Clinical trial results:
A phase IV study to determine the oral and genital tract concentration of Maraviroc required for ex vivo protection from HIV-1 using Maraviroc 300mg stat

Summary

EudraCT number	2012-003778-16
Trial protocol	GB
Global end of trial date	01 July 2015

Results information

Result version number	v1 (current)
This version publication date	06 December 2018
First version publication date	06 December 2018
Summary attachment (see zip file)	FINAL STUDY REPORT (MVC PREP Final Study Report v 17052016.pdf)

Trial information

Trial identification

Sponsor protocol code	J005

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Guy's and St Thomas' NHS Foundation Trust
Sponsor organisation address	Great Maze Pond, London, United Kingdom, SE19RT
Public contact	Dr Julie Fox, Guy's & St. Thomas' NHS Foundation Trust, 44 02071882643, julie.fox@gstt.nhs.uk
Scientific contact	Dr Julie Fox, Guy's & St. Thomas' NHS Foundation Trust, 44 02071882643, julie.fox@gstt.nhs.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	01 July 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 July 2015
Global end of trial reached?	Yes
Global end of trial date	01 July 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine concentration of Maraviroc in directly aspirated fluid and tissue from the genital tract and rectal compartments at different time periods following a single oral administration of Maraviroc 300mg in HIV-1-negative healthy volunteers

Protection of trial subjects:

Patients must refrain from drinking grapefruit juice during the study as very large quantities can affect the pharmacokinetics of Maraviroc. Patients are asked to refrain from caffeine and alcohol for 48 hours prior to dosing (if applicable) and until after biopsy.

Background therapy:

None

Evidence for comparator:

N/A

Actual start date of recruitment	18 December 2012
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 58
Worldwide total number of subjects	58
EEA total number of subjects	58

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)	58

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy adult volunteers were recruited through information presented in community organisations, hospitals, colleges, other institutions and/or advertisements, including email responses to expressed interest. 58 participants were recruited from two centres in London between 2013 and 2015.

Pre-assignment

Screening details:

Inclusion Criteria
Male or non-pregnant, non-lactating females
Age between 18 to 50 years, inclusive.
Body Mass Index (BMI) of 16 to 35 kg/m2, inclusive.
Negative antibody/antigen combined test for HIV-1 and HIV-2.
Absence of any significant health problems (in the opinion of the investigator)

Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Blinding implementation details:

N/A

Arms

Are arms mutually exclusive?	Yes
Arm title	ARM A - CONTROL

Arm description:

1st sampling at end of V2 (baseline)
2nd sampling 4 weeks post V2
No IMP administration

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	ARM B - MARAVIROC 300mg

Arm description:

1st sampling 2 hours post 1stMaraviroc 300g stat dose
2nd sampling 24 hours post 2nd Maraviroc 300mg stat dose

Arm type	Experimental
Investigational medicinal product name	MARAVIROC
Investigational medicinal product code	
Other name	CELSENTRI
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg single dose administered at two timepoints one month apart.

Arm title	ARM C - MARAVIROC 300mg

Arm description:

1st sampling 4 hours post 1stMaraviroc 300g stat dose
2nd sampling 36 hours post 2ndMaraviroc 300mg stat dose

Arm type	Experimental

Investigational medicinal product name	MARAVIROC
Investigational medicinal product code	
Other name	CELSENTRI
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg single dose administered at two timepoints one month apart.

Arm title	ARM D - MARAVIROC 300mg

Arm description:

1st sampling 6 hours post 1stMaraviroc 300mg stat dose
2nd sampling 48 hours post 2ndMaraviroc 300mg stat dose

Arm type	Experimental
Investigational medicinal product name	MARAVIROC
Investigational medicinal product code	
Other name	CELSENTRI
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg single dose administered at two timepoints one month apart.

Arm title	ARM E - MARAVIROC 300mg

Arm description:

1st sampling 12 hours post 1stMaraviroc 300mg stat dose
2nd sampling 72 hours post 2ndMaraviroc 300mg stat dose

Arm type	Experimental
Investigational medicinal product name	MARAVIROC
Investigational medicinal product code	
Other name	CELSENTRI
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg single dose administered at two timepoints one month apart.

Number of subjects in period 1	ARM A - CONTROL	ARM B - MARAVIROC 300mg	ARM C - MARAVIROC 300mg
Started	10	12	12
Completed	10	12	12

Number of subjects in period 1	ARM D - MARAVIROC 300mg	ARM E - MARAVIROC 300mg
Started	12	12
Completed	12	12

Baseline characteristics

Reporting groups

Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	58	58	
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)	58	58	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	28	28	
Male	30	30	

End points

End points reporting groups

Reporting group title	ARM A - CONTROL
Reporting group description:	
1st sampling at end of V2 (baseline) 2nd sampling 4 weeks post V2 No IMP administration	
Reporting group title	ARM B - MARAVIROC 300mg
Reporting group description:	
1st sampling 2 hours post 1stMaraviroc 300g stat dose 2nd sampling 24 hours post 2nd Maraviroc 300mg stat dose	
Reporting group title	ARM C - MARAVIROC 300mg
Reporting group description:	
1st sampling 4 hours post 1stMaraviroc 300g stat dose 2nd sampling 36 hours post 2ndMaraviroc 300mg stat dose	
Reporting group title	ARM D - MARAVIROC 300mg
Reporting group description:	
1st sampling 6 hours post 1stMaraviroc 300mg stat dose 2nd sampling 48 hours post 2ndMaraviroc 300mg stat dose	
Reporting group title	ARM E - MARAVIROC 300mg
Reporting group description:	
1st sampling 12 hours post 1stMaraviroc 300mg stat dose 2nd sampling 72 hours post 2ndMaraviroc 300mg stat dose	

Primary: Concentration of Maraviroc in fluid and tissue

End point title	Concentration of Maraviroc in fluid and tissue[1]
End point description:	
Concentration of Maraviroc in fluid and tissue from the genital tract and rectal compartments at different time periods following a single oral administration of Maraviroc 300mg in HIV-1-negative healthy volunteers	
End point type	Primary
End point timeframe:	
Duration of trial maximum 6 weeks	

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: See attached document for results

End point values	ARM A - CONTROL	ARM B - MARAVIROC 300mg	ARM C - MARAVIROC 300mg	ARM D - MARAVIROC 300mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	12	12	12
Units: whole	10	12	12	12

End point values	ARM E - MARAVIROC 300mg			

Subject group type	Reporting group			
Number of subjects analysed	12			
Units: whole	12			

Attachments (see zip file)	MVC PREP RESULTS TABLES.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Secondary Enpoint

End point title	Secondary Enpoint

End point description:

Level of Maraviroc required in the plasma, vagina, rectum and urethra for 100% ex vivo protection from HIV-1(this will inform on dosing of intermittent PrEP).

End point type	Secondary

End point timeframe:

0-6 weeks Follow up

End point values	ARM A - CONTROL	ARM B - MARAVIROC 300mg	ARM C - MARAVIROC 300mg	ARM D - MARAVIROC 300mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	12	12	12
Units: whole	10	12	12	12

End point values	ARM E - MARAVIROC 300mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: whole	12			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
0 to 6 weeks follow up visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	ARM B
Reporting group description: -	
Reporting group title	ARM C
Reporting group description: -	
Reporting group title	ARM A
Reporting group description: -	
Reporting group title	ARM D
Reporting group description: -	

Serious adverse events	ARM B	ARM C	ARM A
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	ARM D		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	ARM B	ARM C	ARM A
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	2 / 12 (16.67%)	0 / 10 (0.00%)
Nervous system disorders			

Headache subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Immune system disorders Post Exposure Prop (PEP). from sexual exposure subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	1 / 12 (8.33%) 1	0 / 10 (0.00%) 0
Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0	0 / 12 (0.00%) 0	0 / 10 (0.00%) 0

Non-serious adverse events	ARM D		
Total subjects affected by non-serious adverse events subjects affected / exposed	1 / 12 (8.33%)		
Nervous system disorders Headache subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Immune system disorders Post Exposure Prop (PEP). from sexual exposure subjects affected / exposed occurrences (all)	0 / 12 (0.00%) 0		
Gastrointestinal disorders Abdominal Pain subjects affected / exposed occurrences (all)	1 / 12 (8.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 October 2013	* Change in CI to Julie Fox * Label update to reflect change in CI
15 May 2014	Removal of Hep A from exclusion criteria
29 April 2015	Additional Control group included

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported