Clinical trial results:
A Phase I/IIa Sporozoite Challenge Study to Assess the Safety and Protective Efficacy of adjuvanted R21 at different doses and the Combination Malaria Vaccine Candidate Regimen of adjuvanted R21 + ChAd63 and MVA encoding ME-TRAP.

Summary

EudraCT number	2016-001265-92
Trial protocol	GB
Global end of trial date	21 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	VAC065

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02905019
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University of Oxford
Sponsor organisation address	Old Road, Oxford, United Kingdom,
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	21 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 December 2017
Global end of trial reached?	Yes
Global end of trial date	21 December 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This is a clinical trial in which healthy volunteers will be administered experimental malaria vaccines. Three groups of volunteers will receive vaccination with the novel malaria vaccine candidate, R21 at three different dose schedules given in combination with the vaccine adjuvant, Matrix-M1. Vaccines will be delivered at 4 week intervals (ie. At 0, 4 & 8 weeks). A fourth group will receive 10ug R21 with Matrix M1 at 0, 4 and 8 weeks in combination with ChAd63 ME-TRAP and MVA ME-TRAP given at 1 and 9 weeks, respectively. A fifth group will receive a 2-doe schedule of 10/10ug R21/Matrix-M given 4 weeks apart. The vaccine schedule containing R21 alone, and ChAd63 ME-TRAP and MVA ME-TRAP have been tested independently in clinical trials, however, the vaccine schedule containing both R21, ChAd63 ME-TRAP and MVA ME-TRAP has not yet been tested. The first principal research objective is to measure how well this new malaria vaccine strategy acts to prevent malaria disease.

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 30 mins - 2 hours (depending on trial) after vaccination to monitor for any immediate adverse effects.
- Volunteers seen within 1 - 3 days of vaccination (most trials) for safety review and provided with 24/7 contact number for trial clinician and emergency contact card for the department.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2016
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: 66
Worldwide total number of subjects	66
EEA total number of subjects	66

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)	66
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Inclusion / Exclusion criteria
Informed consent
Medical History
Physical Examination
Urinalysis
B-HCG urine test (women only)
Review contraindications
Physical observations
HBV, HCV, HIV
Haematology
Biochemistry

Period 1

Period 1 title	Week 0
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:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 2

Arm description:

2 vaccinations of 50µg R21 and one dose of 10µg R21 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental
Investigational medicinal product name	R21
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

R21 at doses of 10µg and 50µg administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 3

Arm description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 plus single doses of ChAd63 ME-TRAP and MVA ME-TRAP

followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

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 was administered at 5 x 10^10 viral particles intramuscularly in the deltoid muscle of either arm.

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 was administered at 2 x 10^8 plaque forming units intramuscularly in the deltoid muscle of either arm.

Arm title	Group 4a

Arm description:

Served as infectivity controls.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Arm title	Group 4b

Arm description:

Served as infectivity controls.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Arm title	Group 5

Arm description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 and a single dose of 2µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 6

Arm description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite)

at week 12.

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 7

Arm description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Number of subjects in period 1	Group 1	Group 2	Group 3
Started	13	12	12
Completed	12	11	12
Not completed	1	1	0
Consent withdrawn by subject	1	1	-

Number of subjects in period 1	Group 4a	Group 4b	Group 5
Started	6	6	8
Completed	6	6	7
Not completed	0	0	1
Consent withdrawn by subject	-	-	1

Number of subjects in period 1	Group 6	Group 7
Started	2	7
Completed	2	7
Not completed	0	0
Consent withdrawn by subject	-	-

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 2

Arm description:

2 vaccinations of 50µg R21 and one dose of 10µg R21 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 3

Arm description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 plus single doses of ChAd63 ME-TRAP and MVA ME-TRAP followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 5

Arm description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 and a single dose of 2µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Arm type	Experimental

Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 6

Arm description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 7

Arm description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 4a

Arm description:

Served as infectivity controls.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Arm title	Group 4b

Arm description:

Served as infectivity controls.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Number of subjects in period 2	Group 1	Group 2	Group 3
Started	12	11	12
Completed	11	11	10
Not completed	1	0	2
Consent withdrawn by subject	1	-	2

Number of subjects in period 2	Group 5	Group 6	Group 7
Started	7	2	7
Completed	7	2	7
Not completed	0	0	0
Consent withdrawn by subject	-	-	-

Number of subjects in period 2	Group 4a	Group 4b
Started	6	6
Completed	6	6
Not completed	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

Arms	
Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 2

Arm description:

2 vaccinations of 50µg R21 and one dose of 10µg R21 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental

Investigational medicinal product name	R21
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

R21 at doses of 10µg and 50µg administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 3

Arm description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 plus single doses of ChAd63 ME-TRAP and MVA ME-TRAP followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

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 was administered at 5 x 10^10 viral particles intramuscularly in the deltoid muscle of either arm.

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 was administered at 2 x 10^8 plaque forming units intramuscularly in the deltoid muscle of either arm.

Arm title	Group 5

Arm description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 and a single dose of 2µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 6

Arm description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 7

Arm description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 4a

Arm description:

Served as infectivity controls.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Arm title	Group 4b

Arm description:

Served as infectivity controls.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Number of subjects in period 3	Group 1	Group 2	Group 3
Started	11	11	10
Completed	11	11	10

Number of subjects in period 3	Group 5	Group 6	Group 7
Started	7	2	7
Completed	7	2	7

Number of subjects in period 3	Group 4a	Group 4b
Started	6	6
Completed	6	6

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

Arms	
Are arms mutually exclusive?	Yes
Arm title	Group 1

Arm description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 2

Arm description:

2 vaccinations of 50µg R21 and one dose of 10µg R21 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 3

Arm description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 plus single doses of ChAd63 ME-TRAP and MVA ME-TRAP followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Arm type	Experimental

Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 4a

Arm description:

Served as infectivity controls.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Arm title	Group 4b

Arm description:

Served as infectivity controls.

Arm type	CHMI

No investigational medicinal product assigned in this arm

Arm title	Group 5

Arm description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 and a single dose of 2µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 6

Arm description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Arm type	Experimental
Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Arm title	Group 7

Arm description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Arm type	Experimental

Investigational medicinal product name	R21 with adjuvant Matrix-M1
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg R21 adjuvanted with 50µg Matrix-M1 administered intramuscularly in the deltoid muscle of either arm.

Number of subjects in period 4[1]	Group 1	Group 2	Group 3
Started	11	11	9
Completed	11	11	9

Number of subjects in period 4[1]	Group 4a	Group 4b	Group 5
Started	6	6	7
Completed	6	6	7

Number of subjects in period 4[1]	Group 6	Group 7
Started	2	7
Completed	2	7

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: One participant from group 3 withdrew from the study prior to the Challenge time period.

Baseline characteristics

Reporting groups	
Reporting group title	Week 0

Reporting group description: -

Reporting group values	Week 0	Total	
Number of subjects	66	66	
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)	66	66	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	36	36	
Male	30	30	

End points

End points reporting groups

Reporting group title	Group 1
Reporting group description:	
3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12	
Reporting group title	Group 2
Reporting group description:	
2 vaccinations of 50µg R21 and one dose of 10µg R21 followed by CHMI by sporozoite challenge (mosquito bite) at week 12	
Reporting group title	Group 3
Reporting group description:	
3 vaccinations of 10µg R21/ 50µg matrix-M1 plus single doses of ChAd63 ME-TRAP and MVA ME-TRAP followed by CHMI by sporozoite challenge (mosquito bite) at week 12	
Reporting group title	Group 4a
Reporting group description:	
Served as infectivity controls.	
Reporting group title	Group 4b
Reporting group description:	
Served as infectivity controls.	
Reporting group title	Group 5
Reporting group description:	
2 vaccinations of 10µg R21/ 50µg matrix-M1 and a single dose of 2µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.	
Reporting group title	Group 6
Reporting group description:	
3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.	
Reporting group title	Group 7
Reporting group description:	
2 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.	
Reporting group title	Group 1
Reporting group description:	
3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12	
Reporting group title	Group 2
Reporting group description:	
2 vaccinations of 50µg R21 and one dose of 10µg R21 followed by CHMI by sporozoite challenge (mosquito bite) at week 12	
Reporting group title	Group 3
Reporting group description:	
3 vaccinations of 10µg R21/ 50µg matrix-M1 plus single doses of ChAd63 ME-TRAP and MVA ME-TRAP followed by CHMI by sporozoite challenge (mosquito bite) at week 12	
Reporting group title	Group 5
Reporting group description:	
2 vaccinations of 10µg R21/ 50µg matrix-M1 and a single dose of 2µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.	
Reporting group title	Group 6
Reporting group description:	
3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.	
Reporting group title	Group 7

Reporting group description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Reporting group title	Group 4a

Reporting group description:

Served as infectivity controls.

Reporting group title	Group 4b

Reporting group description:

Served as infectivity controls.

Reporting group title	Group 1

Reporting group description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Reporting group title	Group 2

Reporting group description:

2 vaccinations of 50µg R21 and one dose of 10µg R21 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Reporting group title	Group 3

Reporting group description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 plus single doses of ChAd63 ME-TRAP and MVA ME-TRAP followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Reporting group title	Group 5

Reporting group description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 and a single dose of 2µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Reporting group title	Group 6

Reporting group description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Reporting group title	Group 7

Reporting group description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Reporting group title	Group 4a

Reporting group description:

Served as infectivity controls.

Reporting group title	Group 4b

Reporting group description:

Served as infectivity controls.

Reporting group title	Group 1

Reporting group description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Reporting group title	Group 2

Reporting group description:

2 vaccinations of 50µg R21 and one dose of 10µg R21 followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Reporting group title	Group 3

Reporting group description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 plus single doses of ChAd63 ME-TRAP and MVA ME-TRAP followed by CHMI by sporozoite challenge (mosquito bite) at week 12

Reporting group title	Group 4a

Reporting group description:

Served as infectivity controls.

Reporting group title	Group 4b

Reporting group description:

Served as infectivity controls.

Reporting group title	Group 5

Reporting group description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 and a single dose of 2µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Reporting group title	Group 6

Reporting group description:

3 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Reporting group title	Group 7

Reporting group description:

2 vaccinations of 10µg R21/ 50µg matrix-M1 followed by CHMI by sporozoite challenge (mosquito bite) at week 12.

Primary: Efficacy of adjuvanted R21 at two different doses and adjuvanted R21 + ChAd63 and MVA encoding ME-TRAP in healthy malaria-naïve volunteers as assessed by number of completely protected individuals

End point title	Efficacy of adjuvanted R21 at two different doses and adjuvanted R21 + ChAd63 and MVA encoding ME-TRAP in healthy malaria-naïve volunteers as assessed by number of completely protected individuals[1]

End point description:

End point type	Primary

End point timeframe:

6 months

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 trial publication can be uploaded following publication, if required.

End point values	Group 1	Group 2	Group 3	Group 4a
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	11	9	6
Units: ELISpot	11	11	9	6

End point values	Group 4b	Group 5	Group 6	Group 7
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	7	2	7
Units: ELISpot	6	7	2	7

Statistical analyses

No statistical analyses for this end point

Primary: Safety of adjuvanted R21 at two different doses and adjuvanted R21 + ChAd63 and MVA encoding ME-TRAP in healthy malaria-naïve volunteers as assessed by frequency of adverse events

End point title	Safety of adjuvanted R21 at two different doses and adjuvanted R21 + ChAd63 and MVA encoding ME-TRAP in healthy malaria-naïve volunteers as assessed by frequency of adverse events[2]

End point description:

End point type	Primary

End point timeframe:

6 months

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 trial publication can be uploaded following publication, if required.

End point values	Group 1	Group 2	Group 3	Group 4a
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	13	12	12	6
Units: Adverse events	13	12	12	6

End point values	Group 4b	Group 5	Group 6	Group 7
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	8	2	7
Units: Adverse events	6	8	2	7

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

Reporting groups

Reporting group title	Group 1

Reporting group description: -

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, no AEs could be uploaded into this report. This information will be available in the trial publication.

Serious adverse events	Group 1		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 13 (7.69%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Gastrointestinal disorders			
Appendicitis			
subjects affected / exposed	1 / 13 (7.69%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Group 1		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 June 2016	Addition of the chief investigators at sites to the investigator agreement Section 3.5 updated Section 7.4 added – rationale for vaccine doses Tables 9 & 10 – Blood volumes reduced in Group 4 & 5 volunteers Section 11.3 – Reporting procedures for all AEs updated Minor changes throughout the document
15 July 2016	Minor typographical errors corrected on Page 53 and 75
12 September 2016	Timelines updated in synopsis Randomisation removed from the entire protocol Minor changes to the schedule of attendances
28 October 2016	Change of the third dose in Group 2 from 50µg to 10µg
06 April 2017	Addition of a new group to assess the efficacy of 10/10/2µg R21 adjuvanted with Matrix-M1 Addition of a new group to assess the durable efficacy of 10/10/10µg R21 adjuvanted with Matrix-M1
08 May 2017	Addition of a new group to assess the efficacy of a two dose 10/10µg R21 adjuvanted with Matrix-M1 Additional immunology bleed for control group during CHMI follow up. Revised criteria for CHMI follow-up to occur at local site.
22 September 2017	Removal of 50ml immunology bleed at C+7 for Grps 4b,c, 5- 7.

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: