 12-17 Years: MenACWY, Placebo	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, 4-11 Years: MenACWY, Placebo	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	144	48	144
Units: Percentage of subjects				
number (not applicable)				
Post-dose 1 (n=43,298,102,143,48,144,48,144,48)	6.3	20.8	4.2	14.6
Post-dose 2 (n=43,246,86,142,46,143,48,143,48)	2.2	15.4	10.4	4.9
Post-dose 3 (n=29,0,0,0,0,0,0,0,0)	99999	99999	99999	99999

End point values	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Percentage of subjects				
number (not applicable)				
Post-dose 1 (n=43,298,102,143,48,144,48,144,48)	10.4			

Post-dose 2 (n=43,246,86,142,46,143,48,143,48)	0			
Post-dose 3 (n=29,0,0,0,0,0,0,0,0)	99999			

Statistical analyses

No statistical analyses for this end point

Primary: Stages 1 and 2: Percentage of Subjects with Solicited Systemic Adverse Events

End point title	Stages 1 and 2: Percentage of Subjects with Solicited Systemic Adverse Events[2]

End point description:

An AE is any untoward medical occurrence in a clinical study subject administered a medicinal product, it does not necessarily have a causal relationship with the treatment. Solicited systemic AEs included fever (defined as body temperature of 38 degree Celsius or higher), Headache, fatigue/Malaise, myalgia, nausea/vomiting, arthralgia, chills, decreased activity, decreased appetite, and irritability. Full Analysis set included all subjects who received at least one dose of study vaccine, regardless of the occurrence of protocol deviations. Here 'n' indicates the number of subjects who were analyzed at specified timepoint for each arm and '99999' defines that dose 3 was not administered in Stage 2 participants hence no data with systemic AEs is available.

End point type	Primary

End point timeframe:

Until 7 days post each dose (Day 727 for Stage 1 and Day 64 for Stage 2)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, Adults: MenACWY, Placebo	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	298	102	143
Units: Percentage of subjects				
number (not applicable)				
Post-dose 1 (n=43,298,102,143,48,144,48,144,48)	41.9	54.0	50.0	36.4
Post-dose 2 (n=43,246,86,142,46,143,48143,48)	39.5	43.5	45.3	18.3
Post-dose 3 (n=29,0,0,0,0,0,0,0,0)	31.0	99999	99999	99999

End point values	Stage 2, 12-17 Years: MenACWY, Placebo	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, 4-11 Years: MenACWY, Placebo	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	144	48	144
Units: Percentage of subjects				

number (not applicable)				
Post-dose 1 (n=43,298,102,143,48,144,48,144,48)	29.2	31.3	31.3	25.0
Post-dose 2 (n=43,246,86,142,46,143,48143,48)	13.0	18.9	16.7	16.1
Post-dose 3 (n=29,0,0,0,0,0,0,0,0)	99999	99999	99999	99999

End point values	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Percentage of subjects				
number (not applicable)				
Post-dose 1 (n=43,298,102,143,48,144,48,144,48)	25.0			
Post-dose 2 (n=43,246,86,142,46,143,48143,48)	29.2			
Post-dose 3 (n=29,0,0,0,0,0,0,0,0)	99999			

Statistical analyses

No statistical analyses for this end point

Primary: Stages 1 and 2: Percentage of Subjects with Unsolicited Adverse Events

End point title	Stages 1 and 2: Percentage of Subjects with Unsolicited Adverse Events[3]

End point description:

An AE is any untoward medical occurrence in a clinical study subject administered a medicinal product, it does not necessarily have a causal relationship with the treatment. Unsolicited adverse events were all adverse events for which the participant was specifically not questioned in the participant diary. Full Analysis set included all subjects who received at least one dose of study vaccine, regardless of the occurrence of protocol deviations. Here 'n' indicates the number of subjects who were analyzed at specified timepoint for each arm and '99999' defines that Dose 3 was not administered in Stage 2 participants hence no data with unsolicited AEs is available.

End point type	Primary

End point timeframe:

Up to Day 748 (Stage 1) and Up to Day 85 (Stage 2)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, Adults: MenACWY, Placebo	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	298	102	143

Units: Percentage of subjects				
number (not applicable)				
Post-dose 1 (n=43,298,102,143,48,144,48,144,48)	39.5	66.4	63.7	37.8
Post-dose 2 (n=43,246,86,142,46,143,48,143,48)	39.5	58.9	55.8	34.5
Post-dose 3 (n=29,0,0,0,0,0,0,0,0)	17.2	99999	99999	99999

End point values	Stage 2, 12-17 Years: MenACWY, Placebo	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, 4-11 Years: MenACWY, Placebo	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	144	48	144
Units: Percentage of subjects				
number (not applicable)				
Post-dose 1 (n=43,298,102,143,48,144,48,144,48)	41.7	41.7	37.5	61.1
Post-dose 2 (n=43,246,86,142,46,143,48,143,48)	28.3	32.2	27.1	53.8
Post-dose 3 (n=29,0,0,0,0,0,0,0,0)	99999	99999	99999	99999

End point values	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Percentage of subjects				
number (not applicable)				
Post-dose 1 (n=43,298,102,143,48,144,48,144,48)	58.3			
Post-dose 2 (n=43,246,86,142,46,143,48,143,48)	60.4			
Post-dose 3 (n=29,0,0,0,0,0,0,0,0)	99999			

Statistical analyses

No statistical analyses for this end point

Primary: Stages 1 and 2: Percentage of Subjects with Serious Adverse Events (SAEs)

End point title	Stages 1 and 2: Percentage of Subjects with Serious Adverse Events (SAEs)[4]

End point description:

SAEs are any untoward medical occurrence that at any dose results in death, is life-threatening (the subject was at risk of death at the time of the event. It does not refer to an event that hypothetically

might have caused death if it were more severe), requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, is a congenital anomaly/birth defect, is a suspected transmission of any infectious agent via a medicinal product. Full Analysis set included all subjects who received at least one dose of study vaccine, regardless of the occurrence of protocol deviations. Here 'n' indicates the number of subjects who were analyzed at specified timepoint for each arm and '99999' defines that Dose 3 was not administered in Stage 2 participants hence no data for SAEs is available.

End point type	Primary

End point timeframe:

Until end of study (Up to 38 months)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, Adults: MenACWY, Placebo	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	298	102	143
Units: Percentage of subjects				
number (not applicable)	43	298	102	143

End point values	Stage 2, 12-17 Years: MenACWY, Placebo	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, 4-11 Years: MenACWY, Placebo	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	144	48	144
Units: Percentage of subjects				
number (not applicable)	48	144	48	144

End point values	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Percentage of subjects				
number (not applicable)	48			

Statistical analyses

No statistical analyses for this end point

Primary: Stages 1 and 2: Percentage of Subjects with Immediate Reportable Events (IREs)

End point title	Stages 1 and 2: Percentage of Subjects with Immediate Reportable Events (IREs)[5]

End point description:

Any event of neuroimmunologic significance categorized as IREs which includes Cranial nerve disorders, Optic neuritis, Multiple sclerosis, Transverse myelitis, Guillain-Barre syndrome (Miller Fisher syndrome, Bickerstaff's encephalitis), Acute disseminated encephalomyelitis (including site specific variants: non-infectious encephalitis, encephalomyelitis, myelitis, myeloradiculomyelitis), Myasthenia gravis and Lambert-Eaton myasthenic syndrome, Immune-mediated peripheral neuropathies and plexopathies (chronic inflammatory demyelinating polyneuropathy, multifocal motor neuropathy and polyneuropathies associated with monoclonal gammopathy), Narcolepsy, Isolated paresthesia of more than 7 days duration. Full Analysis set included all subjects who received at least one dose of study vaccine, regardless of the occurrence of protocol deviations.

End point type	Primary

End point timeframe:

Until end of study (up to 38 months)

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: Descriptive statistics were done, no inferential statistical analyses were performed.

End point values	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, Adults: MenACWY, Placebo	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	43	298	102	143
Units: Percentage of subjects				
number (not applicable)				
Post-dose 1	0	0	0	0
Post-dose 2	0	0	0	0
Post-dose 3	0	0	0	0

End point values	Stage 2, 12-17 Years: MenACWY, Placebo	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, 4-11 Years: MenACWY, Placebo	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	48	144	48	144
Units: Percentage of subjects				
number (not applicable)				
Post-dose 1	0	0	0	0
Post-dose 2	0	0	0	0
Post-dose 3	0	0	0	0

End point values	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY			

Subject group type	Reporting group			
Number of subjects analysed	48			
Units: Percentage of subjects				
number (not applicable)				
Post-dose 1	0			
Post-dose 2	0			
Post-dose 3	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Stages 1 and 2: Percentage of Subjects with Anti-Ebola Virus (EBOV) Glycoprotein (GP) Binding Antibody Response Rate

End point title	Stages 1 and 2: Percentage of Subjects with Anti-Ebola Virus (EBOV) Glycoprotein (GP) Binding Antibody Response Rate

End point description:

Vaccine-induced binding antibody responses were measured using an EBOV GP Filovirus Animal Nonclinical Group (FANG) enzyme-linked immunosorbent assay (ELISA). The per Protocol analysis set included all randomized and vaccinated subjects, who received both the dose 1 and dose 2 (administered not more than 10 days outside the visit window) vaccinations, had immunogenicity data from baseline and at least one post-vaccination evaluable immunogenicity sample, and had no major protocol violations influencing the immune response. For the participants in Stage 1 who received the booster dose: including all participants who received dose 1, dose 2, and the booster dose (within the protocol-defined window), had at least one post-vaccination (after the date of vaccination) evaluable immunogenicity sample, and had no major protocol deviations influencing the immune response. Here 'N' (number of subjects analyzed) signifies number of subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Stages 1 and 2: Day 78 (21 days post Dose 2)

End point values	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, Adults: MenACWY, Placebo	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	42	182	62	134
Units: Percentage of subjects				
number (not applicable)	97.6	98.3	3.3	97.8

End point values	Stage 2, 12-17 Years: MenACWY, Placebo	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, 4-11 Years: MenACWY, Placebo	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	46	124	42	123
Units: Percentage of subjects				

number (not applicable)	2.2	99.2	7.1	97.5

End point values	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY			
Subject group type	Reporting group			
Number of subjects analysed	38			
Units: Percentage of subjects				
number (not applicable)	2.6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Until end of study (up to 38 months)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV

Reporting group description:

Subjects received 0.5 milliliter (mL) of Ad26.ZEBOV (5*10^10 viral particles [vp]) intramuscular (IM) injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 infectious units [Inf.U]) IM injection as Dose 2 on Day 57. The booster vaccination of 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection was administered to subjects who consented (2 years [Day 720] post Dose 1).

Reporting group title	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo

Reporting group description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.

Reporting group title	Stage 2, Adults: MenACWY, Placebo

Reporting group description:

Subjects received MenACWY vaccine as Dose 1 on Day 1 and then placebo as Dose 2 on Day 57.

Reporting group title	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo

Reporting group description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.

Reporting group title	Stage 2, 12-17 Years: MenACWY, Placebo

Reporting group description:

Subjects received MenACWY vaccine as Dose 1 on Day 1 and then placebo as Dose 2 on Day 57.

Reporting group title	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo

Reporting group description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57.

Reporting group title	Stage 2, 4-11 Years: MenACWY, Placebo

Reporting group description:

Subjects received MenACWY vaccine as Dose 1 on Day 1 and then placebo as Dose 2 on Day 57.

Reporting group title	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo

Reporting group description:

Subjects received 0.5 mL of Ad26.ZEBOV (5*10^10 vp) IM injection as Dose 1 on Day 1 followed by 0.5 mL of MVA-BN-Filo (1*10^8 Inf.U) IM injection as Dose 2 on Day 57. Children aged less than (<) 2 years at randomization received placebo at 3 months post dose 2.

Reporting group title	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY

Reporting group description:

Subjects received MenACWY vaccine as Dose 1 on Day 1 and then placebo as Dose 2 on Day 57. Children aged less than (<) 2 years at randomization received MenACWY at 3 months post dose 2.

Serious adverse events	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, Adults: MenACWY, Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 43 (6.98%)	16 / 298 (5.37%)	4 / 102 (3.92%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Abortion Induced Incomplete			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest Injury			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head Injury			
subjects affected / exposed	0 / 43 (0.00%)	2 / 298 (0.67%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament Sprain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple Injuries			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Open Globe Injury			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius Fracture			

subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Laceration			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypovolaemic Shock			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile Convulsion			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Threatened			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage in Pregnancy			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Placenta Praevia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Premature Labour			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia of Pregnancy			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron Deficiency Anaemia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal Detachment			
subjects affected / exposed	1 / 43 (2.33%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic Ulcer			

subjects affected / exposed	1 / 43 (2.33%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal Haematoma			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 298 (0.67%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain Abscess			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chorioretinitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 43 (0.00%)	2 / 298 (0.67%)	3 / 102 (2.94%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Helminthic Infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	0 / 43 (0.00%)	3 / 298 (1.01%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis Bacterial			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis Chronic			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative Wound Infection			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection			

subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous Abscess			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Typhoid Fever			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 43 (0.00%)	1 / 298 (0.34%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Serious adverse events	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, 12-17 Years: MenACWY, Placebo	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 143 (0.00%)	1 / 48 (2.08%)	5 / 144 (3.47%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Abortion Induced Incomplete			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest Injury			

subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head Injury			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament Sprain			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple Injuries			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Open Globe Injury			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius Fracture			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Laceration			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypovolaemic Shock			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			

Febrile Convulsion			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Threatened			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage in Pregnancy			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Placenta Praevia			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Premature Labour			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia of Pregnancy			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Iron Deficiency Anaemia			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal Detachment			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic Ulcer			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal Haematoma			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			

subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain Abscess			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chorioretinitis			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Helminthic Infection			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	2 / 144 (1.39%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis Bacterial			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			

subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis Chronic			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative Wound Infection			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	1 / 144 (0.69%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous Abscess			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Typhoid Fever			

subjects affected / exposed	0 / 143 (0.00%)	1 / 48 (2.08%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Stage 2, 4-11 Years: MenACWY, Placebo	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 48 (0.00%)	15 / 144 (10.42%)	3 / 48 (6.25%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Abortion Induced Incomplete			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest Injury			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head Injury			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament Sprain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multiple Injuries			

subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Open Globe Injury			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius Fracture			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Laceration			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Hypovolaemic Shock			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Febrile Convulsion			
subjects affected / exposed	0 / 48 (0.00%)	1 / 144 (0.69%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion Threatened			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Haemorrhage in Pregnancy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Placenta Praevia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Premature Labour			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 48 (0.00%)	4 / 144 (2.78%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Anaemia of Pregnancy			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron Deficiency Anaemia			
subjects affected / exposed	0 / 48 (0.00%)	1 / 144 (0.69%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal Detachment			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peptic Ulcer			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal Haematoma			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Brain Abscess			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchiolitis			
subjects affected / exposed	0 / 48 (0.00%)	1 / 144 (0.69%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chorioretinitis			

subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Helminthic Infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaria			
subjects affected / exposed	0 / 48 (0.00%)	14 / 144 (9.72%)	2 / 48 (4.17%)
occurrences causally related to treatment / all	0 / 0	0 / 14	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Meningitis Bacterial			
subjects affected / exposed	0 / 48 (0.00%)	1 / 144 (0.69%)	1 / 48 (2.08%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis Chronic			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			

subjects affected / exposed	0 / 48 (0.00%)	4 / 144 (2.78%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postoperative Wound Infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 48 (0.00%)	6 / 144 (4.17%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous Abscess			
subjects affected / exposed	0 / 48 (0.00%)	1 / 144 (0.69%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Typhoid Fever			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Stage 1, Adults: Ad26.ZEBOV, MVA-BN-Filo, Ad26.ZEBOV	Stage 2, Adults: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, Adults: MenACWY, Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 43 (51.16%)	194 / 298 (65.10%)	63 / 102 (61.76%)
Investigations			
Haemoglobin Decreased			
subjects affected / exposed	0 / 43 (0.00%)	7 / 298 (2.35%)	2 / 102 (1.96%)
occurrences (all)	0	11	2
Nervous system disorders			
Headache			
subjects affected / exposed	9 / 43 (20.93%)	40 / 298 (13.42%)	13 / 102 (12.75%)
occurrences (all)	10	42	13
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 43 (2.33%)	2 / 298 (0.67%)	0 / 102 (0.00%)
occurrences (all)	1	2	0
General disorders and administration site conditions			
Pain			
subjects affected / exposed	3 / 43 (6.98%)	16 / 298 (5.37%)	10 / 102 (9.80%)
occurrences (all)	3	17	10
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 43 (0.00%)	2 / 298 (0.67%)	0 / 102 (0.00%)
occurrences (all)	0	2	0
Peptic Ulcer			
subjects affected / exposed	0 / 43 (0.00%)	15 / 298 (5.03%)	1 / 102 (0.98%)
occurrences (all)	0	16	1
Skin and subcutaneous tissue disorders			
Pruritus Generalised			
subjects affected / exposed	1 / 43 (2.33%)	15 / 298 (5.03%)	5 / 102 (4.90%)
occurrences (all)	1	16	5
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	2 / 43 (4.65%)	16 / 298 (5.37%)	7 / 102 (6.86%)
occurrences (all)	2	16	7
Infections and infestations			

Furuncle			
subjects affected / exposed	6 / 43 (13.95%)	11 / 298 (3.69%)	3 / 102 (2.94%)
occurrences (all)	6	11	3
Gastroenteritis			
subjects affected / exposed	1 / 43 (2.33%)	10 / 298 (3.36%)	2 / 102 (1.96%)
occurrences (all)	1	11	3
Malaria			
subjects affected / exposed	6 / 43 (13.95%)	123 / 298 (41.28%)	40 / 102 (39.22%)
occurrences (all)	6	150	50
Nasopharyngitis			
subjects affected / exposed	0 / 43 (0.00%)	21 / 298 (7.05%)	5 / 102 (4.90%)
occurrences (all)	0	23	5
Respiratory Tract Infection			
subjects affected / exposed	2 / 43 (4.65%)	15 / 298 (5.03%)	4 / 102 (3.92%)
occurrences (all)	2	17	4
Tinea Capitis			
subjects affected / exposed	0 / 43 (0.00%)	0 / 298 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Typhoid Fever			
subjects affected / exposed	1 / 43 (2.33%)	14 / 298 (4.70%)	9 / 102 (8.82%)
occurrences (all)	1	14	9
Upper Respiratory Tract Infection			
subjects affected / exposed	1 / 43 (2.33%)	16 / 298 (5.37%)	8 / 102 (7.84%)
occurrences (all)	1	18	8

Non-serious adverse events	Stage 2, 12-17 Years: Ad26.ZEBOV, MVA-BN-Filo	Stage 2, 12-17 Years: MenACWY, Placebo	Stage 2, 4-11 Years: Ad26.ZEBOV, MVA-BN-Filo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	56 / 143 (39.16%)	18 / 48 (37.50%)	69 / 144 (47.92%)
Investigations			
Haemoglobin Decreased			
subjects affected / exposed	8 / 143 (5.59%)	5 / 48 (10.42%)	3 / 144 (2.08%)
occurrences (all)	9	7	3
Nervous system disorders			
Headache			
subjects affected / exposed	14 / 143 (9.79%)	2 / 48 (4.17%)	4 / 144 (2.78%)
occurrences (all)	14	2	4

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 143 (0.70%)	3 / 48 (6.25%)	6 / 144 (4.17%)
occurrences (all)	1	3	6
General disorders and administration site conditions			
Pain			
subjects affected / exposed	3 / 143 (2.10%)	1 / 48 (2.08%)	0 / 144 (0.00%)
occurrences (all)	3	1	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Peptic Ulcer			
subjects affected / exposed	0 / 143 (0.00%)	1 / 48 (2.08%)	0 / 144 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Pruritus Generalised			
subjects affected / exposed	3 / 143 (2.10%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences (all)	3	0	0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	1 / 143 (0.70%)	0 / 48 (0.00%)	0 / 144 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Furuncle			
subjects affected / exposed	2 / 143 (1.40%)	1 / 48 (2.08%)	1 / 144 (0.69%)
occurrences (all)	2	3	1
Gastroenteritis			
subjects affected / exposed	1 / 143 (0.70%)	0 / 48 (0.00%)	3 / 144 (2.08%)
occurrences (all)	1	0	3
Malaria			
subjects affected / exposed	35 / 143 (24.48%)	9 / 48 (18.75%)	50 / 144 (34.72%)
occurrences (all)	40	11	56
Nasopharyngitis			
subjects affected / exposed	1 / 143 (0.70%)	0 / 48 (0.00%)	5 / 144 (3.47%)
occurrences (all)	1	0	5
Respiratory Tract Infection			

subjects affected / exposed	6 / 143 (4.20%)	2 / 48 (4.17%)	4 / 144 (2.78%)
occurrences (all)	8	2	4
Tinea Capitis			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	2 / 144 (1.39%)
occurrences (all)	0	0	3
Typhoid Fever			
subjects affected / exposed	0 / 143 (0.00%)	0 / 48 (0.00%)	1 / 144 (0.69%)
occurrences (all)	0	0	1
Upper Respiratory Tract Infection			
subjects affected / exposed	3 / 143 (2.10%)	1 / 48 (2.08%)	9 / 144 (6.25%)
occurrences (all)	3	1	9

Non-serious adverse events	Stage 2, 4-11 Years: MenACWY, Placebo	Stage 2, 1-3 Years: Ad26.ZEBOV, MVA-BN-Filo, Placebo	Stage 2, 1-3 Years: MenACWY, Placebo, MenACWY
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 48 (43.75%)	108 / 144 (75.00%)	38 / 48 (79.17%)
Investigations			
Haemoglobin Decreased			
subjects affected / exposed	1 / 48 (2.08%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 48 (8.33%)	13 / 144 (9.03%)	1 / 48 (2.08%)
occurrences (all)	4	16	1
General disorders and administration site conditions			
Pain			
subjects affected / exposed	1 / 48 (2.08%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 48 (0.00%)	8 / 144 (5.56%)	3 / 48 (6.25%)
occurrences (all)	0	9	5
Peptic Ulcer			

subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pruritus Generalised			
subjects affected / exposed	0 / 48 (0.00%)	1 / 144 (0.69%)	0 / 48 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Furuncle			
subjects affected / exposed	2 / 48 (4.17%)	6 / 144 (4.17%)	3 / 48 (6.25%)
occurrences (all)	2	6	3
Gastroenteritis			
subjects affected / exposed	2 / 48 (4.17%)	7 / 144 (4.86%)	5 / 48 (10.42%)
occurrences (all)	2	8	5
Malaria			
subjects affected / exposed	14 / 48 (29.17%)	81 / 144 (56.25%)	26 / 48 (54.17%)
occurrences (all)	18	116	39
Nasopharyngitis			
subjects affected / exposed	0 / 48 (0.00%)	6 / 144 (4.17%)	5 / 48 (10.42%)
occurrences (all)	0	6	5
Respiratory Tract Infection			
subjects affected / exposed	4 / 48 (8.33%)	17 / 144 (11.81%)	5 / 48 (10.42%)
occurrences (all)	4	19	5
Tinea Capitis			
subjects affected / exposed	1 / 48 (2.08%)	2 / 144 (1.39%)	3 / 48 (6.25%)
occurrences (all)	1	3	3
Typhoid Fever			
subjects affected / exposed	0 / 48 (0.00%)	0 / 144 (0.00%)	0 / 48 (0.00%)
occurrences (all)	0	0	0
Upper Respiratory Tract Infection			
subjects affected / exposed	4 / 48 (8.33%)	26 / 144 (18.06%)	9 / 48 (18.75%)
occurrences (all)	4	32	11

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 May 2015	The first amendment was written in response to the Assisted Review of the Janssen Ebola Zaire Vaccine Clinical Trials Application meeting in April 2015.
30 November 2015	With the declaration of Sierra Leone as Ebola-free on 07 November 2015, and in line with feedback from the Food and Drug Administration (FDA) and European Medicines Agency (EMA), a control arm was added to Stage 2, which would now become an individually randomized, double-blinded, active-controlled study.
28 January 2016	The main objective of an originally planned Stage 3 of the study was to assess vaccine effectiveness in preventing cases of ebola virus disease (EVD).
07 September 2016	The sponsor halted vaccinations in the clinical program after receipt of a serious case of Miller Fisher syndrome post MVA-BN-Filo vaccination in Phase 2 study VAC52150EBL2001, as well as reports of mild transient paresthesia in the same study that required further assessment to rule out a neurologic and autoimmune event. Stage 1 was extended for 24 months beyond Day 360 post dose 1 for long-term follow-up of safety and immunogenicity.
04 May 2017	This amendment was developed in response to emerging clinical data and changes to the global clinical development plan.
20 June 2018	This amendment was made to replace information on VAC52150 Vaccine Development Rollover study VAC52150EBL4001 with information on long-term follow-up study VAC52150EBL3005.
02 October 2018	This amendment was made to clarify that for each age group of Stage 2, participants and studysite personnel were blinded to study vaccine allocation until the last participant in that age group completed at least the 6-month post-dose 2 visit or discontinued earlier and the database had been locked for that part.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
28 April 2016	The site was notified to halt all vaccinations due to the occurrence of Miller Fisher syndrome in a study participant in the Phase 2 study VAC52150EBL2001.	25 July 2016

Notes:

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

In Stage 2, 140 adult participants either did not receive the dose 2 vaccination (N=68) or received it later than planned (that is, outside of the protocol-defined interval), mainly due to the study pause (N=72).

Notes: