



Clinical trial results:

A Phase I/IIa clinical trial to assess the safety, immunogenicity and efficacy of the blood-stage Plasmodium falciparum malaria vaccine candidate RH5.1/AS01

Summary

EudraCT number	2016-001718-31
Trial protocol	GB
Global end of trial date	27 June 2019

Results information

Result version number	v1 (current)
This version publication date	17 September 2020
First version publication date	17 September 2020

Trial information

Trial identification

Sponsor protocol code	VAC063
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02927145
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	Angela Minasian, University of Oxford, 0044 01865611425, angela.minassian@ndm.ox.ac.uk
Scientific contact	Angela Minasian, University of Oxford, 0044 01865611425, angela.minassian@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	27 June 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 June 2019
Global end of trial reached?	Yes
Global end of trial date	27 June 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety of the RH5.1/AS01 vaccine in healthy volunteers at different doses.

To establish whether the RH5.1/AS01 vaccine can demonstrate a reduced parasite multiplication rate in vaccinated subjects compared to infectivity controls in a blood-stage controlled human malaria infection model.

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.
- Volunteers for Groups 5-9 asked to complete a questionnaire testing their understanding of the trial as part of the consent process to ensure that individuals understand the trial sufficiently to give informed consent.
- 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) - Volunteers seen within 1 - 3 days of vaccination for safety review and provided with 24/7 contact number for trial clinician and emergency contact card for the department.
- Inclusion of AE related safety stopping/holding rules at both a group and individual level in the protocol.
- 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 who remained undiagnosed with malaria at Day 21 given a treatment course of anti-malarials.
- Volunteers followed up until at least 2 consecutive negative blood films seen or two consecutive qPCR results with substantial reduction in genome copies/mL.
- Volunteers observed for 1 hour after vaccination to monitor for any immediate adverse effects.
- Total blood volume taken during study kept to volume that should not compromise healthy volunteers.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 September 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Scientific research
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 90
Worldwide total number of subjects	90
EEA total number of subjects	90

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)	90
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Volunteers were recruited by use of advertisements, formally approved by the ethics committee, distributed or posted in public places (including newspapers, social media, stalls at fairs and public transport) or via email distribution, including to individuals who have registered an interest in taking part in clinical trials at the study sites.

Pre-assignment

Screening details:

Inclusion / Exclusion criteria
Informed Consent Questionnaire
Informed Consent
Medical History
Physical Examination
Urinalysis
Electrocardiogram (Groups 5, 6, 9)
beta-HCG urine (women only)
Review contraindications
Physical Observations
HBV, HCV, HIV
Haematology
Biochemistry

Period 1

Period 1 title	Phase I & IIa
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Group 1 - Phase 1a

Arm description:

3 vaccinations (Days 0/28/56) of 2µg RH5.1/0.5 mL AS01 intramuscularly

Arm type	Experimental
Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2µg RH5.1 in 0.5mL AS01

Arm title	Group 2 - Phase 1a
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Arm description:

3 vaccinations (Days 0/28/56) of 10µg RH5.1 in 0.5mL AS01 intramuscularly

Arm type	Experimental
Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg RH5.1 in 0.5mL AS01

Arm title	Group 3 - Phase 1a
Arm description: 2 vaccinations (Days 0/28) 50µg RH5.1 in 0.5mL AS01 followed by a third vaccination (Day 182) of 10µg RH5.1 in 0.5mL AS01.	
Arm type	Experimental
Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: 50µg RH5.1 in 0.5mL AS01	
Arm title	Group 4 - Phase 1a
Arm description: 3 vaccinations (Days 0/28/56) of 50µg RH5.1 in 0.5mL AS01 intramuscularly	
Arm type	Experimental
Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: 50µg RH5.1 in 0.5mL AS01	
Arm title	Group 5 - Phase 2a
Arm description: 3 vaccinations (Days 0/28/56) of 10µg RH5.1 in 0.5mL AS01 intramuscularly, followed by primary CHMI 2 weeks post 3rd vaccination.	
Arm type	Experimental
Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: 10µg RH5.1 in 0.5mL AS01	
Arm title	Group 6 - Phase 2a
Arm description: Primary CHMI controls (for primary CHMI in Group 5 and 7)	
Arm type	CHMI controls
No investigational medicinal product assigned in this arm	
Arm title	Group 7 - Phase 2a
Arm description: Subset of Group 5. 4 vaccinations (Days 0/28/56/~4 months after 3rd vaccination) of 10µg RH5.1 in 0.5mL AS01. Primary CHMI 2 weeks post 3rd vaccination. Secondary CHMI 1-2 weeks post 4th vaccination.	
Arm type	Experimental
Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:
10µg RH5.1 in 0.5mL AS01

Arm title	Group 8 - Phase 2a
Arm description: Subset of Group 6 undergoing secondary CHMI. Controls for secondary CHMI in Group 7.	
Arm type	CHMI controls
No investigational medicinal product assigned in this arm	
Arm title	Group 9 - Phase 2a
Arm description: Primary CHMI controls (for secondary CHMI in Group 7 and 8)	
Arm type	CHMI controls
No investigational medicinal product assigned in this arm	

Number of subjects in period 1	Group 1 - Phase 1a	Group 2 - Phase 1a	Group 3 - Phase 1a
Started	12	12	12
Completed	12	12	12
Not completed	0	0	0
Consent withdrawn by subject	-	-	-
Physician decision	-	-	-
Pregnancy	-	-	-
Back-up volunteers for CHMI (not required)	-	-	-

Number of subjects in period 1	Group 4 - Phase 1a	Group 5 - Phase 2a	Group 6 - Phase 2a
Started	14	17	17
Completed	11	17	14
Not completed	3	0	3
Consent withdrawn by subject	2	-	1
Physician decision	1	-	-
Pregnancy	-	-	-
Back-up volunteers for CHMI (not required)	-	-	2

Number of subjects in period 1	Group 7 - Phase 2a	Group 8 - Phase 2a	Group 9 - Phase 2a
Started	9	8	6
Completed	8	8	4
Not completed	1	0	2
Consent withdrawn by subject	-	-	2
Physician decision	-	-	-
Pregnancy	1	-	-

Back-up volunteers for CHMI (not required)	-	-	-
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Period 2

Period 2 title	Optional long-term follow-up
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Group 1 - Phase 1a

Arm description:

3 vaccinations (Days 0/28/56) of 2µg RH5.1/0.5 mL AS01 intramuscularly. Optional long term follow-up at approximately 1.5-2.5 years after 3rd vaccination.

Arm type	Experimental
Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

2µg RH5.1 in 0.5mL AS01

Arm title	Group 2 - Phase 1a
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Arm description:

3 vaccinations (Days 0/28/56) of 10µg RH5.1 in 0.5mL AS01 intramuscularly. Optional long term follow-up at approximately 1.5-2.5 years after 3rd vaccination.

Arm type	Experimental
Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use

Dosage and administration details:

10µg RH5.1 in 0.5mL AS01

Arm title	Group 3 - Phase 1a
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Arm description:

2 vaccinations (Days 0/28) 50µg RH5.1 in 0.5mL AS01 followed by a third vaccination (Day 182) of 10µg RH5.1 in 0.5mL AS01. Optional long term follow-up at approximately 1.5-2.5 years after 3rd vaccination.

Arm type	Experimental
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Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: 50µg RH5.1 in 0.5mL AS01	
Arm title	Group 4 - Phase 1a
Arm description: 3 vaccinations (Days 0/28/56) of 50µg RH5.1 in 0.5mL AS01 intramuscularly	
Arm type	Experimental
Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: 50µg RH5.1 in 0.5mL AS01	
Arm title	Group 5 - Phase 2a
Arm description: 3 vaccinations (Days 0/28/56) of 10µg RH5.1 in 0.5mL AS01 intramuscularly, followed by primary CHMI 2 weeks post 3rd vaccination. Optional long term follow-up at approximately 1.5-2.5 years after 3rd vaccination.	
Arm type	Experimental
Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: 10µg RH5.1 in 0.5mL AS01	
Arm title	Group 7 - Phase 2a
Arm description: Subset of Group 5 . 4 vaccinations (Days 0/28/56/~4 months after 3rd vaccination) of 10µg RH5.1 in 0.5mL AS01. Primary CHMI 2 weeks post 3rd vaccination. Secondary CHMI 1-2 weeks post 4th vaccination.	
Arm type	Experimental
Investigational medicinal product name	RH5.1 with adjuvant AS01
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intramuscular use
Dosage and administration details: 10µg RH5.1 in 0.5mL AS01	

Number of subjects in period 2	Group 1 - Phase 1a	Group 2 - Phase 1a	Group 3 - Phase 1a
Started	9	10	7
Completed	9	10	7

Number of subjects in period 2	Group 4 - Phase 1a	Group 5 - Phase 2a	Group 7 - Phase 2a
Started	4	3	6
Completed	4	3	6

Baseline characteristics

Reporting groups

Reporting group title	Phase I & IIa
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Reporting group description: -

Reporting group values	Phase I & IIa	Total	
Number of subjects	90	90	
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)	90	90	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	56	56	
Male	34	34	

End points

End points reporting groups

Reporting group title	Group 1 - Phase 1a
Reporting group description: 3 vaccinations (Days 0/28/56) of 2µg RH5.1/0.5 mL AS01 intramuscularly	
Reporting group title	Group 2 - Phase 1a
Reporting group description: 3 vaccinations (Days 0/28/56) of 10µg RH5.1 in 0.5mL AS01 intramuscularly	
Reporting group title	Group 3 - Phase 1a
Reporting group description: 2 vaccinations (Days 0/28) 50µg RH5.1 in 0.5mL AS01 followed by a third vaccination (Day 182) of 10µg RH5.1 in 0.5mL AS01.	
Reporting group title	Group 4 - Phase 1a
Reporting group description: 3 vaccinations (Days 0/28/56) of 50µg RH5.1 in 0.5mL AS01 intramuscularly	
Reporting group title	Group 5 - Phase 2a
Reporting group description: 3 vaccinations (Days 0/28/56) of 10µg RH5.1 in 0.5mL AS01 intramuscularly, followed by primary CHMI 2 weeks post 3rd vaccination.	
Reporting group title	Group 6 - Phase 2a
Reporting group description: Primary CHMI controls (for primary CHMI in Group 5 and 7)	
Reporting group title	Group 7 - Phase 2a
Reporting group description: Subset of Group 5. 4 vaccinations (Days 0/28/56/~4 months after 3rd vaccination) of 10µg RH5.1 in 0.5mL AS01. Primary CHMI 2 weeks post 3rd vaccination. Secondary CHMI 1-2 weeks post 4th vaccination.	
Reporting group title	Group 8 - Phase 2a
Reporting group description: Subset of Group 6 undergoing secondary CHMI. Controls for secondary CHMI in Group 7.	
Reporting group title	Group 9 - Phase 2a
Reporting group description: Primary CHMI controls (for secondary CHMI in Group 7 and 8)	
Reporting group title	Group 1 - Phase 1a
Reporting group description: 3 vaccinations (Days 0/28/56) of 2µg RH5.1/0.5 mL AS01 intramuscularly. Optional long term follow-up at approximately 1.5-2.5 years after 3rd vaccination.	
Reporting group title	Group 2 - Phase 1a
Reporting group description: 3 vaccinations (Days 0/28/56) of 10µg RH5.1 in 0.5mL AS01 intramuscularly. Optional long term follow-up at approximately 1.5-2.5 years after 3rd vaccination.	
Reporting group title	Group 3 - Phase 1a
Reporting group description: 2 vaccinations (Days 0/28) 50µg RH5.1 in 0.5mL AS01 followed by a third vaccination (Day 182) of 10µg RH5.1 in 0.5mL AS01. Optional long term follow-up at approximately 1.5-2.5 years after 3rd vaccination.	
Reporting group title	Group 4 - Phase 1a
Reporting group description: 3 vaccinations (Days 0/28/56) of 50µg RH5.1 in 0.5mL AS01 intramuscularly	
Reporting group title	Group 5 - Phase 2a
Reporting group description: 3 vaccinations (Days 0/28/56) of 10µg RH5.1 in 0.5mL AS01 intramuscularly, followed by primary CHMI	

2 weeks post 3rd vaccination. Optional long term follow-up at approximately 1.5-2.5 years after 3rd vaccination.

Reporting group title	Group 7 - Phase 2a
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Reporting group description:

Subset of Group 5 . 4 vaccinations (Days 0/28/56/~4 months after 3rd vaccination) of 10µg RH5.1 in 0.5mL AS01. Primary CHMI 2 weeks post 3rd vaccination. Secondary CHMI 1-2 weeks post 4th vaccination.

Primary: Efficacy of the RH5.1/AS01 vaccine as assessed by a reduction in the PCR-derived parasite multiplication rate (PMR) in vaccinated subjects compared to infectivity controls

End point title	Efficacy of the RH5.1/AS01 vaccine as assessed by a reduction in the PCR-derived parasite multiplication rate (PMR) in vaccinated subjects compared to infectivity controls ^{[1][2]}
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End point description:

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

End point type	Primary
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End point timeframe:

8 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 data, we have not provided this analysis at this time. The scientific paper can be uploaded following publication, if required.

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

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

End point values	Group 6 - Phase 2a	Group 7 - Phase 2a	Group 8 - Phase 2a	Group 9 - Phase 2a
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	9	8	4
Units: no of participants	14	9	8	4

Statistical analyses

No statistical analyses for this end point

Primary: Safety of RH5.1/AS01 in healthy malaria-naïve adults in the UK assed by actively and passively collected data on adverse events.

End point title	Safety of RH5.1/AS01 in healthy malaria-naïve adults in the UK assed by actively and passively collected data on adverse events. ^[3]
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End point description:

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

End point type	Primary
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End point timeframe:

Main study: 8 months.

For subset of subjects: up to 2.5 years (optional long-term follow-up).

Notes:

[3] - 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 data, we have not provided this analysis at this time. The scientific paper can be uploaded following publication, if required.

End point values	Group 1 - Phase 1a	Group 2 - Phase 1a	Group 3 - Phase 1a	Group 4 - Phase 1a
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	11
Units: Percentage	12	12	12	11

End point values	Group 1 - Phase 1a	Group 2 - Phase 1a	Group 3 - Phase 1a	Group 4 - Phase 1a
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	9	10	7	4
Units: Percentage	9	10	7	4

End point values	Group 5 - Phase 2a	Group 7 - Phase 2a	Group 5 - Phase 2a	Group 6 - Phase 2a
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	6	17	14
Units: Percentage	3	6	17	14

End point values	Group 7 - Phase 2a	Group 8 - Phase 2a	Group 9 - Phase 2a	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	9	8	4	
Units: Percentage	9	8	4	

Statistical analyses

No statistical analyses for this end point

Secondary: Humoral and cellular immunogenicity of RH5.1/AS01 when administered to healthy volunteers at different doses.

End point title	Humoral and cellular immunogenicity of RH5.1/AS01 when administered to healthy volunteers at different doses. ^[4]
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End point description:

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

End point type	Secondary
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End point timeframe:

8 months

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Due to the confidential nature of this data, we have not provided this analysis at this time. The scientific paper can be uploaded following publication, if required.

End point values	Group 1 - Phase 1a	Group 2 - Phase 1a	Group 3 - Phase 1a	Group 4 - Phase 1a
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	12	12	11
Units: n/a (multiple units)				
number (not applicable)	12	12	12	11

End point values	Group 5 - Phase 2a	Group 7 - Phase 2a		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	9		
Units: n/a (multiple units)				
number (not applicable)	17	9		

Statistical analyses

No statistical analyses for this end point

Secondary: Immunological readouts for association with a reduced parasite multiplication rate.

End point title	Immunological readouts for association with a reduced parasite multiplication rate. ^[5]
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End point description:

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

End point type	Secondary
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End point timeframe:

8 months

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Due to the confidential nature of this data, we have not provided this analysis at this time. The scientific paper can be uploaded following publication, if required.

End point values	Group 5 - Phase 2a	Group 6 - Phase 2a	Group 7 - Phase 2a	Group 8 - Phase 2a
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	14	9	8
Units: n/a (multiple units)				
number (not applicable)	17	14	9	8

End point values	Group 9 - Phase 2a			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: n/a (multiple units)				
number (not applicable)	4			

Statistical analyses

No statistical analyses for this end point

Secondary: Durability of any reduction in parasite multiplication rate (PMR) in vaccinated subjects in a second CHMI, ~4 months after the primary CHMI, compared to unvaccinated controls receiving a second challenge and newly recruited malaria-naïve primary controls

End point title	Durability of any reduction in parasite multiplication rate (PMR) in vaccinated subjects in a second CHMI, ~4 months after the primary CHMI, compared to unvaccinated controls receiving a second challenge and newly recruited malaria-naïve primary controls ^[6]
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End point description:

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

End point type	Secondary
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End point timeframe:

12 months

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Due to the confidential nature of this data, we have not provided this analysis at this time. The scientific paper can be uploaded following publication, if required.

End point values	Group 5 - Phase 2a	Group 6 - Phase 2a	Group 7 - Phase 2a	Group 8 - Phase 2a
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	14	9	8
Units: no of participants	17	14	9	8

End point values	Group 9 - Phase 2a			
Subject group type	Reporting group			
Number of subjects analysed	4			
Units: no of participants	4			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Data on solicited adverse events were collected for 7 days after vaccinated and unsolicited adverse events for 28 days post-vaccination.

Data on serious adverse events and adverse events of special interest were collected for the study duration.

Adverse event reporting additional description:

Following each vaccination, volunteers completed an electronic diary card for 28 days with adverse event data. Solicited AEs, collected for 7 days, included local AEs (pain, erythema, warmth, swelling and itching) and systemic AEs (headache, malaise, myalgia, arthralgia, feverishness, nausea, fatigue, and measured fever

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	Group 1 - Phase 1a
Reporting group description: -	
Reporting group title	Group 2 - Phase 1a
Reporting group description: -	
Reporting group title	Group 3 - Phase 1a
Reporting group description: -	
Reporting group title	Group 4 - Phase 1a
Reporting group description: -	
Reporting group title	Group 5 - Phase 2a
Reporting group description: -	
Reporting group title	Group 7 - Phase 2a
Reporting group description: -	

Serious adverse events	Group 1 - Phase 1a	Group 2 - Phase 1a	Group 3 - Phase 1a
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Tonsillectomy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			

subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 12 (8.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Group 4 - Phase 1a	Group 5 - Phase 2a	Group 7 - Phase 2a
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 14 (0.00%)	1 / 17 (5.88%)	1 / 9 (11.11%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Surgical and medical procedures			
Tonsillectomy			
subjects affected / exposed	0 / 14 (0.00%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pregnancy			
subjects affected / exposed	0 / 14 (0.00%)	0 / 17 (0.00%)	1 / 9 (11.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Psoriasis			
subjects affected / exposed	0 / 14 (0.00%)	0 / 17 (0.00%)	0 / 9 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Group 1 - Phase 1a	Group 2 - Phase 1a	Group 3 - Phase 1a
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	1 / 12 (8.33%)

General disorders and administration site conditions			
Local reaction	Additional description: Reaction at injection site		
subjects affected / exposed	1 / 12 (8.33%)	1 / 12 (8.33%)	1 / 12 (8.33%)
occurrences (all)	1	1	1
Chills			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 12 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Group 4 - Phase 1a	Group 5 - Phase 2a	Group 7 - Phase 2a
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 14 (21.43%)	5 / 17 (29.41%)	0 / 9 (0.00%)
General disorders and administration site conditions			
Local reaction	Additional description: Reaction at injection site		
subjects affected / exposed	3 / 14 (21.43%)	1 / 17 (5.88%)	0 / 9 (0.00%)
occurrences (all)	3	1	0
Chills			
subjects affected / exposed	0 / 14 (0.00%)	4 / 17 (23.53%)	0 / 9 (0.00%)
occurrences (all)	0	4	0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
15 September 2016	Addition of information regarding the use of the informed consent questionnaire. Correction of schedule of attendances table/blood volumes. Addition of wording to clarify that stated vaccine and adjuvant doses are nominal and may vary slightly due to dilution, mixing and administration techniques. Clarification added regarding ECG as part of screening procedures for Group 5-6. Change in wording of exclusion criterion regarding prior receipt of an investigational malaria vaccine. "History of splenectomy" removed as a separate exclusion criterion.
29 May 2017	Selection of dose of RH5.1/AS01 (10 µg) for Group 5 in the Phase IIa study. Guy's and St. Thomas' NIHR CRF to continue as a recruitment and vaccination site for the Phase IIa study. Removal of Cardiovascular Risk Score and checking of cholesterol levels from the protocol. Correction of blood volumes in schedule of attendances. Clarification of vaccination of 2 back-up volunteers in Group 5. Clarification of challenge at 2 weeks post final vaccination. Blinding of all Investigators (except the Principal Laboratory Investigator) to the malaria qPCR results during the post-challenge phase.
11 September 2017	Modification of bleed schedule for Groups 5 and 6. Correction/clarifications to footer of schedule of attendances tables.
23 November 2017	Addition of conflicts of interest statements of Investigators. Correction of minor typographical errors in the bleeding schedule tables.
23 January 2018	Addition of 3 new groups to assess the durability of the vaccine-induced reduction in PMR (Group 7 = Phase IIa malaria-exposed vaccinees; Group 8 = Phase IIa malaria-exposed controls; Group 9 = newly recruited malaria-naïve controls). Removal of microscopy as a diagnostic tool in the second homologous CHMI, and adjustment of the qPCR diagnostic criteria for commencing anti-malarials. Addition of 2 new exclusion criteria (Groups 5-9): G6PD deficiency and abnormal haemoglobinopathy screen. Clarification of 2 exclusion criteria (relating to Hepatitis C serology and contraindications relating to use of malarone and riamet).
07 February 2018	Clarification of scientific rationale for re-challenge of healthy volunteers.
10 October 2018	Addition of last visit for all vaccinated volunteers (Groups 1-4, 5 and 7) to assess durability of immune responses 1-2.5 years since their final vaccination.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported