



## Clinical trial results:

### Evaluating the Long Term Immunogenicity of adenoviral and MVA vectored Ebola vaccine schedules and response to late boosting with AD26.ZEBOV vaccine: an open-label clinical trial

#### Summary

EudraCT number	2017-004610-26
Trial protocol	GB
Global end of trial date	09 March 2021

#### Results information

Result version number	v1 (current)
This version publication date	06 July 2022
First version publication date	06 July 2022

#### Trial information

##### Trial identification

Sponsor protocol code	OVG2017/10
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##### Additional study identifiers

ISRCTN number	ISRCTN10481319
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

##### Sponsors

Sponsor organisation name	University of Oxford, Clinical Trials and Research Governance (CTRG)
Sponsor organisation address	Boundary Brook House, Oxford, United Kingdom, OX3 7GB
Public contact	Matthew Snape, University of Oxford, 44 1865611400, matthew.snape@paediatrics.ox.ac.uk
Scientific contact	Matthew Snape, University of Oxford, 44 1865611400, matthew.snape@paediatrics.ox.ac.uk

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:

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## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 June 2022
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	09 March 2021
Was the trial ended prematurely?	No

Notes:

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## General information about the trial

Main objective of the trial:

To evaluate the long-term persistence of immunity (both cellular immunity and antibody levels) in healthy volunteers who were vaccinated approximately 2-5 years previously with investigational Ebola vaccines (ChAd3-EBO Z, MVA-BN-FILO, MVA-EBO-Z and Ad26.ZEBOV), and to assess the response to a booster dose of an investigational Ebola vaccine (Ad26.ZEBOV) given approximately 2-5 years after the initial vaccines.

Protection of trial subjects:

The trial complied with the General Data Protection Regulations and the Data Protection Act. Participants were enrolled with fully informed consent, including the safety data known about the vaccines up to that point, i.e. mild vaccine reactions are common and include local reactions such as pain, tenderness and swelling at the injection site and systemic reactions such as mild fever, fatigue and headache. Fever is the most commonly reported systemic reaction with an incidence of up to 10%. There is a small risk of pain and bruising as a result of blood sampling. Very occasionally, participants may feel faint or experience a vaso-vagal episode as a result of taking blood. Possible side effects were explained to the participants and they were told they can take painkillers/ antipyretics (e.g. paracetamol). Participants were observed for 30 minutes after receiving the vaccine in case of any immediate reactions. They were also given a phone number for 24 hour contact with a study doctor if they were concerned about vaccine reactions and asked to keep a diary card reporting solicited reactions, and to report any serious adverse events. The possible adverse effects of blood sampling were minimised by ensuring that the participant was aware of when and how the blood was taken and provided an opportunity to ask questions about the procedure. Blood was taken by a doctor or nurse experienced and trained in taking blood and in managing any adverse events associated with the procedure. Participants were compensated for the inconvenience of having blood taken. As with any vaccine there was the rare risk of an anaphylactic reactions to these Ebola vaccines and study staff were trained to manage this. The investigational nature of Ad26.ZEBOV with the potential for unknown side effects, was made clear to participants as part of the informed consent process, however adenoviral based vaccines have been given to thousands of participants without significant safety concerns.

Background therapy:

The study population consisted of participants who had received immunisation with Ebola vaccines (ChAd3-EBO-Z, MVA-BN-FILO, MVA-EBO-Z or AD26.ZEBOV) in previous Ebola vaccine studies EBL01, EBL04 and EBL05.

Evidence for comparator:

The aim of the study was to assess the impact on the duration of the immune response of giving a booster dose of an Ebola vaccine (AD26.ZEBOV), 2-5 years after the initial immunisation regimens. The duration of a persistent immunological response from Ebola vaccine would determine whether additional booster dosage would be required to maintain a protective level of immunity in such a cohort. The sustainability of an immune response would also indicate how many such boosters would be required and at what intervals. All such information would be crucial in determining the Ebola vaccination policy by WHO and countries in the Ebola endemic zone.

Actual start date of recruitment	30 April 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

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### Population of trial subjects

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#### Subjects enrolled per country

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Country: Number of subjects enrolled	United Kingdom: 48
Worldwide total number of subjects	48
EEA total number of subjects	0

Notes:

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#### Subjects enrolled per age group

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In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	48
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

The study population consisted of participants who had received immunisation with Ebola vaccines (ChAd3-EBO-Z, MVA-BN-FILO, MVA-EBO-Z or AD26.ZEBOV) in previous Ebola vaccine studies EBL01, EBL04 and EBL05.

Recruitment period: September - December 2019; territories - United Kingdom.

### Pre-assignment

Screening details:

Baseline assessments and information collection was carried out by trained study team member. Participants were to have received at least one vaccine during Ebola vaccine studies. Exclusion criteria was previous malignancy, pregnancy, breast feeding, new significant medical or surgical history, receipt of other adeno virus vaccine.

### Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	Ebola vaccine AD26.ZEBOV boosted group

Arm description:

Investigational medicinal product, Ebola vaccine AD26.ZEBOV, was administered as a booster vaccine following previous participation in studies of regimens of Ebola vaccines ChAd3-EBO-Z, MVA-EBO-Z, MVA-BN-FILO and AD26.ZEBOV.

Arm type	Active comparator
Investigational medicinal product name	AD26.ZEBOV
Investigational medicinal product code	AS1
Other name	
Pharmaceutical forms	Solution for injection, Solution for injection in multidose container
Routes of administration	Injection , Intramuscular use

Dosage and administration details:

The vaccine dosage was a 0.5 ml dose of AD26.ZEBOV, containing  $5 \times 10^{10}$  vp. The vaccine was administered as an IM injection in either deltoid. The dosage and route of administration have been shown to be immunogenic in Phase I and II studies of the IMP, with an acceptable safety profile. The vaccine was administered as a single dose (booster).

AD26.ZEBOV is a monovalent, recombinant, replication incompetent AD26-based vaccine expressing the full length Ebola virus (EBOV, formerly known as Zaire ebolavirus) Mayinga glycoprotein (GP), produced in the human cell line PER.C6®. It was supplied in a single use 2mL glass vial with an extractable volume of 0.5mL at a concentration of  $1 \times 10^{11}$  virus particles (vp)/mL. The vaccine was formulated in final formulation buffer.

<b>Arm title</b>	Non-boosted group
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Arm description:

Previous participants in studies of regimens of Ebola vaccines ChAd3-EBO-Z, MVA-EBO-Z, MVA-BN-FILO and AD26.ZEBOV who wished to participate in the study but did not wish to receive a booster vaccine.

Arm type	No intervention
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Ebola vaccine AD26.ZEBOV boosted group	Non-boosted group
Started	28	20
Completed	27	15
Not completed	1	5
Consent withdrawn by subject	1	1
Adverse event, non-fatal	-	1
Left UK	-	1
Lost to follow-up	-	1
Withdrawn due to other commitments	-	1

## Baseline characteristics

### Reporting groups

Reporting group title	Ebola vaccine AD26.ZEBOV boosted group
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Reporting group description:

Investigational medicinal product, Ebola vaccine AD26.ZEBOV, was administered as a booster vaccine following previous participation in studies of regimens of Ebola vaccines ChAd3-EBO-Z, MVA-EBO-Z, MVA-BN-FILO and AD26.ZEBOV.

Reporting group title	Non-boosted group
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Reporting group description:

Previous participants in studies of regimens of Ebola vaccines ChAd3-EBO-Z, MVA-EBO-Z, MVA-BN-FILO and AD26.ZEBOV who wished to participate in the study but did not wish to receive a booster vaccine.

Reporting group values	Ebola vaccine AD26.ZEBOV boosted group	Non-boosted group	Total
Number of subjects	28	20	48
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	28	20	48
From 65-84 years	0	0	0
85 years and over	0	0	0
Gender categorical Units: Subjects			
Female	11	11	22
Male	17	9	26

## End points

### End points reporting groups

Reporting group title	Ebola vaccine AD26.ZEBOV boosted group
Reporting group description: Investigational medicinal product, Ebola vaccine AD26.ZEBOV, was administered as a booster vaccine following previous participation in studies of regimens of Ebola vaccines ChAd3-EBO-Z, MVA-EBO-Z, MVA-BN-FILO and AD26.ZEBOV.	
Reporting group title	Non-boosted group
Reporting group description: Previous participants in studies of regimens of Ebola vaccines ChAd3-EBO-Z, MVA-EBO-Z, MVA-BN-FILO and AD26.ZEBOV who wished to participate in the study but did not wish to receive a booster vaccine.	

### Primary: Humoral immunity: Ebola GP specific IgG (GM)

End point title	Humoral immunity: Ebola GP specific IgG (GM) <sup>[1]</sup>
End point description: Ebola specific (Anti-Zaire) GP IgG as measured by ELISA - presented as Geometric Mean (95% CI)	
End point type	Primary
End point timeframe: First visit (V1, day 0) and 12 months from V1 (day 365)	

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 statistical analysis - reported as Geometric Mean (95% CI).

End point values	Ebola vaccine AD26.ZEBOV boosted group	Non-boosted group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	20		
Units: ELISA Units				
geometric mean (confidence interval 95%)				
Day 0	109 (53 to 224)	91 (38 to 223)		
Day 365	2162 (1341 to 3484)	84 (21 to 337)		

### Statistical analyses

No statistical analyses for this end point

### Primary: Cellular immunity: Ebola GP specific T cell cytokine response

End point title	Cellular immunity: Ebola GP specific T cell cytokine response <sup>[2]</sup>
End point description: Ebola GP specific T cell cytokine response measured using ex vivo interferon-γ enzyme-linked immunosorbent spot (ELISPOT)	
End point type	Primary

End point timeframe:

First visit (V1, day 0) and 12 months from V1 (day 365)

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 statistical analysis - reported as Median (IQR).

End point values	Ebola vaccine AD26.ZEBOV boosted group	Non-boosted group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	20		
Units: spot-forming cells (SFC) per 10 <sup>6</sup>				
median (inter-quartile range (Q1-Q3))				
Day 0	91 (64 to 194)	361 (207 to 519)		
Day 365	953 (268 to 1464)	185 (88 to 248)		

## Statistical analyses

No statistical analyses for this end point

## Primary: Humoral immunity: Ebola GP specific IgG (titre ≥ 166 EU)

End point title	Humoral immunity: Ebola GP specific IgG (titre ≥ 166 EU) <sup>[3]</sup>
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End point description:

Ebola specific (Anti-Zaire) GP IgG as measured by ELISA - presented as percentage participants with IgG titre ≥ 166 EU

End point type	Primary
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End point timeframe:

First visit (V1, day 0) and 12 months from V1 (day 365)

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 statistical analysis - reported as percentage participants with IgG titre ≥ 166 EU.

End point values	Ebola vaccine AD26.ZEBOV boosted group	Non-boosted group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	28	20		
Units: IgG titre ≥ 166 EU				
number (not applicable)				
Day 0	46.4	42.1		
Day 365	100	38.5		

## Statistical analyses





## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Days 0-3 post immunisation

Days 0-28 post immunisation

Days 0-365 post immunisation

Adverse event reporting additional description:

Solicited adverse events within first 3 days after immunisation 0 - eDiary

Unsolicited medically attended adverse events within first month after immunisation - eDiary, vital signs at D0, D7, D28

Serious adverse events experienced by any participant throughout study

Solicited non-SAEs are not reported here but will be reported in a publication.

Assessment type

Systematic

### Dictionary used

Dictionary name

Protocol

Dictionary version

v5.1

### Reporting groups

Reporting group title

Ebola vaccine AD26.ZEBOV boosted group

Reporting group description:

Investigational medicinal product, Ebola vaccine AD26.ZEBOV, was administered as a booster vaccine following previous participation in studies of regimens of Ebola vaccines ChAd3-EBO-Z, MVA-EBO-Z, MVA-BN-FILO and AD26.ZEBOV.

Reporting group title

Non-boosted group

Reporting group description:

Previous participants in studies of regimens of Ebola vaccines ChAd3-EBO-Z, MVA-EBO-Z, MVA-BN-FILO and AD26.ZEBOV who wished to participate in the study but did not wish to receive a booster vaccine.

Serious adverse events	Ebola vaccine AD26.ZEBOV boosted group	Non-boosted group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 28 (3.57%)	2 / 20 (10.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Surgical and medical procedures			
Gall Bladder Removal	Additional description: Elective procedure		
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Immune system disorders			
Autoimmune hypothyroidism	Additional description: Family history of hypothyroidism		
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	
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: 0 %

<b>Non-serious adverse events</b>	Ebola vaccine AD26.ZEBOV boosted group	Non-boosted group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	5 / 28 (17.86%)	1 / 20 (5.00%)	
Injury, poisoning and procedural complications			
Faint/syncope			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Autoimmune hypothyroidism	Additional description: Family history of hypothyroidism		
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Loose stool			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Respiratory, thoracic and mediastinal disorders			
Laboured breathing			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Shorten of breath			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			

COVID-19			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
sore throat			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Dry cough			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Coryza			
subjects affected / exposed	1 / 28 (3.57%)	0 / 20 (0.00%)	
occurrences (all)	1	0	
Schistosomiasis			
subjects affected / exposed	0 / 28 (0.00%)	1 / 20 (5.00%)	
occurrences (all)	0	1	

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 January 2019	<ul style="list-style-type: none"><li>- Addition of a PI signature page.</li><li>- Update to planned trial dates.</li><li>- Clarification and strengthening of safety reporting wording in section 10.</li></ul>
01 April 2019	<ul style="list-style-type: none"><li>- Update to full study title to aid clarity</li><li>- Update to objectives to be inclusive of all participants who received completed immunisation regimens in EBL01, EBL04 and EBL05</li><li>- Addition of Visit 2, 7 days post immunisation for booster only group in order to study the early response to immunisation</li><li>- Update to risk safety language and clarification on safety reporting and vaccine storage, which have come about following discussions with the vaccine supplier Janssen</li><li>- Update to text relating to intellectual property as these details were to be covered in the Agreement with Janssen</li><li>- Update to number of participants who received AD26.ZEBOV (as opposed to placebo) in previous studies in line with the updated IB</li><li>- Correction of information relating to asking GPs to inform OVG of any reason a participant should not take part in the study</li><li>- Correction of summary study design</li></ul>
10 December 2019	<ul style="list-style-type: none"><li>- Change of PI at the NIHR/Wellcome Trust Imperial Clinical Research Facility Hammersmith Hospital Site</li></ul>

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

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

Results will be published later in 2022 and distributed to participants. The publication will contain the data for the secondary objectives and solicited non-SAE, which are not reported here.

Notes: