Clinical trial results:
A multicentre, 48 week randomised controlled factorial trial of adding maraviroc and/or metformin for hepatic steatosis in HIV-1-infected adults on combination antiretroviral therapy.

Summary

EudraCT number	2016-003575-21
Trial protocol	GB
Global end of trial date	06 November 2020

Results information

Result version number	v1 (current)
This version publication date	18 December 2021
First version publication date	18 December 2021

Trial information

Trial identification

Sponsor protocol code	N/A

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03129113
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	University College London
Sponsor organisation address	90 High Holborn, London, United Kingdom,
Public contact	Chief Investigator for MAVMET Trial, University College London, +44 07983806215, mrcctu.mavmet@ucl.ac.uk
Scientific contact	Chief Investigator for MAVMET Trial, University College London, +44 07983806215, mrcctu.mavmet@ucl.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	17 May 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 November 2020
Global end of trial reached?	Yes
Global end of trial date	06 November 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

MAVMET is trying to find out if maraviroc, metformin or a combination of both results in a change in percentage of liver fat as measured by MR PDFF a type of MRI imaging over 48 weeks.

Protection of trial subjects:

In consenting to the trial, patients are consenting to trial treatment, trial follow-up and data collection. However, an individual patient may stop treatment early or be stopped early for any of the following reasons:
Unacceptable toxicity or adverse event
Intercurrent illness that prevents further treatment
Any change in the patient's condition that justifies the discontinuation of treatment in the clinician's opinion
Inadequate compliance with the protocol treatment in the judgement of the treating physician
Withdrawal of consent for treatment by the patient

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 August 2017
Long term follow-up planned	No
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	0

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)	86
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment took place in 6 London hospitals between 19/03/2018 and 11/11/2019.

Pre-assignment

Screening details:

Males or females ≥35 years of age; Chronic HIV-1-infection for ≥5 years; On cART and with virological suppression (<50
copies/mL) for ≥1 year; either i) >1 abnormal (above the upper limit) of LFTS (ALT or AST) in the last 2 years with no other
explanation, ii) increased waist circumference, confirmed diagnosis of NAFLD on imaging or biopsy.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Maraviroc

Arm description:

Maraviroc p/o BID dosed as follows: 150mg BID in those on ritonavir-boosted PI, cobicistat-boosted PI, or ritonavir-boosted or cobicistat-boosted elvitegravir; 600mg BID in those on efavirenz (EFV)-based regimens, or 300mg BID in those on raltegravir (RAL), dolutegravir (DTG) or nevirapine (NVP)-based regimens.

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

Dosage and administration details:

Maraviroc p/o BID dosed as follows: 150mg BID in those on ritonavir-boosted PI, cobicistat-boosted PI, or ritonavir-boosted or cobicistat-boosted elvitegravir; 600mg BID in those on efavirenz (EFV)-based regimens, or 300mg BID in those on raltegravir (RAL), dolutegravir (DTG) or nevirapine (NVP)-based regimens.

Arm title	Metformin

Arm description:

Metformin p/o 500mg BID with or after food.

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

Dosage and administration details:

Metformin p/o 500mg BID with or after food.

Arm title	Maraviroc and metformin

Arm description: -

Arm type	Experimental

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

Dosage and administration details:

Maraviroc p/o BID dosed as follows: 150mg BID in those on ritonavir-boosted PI, cobicistat-boosted PI, or ritonavir-boosted or cobicistat-boosted elvitegravir; 600mg BID in those on efavirenz (EFV)-based regimens, or 300mg BID in those on raltegravir (RAL), dolutegravir (DTG) or nevirapine (NVP)-based regimens.

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

Dosage and administration details:

Metformin p/o 500mg BID with or after food.

Arm title	No drug

Arm description:

Control arm

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Maraviroc	Metformin	Maraviroc and metformin
Started	23	21	22
Completed	21	20	19
Not completed	2	1	3
Consent withdrawn by subject	2	1	2
Lost to follow-up	-	-	1

Number of subjects in period 1	No drug
Started	24
Completed	24
Not completed	0
Consent withdrawn by subject	-
Lost to follow-up	-

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	90	90	
Age categorical Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
median	52		
inter-quartile range (Q1-Q3)	47 to 57	-	
Gender categorical Units: Subjects			
Female	6	6	
Male	84	84	
Ethnicity Units: Subjects			
White	73	73	
Hispanic/Latino	3	3	
Black Caribbean/American	1	1	
Black African	9	9	
Mixed ethnic group	2	2	
Other	2	2	
Entry criteria Units: Subjects			
Raised LFTs only	1	1	
Increased waist circumference only	20	20	
Scan or biopsy diagnosis only	2	2	
Raised LFTs and large waist circumference	4	4	
Scan or biopsy diagnosis plus 1+ another criteria	63	63	
Baseline ART Units: Subjects			
INSTI	43	43	
PI	15	15	

NNRTI	32	32	

BMI			
Units: kg/m^2			
median	28		
inter-quartile range (Q1-Q3)	26 to 33	-	
Waist circumference			
Units: cm			
median	104		
inter-quartile range (Q1-Q3)	97 to 112	-	
ALT			
Units: U/L			
median	41		
inter-quartile range (Q1-Q3)	31 to 61	-	
AST			
Units: U/L			
median	32		
inter-quartile range (Q1-Q3)	27 to 41	-	
ALP			
Units: U/L			
median	83		
inter-quartile range (Q1-Q3)	66 to 103	-	
GGT			
Units: U/L			
median	44		
inter-quartile range (Q1-Q3)	27 to 70	-	
CD4 count			
Units: cells/mm^3			
median	672		
inter-quartile range (Q1-Q3)	451 to 831	-	
CD4 %			
Units: percent			
median	34		
inter-quartile range (Q1-Q3)	29 to 41	-	
CD8 count			
Units: cells/mm^3			
median	661		
inter-quartile range (Q1-Q3)	543 to 834	-	
CD8 %			
Units: percent			
median	35		
inter-quartile range (Q1-Q3)	31 to 43	-	

Subject analysis sets

Subject analysis set title	Scans as initially planned
Subject analysis set type	Per protocol

Subject analysis set description:

This dataset is limited to those who had their W48 scans within a +/-6 week window around W48. This excludes those who had their treatment lengthened due to the pandemic.

Reporting group values	Scans as initially planned		
Number of subjects	62		
Age categorical			
Units: Subjects			
In utero			
Preterm newborn infants (gestational age < 37 wks)			
Newborns (0-27 days)			
Infants and toddlers (28 days-23 months)			
Children (2-11 years)			
Adolescents (12-17 years)			
Adults (18-64 years)			
From 65-84 years			
85 years and over			
Age continuous			
Units: years			
median	53		
inter-quartile range (Q1-Q3)	47 to 57		
Gender categorical			
Units: Subjects			
Female	57		
Male	5		
Ethnicity			
Units: Subjects			
White	51		
Hispanic/Latino	2		
Black Caribbean/American	1		
Black African	5		
Mixed ethnic group	2		
Other	1		
Entry criteria			
Units: Subjects			
Raised LFTs only	1		
Increased waist circumference only	14		
Scan or biopsy diagnosis only	2		
Raised LFTs and large waist circumference	4		
Scan or biopsy diagnosis plus 1+ another criteria	41		
Baseline ART			
Units: Subjects			
INSTI	27		
PI	11		
NNRTI	24		
BMI			
Units: kg/m^2			
median	28		
inter-quartile range (Q1-Q3)	26 to 32		
Waist circumference			
Units: cm			
median	105		

inter-quartile range (Q1-Q3)	98 to 112		
ALT Units: U/L median inter-quartile range (Q1-Q3)	 39 31 to 57		
AST Units: U/L median inter-quartile range (Q1-Q3)	 31 27 to 41		
ALP Units: U/L median inter-quartile range (Q1-Q3)	 79 62 to 102		
GGT Units: U/L median inter-quartile range (Q1-Q3)	 42 25 to 70		
CD4 count Units: cells/mm^3 median inter-quartile range (Q1-Q3)	 677 430 to 801		
CD4 % Units: percent median inter-quartile range (Q1-Q3)	 35 29 to 41		
CD8 count Units: cells/mm^3 median inter-quartile range (Q1-Q3)	 663 543 to 834		
CD8 % Units: percent median inter-quartile range (Q1-Q3)	 35 31 to 44		

End points

End points reporting groups

Reporting group title	Maraviroc
Reporting group description:	
Maraviroc p/o BID dosed as follows: 150mg BID in those on ritonavir-boosted PI, cobicistat-boosted PI, or ritonavir-boosted or cobicistat-boosted elvitegravir; 600mg BID in those on efavirenz (EFV)-based regimens, or 300mg BID in those on raltegravir (RAL), dolutegravir (DTG) or nevirapine (NVP)-based regimens.	
Reporting group title	Metformin
Reporting group description:	
Metformin p/o 500mg BID with or after food.	
Reporting group title	Maraviroc and metformin
Reporting group description: -	
Reporting group title	No drug
Reporting group description:	
Control arm	
Subject analysis set title	Scans as initially planned
Subject analysis set type	Per protocol
Subject analysis set description:	
This dataset is limited to those who had their W48 scans within a +/-6 week window around W48. This excludes those who had their treatment lengthened due to the pandemic.	

Primary: Change in % liver fat to 48 weeks (all participants)

End point title	Change in % liver fat to 48 weeks (all participants)
End point description:	
End point type	Primary
End point timeframe:	
48 weeks from randomisation	

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	19	22
Units: liver fat %				
arithmetic mean (standard deviation)	2.2 (± 4.6)	1.3 (± 4.1)	0.8 (± 5.7)	1.4 (± 4.0)

Statistical analyses

Statistical analysis title	Absolute change: maraviroc
Comparison groups	No drug v Maraviroc

Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.45
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.53
upper limit	0.68

Statistical analysis title	Absolute change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.81
upper limit	0.56

Statistical analysis title	Absolute change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.23
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-1.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.74
upper limit	0.65

Statistical analysis title	Relative change: maraviroc

Comparison groups	Maraviroc v No drug
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.14

Statistical analysis title	Relative change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.14

Statistical analysis title	Relative change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.57
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.18

Primary: Change in % liver fat to 48 weeks (scans performed as planned)	
End point title	Change in % liver fat to 48 weeks (scans performed as planned)

End point description:

End point type	Primary

End point timeframe:

Only scans performed in original W48 window (+/- 6 weeks)

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	14	16	15	17
Units: liver fat %				
arithmetic mean (standard deviation)	0.3 (± 2.6)	0.6 (± 4.2)	-0.2 (± 5.8)	1.7 (± 2.2)

Statistical analyses

Statistical analysis title	Absolute change: maraviroc
Comparison groups	Maraviroc v No drug
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.15
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.64
upper limit	0.25

Statistical analysis title	Absolute change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.008
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-1.45

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.53
upper limit	-0.38

Statistical analysis title	Absolute change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-2.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.66
upper limit	-0.63

Statistical analysis title	Relative change: maraviroc
Comparison groups	Maraviroc v No drug
Number of subjects included in analysis	31
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.31
upper limit	0.1

Statistical analysis title	Relative change: metformin
Comparison groups	No drug v Metformin

Number of subjects included in analysis	33
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.37
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.12

Statistical analysis title	Relative change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.17
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.09

Secondary: Change in hepatic steatosis grade

End point title	Change in hepatic steatosis grade
End point description:	

End point type	Secondary
End point timeframe:	
Up to W48	

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	19	22
Units: Change in grade				
-2	0	0	0	1
-1	1	1	3	0
None	13	14	12	17

+1	6	4	4	4
+2	1	1	0	0

Statistical analyses

Statistical analysis title	Change in grade: all four arms
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin v No drug
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.55
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Change in grade: maraviroc vs control
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin v No drug
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Change in grade: metformin vs control
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin v No drug
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.56
Method	Wilcoxon (Mann-Whitney)

Secondary: Quality of life: mobility

End point title	Quality of life: mobility

End point description:

End point type	Secondary

End point timeframe:

At 48 weeks

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	19	24
Units: EQ-5D				
No change	20	15	15	17
Improved	1	3	2	4
Worsened	0	2	2	3

Statistical analyses

Statistical analysis title	Comparison of all arms
Comparison groups	Metformin v Maraviroc and metformin v No drug v Maraviroc
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.53
Method	Wilcoxon (Mann-Whitney)

Secondary: Quality of life: Self-care

End point title	Quality of life: Self-care

End point description:

End point type	Secondary

End point timeframe:

At W48

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	19	24
Units: EQ-5D level change				
No Change	21	15	16	23
Improved	0	3	0	1
Worsened	0	2	3	0

Statistical analyses

Statistical analysis title	Comparison of all arms
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin v No drug

Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015
Method	Wilcoxon (Mann-Whitney)

Secondary: Quality of life: activities

End point title	Quality of life: activities

End point description:

End point type	Secondary

End point timeframe:

At W48

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	19	24
Units: EQ-5D level change				
No change	21	19	15	14
Improved	0	1	1	5
Worsened	0	0	3	5

Statistical analyses

Statistical analysis title	Comparison of all arms
Comparison groups	Metformin v Maraviroc and metformin v Maraviroc v No drug
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.003
Method	Wilcoxon (Mann-Whitney)

Secondary: Quality of life: pain

End point title	Quality of life: pain

End point description:

End point type	Secondary

End point timeframe:

At W48

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	19	24
Units: EQ-5D level change				
No change	15	12	13	8
Improved	4	4	2	4
Worsened	2	4	4	12

Statistical analyses

Statistical analysis title	Comparison of all arms
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin v No drug
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.065
Method	Wilcoxon (Mann-Whitney)

Secondary: Quality of life: anxiety

End point title	Quality of life: anxiety
End point description:	
End point type	Secondary
End point timeframe:	
At W48	

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	19	24
Units: EQ-5D level change				
No change	11	12	14	16
Improved	3	4	1	1
Worsened	7	4	4	7

Statistical analyses

Statistical analysis title	Comparison of all arms
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin v No drug
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.58
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in self-reported health score

End point title	Change in self-reported health score

End point description:

End point type	Secondary

End point timeframe:

At W48

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	19	24
Units: health score				
median (inter-quartile range (Q1-Q3))	0 (-10 to 8)	5 (-5 to 8)	-5 (-8 to 10)	0 (-20 to 5)

Statistical analyses

Statistical analysis title	Comparison of all arms
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin v No drug
Number of subjects included in analysis	84
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.63
Method	Wilcoxon (Mann-Whitney)

Secondary: Adherence to trial drugs

End point title	Adherence to trial drugs[1]

End point description:

End point type	Secondary

End point timeframe:

Over all treatment

Notes:

[1] - 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: Outcome is adherence to trial drugs so is limited only to the arms that are taking trial drugs.

End point values	Maraviroc	Metformin	Maraviroc and metformin	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	23	21	22	
Units: Stopped treatment early				
Yes	3	4	4	
No	20	17	18	

Statistical analyses

Statistical analysis title	Stopped early
Comparison groups	Maraviroc and metformin v Metformin v Maraviroc
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.84
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Had at least one dose decrease
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.27
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Missed any doses
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.28
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Adherence at W4
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin

Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.36
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Adherence at W12
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.23
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Adherence at W24
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.94
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Adherence at W36
Comparison groups	Maraviroc v Metformin v Maraviroc and metformin
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Adherence at W48
Comparison groups	Maraviroc and metformin v Maraviroc v Metformin
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.55
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in CD4 count	
End point title	Change in CD4 count
End point description:	
End point type	Secondary
End point timeframe:	
Up to W48	

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	23
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	667 (614 to 720)	665 (610 to 720)	737 (683 to 791)	648 (599 to 698)

Statistical analyses

Statistical analysis title	Absolute change: maraviroc
Comparison groups	Maraviroc v No drug
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.63
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-61
upper limit	99

Statistical analysis title	Absolute change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	16

Confidence interval	
level	95 %
sides	2-sided
lower limit	-63
upper limit	95

Statistical analysis title	Absolute change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	89
Confidence interval	
level	95 %
sides	2-sided
lower limit	12
upper limit	166

Statistical analysis title	Relative change: maraviroc
Comparison groups	No drug v Maraviroc
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.82
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.15

Statistical analysis title	Relative change: metformin
Comparison groups	No drug v Metformin

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.94
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.16

Statistical analysis title	Relative change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.25

Secondary: Change in CD4 %	
End point title	Change in CD4 %
End point description:	

End point type	Secondary
End point timeframe:	
Up to W48	

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	23
Units: CD4%				
arithmetic mean (confidence interval 95%)	34 (32 to 35)	34 (32 to 35)	34 (33 to 36)	35 (33 to 36)

Statistical analyses

Statistical analysis title	Absolute change: maraviroc
Comparison groups	Maraviroc v No drug
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.44
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.5
upper limit	1.54

Statistical analysis title	Absolute change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.43
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.97
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.4
upper limit	1.44

Statistical analysis title	Absolute change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.76
upper limit	2.32

Statistical analysis title	Relative change: maraviroc
Comparison groups	No drug v Maraviroc
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.04
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.04

Statistical analysis title	Relative change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.12
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.02

Statistical analysis title	Relative change: maraviroc and metformin

Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.87
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.08

Secondary: Change in CD8 count

End point title	Change in CD8 count
End point description:	
End point type	Secondary
End point timeframe:	
Up to W48	

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	23
Units: cells/mm^3				
arithmetic mean (confidence interval 95%)	752 (664 to 840)	767 (676 to 858)	817 (727 to 908)	689 (606 to 770)

Statistical analyses

Statistical analysis title	Absolute change: maraviroc
Comparison groups	No drug v Maraviroc
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.28
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	62

Confidence interval	
level	95 %
sides	2-sided
lower limit	-51
upper limit	175

Statistical analysis title	Absolute change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.25
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	80
Confidence interval	
level	95 %
sides	2-sided
lower limit	-58
upper limit	217

Statistical analysis title	Absolute change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.02
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	128
Confidence interval	
level	95 %
sides	2-sided
lower limit	20
upper limit	236

Statistical analysis title	Relative change: maraviroc
Comparison groups	No drug v Maraviroc

Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.24
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.07
upper limit	0.25

Statistical analysis title	Relative change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.36
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.25

Statistical analysis title	Relative change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.03
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.02
upper limit	0.33

Secondary: Change in CD8 %

End point title	Change in CD8 %

End point description:

End point type	Secondary

End point timeframe:

Up to W48

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	17	17	18	22
Units: CD8 %				
arithmetic mean (confidence interval 95%)	37 (34 to 41)	38 (35 to 41)	37 (34 to 41)	40 (36 to 42)

Statistical analyses

Statistical analysis title	Absolute change: maraviroc
Comparison groups	No drug v Maraviroc
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.44
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-2.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.58
upper limit	3.32

Statistical analysis title	Absolute change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.58
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-1.33

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.11
upper limit	3.45

Statistical analysis title	Absolute change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-1.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.96
upper limit	3.16

Statistical analysis title	Relative change: maraviroc
Comparison groups	No drug v Maraviroc
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.92
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.13

Statistical analysis title	Relative change: metformin
Comparison groups	No drug v Metformin

Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.67
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.09

Statistical analysis title	Relative change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.98
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	0.12

Secondary: Change in ALT over time
End point title: Change in ALT over time
End point description:
End point type: Secondary
End point timeframe: Up to W48

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	18	24
Units: U/L				
arithmetic mean (confidence interval 95%)	47 (35 to 59)	46 (33 to 58)	44 (31 to 57)	52 (40 to 63)

Statistical analyses

Statistical analysis title	Absolute change: maraviroc
Comparison groups	Maraviroc v No drug
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.62
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23
upper limit	14

Statistical analysis title	Absolute change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.48
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23
upper limit	11

Statistical analysis title	Absolute change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-26
upper limit	11

Statistical analysis title	Relative change: maraviroc
Comparison groups	No drug v Maraviroc
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.99
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.32
upper limit	0.32

Statistical analysis title	Relative change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.55
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.37
upper limit	0.2

Statistical analysis title	Relative change: maraviroc and metformin

Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	0.2

Secondary: Change in AST	
End point title	Change in AST
End point description:	
End point type	Secondary
End point timeframe:	
Up to W48	

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	19	19	22
Units: U/L				
arithmetic mean (confidence interval 95%)	35 (29 to 40)	33 (27 to 39)	35 (29 to 41)	39 (34 to 44)

Statistical analyses

Statistical analysis title	Absolute change: maraviroc
Comparison groups	No drug v Maraviroc
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-5

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	5

Statistical analysis title	Absolute change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.16
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	2

Statistical analysis title	Absolute change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.41
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13
upper limit	5

Statistical analysis title	Relative change: maraviroc
Comparison groups	No drug v Maraviroc

Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.46
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	0.12

Statistical analysis title	Relative change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.06

Statistical analysis title	Relative change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.65
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.16

Secondary: Change in ALP

End point title	Change in ALP

End point description:

End point type	Secondary

End point timeframe:

Up to W48

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	20	19	24
Units: U/L				
arithmetic mean (confidence interval 95%)	80 (74 to 85)	77 (71 to 83)	70 (64 to 76)	84 (78 to 89)

Statistical analyses

Statistical analysis title	Absolute change: maraviroc
Comparison groups	Maraviroc v No drug
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.29
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	4

Statistical analysis title	Absolute change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.15
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-6

Confidence interval	
level	95 %
sides	2-sided
lower limit	-14
upper limit	2

Statistical analysis title	Absolute change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21
upper limit	-5

Statistical analysis title	Relative change: maraviroc
Comparison groups	No drug v Maraviroc
Number of subjects included in analysis	45
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.26
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.05

Statistical analysis title	Relative change: metformin
Comparison groups	No drug v Metformin

Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.16
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.17
upper limit	0.03

Statistical analysis title	Relative change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.002
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	-0.07

Secondary: Change in GGT	
End point title	Change in GGT
End point description:	

End point type	Secondary
End point timeframe:	
Up to W48	

End point values	Maraviroc	Metformin	Maraviroc and metformin	No drug
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	20	18	19	24
Units: U/L				
arithmetic mean (confidence interval 95%)	61 (47 to 74)	51 (37 to 65)	62 (48 to 76)	53 (40 to 65)

Statistical analyses

Statistical analysis title	Absolute change: maraviroc
Comparison groups	Maraviroc v No drug
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.38
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	26

Statistical analysis title	Absolute change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.62
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15
upper limit	9

Statistical analysis title	Absolute change: maraviroc and metformin
Comparison groups	No drug v Maraviroc and metformin

Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.35
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11
upper limit	30

Statistical analysis title	Relative change: maraviroc
Comparison groups	No drug v Maraviroc
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.21
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.09
upper limit	0.43

Statistical analysis title	Relative change: metformin
Comparison groups	No drug v Metformin
Number of subjects included in analysis	42
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.84
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.2

Statistical analysis title	Relative change: maraviroc and metformin

Comparison groups	No drug v Maraviroc and metformin
Number of subjects included in analysis	43
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	Regression, Linear
Parameter estimate	Mean difference (net)
Point estimate	0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.49

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Across the entire trial - up to W48 visit	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21

Reporting groups	
Reporting group title	Maraviroc
Reporting group description:	
Maraviroc p/o BID dosed as follows: 150mg BID in those on ritonavir-boosted PI, cobicistat-boosted PI, or ritonavir-boosted or cobicistat-boosted elvitegravir; 600mg BID in those on efavirenz (EFV)-based regimens, or 300mg BID in those on raltegravir (RAL), dolutegravir (DTG) or nevirapine (NVP)-based regimens.	
Reporting group title	Metformin
Reporting group description:	
Metformin p/o 500mg BID with or after food.	
Reporting group title	Maraviroc and metformin
Reporting group description: -	
Reporting group title	No drug
Reporting group description:	
Control arm	

Serious adverse events	Maraviroc	Metformin	Maraviroc and metformin
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 23 (8.70%)	1 / 21 (4.76%)	3 / 22 (13.64%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 23 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 23 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac ischemia			

subjects affected / exposed	1 / 23 (4.35%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Right retinal 'u' tear			
subjects affected / exposed	0 / 23 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	1 / 23 (4.35%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza A pneumonia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	No drug		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac ischemia			

subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Right retinal 'u' tear			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pyelonephritis			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Influenza A pneumonia			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Maraviroc	Metformin	Maraviroc and metformin
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 23 (13.04%)	7 / 21 (33.33%)	7 / 22 (31.82%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma of skin			
subjects affected / exposed	1 / 23 (4.35%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Squamous cell carcinoma			
subjects affected / exposed	0 / 23 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 23 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	2
Nervous system disorders			

Migraine			
subjects affected / exposed	0 / 23 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Dizziness			
subjects affected / exposed	0 / 23 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 23 (0.00%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Labyrinthitis			
subjects affected / exposed	1 / 23 (4.35%)	0 / 21 (0.00%)	0 / 22 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	1 / 23 (4.35%)	1 / 21 (4.76%)	1 / 22 (4.55%)
occurrences (all)	1	1	1
Diarrhoea			
subjects affected / exposed	0 / 23 (0.00%)	5 / 21 (23.81%)	3 / 22 (13.64%)
occurrences (all)	0	7	4
Flatulance			
subjects affected / exposed	0 / 23 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
GI upset			
subjects affected / exposed	0 / 23 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Stomach discomfort			
subjects affected / exposed	0 / 23 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Vomiting			
subjects affected / exposed	0 / 23 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1
Psychiatric disorders			
Grief reaction			
subjects affected / exposed	0 / 23 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1

Musculoskeletal and connective tissue disorders			
Knee cramp			
subjects affected / exposed	0 / 23 (0.00%)	1 / 21 (4.76%)	0 / 22 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Surgical site infection			
subjects affected / exposed	0 / 23 (0.00%)	0 / 21 (0.00%)	1 / 22 (4.55%)
occurrences (all)	0	0	1

Non-serious adverse events	No drug		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 24 (4.17%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant melanoma of skin			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Squamous cell carcinoma			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Migraine			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 24 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 24 (4.17%)		
occurrences (all)	1		
Ear and labyrinth disorders			
Labyrinthitis			

subjects affected / exposed occurrences (all)	0 / 24 (0.00%) 0		
Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Flatulance subjects affected / exposed occurrences (all) GI upset subjects affected / exposed occurrences (all) Stomach discomfort subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all)	 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0 0 / 24 (0.00%) 0		
Psychiatric disorders Grief reaction subjects affected / exposed occurrences (all)	 0 / 24 (0.00%) 0		
Musculoskeletal and connective tissue disorders Knee cramp subjects affected / exposed occurrences (all)	 0 / 24 (0.00%) 0		
Infections and infestations Surgical site infection subjects affected / exposed occurrences (all)	 0 / 24 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 April 2020	Due to the Covid-19 pandemic, participants were not able to attend their final visit as planned. The protocol was changed to allow those participants to continue on their randomised treatments until it was safe for them to visit clinics again.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported