Clinical trial results:
A Phase I/IIa Sporozoite Challenge Study to assess the safety, immunogenicity and protective efficacy of intravenous boosting with malaria vaccine candidates ChAd63 and MVA encoding ME-TRAP

Summary

EudraCT number	2017-001075-23
Trial protocol	GB
Global end of trial date	10 June 2019

Results information

Result version number	v1 (current)
This version publication date	04 December 2021
First version publication date	04 December 2021

Trial information

Trial identification

Sponsor protocol code	VAC066

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03707353
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Oxford
Sponsor organisation address	Churchill Hospital, Old road, Headington, Oxford, United Kingdom, OX3 7LE
Public contact	Professor Adrian Hill, University of Oxford, +44 1865617610, adrian.hill@ndm.ox.ac.uk
Scientific contact	Professor Adrian Hill, University of Oxford, +44 1865617610, 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	10 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 June 2019
Global end of trial reached?	Yes
Global end of trial date	10 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess the efficacy (occurrence of P. falciparum parasitemia, assessed by PCR) of intramuscular vaccination followed by intravenous boosting with ChAd63 and MVA encoding ME-TRAP, against malaria sporozoite challenge, in healthy malaria-naïve volunteers.
- To assess the safety of intramuscular vaccination followed by intravenous boosting with ChAd63 and MVA encoding ME-TRAP, in healthy malaria-naïve volunteers

Protection of trial subjects:

- Volunteers given at least 24 hours to read VIS before being seen and then given plenty of opportunity to ask questions prior to agreeing to take part in a study.
- Screening visit including full medical history, physical examination and baseline blood tests to ensure volunteers are healthy prior to enrolment.
- Vaccination carried out in clinical environment with staff trained in resuscitation in case of allergic reaction.
- Safety review prior to dose escalation (LSM)
- Total blood volume taken during study kept to volume that should not compromise healthy volunteers (i.e. less than regular donation to blood transfusion service).
- Volunteers observed for 1-2 hours after vaccination to monitor for any immediate adverse effects.
- Volunteers seen within 3 days of vaccination for safety review and provided with 24/7 contact number for trial clinician and emergency contact card for the department.
-Volunteers phoned daily by the clinic team prior to first in-person follow up after CHMI

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 October 2018
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: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	42
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The first enrolment (recruitment start) took place on 30th October 2018.
The last enrolment (recruitment end) took place on 4th February 2019.
Note: Group 3 and 4 were first enrolled in parallel with Week 4 for groups A, 1 and 2. Groups 3 and 4 have been included in Week 0 for clarity of baseline information.

Pre-assignment

Screening details:

Inclusion / Exclusion criteria
Informed consent
Medical History
Physical Examination
Biochemistry
Haematology
Urinalysis
Serum B-HCG (women only)
Coagulation profile
Review contraindications
HBV,HCV,HIV serology
Anti- P. falciparum serology (if deemed necessary)

Period 1

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

Blinding implementation details:

Laboratory investigators processing blood films and samples for PCR analysis were blinded to group allocation. No other blinding was used.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3-dose regimen)

Arm type	Experimental
Investigational medicinal product name	ChAd63 ME-TRAP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

ChAd63 ME-TRAP 5x10^10 vp administered intramuscularly into the deltoid of the arm at week 0

Arm title	Group 1

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with ChAd63-ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	Experimental

Investigational medicinal product name	ChAd63 ME-TRAP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

ChAd63 ME-TRAP 5x10^10 vp administered intramuscularly into the deltoid of the arm at week 0

Arm title	Group 2

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	Experimental
Investigational medicinal product name	ChAd63 ME-TRAP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

ChAd63 ME-TRAP 5x10^10 vp administered intramuscularly into the deltoid of the arm at week 0

Arm title	Group 3

Arm description:

ChAd63 ME-TRAP in a homologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 4

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Group 5

Arm description:

Controlled human malaria infection (CHMI) only at week 11-12

Arm type	CHMI

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Group A	Group 1	Group 2
Started	3	9	10
Completed	3	9	9
Not completed	0	0	1
Non-attendance post D0	-	-	1

Number of subjects in period 1	Group 3	Group 4	Group 5
Started	7	7	6
Completed	7	7	6
Not completed	0	0	0

Non-attendance post D0	-	-	-

Period 2

Period 2 title	Week 4
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Laboratory investigators processing blood films and samples for PCR analysis were blinded to group allocation. No other blinding was used.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3-dose regimen)

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

Dosage and administration details:

MVA ME-TRAP 2 x 10^8 pfu administered intramuscularly into the deltoid of the arm at week 4

Arm title	Group 1

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with ChAd63-ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

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

Dosage and administration details:

MVA ME-TRAP 2 x 10^8 pfu administered intramuscularly into the deltoid of the arm at week 4

Arm title	Group 2

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	Experimental

Investigational medicinal product name	MVA ME-TRAP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

MVA ME-TRAP 2 x 10^8 pfu administered intramuscularly into the deltoid of the arm at week 4

Arm title	Group 3

Arm description:

ChAd63 ME-TRAP in a homologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	Experimental
Investigational medicinal product name	ChAd63 ME-TRAP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

ChAd63 ME-TRAP 5x10^10vp administered intramuscularly into the deltoid of the arm at week 4

Arm title	Group 4

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	Experimental
Investigational medicinal product name	ChAd63 ME-TRAP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

ChAd63 ME-TRAP 5x10^10vp administered intramuscularly into the deltoid of the arm

Arm title	Group 5

Arm description:

Controlled human malaria infection (CHMI) only at week 11-12

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Group A	Group 1	Group 2
Started	3	9	9
Completed	3	8	9
Not completed	0	1	0
Consent withdrawn by subject	-	1	-

Number of subjects in period 2	Group 3	Group 4	Group 5

Started	7	7	6
Completed	7	7	6
Not completed	0	0	0
Consent withdrawn by subject	-	-	-

Period 3

Period 3 title	Week 8
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Laboratory investigators processing blood films and samples for PCR analysis were blinded to group allocation. No other blinding was used

Arms

Are arms mutually exclusive?	Yes
Arm title	Group A

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3-dose regimen)

Arm type	Experimental
Investigational medicinal product name	MVA ME-TRAP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

MVA ME-TRAP 2 x 10^7 pfu administered intravenously via peripheral cannula at week 8

Arm title	Group 1

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with ChAd63-ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	Experimental
Investigational medicinal product name	ChAd63 ME-TRAP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

ChAd63 ME-TRAP 5 x 10^10vp administered intravenously via peripheral cannula at week 8

Arm title	Group 2

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	Experimental

Investigational medicinal product name	MVA ME-TRAP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

MVA ME-TRAP 2 x 10^7 pfu administered intravenously via peripheral cannula at week 8

Arm title	Group 3

Arm description:

ChAd63 ME-TRAP in a homologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	Experimental
Investigational medicinal product name	ChAd63 ME-TRAP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

ChAd63 ME-TRAP 5 x 10^10vp administered intravenously via peripheral cannula at week 8

Arm title	Group 4

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	Experimental
Investigational medicinal product name	MVA ME-TRAP
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

MVA ME-TRAP 2 x 10^7 pfu administered intravenously via peripheral cannula at week 8

Arm title	Group 5

Arm description:

Controlled human malaria infection (CHMI) only at week 11-12

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 3	Group A	Group 1	Group 2
Started	3	8	9
Completed	2	8	9
Not completed	1	0	0
Physician decision	-	-	-
Lost to follow-up	1	-	-

Number of subjects in period 3	Group 3	Group 4	Group 5
Started	7	7	6

Completed	6	7	6
Not completed	1	0	0
Physician decision	1	-	-
Lost to follow-up	-	-	-

Period 4

Period 4 title	Week 11-12: CHMI
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

Laboratory investigators processing blood films and samples for PCR analysis were blinded to group allocation. No other blinding was used.

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with ChAd63-ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Arm title	Group 2

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with ChAd63-ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Arm title	Group 3

Arm description:

ChAd63 ME-TRAP in a homologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Arm title	Group 4

Arm description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Arm title	Group 5

Arm description:

Controlled human malaria infection (CHMI) only at week 11-12

Arm type	CHMI Control group

No investigational medicinal product assigned in this arm

Number of subjects in period 4[1]	Group 1	Group 2	Group 3
Started	8	9	6
Completed	8	9	6
Not completed	0	0	0
Consent withdrawn by subject	-	-	-

Number of subjects in period 4[1]	Group 4	Group 5
Started	7	6
Completed	7	5
Not completed	0	1
Consent withdrawn by subject	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Group A was not included in the challenge at Week 11-12.

Baseline characteristics

Reporting groups	
Reporting group title	Week 0

Reporting group description: -

Reporting group values	Week 0	Total	
Number of subjects	42	42	
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)	42	42	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	25		
full range (min-max)	18 to 45	-	
Gender categorical Units: Subjects			
Female	12	12	
Male	30	30	

End points

End points reporting groups

Reporting group title	Group A
Reporting group description:	
ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3-dose regimen)	

Reporting group title	Group 1
Reporting group description:	
ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with ChAd63-ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.	

Reporting group title	Group 2
Reporting group description:	
ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.	

Reporting group title	Group 3
Reporting group description:	
ChAd63 ME-TRAP in a homologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.	

Reporting group title	Group 4
Reporting group description:	
ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.	

Reporting group title	Group 5
Reporting group description:	
Controlled human malaria infection (CHMI) only at week 11-12	

Reporting group title	Group A
Reporting group description:	
ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3-dose regimen)	

Reporting group title	Group 1
Reporting group description:	
ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with ChAd63-ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.	

Reporting group title	Group 2
Reporting group description:	
ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.	

Reporting group title	Group 3
Reporting group description:	
ChAd63 ME-TRAP in a homologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.	

Reporting group title	Group 4
Reporting group description:	
ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.	

Reporting group title	Group 5
Reporting group description:	
Controlled human malaria infection (CHMI) only at week 11-12	

Reporting group title	Group A

Reporting group description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3-dose regimen)

Reporting group title	Group 1

Reporting group description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with ChAd63-ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 2

Reporting group description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 3

Reporting group description:

ChAd63 ME-TRAP in a homologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 4

Reporting group description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 5

Reporting group description:

Controlled human malaria infection (CHMI) only at week 11-12

Reporting group title	Group 1

Reporting group description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with ChAd63-ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 2

Reporting group description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with ChAd63-ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 3

Reporting group description:

ChAd63 ME-TRAP in a homologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 4

Reporting group description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 5

Reporting group description:

Controlled human malaria infection (CHMI) only at week 11-12

Primary: To assess the efficacy (occurrence of P. falciparum parasitemia, assessed by PCR) of intramuscular vaccination followed by intravenous boosting with ChAd63 and MVA encoding ME-TRAP, against malaria sporozoite challenge, in healthy malaria-naïve volunteers

End point title	To assess the efficacy (occurrence of P. falciparum parasitemia, assessed by PCR) of intramuscular vaccination followed by intravenous boosting with ChAd63 and MVA encoding ME-TRAP, against malaria sporozoite challenge, in healthy malaria-naïve volunteers[1]

End point description:

End point type	Primary

End point timeframe:

Duration of the trial

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. A link to the paper can be shared following publication, if required.

End point values	Group 1	Group 2	Group 3	Group 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	8	9	6	7
Units: Number of negative cases	8	9	6	7

End point values	Group 5			
Subject group type	Reporting group			
Number of subjects analysed	6			
Units: Number of negative cases	6			

Statistical analyses

No statistical analyses for this end point

Primary: To assess the safety of intramuscular vaccination followed by intravenous boosting with ChAd63 and MVA encoding ME-TRAP, in healthy malaria-naïve volunteers

End point title	To assess the safety of intramuscular vaccination followed by intravenous boosting with ChAd63 and MVA encoding ME-TRAP, in healthy malaria-naïve volunteers[2]

End point description:

End point type	Primary

End point timeframe:

Duration of trial

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: This is a descriptive safety endpoint, where volunteers were vaccinated with MVA ME-TRAP and ChAd63 ME-TRAP. Forty two volunteers were vaccinated in total. This sample size should allow an estimation to be made of the frequency and magnitude of outcome measures, rather than aiming to obtain statistical significance for differences between groups.

End point values	Group A	Group 1	Group 2	Group 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	8	9	6
Units: Adverse Events	2	8	9	6

End point values	Group 4	Group 5		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: Adverse Events	7	6		

Statistical analyses

No statistical analyses for this end point

Secondary: To assess cell-mediated immunogenicity generated in malaria naïve individuals of vaccination schedules incorporating intramuscular prime dose(s) followed by intravenous booster with ChAd63 and MVA encoding ME-TRAP

End point title	To assess cell-mediated immunogenicity generated in malaria naïve individuals of vaccination schedules incorporating intramuscular prime dose(s) followed by intravenous booster with ChAd63 and MVA encoding ME-TRAP

End point description:

End point type	Secondary

End point timeframe:

T Cell responses to ME-TRAP measured before the intravenous vaccination and approximately 28 days after intravenous vaccination, prior to challenge.

End point values	Group A	Group 1	Group 2	Group 3
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	8	9	6
Units: ELISPOT Responses	2	8	9	6

End point values	Group 4	Group 5		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	6		
Units: ELISPOT Responses	7	6		

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	21

Reporting groups

Reporting group title	Group A

Reporting group description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3-dose regimen)

Reporting group title	Group 1

Reporting group description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with ChAd63-ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 2

Reporting group description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by a further boost with MVA ME-TRAP (3 dose regimen) and CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 3

Reporting group description:

ChAd63 ME-TRAP in a homologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 4

Reporting group description:

ChAd63 ME-TRAP and MVA ME-TRAP in a heterologous prime-boost regime, followed by CHMI. Repeat CHMI for sterilely protected volunteers.

Reporting group title	Group 5

Reporting group description:

Controlled human malaria infection (CHMI) only at week 11-12

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 the confidential nature of this information, we have not provided this analysis at this time. A link to the paper can be shared following publication, if required. Please note, a single SAE was reported in this trial and has been included in these results.

Serious adverse events	Group A	Group 1	Group 2
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Infection	Additional description: Volunteer hospitalised for possible bacterial/viral infection 3 weeks following administration of intravenous ChAd63 ME-TRAP. Deemed unlikely to be related to vaccination.		

subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 10 (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	Group 3	Group 4	Group 5
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 6 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Infections and infestations			
Infection	Additional description: Volunteer hospitalised for possible bacterial/viral infection 3 weeks following administration of intravenous ChAd63 ME-TRAP. Deemed unlikely to be related to vaccination.		
subjects affected / exposed	1 / 7 (14.29%)	0 / 7 (0.00%)	0 / 6 (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

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

Non-serious adverse events	Group A	Group 1	Group 2
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)

Non-serious adverse events	Group 3	Group 4	Group 5
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 7 (0.00%)	0 / 7 (0.00%)	0 / 6 (0.00%)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 September 2018	REC only amendment to align with comments from MHRA Inclusion of serum beta hCG measurement at screening Clarification on SUSAR reporting Reduction in IV MVA ME-TRAP dose to 2 x 10^7 pfu
10 September 2018	Addition of lead-in group (Group A) in order to provide further safety data Extension of vaccination windows to +/-10 days Addition of Southampton and Imperial sites Revision to compensation amounts IMPD update for the intravenous route
14 January 2019	Addition of John Radcliffe Hospital site Addition of NHS consent form for use for volunteers undergoing procedures at the John Radcliffe Hospital site only Correction of typographical errors in protocol

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.

A second challenge was originally planned for groups 1, 2, 3 and 4 in addition to the introduction of Group 6 as a challenge only control. The second challenge did no go ahead before trial end.

Notes: