Clinical trial results:
A Phase I/II Study to assess the safety, immunogenicity and protective efficacy of novel malaria vaccine candidates ChAdOx1 LS2 and MVA LS2 in healthy UK adults

Summary

EudraCT number	2017-001049-28
Trial protocol	GB
Global end of trial date	20 December 2017

Results information

Result version number	v1 (current)
This version publication date	04 January 2019
First version publication date	04 January 2019

Trial information

Trial identification

Sponsor protocol code	VAC067

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03203421
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Oxford
Sponsor organisation address	Old Road, Oxford, United Kingdom, OX3 7LE
Public contact	Professor Adrian Hill, University of Oxford, 01865 617610, adrian.hill@ndm.ox.ac.uk
Scientific contact	Professor Adrian Hill, University of Oxford, 01865 617610, adrian.hill@ndm.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:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 December 2017
Global end of trial reached?	Yes
Global end of trial date	20 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of new candidate malaria vaccines ChAdOx1 LS2 administered alone, and with MVA LS2 in a prime-boost regimen by the intramuscular routes in healthy malaria-naïve volunteers

To assess the efficacy (occurrence of P. falciparum parasitemia, assessed by blood slide) of ChAdOx1 LS2 and MVA LS2 administered in prime-boost vaccination regimen against malaria sporozoite challenge, in healthy malaria-naïve volunteers.

Protection of trial subjects:

- Volunteers given at least 24 hours to read Participant Information Leaflet before being seen for screening, and then given plenty of opportunity to ask questions prior to agreeing to take part in a study.
- Written informed consent is obtained before performing any study procedures.
- Volunteers given the opportunity to withdraw from the rial at any time without affecting their normal medical care.
- Screening visit including full medical history, physical examination and baseline blood tests to ensure volunteers are eligible.
- Vaccination carried out in clinical environment with staff trained in resuscitation in case of allergic reaction.
- Safety review prior to dose escalation (Local safety monitor)

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 July 2017
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 18
Worldwide total number of subjects	18
EEA total number of subjects	18

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

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

Subject disposition

Recruitment

Recruitment details:

Volunteers were recruited through advertisements distributed or posted in public places - including buses and trains, newspapers, radio, website or social media, and Oxford vaccine centre databases. Information sheet was available to the volunteer at least 24 hours prior to the screening visit.

Pre-assignment

Screening details:

- Review of inclusion/exclusion criteria
- Informed consent
- Medical history, concomitant medication
- Physical examination
- Urinalysis, B-HCG urine test (women only)
- Haematology, biochemistry
- Diagnostic serology: HBsAg, HCV and HIV antibodies
- Immunology: Human Leukocyte Antigen (HLA) typing

Period 1

Period 1 title	Week 0 - Prime
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

Single dose ChAdOx1 LS2 5 x 10^9 vp

Arm type	Experimental
Investigational medicinal product name	ChAdOx1 LS2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

ChAdOx1 LS2 5x10^9 vp administered intramuscularly into the deltoid of the non-dominant arm.

Arm title	Group 2

Arm description:

ChAdOx1 LS2 and MVA LS2 in a heterologous prime-boost regime followed by CHMI

Arm type	Experimental
Investigational medicinal product name	ChAdOx1 LS2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

ChAdOx1 LS2 2.5 x 10^10 vp administered intramuscularly into the deltoid of the non-dominant arm.

Arm title	Control Group

Arm description:

Controlled human malaria infection (CHMI) of unvaccinated group.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Group 1	Group 2	Control Group
Started	3	10	5
Completed	3	10	5

Period 2	
Period 2 title	Week 8 (window: 1-10 weeks post prime)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms	
Are arms mutually exclusive?	Yes
Arm title	Group 2

Arm description:

ChAdOx1 LS2 and MVA LS2 in a heterologous prime-boost regime followed by CHMI

Arm type	Experimental
Investigational medicinal product name	MVA LS2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

MVA LS2 2 x 10^8 pfu administered intramuscularly into the deltoid of the non-dominant arm.

Arm title	Group 1

Arm description:

Single dose ChAdOx1 LS2 5 x 10^9 vp

Arm type	Experimental
Investigational medicinal product name	ChAdOx1 LS2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

ChAdOx1 LS2 5x10^9 vp administered intramuscularly into the deltoid of the non-dominant arm.

Arm title	Control Group

Arm description:

Controlled human malaria infection (CHMI) of unvaccinated group.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Group 2	Group 1	Control Group
Started	10	3	5
Completed	10	3	6
Not completed	0	0	2
Consent withdrawn by subject	-	-	2
Joined	0	0	3
Additional controls added	-	-	3

Period 3	
Period 3 title	Week 11 - CHMI (2-4 weeks post boost)
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 2

Arm description:

ChAdOx1 LS2 and MVA LS2 in a heterologous prime-boost regime followed by CHMI

Arm type	Experimental
Investigational medicinal product name	ChAdOx1 LS2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

ChAdOx1 LS2 5x10^9 vp administered intramuscularly into the deltoid of the non-dominant arm.

Arm title	Control Group

Arm description:

Controlled human malaria infection (CHMI) of unvaccinated group.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Arm title	Group 1

Arm description:

Single dose ChAdOx1 LS2 5 x 10^9 vp

Arm type	Experimental
Investigational medicinal product name	ChAdOx1 LS2
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:
ChAdOx1 LS2 5x10^9 vp administered intramuscularly into the deltoid of the non-dominant arm.

Number of subjects in period 3	Group 2	Control Group	Group 1
Started	10	6	3
Completed	9	6	2
Not completed	1	0	1
Consent withdrawn by subject	1	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Week 0 - Prime

Reporting group description: -

Reporting group values	Week 0 - Prime	Total	
Number of subjects	18	18	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	18	18	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	8	8	
Male	10	10	

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description: Single dose ChAdOx1 LS2 5 x 10^9 vp	
Reporting group title	Group 2
Reporting group description: ChAdOx1 LS2 and MVA LS2 in a heterologous prime-boost regime followed by CHMI	
Reporting group title	Control Group
Reporting group description: Controlled human malaria infection (CHMI) of unvaccinated group.	
Reporting group title	Group 2
Reporting group description: ChAdOx1 LS2 and MVA LS2 in a heterologous prime-boost regime followed by CHMI	
Reporting group title	Group 1
Reporting group description: Single dose ChAdOx1 LS2 5 x 10^9 vp	
Reporting group title	Control Group
Reporting group description: Controlled human malaria infection (CHMI) of unvaccinated group.	
Reporting group title	Group 2
Reporting group description: ChAdOx1 LS2 and MVA LS2 in a heterologous prime-boost regime followed by CHMI	
Reporting group title	Control Group
Reporting group description: Controlled human malaria infection (CHMI) of unvaccinated group.	
Reporting group title	Group 1
Reporting group description: Single dose ChAdOx1 LS2 5 x 10^9 vp	

Primary: The safety and tolerability of ChAdOx1 LS2 administered alone and with MVA LS2 in a prime-boost vaccination regimen in healthy malaria-naive volunteers assessed by the frequency and severity of adverse events

End point title	The safety and tolerability of ChAdOx1 LS2 administered alone and with MVA LS2 in a prime-boost vaccination regimen in healthy malaria-naive volunteers assessed by the frequency and severity of adverse events[1]
End point description:	
End point type	Primary
End point timeframe: All AEs occurring in the 28 days following each vaccination collected from diary cards, clinical review, clinical examination and laboratory results.	

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: Due to the confidential nature of this information, we have not provided this analysis at this time. The scientific paper can be uploaded following publication if required.

End point values	Group 2	Control Group	Group 1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	2	
Units: Adverse events	9	6	2	

Statistical analyses

No statistical analyses for this end point

Primary: The efficacy of ChAdOx2 LS2 and MVA LS2 administered in a prime-boost vaccination regimen against malaria sporozoite challenge, in healthy malaria-naive volunteers

End point title	The efficacy of ChAdOx2 LS2 and MVA LS2 administered in a prime-boost vaccination regimen against malaria sporozoite challenge, in healthy malaria-naive volunteers[2]

End point description:

End point type	Primary

End point timeframe:

Completely protected individuals who did not develop blood stage infection by Day 21 following sporozoite challenge.

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: Due to the confidential nature of this information, we have not provided this analysis at this time. The scientific paper can be uploaded following publication if required.

End point values	Group 2	Control Group	Group 1	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	6	2	
Units: volunteer	9	6	2	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

All AEs occurring in the 28 days following each vaccination collected from diary cards, clinical review, clinical examination, laboratory results, or reported by the volunteer, whether or not attributed to study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19

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

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Due to technical difficulties, non-serious AE could not be uploaded in this report. these will be available in the trial publication.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 May 2017	Minor clarifications as requested by MHRA. Table 6 - Additional 2.5mls at C-1 visit for Group 2 volunteers; Tables 8 and 9 updated to reflect this
09 June 2017	Addition of MVA LS2 to replace homologous regimen with heterologous prime-boost trial design. Clarification Imperial College London premises to be used for sporozoite challenge procedures but not to be listed as trial site. Correction of typographical errors incl. section 7.3 IMP storage.

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.

None reported

Notes: