



## Clinical trial results:

### A Phase I/IIa Sporozoite Challenge Study to Assess the Safety and Protective Efficacy of the Combination Malaria Vaccine Candidate Regimen of RTS,S/AS01B + ChAd63 and MVA encoding ME-TRAP and also RTS,S/A01B alone.

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2013-000393-30 |
| Trial protocol           | GB             |
| Global end of trial date | 21 August 2014 |

#### Results information

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

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | VAC055 |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT01883609 |
| 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               | 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:

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## Results analysis stage

|                                                      |                |
|------------------------------------------------------|----------------|
| Analysis stage                                       | Final          |
| Date of interim/final analysis                       | 21 August 2014 |
| Is this the analysis of the primary completion data? | Yes            |
| Primary completion date                              | 21 August 2014 |
| Global end of trial reached?                         | Yes            |
| Global end of trial date                             | 21 August 2014 |
| Was the trial ended prematurely?                     | No             |

Notes:

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## General information about the trial

Main objective of the trial:

Primary Objectives:

To assess the efficacy (occurrence of *P. falciparum* parasitemia, assessed by blood slide) of a combination immunization regimen with ChAd63/MVA ME-TRAP and RTS,S/AS01B, and of RTS,S/AS01B alone, against malaria sporozoite challenge, in healthy malaria-naïve volunteers.

To assess the safety of a combination immunization regimen with ChAd63/MVA ME-TRAP and RTS,S/AS01B, and of RTS,S/AS01B alone, in healthy malaria-naïve volunteers.

Secondary Objectives:

To assess immunogenicity generated in malaria naïve individuals of a malaria vaccine schedule containing RTS,S/AS01B and ChAd63/MVA ME-TRAP, and of RTS,S/AS01B alone.

To assess the efficacy (measured as time to *P. falciparum* parasitemia assessed by blood slide, by PCR, and parasite density dynamics assessed by PCR) of a combination immunization regimen with ChAd63/MVA ME-TRAP and RTS,S/AS01B, and of RTS,S/AS01B alone, against malaria sporozoite challenge, in healthy malaria-naïve volunteers.

Protection of trial subjects:

- Volunteers were 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.
- Total blood volume taken during study kept to 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, symptom review 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.

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Background therapy: -

Evidence for comparator: -

|                                                           |                   |
|-----------------------------------------------------------|-------------------|
| Actual start date of recruitment                          | 02 September 2013 |
| Long term follow-up planned                               | No                |
| Independent data monitoring committee (IDMC) involvement? | No                |

Notes:

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### Population of trial subjects

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#### Subjects enrolled per country

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

Notes:

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#### Subjects enrolled per age group

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

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Inclusion / Exclusion criteria  
Informed Consent Questionnaire  
Informed consent  
Medical History  
Physical Examination  
Urinalysis  
Electrocardiogram  
 $\beta$ -HCG urine (women only)  
Review contraindications  
Physical Observations  
HBV,HCV,HIV  
Haematology  
Biochemistry

### Period 1

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

### Arms

|                              |     |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Group 1 |
|------------------|---------|

Arm description:

RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP.

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | RTS,S/AS01B            |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

50mcg of RTS,S and standard adult dose of AS01.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Group 2 |
|------------------|---------|

Arm description:

RTS,S/AS01B

|                                        |                        |
|----------------------------------------|------------------------|
| Arm type                               | Experimental           |
| Investigational medicinal product name | RTS,S/AS01B            |
| Investigational medicinal product code |                        |
| Other name                             |                        |
| Pharmaceutical forms                   | Solution for injection |
| Routes of administration               | Intramuscular use      |

Dosage and administration details:

50mcg of RTS,S and standard adult dose of AS01.

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Group 3 |
|------------------|---------|

Arm description:

Unvaccinated controls.

|                                                           |                      |
|-----------------------------------------------------------|----------------------|
| Arm type                                                  | Unvaccinated Control |
| No investigational medicinal product assigned in this arm |                      |
| <b>Arm title</b>                                          | Group 4              |
| Arm description:<br>Unvaccinated controls.                |                      |
| Arm type                                                  | Unvaccinated Control |
| No investigational medicinal product assigned in this arm |                      |

| Number of subjects in period 1 | Group 1 | Group 2 | Group 3 |
|--------------------------------|---------|---------|---------|
| Started                        | 20      | 17      | 6       |
| Completed                      | 20      | 17      | 6       |

| Number of subjects in period 1 | Group 4 |
|--------------------------------|---------|
| Started                        | 5       |
| Completed                      | 5       |

|                              |                         |
|------------------------------|-------------------------|
| <b>Period 2</b>              |                         |
| Period 2 title               | Day 14                  |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

|                              |         |
|------------------------------|---------|
| <b>Arms</b>                  |         |
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Group 1 |

|                                                                          |                        |
|--------------------------------------------------------------------------|------------------------|
| Arm description:<br>RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP.         |                        |
| 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:<br>A dose of 5 x 10 <sup>10</sup> vp. |                        |
| <b>Arm title</b>                                                         | Group 2                |
| Arm description:<br>RTS,S/AS01B                                          |                        |
| Arm type                                                                 | No intervention        |
| No investigational medicinal product assigned in this arm                |                        |
| <b>Arm title</b>                                                         | Group 4                |

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Arm description:                                          |                 |
| Unvaccinated controls                                     |                 |
| Arm type                                                  | No intervention |
| No investigational medicinal product assigned in this arm |                 |
| <b>Arm title</b>                                          | Group 4         |
| Arm description:                                          |                 |
| Unvaccinated controls                                     |                 |
| Arm type                                                  | No intervention |
| No investigational medicinal product assigned in this arm |                 |

| <b>Number of subjects in period 2</b> | Group 1 | Group 2 | Group 4 |
|---------------------------------------|---------|---------|---------|
| Started                               | 20      | 17      | 6       |
| Completed                             | 20      | 17      | 6       |

| <b>Number of subjects in period 2</b> | Group 4 |
|---------------------------------------|---------|
| Started                               | 5       |
| Completed                             | 5       |

|                                                 |                         |
|-------------------------------------------------|-------------------------|
| <b>Period 3</b>                                 |                         |
| Period 3 title                                  | Day 28                  |
| Is this the baseline period?                    | No                      |
| Allocation method                               | Randomised - controlled |
| Blinding used                                   | Not blinded             |
| <b>Arms</b>                                     |                         |
| Are arms mutually exclusive?                    | Yes                     |
| <b>Arm title</b>                                | Group 1                 |
| Arm description:                                |                         |
| RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP.    |                         |
| Arm type                                        | Experimental            |
| Investigational medicinal product name          | RTS,S/AS01B             |
| Investigational medicinal product code          |                         |
| Other name                                      |                         |
| Pharmaceutical forms                            | Solution for injection  |
| Routes of administration                        | Intramuscular use       |
| Dosage and administration details:              |                         |
| 50mcg of RTS,S and standard adult dose of AS01. |                         |
| <b>Arm title</b>                                | Group 2                 |
| Arm description:                                |                         |
| RTS,S/AS01B                                     |                         |
| Arm type                                        | Experimental            |

|                                                                                       |                        |
|---------------------------------------------------------------------------------------|------------------------|
| Investigational medicinal product name                                                | RTS,S/AS01B            |
| Investigational medicinal product code                                                |                        |
| Other name                                                                            |                        |
| Pharmaceutical forms                                                                  | Solution for injection |
| Routes of administration                                                              | Intramuscular use      |
| Dosage and administration details:<br>50mcg of RTS,S and standard adult dose of AS01. |                        |
| <b>Arm title</b>                                                                      | Group 3                |
| Arm description:<br>Unvaccinated controls                                             |                        |
| Arm type                                                                              | No intervention        |
| No investigational medicinal product assigned in this arm                             |                        |
| <b>Arm title</b>                                                                      | Group 4                |
| Arm description:<br>Unvaccinated controls                                             |                        |
| Arm type                                                                              | No intervention        |
| No investigational medicinal product assigned in this arm                             |                        |

| Number of subjects in period 3 | Group 1 | Group 2 | Group 3 |
|--------------------------------|---------|---------|---------|
| Started                        | 20      | 17      | 6       |
| Completed                      | 20      | 17      | 6       |

| Number of subjects in period 3 | Group 4 |
|--------------------------------|---------|
| Started                        | 5       |
| Completed                      | 5       |

|                                                                  |                         |
|------------------------------------------------------------------|-------------------------|
| <b>Period 4</b>                                                  |                         |
| Period 4 title                                                   | Day 56                  |
| Is this the baseline period?                                     | No                      |
| Allocation method                                                | Randomised - controlled |
| Blinding used                                                    | Not blinded             |
| <b>Arms</b>                                                      |                         |
| Are arms mutually exclusive?                                     | Yes                     |
| <b>Arm title</b>                                                 | Group 1                 |
| Arm description:<br>RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP. |                         |
| Arm type                                                         | Experimental            |

|                                                                                       |                        |
|---------------------------------------------------------------------------------------|------------------------|
| Investigational medicinal product name                                                | RTS,S/AS01B            |
| Investigational medicinal product code                                                |                        |
| Other name                                                                            |                        |
| Pharmaceutical forms                                                                  | Solution for injection |
| Routes of administration                                                              | Intramuscular use      |
| Dosage and administration details:<br>50mcg of RTS,S and standard adult dose of AS01. |                        |
| <b>Arm title</b>                                                                      | Group 2                |
| Arm description:<br>RTS,S/AS01B                                                       |                        |
| Arm type                                                                              | Experimental           |
| Investigational medicinal product name                                                | RTS,S/AS01B            |
| Investigational medicinal product code                                                |                        |
| Other name                                                                            |                        |
| Pharmaceutical forms                                                                  | Solution for injection |
| Routes of administration                                                              | Intramuscular use      |
| Dosage and administration details:<br>50mcg of RTS,S and standard adult dose of AS01. |                        |
| <b>Arm title</b>                                                                      | Group 3                |
| Arm description:<br>Unvaccinated controls                                             |                        |
| Arm type                                                                              | No intervention        |
| No investigational medicinal product assigned in this arm                             |                        |
| <b>Arm title</b>                                                                      | Group 4                |
| Arm description:<br>Unvaccinated controls                                             |                        |
| Arm type                                                                              | No intervention        |
| No investigational medicinal product assigned in this arm                             |                        |

| <b>Number of subjects in period 4</b> | Group 1 | Group 2 | Group 3 |
|---------------------------------------|---------|---------|---------|
| Started                               | 20      | 17      | 6       |
| Completed                             | 20      | 17      | 6       |

| <b>Number of subjects in period 4</b> | Group 4 |
|---------------------------------------|---------|
| Started                               | 5       |
| Completed                             | 5       |

**Period 5**

|                              |                         |
|------------------------------|-------------------------|
| Period 5 title               | Day 70                  |
| Is this the baseline period? | No                      |
| Allocation method            | Randomised - controlled |
| Blinding used                | Not blinded             |

**Arms**

|                              |         |
|------------------------------|---------|
| Are arms mutually exclusive? | Yes     |
| <b>Arm title</b>             | Group 1 |

Arm description:

RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP.

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

2 x 10<sup>8</sup> pfu

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Group 2 |
|------------------|---------|

Arm description:

RTS,S/AS01B

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

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Group 3 |
|------------------|---------|

Arm description:

Unvaccinated controls

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

|                  |         |
|------------------|---------|
| <b>Arm title</b> | Group 4 |
|------------------|---------|

Arm description:

Unvaccinated controls

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

| <b>Number of subjects in period 5</b> | Group 1 | Group 2 | Group 3 |
|---------------------------------------|---------|---------|---------|
| Started                               | 20      | 17      | 6       |
| Completed                             | 20      | 17      | 6       |

| <b>Number of subjects in period 5</b> | Group 4 |
|---------------------------------------|---------|
| Started                               | 5       |
| Completed                             | 5       |

|                                                                  |                         |
|------------------------------------------------------------------|-------------------------|
| <b>Period 6</b>                                                  |                         |
| Period 6 title                                                   | Malaria Challenge       |
| Is this the baseline period?                                     | No                      |
| Allocation method                                                | Randomised - controlled |
| Blinding used                                                    | Not blinded             |
| <b>Arms</b>                                                      |                         |
| Are arms mutually exclusive?                                     | Yes                     |
| <b>Arm title</b>                                                 | Group 1                 |
| Arm description:<br>RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP. |                         |
| Arm type                                                         | Malaria Challenge       |
| No investigational medicinal product assigned in this arm        |                         |
| <b>Arm title</b>                                                 | Group 2                 |
| Arm description:<br>RTS,S/AS01B                                  |                         |
| Arm type                                                         | Malaria Challenge       |
| No investigational medicinal product assigned in this arm        |                         |
| <b>Arm title</b>                                                 | Group 3                 |
| Arm description:<br>Unvaccinated controls                        |                         |
| Arm type                                                         | No intervention         |
| No investigational medicinal product assigned in this arm        |                         |

| <b>Number of subjects in period 6<sup>[1]</sup></b> | Group 1 | Group 2 | Group 3 |
|-----------------------------------------------------|---------|---------|---------|
| Started                                             | 17      | 16      | 6       |
| Completed                                           | 17      | 16      | 6       |

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: Three volunteers withdrew from Group 1 and one volunteer withdrew from Group 2 prior to the malaria challenge.

|                              |                                    |
|------------------------------|------------------------------------|
| <b>Period 7</b>              |                                    |
| Period 7 title               | Repeat Challenge/Group 4 Challenge |
| Is this the baseline period? | No                                 |
| Allocation method            | Randomised - controlled            |
| Blinding used                | Not blinded                        |
| <b>Arms</b>                  |                                    |
| Are arms mutually exclusive? | Yes                                |

|                                                                  |                          |
|------------------------------------------------------------------|--------------------------|
| <b>Arm title</b>                                                 | Group 1                  |
| Arm description:<br>RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP. |                          |
| Arm type                                                         | Repeat Malaria Challenge |
| No investigational medicinal product assigned in this arm        |                          |
| <b>Arm title</b>                                                 | Group 2                  |
| Arm description:<br>RTS,S/AS01B                                  |                          |
| Arm type                                                         | Repeat Malaria Challenge |
| No investigational medicinal product assigned in this arm        |                          |
| <b>Arm title</b>                                                 | Group 4                  |
| Arm description:<br>Unvaccinated controls                        |                          |
| Arm type                                                         | No intervention          |
| No investigational medicinal product assigned in this arm        |                          |

| <b>Number of subjects in period 7<sup>[2]</sup></b> | Group 1 | Group 2 | Group 4 |
|-----------------------------------------------------|---------|---------|---------|
| Started                                             | 8       | 6       | 5       |
| Completed                                           | 8       | 6       | 5       |

Notes:

[2] - 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 2 volunteers did not take part in this stage of the study. Only sterilely protected volunteers from groups 1 and 2 took part in this stage.

## Baseline characteristics

### Reporting groups

|                                                                              |         |
|------------------------------------------------------------------------------|---------|
| Reporting group title                                                        | Group 1 |
| Reporting group description:<br>RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP. |         |
| Reporting group title                                                        | Group 2 |
| Reporting group description:<br>RTS,S/AS01B                                  |         |
| Reporting group title                                                        | Group 3 |
| Reporting group description:<br>Unvaccinated controls.                       |         |
| Reporting group title                                                        | Group 4 |
| Reporting group description:<br>Unvaccinated controls.                       |         |

| Reporting group values                | Group 1 | Group 2 | Group 3 |
|---------------------------------------|---------|---------|---------|
| Number of subjects                    | 20      | 17      | 6       |
| Age categorical<br>Units: Subjects    |         |         |         |
| Adults (18-64 years)                  | 20      | 17      | 6       |
| Gender categorical<br>Units: Subjects |         |         |         |
| Female                                | 8       | 8       | 3       |
| Male                                  | 12      | 9       | 3       |

| Reporting group values                | Group 4 | Total |  |
|---------------------------------------|---------|-------|--|
| Number of subjects                    | 5       | 48    |  |
| Age categorical<br>Units: Subjects    |         |       |  |
| Adults (18-64 years)                  | 5       | 48    |  |
| Gender categorical<br>Units: Subjects |         |       |  |
| Female                                | 3       | 22    |  |
| Male                                  | 2       | 26    |  |

## End points

### End points reporting groups

|                                                                              |         |
|------------------------------------------------------------------------------|---------|
| Reporting group title                                                        | Group 1 |
| Reporting group description:<br>RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP. |         |
| Reporting group title                                                        | Group 2 |
| Reporting group description:<br>RTS,S/AS01B                                  |         |
| Reporting group title                                                        | Group 3 |
| Reporting group description:<br>Unvaccinated controls.                       |         |
| Reporting group title                                                        | Group 4 |
| Reporting group description:<br>Unvaccinated controls.                       |         |
| Reporting group title                                                        | Group 1 |
| Reporting group description:<br>RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP. |         |
| Reporting group title                                                        | Group 2 |
| Reporting group description:<br>RTS,S/AS01B                                  |         |
| Reporting group title                                                        | Group 4 |
| Reporting group description:<br>Unvaccinated controls                        |         |
| Reporting group title                                                        | Group 4 |
| Reporting group description:<br>Unvaccinated controls                        |         |
| Reporting group title                                                        | Group 1 |
| Reporting group description:<br>RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP. |         |
| Reporting group title                                                        | Group 2 |
| Reporting group description:<br>RTS,S/AS01B                                  |         |
| Reporting group title                                                        | Group 3 |
| Reporting group description:<br>Unvaccinated controls                        |         |
| Reporting group title                                                        | Group 4 |
| Reporting group description:<br>Unvaccinated controls                        |         |
| Reporting group title                                                        | Group 1 |
| Reporting group description:<br>RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP. |         |
| Reporting group title                                                        | Group 2 |
| Reporting group description:<br>RTS,S/AS01B                                  |         |
| Reporting group title                                                        | Group 3 |
| Reporting group description:<br>Unvaccinated controls                        |         |
| Reporting group title                                                        | Group 4 |
| Reporting group description:<br>Unvaccinated controls                        |         |
| Reporting group title                                                        | Group 1 |
| Reporting group description:<br>RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP. |         |
| Reporting group title                                                        | Group 2 |
| Reporting group description:<br>RTS,S/AS01B                                  |         |
| Reporting group title                                                        | Group 3 |
| Reporting group description:<br>Unvaccinated controls                        |         |
| Reporting group title                                                        | Group 4 |

Reporting group description:

Unvaccinated controls

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

Reporting group description:

RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP.

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

Reporting group description:

RTS,S/AS01B

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

Reporting group description:

Unvaccinated controls

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

Reporting group description:

Unvaccinated controls

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

Reporting group description:

RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP.

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

Reporting group description:

RTS,S/AS01B

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

Reporting group description:

Unvaccinated controls

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

Reporting group description:

RTS,S/AS01B, ChAd63 ME-TRAP and MVA ME-TRAP.

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

Reporting group description:

RTS,S/AS01B

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

Reporting group description:

Unvaccinated controls

---

## Primary: Primary efficacy

|                 |                                 |
|-----------------|---------------------------------|
| End point title | Primary efficacy <sup>[1]</sup> |
|-----------------|---------------------------------|

End point description:

The number of completely protected individuals will be presented between each vaccination group and controls. Completely protected individuals are those who do not, by Day 21 following sporozoite challenge, develop blood stage malaria infection.

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

End point timeframe:

Diagnosis of malaria infection following challenge will be defined as positive thick film microscopy up to 21 days 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 study, we will provide additional statistical information following publication.

| <b>End point values</b>     | Group 1         | Group 2         | Group 3         |  |
|-----------------------------|-----------------|-----------------|-----------------|--|
| Subject group type          | Reporting group | Reporting group | Reporting group |  |
| Number of subjects analysed | 17              | 16              | 6               |  |
| Units: Number of subjects   | 17              | 16              | 6               |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

AEs reviewed from day of vaccination at multiple time points according to visit schedule until trial end

SAEs reported within 24 hours of awareness to sponsor.

SUSARs reported within 15 days of awareness (7 days for fatal or life threatening events)

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

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### Dictionary used

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|                    |        |
|--------------------|--------|
| Dictionary name    | MedDRA |
| Dictionary version | 17.0   |

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

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### 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 will be uploaded at a later date.

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 05 July 2013     | <p>Amendment to IMPD to document that the shelf-life of the RTS,S purified bulk lot ARTSAPA004 has been extended to 48 months based on satisfactory real-time stability data for up to 36 months storage at -70C.</p> <p>In addition, the long term stability protocol applied to RTS,S drug substance was modified to introduce changes such as addition of a 42-month stability testing time point as well as addition, replacement and removal of certain tests.</p>                                                                                                                                                                                                                                      |
| 29 August 2013   | <p>Correction of an error in the exclusion criteria.</p> <p>The previous text read:</p> <ul style="list-style-type: none"><li>• Use of medications known to cause prolongation of the QT interval or to otherwise have a potentially clinically significant interaction with Riamet and Malarone</li></ul> <p>The new text now reads:</p> <ul style="list-style-type: none"><li>• Use of medications known to cause prolongation of the QT interval and existing contraindication to the use of Malarone</li><li>• Use of medications known to have a potentially clinically significant interaction with Riamet and Malarone</li></ul> <p>The protocol and GP screening letter were updated accordingly</p> |
| 25 November 2013 | Addition of post-challenge diary card.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| 27 November 2013 | To extend the shelf life of ChAd63 ME-TRAP (AdCh63 ME-TRAP) lot 01S11-01 to 6th January 2015.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported