# Clinical trial results:
# A Phase I/IIa Sporozoite Challenge Study to Assess the Efficacy of Candidate Combination Malaria Vaccine Approaches using the ChAd63 and MVA vectors encoding the antigens ME-TRAP, CS and AMA1.

## Summary

| | |
|---|---|
| EudraCT number | 2012-004416-66 |
| Trial protocol | GB |
| Global end of trial date | 14 October 2013 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 15 July 2016 |
| First version publication date | 07 August 2015 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | VAC052 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01739036 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | University of Oxford, CTRG |
| Sponsor organisation address | Old Road, Oxford, United Kingdom, OX3 7LE |
| Public contact | Dr Alison Lawrie, University of Oxford, +44 1865857382, alison.lawrie@ndm.ox.ac.uk |
| Scientific contact | Dr Alison Lawrie, University of Oxford, +44 1865857382, alison.lawrie@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 | 14 October 2013 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 October 2013 |
| Global end of trial reached? | Yes |
| Global end of trial date | 14 October 2013 |
| Was the trial ended prematurely? | No |

Notes:

## General information about the trial

Main objective of the trial:

Primary Objective: To assess the efficacy of each of two combinations of heterologous prime-boost immunisation strategies:

1. ChAd63-MVA ME-TRAP combined with ChAd63-MVA CS
2. ChAd63-MVA ME-TRAP combined with ChAd63-MVA CS and ChAd63-MVA AMA1

Secondary Objectives: To assess the safety and immunogenicity of heterologous prime-boost immunisation of malaria-naïve individuals with ChAd63-MVA ME-TRAP combined with ChAd63-MVA CS. To assess the safety and immunogenicity of heterologous prime-boost immunisation of malaria-naïve individuals with ChAd63-MVA ME-TRAP combined with ChAd63-MVA CS and ChAd63-MVA AMA1.

Protection of trial subjects:

- Volunteers given at least 24 hours to read the VIS before being seen and then given plenty of opportunity to ask questions prior to agreeing to take part in the 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 escalations (LSM)
- Total blood volume taken during the study was kept to a volume that should not compromise healthy volunteers.
- Volunteers observed for 30 mins after vaccination to monitor for any immediate adverse effects.
- Volunteers seen within 1 day of vaccination for safety review and provided with 24/7 contact number for trial clinician and emergency contact card for the department.
- ECG and cholesterol checked prior to enrolment to aid cardiac risk assessment
- Age range 18 – 45 years
- Volunteers given emergency contact card detailing that they have been infected with malaria.
- Volunteers seen twice daily once blood stage malaria is possible with twice daily malaria films and PCR
- Malaria treated promptly when diagnosed with highly efficacious medication and at least half of doses directly observed.
- Volunteers provided with symptomatic treatment (antipyretic/analgesic and antiemetic) in case of malaria symptoms.
- Volunteers followed up until at least 2 consecutive negative blood films seen.

Background therapy:

Riamet, Malerone or Chloroquine for treatment of malaria infection.
Paracetamol for pain relief.

Evidence for comparator:

No comparator

| | |
|---|---|
| Actual start date of recruitment | 04 April 2013 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United Kingdom: 37 |
| Worldwide total number of subjects | 37 |
| EEA total number of subjects | 37 |

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) | 37 |
| 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 Questionnaire
Informed consent
Medical History
Physical Examination
Urinalysis
β-HCG urine (women only)
Review contraindications
Physical Observations
HBV,HCV,HIV
Haematology
Biochemistry
Anti- P. Falciparum serology

### Pre-assignment period milestones

| | |
|---|---|
| Number of subjects started | 37 |
| Number of subjects completed | 37 |

### Period 1

| | |
|---|---|
| Period 1 title | Day 0 |
| Is this the baseline period? | Yes |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Group 1 |

Arm description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp,

followed by intramuscular administration of a mixture of MVA ME-TRAP 2 x 108 pfu and MVA CS 2 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| | |
|---|---|
| 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:

Mixture of ChAd63 CS 5 x 1010 vp and ChAd63 ME-TRAP 5 x 1010 vp to be administered as the first vaccination of Group 1 participants

| | |
|---|---|
| Investigational medicinal product name | ChAd63 CS |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Solution for injection |

| | |
|---|---|
| Routes of administration | Intramuscular use |

Dosage and administration details:

Mixture of ChAd63 CS 5 x 1010 vp and ChAd63 ME-TRAP 5 x 1010 vp to be administered as the first vaccination of Group 1 participants

| | |
|---|---|
| **Arm title** | Group 2 |

Arm description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp and ChAd63 AMA1 5 x 1010 vp

followed by intramuscular administration of a mixture of MVA ME-TRAP 1.33 x 108 pfu and MVA CS 1.33 x 108 pfu and MVA AMA1 1.33 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| | |
|---|---|
| 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:

Mixture of ChAd63 CS 5 x 1010 vp, ChAd63 ME-TRAP 5 x 1010 vp, and ChAd63 AMA1 5 x 1010 vp to be administered as the first vaccination of Group 2 participants

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

Dosage and administration details:

Mixture of ChAd63 CS 5 x 1010 vp, ChAd63 ME-TRAP 5 x 1010 vp, and ChAd63 AMA1 5 x 1010 vp to be administered as the first vaccination of Group 2 participants

| | |
|---|---|
| **Arm title** | Group 3 |

Arm description:

Controlled human malaria infection administered at an interval of approximately 8-12 months after the initial controlled human malaria infection that the volunteers received in the VAC045 clinical trial.

| | |
|---|---|
| Arm type | Re-challenge/Previously vaccinated |

No investigational medicinal product assigned in this arm

| | |
|---|---|
| **Arm title** | Group 4 |

Arm description:

Unvaccinated control volunteers who undergo controlled human malaria infection.

| | |
|---|---|
| Arm type | No intervention |

No investigational medicinal product assigned in this arm

| Number of subjects in period 1 | Group 1 | Group 2 | Group 3 |
|---|---|---|---|
| Started | 15 | 15 | 1 |
| Completed | 15 | 15 | 1 |

| Number of subjects in period 1 | Group 4 |
|---|---|
| Started | 6 |
| Completed | 6 |

**Period 2**

| | |
|---|---|
| Period 2 title | Day 56 |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

**Arms**

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Group 1 |

Arm description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp,

followed by intramuscular administration of a mixture of MVA ME-TRAP 2 x 108 pfu and MVA CS 2 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| | |
|---|---|
| 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:

2. Mixture of MVA CS 2 x 108 pfu and MVA ME-TRAP 2 x 108 pfu to be administered as the second vaccination of Group 1 participants

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

Dosage and administration details:

2. Mixture of MVA CS 2 x 108 pfu and MVA ME-TRAP 2 x 108 pfu to be administered as the second vaccination of Group 1 participants

| | |
|---|---|
| **Arm title** | Group 2 |

Arm description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp and ChAd63 AMA1 5 x 1010 vp

followed by intramuscular administration of a mixture of MVA ME-TRAP 1.33 x 108 pfu and MVA CS 1.33 x 108 pfu and MVA AMA1 1.33 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| | |
|---|---|
| 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:

Mixture of MVA CS 1.33 x 108 pfu, MVA ME-TRAP 1.33 x 108 pfu, and MVA AMA1 1.33 x 108 pfu to be administered as the second vaccination of Group 2 participants

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

Dosage and administration details:

Mixture of MVA CS 1.33 x 108 pfu, MVA ME-TRAP 1.33 x 108 pfu, and MVA AMA1 1.33 x 108 pfu to be administered as the second vaccination of Group 2 participants

| | |
|---|---|
| **Arm title** | Group 3 |

Arm description:

Controlled human malaria infection administered at an interval of approximately 8-12 months after the initial controlled human malaria infection that the volunteers received in the VAC045 clinical trial.

| | |
|---|---|
| Arm type | Re-challenge/Previously vaccinated |

No investigational medicinal product assigned in this arm

| | |
|---|---|
| **Arm title** | Group 4 |

Arm description:

Unvaccinated control volunteers who undergo controlled human malaria infection.

| | |
|---|---|
| Arm type | No intervention |

No investigational medicinal product assigned in this arm

| **Number of subjects in period 2** | Group 1 | Group 2 | Group 3 |
|---|---|---|---|
| Started | 15 | 15 | 1 |
| Completed | 15 | 14 | 1 |
| Not completed | 0 | 1 | 0 |
| Consent withdrawn by subject | - | 1 | - |

| **Number of subjects in period 2** | Group 4 |
|---|---|
| Started | 6 |
| Completed | 6 |
| Not completed | 0 |
| Consent withdrawn by subject | - |

## Period 3

| | |
|---|---|
| Period 3 title | Malaria Challenge |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

## Arms

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Group 1 |

Arm description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp,

followed by intramuscular administration of a mixture of MVA ME-TRAP 2 x 108 pfu and MVA CS 2 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| | |
|---|---|
| Arm type | Malaria Challenge |
| No investigational medicinal product assigned in this arm | |
| **Arm title** | Group 2 |

Arm description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp and ChAd63 AMA1 5 x 1010 vp

followed by intramuscular administration of a mixture of MVA ME-TRAP 1.33 x 108 pfu and MVA CS 1.33 x 108 pfu and MVA AMA1 1.33 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| | |
|---|---|
| Arm type | Malaria Challenge |
| No investigational medicinal product assigned in this arm | |
| **Arm title** | Group 3 |

Arm description:

Controlled human malaria infection administered at an interval of approximately 8-12 months after the initial controlled human malaria infection that the volunteers received in the VAC045 clinical trial.

| | |
|---|---|
| Arm type | Re-challenge/Previously vaccinated |
| No investigational medicinal product assigned in this arm | |
| **Arm title** | Group 4 |

Arm description:

Unvaccinated control volunteers who undergo controlled human malaria infection.

| | |
|---|---|
| Arm type | Malaria Challenge |
| No investigational medicinal product assigned in this arm | |

| Number of subjects in period 3 | Group 1 | Group 2 | Group 3 |
|---|---|---|---|
| Started | 15 | 14 | 1 |
| Completed | 13 | 13 | 1 |
| Not completed | 2 | 1 | 0 |
| Consent withdrawn by subject | 2 | 1 | - |

| Number of subjects in period 3 | Group 4 |
|---|---|
| Started | 6 |
| Completed | 6 |
| Not completed | 0 |
| Consent withdrawn by subject | - |

**Period 4**

| | |
|---|---|
| Period 4 title | Follow Up |
| Is this the baseline period? | No |
| Allocation method | Randomised - controlled |
| Blinding used | Not blinded |

**Arms**

| | |
|---|---|
| Are arms mutually exclusive? | Yes |
| **Arm title** | Group 1 |

Arm description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp,

followed by intramuscular administration of a mixture of MVA ME-TRAP 2 x 108 pfu and MVA CS 2 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| | |
|---|---|
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |
| **Arm title** | Group 2 |

Arm description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp and ChAd63 AMA1 5 x 1010 vp

followed by intramuscular administration of a mixture of MVA ME-TRAP 1.33 x 108 pfu and MVA CS 1.33 x 108 pfu and MVA AMA1 1.33 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| | |
|---|---|
| Arm type | No intervention |
| No investigational medicinal product assigned in this arm | |
| **Arm title** | Group 3 |

Arm description:

Controlled human malaria infection administered at an interval of approximately 8-12 months after the initial controlled human malaria infection that the volunteers received in the VAC045 clinical trial.

| | |
|---|---|
| Arm type | No intervention |

| |
|---|
| No investigational medicinal product assigned in this arm |

| | |
|---|---|
| **Arm title** | Group 4 |

Arm description:

Unvaccinated control volunteers who undergo controlled human malaria infection.

| | |
|---|---|
| Arm type | No intervention |

| |
|---|
| No investigational medicinal product assigned in this arm |

| **Number of subjects in period 4** | Group 1 | Group 2 | Group 3 |
|---|---|---|---|
| Started | 13 | 13 | 1 |
| Completed | 13 | 13 | 1 |

| **Number of subjects in period 4** | Group 4 |
|---|---|
| Started | 6 |
| Completed | 6 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Group 1 |
| Reporting group description: | |
| Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp,<br><br>followed by intramuscular administration of a mixture of MVA ME-TRAP 2 x 108 pfu and MVA CS 2 x 108 pfu eight weeks later,<br><br>followed by controlled human malaria infection 17-24 days later. | |

| Reporting group title | Group 2 |
|---|---|
| Reporting group description: | |
| Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp and ChAd63 AMA1 5 x 1010 vp<br><br>followed by intramuscular administration of a mixture of MVA ME-TRAP 1.33 x 108 pfu and MVA CS 1.33 x 108 pfu and MVA AMA1 1.33 x 108 pfu eight weeks later,<br><br>followed by controlled human malaria infection 17-24 days later. | |

| Reporting group title | Group 3 |
|---|---|
| Reporting group description: | |
| Controlled human malaria infection administered at an interval of approximately 8-12 months after the initial controlled human malaria infection that the volunteers received in the VAC045 clinical trial. | |

| Reporting group title | Group 4 |
|---|---|
| Reporting group description: | |
| Unvaccinated control volunteers who undergo controlled human malaria infection. | |

| Reporting group values | Group 1 | Group 2 | Group 3 |
|---|---|---|---|
| Number of subjects | 15 | 15 | 1 |
| Age categorical | | | |
| Healthy adult volunteers | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 15 | 15 | 1 |
| 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 |
| From 65-84 years | 0 | 0 | 0 |
| 85 years and over | 0 | 0 | 0 |
| Gender categorical<br>Units: Subjects | | | |
| Female | 2 | 5 | 0 |
| Male | 13 | 10 | 1 |

| Reporting group values | Group 4 | Total | |
|---|---|---|---|
| Number of subjects | 6 | 37 | |

| Age categorical | | | |
|---|---|---|---|
| Healthy adult volunteers | | | |
| Units: Subjects | | | |
| Adults (18-64 years) | 6 | 37 | |
| 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 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 5 | 12 | |
| Male | 1 | 25 | |

## End points

### End points reporting groups

| Reporting group title | Group 1 |
|---|---|

Reporting group description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp,

followed by intramuscular administration of a mixture of MVA ME-TRAP 2 x 108 pfu and MVA CS 2 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| Reporting group title | Group 2 |
|---|---|

Reporting group description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp and ChAd63 AMA1 5 x 1010 vp

followed by intramuscular administration of a mixture of MVA ME-TRAP 1.33 x 108 pfu and MVA CS 1.33 x 108 pfu and MVA AMA1 1.33 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| Reporting group title | Group 3 |
|---|---|

Reporting group description:

Controlled human malaria infection administered at an interval of approximately 8-12 months after the initial controlled human malaria infection that the volunteers received in the VAC045 clinical trial.

| Reporting group title | Group 4 |
|---|---|

Reporting group description:

Unvaccinated control volunteers who undergo controlled human malaria infection.

| Reporting group title | Group 1 |
|---|---|

Reporting group description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp,

followed by intramuscular administration of a mixture of MVA ME-TRAP 2 x 108 pfu and MVA CS 2 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| Reporting group title | Group 2 |
|---|---|

Reporting group description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp and ChAd63 AMA1 5 x 1010 vp

followed by intramuscular administration of a mixture of MVA ME-TRAP 1.33 x 108 pfu and MVA CS 1.33 x 108 pfu and MVA AMA1 1.33 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| Reporting group title | Group 3 |
|---|---|

Reporting group description:

Controlled human malaria infection administered at an interval of approximately 8-12 months after the initial controlled human malaria infection that the volunteers received in the VAC045 clinical trial.

| Reporting group title | Group 4 |
|---|---|

Reporting group description:

Unvaccinated control volunteers who undergo controlled human malaria infection.

| Reporting group title | Group 1 |
|---|---|

Reporting group description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp,

followed by intramuscular administration of a mixture of MVA ME-TRAP 2 x 108 pfu and MVA CS 2 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| Reporting group title | Group 2 |
|---|---|

Reporting group description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp and ChAd63 AMA1 5 x 1010 vp

followed by intramuscular administration of a mixture of MVA ME-TRAP 1.33 x 108 pfu and MVA CS 1.33 x 108 pfu and MVA AMA1 1.33 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| Reporting group title | Group 3 |
|---|---|

Reporting group description:

Controlled human malaria infection administered at an interval of approximately 8-12 months after the initial controlled human malaria infection that the volunteers received in the VAC045 clinical trial.

| Reporting group title | Group 4 |
|---|---|

Reporting group description:

Unvaccinated control volunteers who undergo controlled human malaria infection.

| Reporting group title | Group 1 |
|---|---|

Reporting group description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp,

followed by intramuscular administration of a mixture of MVA ME-TRAP 2 x 108 pfu and MVA CS 2 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| Reporting group title | Group 2 |
|---|---|

Reporting group description:

Intramuscular administration of a mixture of ChAd63 ME-TRAP 5 x 1010 vp and ChAd63 CS 5 x 1010 vp and ChAd63 AMA1 5 x 1010 vp

followed by intramuscular administration of a mixture of MVA ME-TRAP 1.33 x 108 pfu and MVA CS 1.33 x 108 pfu and MVA AMA1 1.33 x 108 pfu eight weeks later,

followed by controlled human malaria infection 17-24 days later.

| Reporting group title | Group 3 |
|---|---|

Reporting group description:

Controlled human malaria infection administered at an interval of approximately 8-12 months after the initial controlled human malaria infection that the volunteers received in the VAC045 clinical trial.

| Reporting group title | Group 4 |
|---|---|

Reporting group description:

Unvaccinated control volunteers who undergo controlled human malaria infection.

## Primary: Controlled human malaria infection of sporozoites

| End point title | Controlled human malaria infection of sporozoites[1] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

Diagnosis of malaria infection following challenge as defined as positive thick film microscopy up to day 21 post challenge.

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 publication wil be uploaded at a later date.

| **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 | 13 | 13 | 1 | 6 |
| Units: 33 | 13 | 13 | 1 | 6 |

## Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information[1]

Timeframe for reporting adverse events:

AEs collected and reviewed from day of vaccination to 90 days post challenge (total 160 days).
SAEs reported within 24 hours of awareness to sponsor.
SUSARs reported within 15 days of awareness (7 days for fatal or life threatening events).

| | |
|---|---|
| Assessment type | Systematic |

### Dictionary used

| | |
|---|---|
| Dictionary name | None |
| Dictionary version | N/A |

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 the confidential nature of this information, we have not provided this data at this time. The publication wil be uploaded at a later date.
There were a total of 3 SAEs, none of which were realted to any of the IMPs or challenge procedures.

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|---|---|
| 21 February 2013 | Addition of electrocardiogram as a study procedure.<br>Change of timing of post-vaccination follow-up visit.<br>Corrections to the VIS to match the protocol.<br>Addition of emergency contact cards.<br>Shelf life extension of MVA CS lot 0010210. |
| 25 March 2013 | Change of diary card. |
| 20 May 2013 | Change to the protocol for day 7 post-CHMI visit<br>Amendment to the phrasing used regarding the day 7 follow up visits after the controlled human malaria infection (CHMI) procedure. The protocol stated that volunteers will be seen for blood tests 3 times on the day, with a gap of 6-8 hours between each visit. This was not possible in practice, and therefore the phrasing was changed to 'The interval between visits will be as evenly spaced as practicable'. |
| 31 May 2013 | To extend the shelf life of vaccine ChAd63 CS (Batch No 03O11-01) for a further year to 16th June 2014.<br>To extend the shelf life of vaccine AdCh63 AMA1 (Lot 01 Fill 09-04) for a further year to 17th June 2014. |
| 17 July 2013 | To extend the shelf life of vaccine MVA AMA1 to 3rd August 2014. |

Notes:

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported