



## 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
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##### 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**

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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**

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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: -

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Evidence for comparator: -

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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
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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
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Arm description:

Unvaccinated controls.

Arm type	Unvaccinated Control
No investigational medicinal product assigned in this arm	
<b>Arm title</b>	Group 4
Arm description: 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: 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: A dose of 5 x 10 <sup>10</sup> vp.	
<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 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: 50mcg of RTS,S and standard adult dose of AS01.	
<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	

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: 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	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 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
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Arm description:

RTS,S/AS01B

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

<b>Arm title</b>	Group 3
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Arm description:

Unvaccinated controls

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

<b>Arm title</b>	Group 4
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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: 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: RTS,S/AS01B	
Arm type	Malaria Challenge
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	

Number of subjects in period 6 <sup>[1]</sup>	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: 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: RTS,S/AS01B	
Arm type	Repeat Malaria Challenge
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 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: 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 values	Group 1	Group 2	Group 3
Number of subjects	20	17	6
Age categorical Units: Subjects			
Adults (18-64 years)	20	17	6
Gender categorical Units: Subjects			
Female	8	8	3
Male	12	9	3

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

## End points

### End points reporting groups

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 4
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 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 4

Reporting group description:

Unvaccinated controls

Reporting group title	Group 1
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Reporting group description:

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

Reporting group title	Group 2
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Reporting group description:

RTS,S/AS01B

Reporting group title	Group 3
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Reporting group description:

Unvaccinated controls

Reporting group title	Group 4
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Reporting group description:

Unvaccinated controls

Reporting group title	Group 1
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Reporting group description:

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

Reporting group title	Group 2
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Reporting group description:

RTS,S/AS01B

Reporting group title	Group 3
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Reporting group description:

Unvaccinated controls

Reporting group title	Group 1
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Reporting group description:

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

Reporting group title	Group 2
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Reporting group description:

RTS,S/AS01B

Reporting group title	Group 4
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Reporting group description:

Unvaccinated controls

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### Primary: Primary efficacy

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

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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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