Clinical trial results:
SSAT058: A phase IV, open-label, multi centre pilot study to assess changes in cerebral function parameters in patients without perceived Central Nervous System (CNS) symptoms when switched from tenofovir/emtricitabine/efavirenz (Atripla®) to a fixed dose combination of tenofovir/emtricitabine/rilpivirine (Eviplera®).

Summary

EudraCT number	2014-002284-15
Trial protocol	GB
Global end of trial date	10 February 2017

Results information

Result version number	v1 (current)
This version publication date	28 June 2018
First version publication date	28 June 2018

Trial information

Trial identification

Sponsor protocol code	SSAT058

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02529059
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	St Stephen's AIDS Trust
Sponsor organisation address	Chelsea Chambers, 262a Fulham Road, London, United Kingdom, SW10 9EL
Public contact	Marita Marshall, St Stephen's AIDS Trust, +44 2038280567, marita.marshall@ststcr.com
Scientific contact	Prof. Mark Nelson, Chelsea and Westminster Hospital, mark.nelson@chelwest.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	18 December 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	10 February 2017
Global end of trial reached?	Yes
Global end of trial date	10 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess changes in neuropsychiatric and central nervous system (CNS) parameters in patients without perceived Central Nervous System (CNS) symptoms after 4 weeks of switching from Atripla (TDF/FTC/EFV) to Eviplera (TDF/FTC/RPV).

Protection of trial subjects:

The protocol was written, and the study was conducted according to the ICH Harmonized Tripartite Guideline on Good Clinical Practice, E6 and the principles of the Declaration of Helsinki. The protocol was approved by the National Regulator and an Independent Ethics Committee as required by national legislation.

Written informed consent was obtained from each subject prior to evaluations being performed for eligibility. Subjects were given adequate time to review the information in the informed consent and were encouraged to ask questions concerning all portions of the conduct of the study to ensure understanding. The purpose of the study together with the procedures benefits and risks of the study; any discomforts and the precautions taken was described during the consent process; allowing subject to make an informed decision about participation. Subjects were also informed of their right to discontinue from the study at any time without any detriment.

The inclusion/exclusion criteria were designed to eliminate subjects who may have been put at risk by participating in the study. Women of childbearing potential were required to have a negative pregnancy test at screening in order to exclude any participants who may have been pregnant, and these participants (along with heterosexually active males) were required to use effective birth control for the duration of the study.

Safety and tolerability of medications were assessed by questions, physical examination (as required) and laboratory parameters. Any changes in health status during the study were recorded and followed up by the clinical team.

Background therapy:

Only patients who were taking Atripla for at least 12 weeks, with established viral load suppression to undetectable levels (by local assay), were included in this study.

Evidence for comparator: -

Actual start date of recruitment	14 December 2015
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: 42
Worldwide total number of subjects	42
EEA total number of subjects	42

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)	40
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Patients were competitively recruited from 4 sites in the UK; Elton John Centre (Brighton), Chelsea & Westminster Hospital (London), St Mary's Hospital (London) and Guy's & St. Thomas' Hospital (London).

42 patients were recruited from Dec 2015 to June 2016. One patient was deemed non-evaluable at baseline and is not included in the analysis.

Pre-assignment

Screening details:

Four patients screened for the study were deemed ineligible:
- Due to previous nRTI treatment
- Could not comply with contraception requirements
- Could not comply with treatment switch requirements
- Presented with pre-existing cognitive issues at screening

Period 1

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

Arms

Arm title	Experimental Arm

Arm description:

Single Arm Study - all patients were switched from tenofovir/emtricitabine/efavirenz (Atripla®) to a fixed dose combination of tenofovir/emtricitabine/rilpivirine (Eviplera®).

Arm type	Experimental
Investigational medicinal product name	Eviplera
Investigational medicinal product code	J05AR08
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

A single-pill fixed dose combination of tenofovir 245mg, emtricitabine 200mg and rilpivirine 25mg once daily.

Number of subjects in period 1	Experimental Arm
Started	42
Week 4	40
Week 12	39
week 24	39
Completed	39
Not completed	3
Consent withdrawn by subject	1
Adverse event, non-fatal	1

Determined ineligible	1

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	42	42	
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)	40	40	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	47.3		
full range (min-max)	31.2 to 68.4	-	
Gender categorical Units: Subjects			
Female	3	3	
Male	39	39	
Ethnicity Units: Subjects			
Unknown	2	2	
English/Welsh/Scottish/Northern Irish/British	26	26	
Irish	1	1	
other White	7	7	
White & Black African	1	1	
Mixed/multiple ethnicity)	1	1	
African	2	2	
Caribbean	1	1	
other	1	1	
Duration of prior Atripla treatment Units: Days			
median	1778		
inter-quartile range (Q1-Q3)	938 to 2656	-	

End points

End points reporting groups

Reporting group title	Experimental Arm

Reporting group description:

Single Arm Study - all patients were switched from tenofovir/emtricitabine/efavirenz (Atripla®) to a fixed dose combination of tenofovir/emtricitabine/rilpivirine (Eviplera®).

Subject analysis set title	Baseline
Subject analysis set type	Full analysis

Subject analysis set description:

All patients attending baseline visit (pre-switch).

Note: 1 patient excluded from analysis due to protocol deviation

Subject analysis set title	Week 4
Subject analysis set type	Full analysis

Subject analysis set description:

All patients attending Week 4 visit post switch

Subject analysis set title	Week 12
Subject analysis set type	Full analysis

Subject analysis set description:

All patients attending Week 12 visit post switch

Subject analysis set title	Week 24
Subject analysis set type	Full analysis

Subject analysis set description:

All patients attending Week 24 visit (post switch)

Primary: Proportion of patients with grade 2-4 CNS AE at Baseline, Week 4 and Week 12 , as reported in the CNS questionnaire:

End point title	Proportion of patients with grade 2-4 CNS AE at Baseline, Week 4 and Week 12 , as reported in the CNS questionnaire:[1]

End point description:

AEs were graded using a study questionnaire based on the AIDS Clinical Trials Group (ACTG) grading scale.

These were then coded as:
0 - None
1 - Mild
2 - Moderate
3 - Severe

The following results represent frequency of patients with at least one moderate (or severe) AE from this questionnaire.

McNemars Chi squared value for change in individual toxicities given in attached report.

End point type	Primary

End point timeframe:

Baseline, Week 4 and Week 12 post switch

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: A summary listing of the 'proportion of patients affected' is the only measure required by protocol

End point values	Baseline	Week 4	Week 12	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	41	40	39	
Units: Patients				
Any	14	7	9	
Dizziness	3	1	1	
Depression/low mood	3	1	3	
Insomnia/sleeplessness	5	4	5	
Anxiety/nervousness	3	1	0	
Confusion	1	1	0	
Impaired concentration/attention	3	1	1	
Headache	3	1	1	
Somnolence/daytime sleepiness	2	5	2	
Aggressive mood/behaviour	2	0	1	
Abnormal dreams	9	1	1	

Attachments (see zip file)	SSAT058 CNS Questionnaire results.pdf

Statistical analyses

No statistical analyses for this end point

Primary: Median number of grade 2+ neuropsychiatric and CNS AEs, as reported in the CNS questionnaire at Baseline, Week 4 and Week 12

End point title	Median number of grade 2+ neuropsychiatric and CNS AEs, as reported in the CNS questionnaire at Baseline, Week 4 and Week 12

End point description:

Please note that this was not considered a normalised dataset, and therefore range is given instead of the originally intended 95% CI. Incidence of grade 2+ AEs were transformed into a score out of 100 to facilitate comparison.

End point type	Primary

End point timeframe:

Basseline, Week 4 and Week 12

End point values	Baseline	Week 4	Week 12	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	41	40	39	
Units: Score (/100)				
median (full range (min-max))	0 (0 to 30)	0 (0 to 25)	0 (0 to 25)	

Statistical analyses

Statistical analysis title	Baseline to week 4
Statistical analysis description: % improvement in total CNS score from baseline	
Comparison groups	Baseline v Week 4
Number of subjects included in analysis	81
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.064
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Baseline to week 12
Statistical analysis description: % improvement in total CNS score from baseline	
Comparison groups	Baseline v Week 12
Number of subjects included in analysis	80
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.022
Method	Wilcoxon (Mann-Whitney)

Primary: Median CNS toxicity score (from CNS questionnaire) from baseline compared to Week 4 and Week 12

End point title	Median CNS toxicity score (from CNS questionnaire) from baseline compared to Week 4 and Week 12
End point description: All grades of CNS adverse events reported in the questionnaire were summed together. This total was then transformed into a score from 0 to 100, where a score of 0 represents no adverse events, and 100 is all events reported as 'Severe'. Due to this dataset not being normalised, inter-quartile range is given instead of the protocol specified 95% CI.	
End point type	Primary
End point timeframe: Baseline to Week 4 and Week 12	

End point values	Baseline	Week 4	Week 12	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	41	40	39	
Units: Score (/100)				
median (inter-quartile range (Q1-Q3))	10 (3 to 23)	7 (3 to 13)	10 (3 to 17)	

Statistical analyses

Statistical analysis title	Baseline to week 4
Comparison groups	Baseline v Week 4
Number of subjects included in analysis	81
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.028
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Baseline to week 12
Comparison groups	Baseline v Week 12
Number of subjects included in analysis	80
Analysis specification	Post-hoc
Analysis type	other
P-value	= 0.064
Method	Wilcoxon (Mann-Whitney)

Primary: Rate of toxicity as measured by change in sleep score from baseline to Week 4, Week 12 & Week 24

End point title	Rate of toxicity as measured by change in sleep score from baseline to Week 4, Week 12 & Week 24

End point description:

Please note that this was not considered a normalised dataset, and therefore inter-quartile range is given instead of the originally intended 95% CI.

All reported sleep adverse effects were transformed into a score out of 100 for ease of comparison.

'Change from baseline' measures the improvement in responses. A positive value indicates a reduction in reported adverse events.

Note: Week 24 time-point is considered a secondary endpoint.

End point type	Primary

End point timeframe:

Baseline to week 4 / week 12

End point values	Baseline	Week 4	Week 12	Week 24
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	40	39	39[2]
Units: Score (/100)				
median (inter-quartile range (Q1-Q3))				
Sleep score	22 (20 to 32)	20 (14 to 29)	19 (14 to 27)	20 (14 to 26)
Change from baseline	0 (0 to 0)	2 (-1 to 8)	4 (-1 to 10)	3 (-2 to 10)

Notes:

[2] - Secondary endpoint

Attachments (see zip file)	SSAT058 Sleep questionnaire results.pdf

Statistical analyses

Statistical analysis title	Baseline to week 4
Comparison groups	Baseline v Week 4
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.008
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Baseline to week 12
Comparison groups	Week 12 v Baseline
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Baseline to week 24
Comparison groups	Week 24 v Baseline
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.009
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Friedman's test
Comparison groups	Baseline v Week 4 v Week 12 v Week 24
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.03
Method	Friedman's test

Secondary: Proportion of patients with grade 2-4 CNS AE at Week 24 , as reported in the CNS questionnaire:

End point title	Proportion of patients with grade 2-4 CNS AE at Week 24 , as reported in the CNS questionnaire:

End point description:	
McNemars Chi squared value for change in individual toxicities given in attached report.	
End point type	Secondary
End point timeframe:	
Week 24 post treatment switch	

End point values	Week 24			
Subject group type	Subject analysis set			
Number of subjects analysed	37[3]			
Units: Patients				
Any	10			
Dizziness	0			
Depression/low mood	2			
Insomnia/sleeplessness	6			
Anxiety/nervousness	2			
Confusion	0			
Impaired concentration/attention	1			
Headache	1			
Somnolence/daytime sleepiness	3			

Notes:

[3] - 2 patients DNA

Statistical analyses

No statistical analyses for this end point

Secondary: Median number of grade 2+ neuropsychiatric and CNS AEs, as reported in the CNS questionnaire at Week 24

End point title	Median number of grade 2+ neuropsychiatric and CNS AEs, as reported in the CNS questionnaire at Week 24
End point description:	
End point type	Secondary
End point timeframe:	
Week 24 visit only	

End point values	Week 24			
Subject group type	Subject analysis set			
Number of subjects analysed	37[4]			
Units: Adverse Events				
median (full range (min-max))	0 (0 to 5)			

Notes:

[4] - 2 patients DNA

Statistical analyses

No statistical analyses for this end point

Secondary: Median CNS toxicity score (from CNS questionnaire) at Week 24

End point title	Median CNS toxicity score (from CNS questionnaire) at Week 24

End point description:

All grades of CNS adverse events reported in the questionnaire were summed together. This total was then transformed into a score from 0 to 100, where a score of 0 represents no adverse events, and 100 is all events reported as 'Severe'. Due to this dataset not being normalised, inter-quartile range is given instead of the protocol specified 95% CI.

End point type	Secondary

End point timeframe:

Week 24

End point values	Week 24			
Subject group type	Subject analysis set			
Number of subjects analysed	37[5]			
Units: Score (/100)				
median (inter-quartile range (Q1-Q3))	7 (3 to 17)			

Notes:

[5] - 2 patients DNA

Statistical analyses

No statistical analyses for this end point

Secondary: Rate of change in CNS parameters as measured using the Hospital Anxiety and Depression Scale (HADS) at Week12/24 compared to baseline

End point title	Rate of change in CNS parameters as measured using the Hospital Anxiety and Depression Scale (HADS) at Week12/24 compared to baseline

End point description:

A HAD score was derived based on responses in the HAD scale questionnaire. The responses to each question were given scores that ranged from 0 to 3 where response with a score of 0 gave a positive response while 3 gave negative response. All missing responses were scored 3.

The total HAD scores from each patient responses were taken as a fraction of the observed HAD score relative to the expected total HAD score. These have been expressed as that out of 100. So the minimum possible score that could be observed could be 0 and maximum possible score that could be observed is 100 (‘worse’).

Please note that this was not considered a normalised dataset, and therefore inter-quartile range is given instead of the originally intended 95% CI.

End point type	Secondary

End point timeframe:

Baseline to Week 12 / Week 24

End point values	Baseline	Week 12	Week 24	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	41	39	39	
Units: Score (/100)				
median (inter-quartile range (Q1-Q3))				
Absolute value	14.3 (7.1 to 26.2)	16.7 (2.4 to 23.8)	9.5 (0.0 to 26.2)	
Change from Baselnie	0.0 (0.0 to 0.0)	2.4 (-2.4 to 7.1)	2.4 (0.0 to 7.1)	

Attachments (see zip file)	SSAT058 HAD Results.pdf

Statistical analyses

Statistical analysis title	Baseline to week 12
Comparison groups	Baseline v Week 12
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.049
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Baseline to week 24
Comparison groups	Baseline v Week 24
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.024
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Friedman's test
Comparison groups	Baseline v Week 12 v Week 24
Number of subjects included in analysis	119
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.004
Method	Friedman's test

Secondary: Proportion of patients with undetectable viral load at weeks 4, 12 and 24

End point title	Proportion of patients with undetectable viral load at weeks 4, 12 and 24

End point description: Undetectable by local assay	
End point type	Secondary
End point timeframe: Weeks 4, 12 and 24	

End point values	Baseline	Week 4	Week 12	Week 24
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	40	39	39
Units: Patients	40	40	38	39

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with viral load below 400 copies/ml at Weeks 4, 12 and 24

End point title	Proportion of patients with viral load below 400 copies/ml at Weeks 4, 12 and 24
End point description:	
End point type	Secondary
End point timeframe: Weeks 4, 12 and 24.	

End point values	Baseline	Week 4	Week 12	Week 24
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	40	39	39
Units: Patients				
<400	41	40	39	39
>=400	0	0	0	0

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline CD4+ count at Week 12 and Week 24

End point title	Change from baseline CD4+ count at Week 12 and Week 24
End point description:	
End point type	Secondary

End point timeframe:
Baseline to Weeks 12 and 24

End point values	Baseline	Week 12	Week 24	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	41	39	39	
Units: cells/millilitre				
median (inter-quartile range (Q1-Q3))				
Absolute value	563 (465 to 679)	590 (481 to 719)	600 (488 to 682)	
Change from baseline	0 (0 to 0)	16 (-34 to 60)	-2 (-55 to 75)	

Statistical analyses

Statistical analysis title	Baseline to week 12
Comparison groups	Week 12 v Baseline
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.238
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Baseline to week 24
Comparison groups	Baseline v Week 24
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.995
Method	Wilcoxon (Mann-Whitney)

Secondary: Proportion of patients with grade 2-4 non-lipid laboratory AEs at Weeks, 4, 12 and 24 compared with Baseline

End point title	Proportion of patients with grade 2-4 non-lipid laboratory AEs at Weeks, 4, 12 and 24 compared with Baseline

End point description:

End point type	Secondary

End point timeframe:
Baseline to Weeks 4, 12 and 24

End point values	Baseline	Week 4	Week 12	Week 24
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	40	39	39
Units: Patients				
Sodium (high)	0	0	0	0
Sodium (low)	0	0	0	0
Potassium (high)	0	0	0	0
Potassium (low)	0	0	0	0
Creatinine	0	1	2	1
Albumin	0	0	0	0
glucose	1	2	2	2
ALT	0	0	0	0
ALP	0	0	0	0
AST	0	0	0	0
Total Bilirubin	0	0	0	0
Serum Phosphate	4	4	1	3
Haemoglobin	0	0	0	0
White Blood Cells	0	0	0	0
Platelets	0	0	0	0
Neutrophils	0	0	0	0

Attachments (see zip file)	SSAT058 Lab reults.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of patients with grade 2-4 non-CNS adverse events at Weeks, 4, 12 and 24 compared with Baseline

End point title	Proportion of patients with grade 2-4 non-CNS adverse events at Weeks, 4, 12 and 24 compared with Baseline

End point description:

Proportion of patients experiencing at least one Grade 2+ (moderate or severe) AE. As assessed by the CNS questionnaire.

End point type	Secondary

End point timeframe:

Baseline, Week 4,12 and 24

End point values	Baseline	Week 4	Week 12	Week 24
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	40	39	37
Units: Patients				
None	27	33	30	27
1+ Moderate/Severe	14	7	9	10

Statistical analyses

No statistical analyses for this end point

Secondary: Change in lipid parameters from Baseline to Weeks 4, 12 and 24

End point title	Change in lipid parameters from Baseline to Weeks 4, 12 and 24

End point description:

p-values from Wilcoxon signed rank tests listed in attached lab data table.

Additionally this analysis has been performed both with and without protocol deviating patients, as listed in the table attached to the first laboratory parameters endpoint.

End point type	Secondary

End point timeframe:

From Baseline to Weeks 4, 12 and 24.

End point values	Baseline	Week 4	Week 12	Week 24
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	40	39	39
Units: mmol/l				
median (inter-quartile range (Q1-Q3))				
Total cholesterol values	5.2 (4.6 to 5.7)	4.7 (4.2 to 5.0)	4.5 (3.8 to 5.0)	4.4 (4.0 to 5.2)
Total cholesterol change from baseline	0.0 (0.0 to 0.0)	-0.6 (-0.8 to -0.2)	-0.7 (-1.0 to -0.5)	-0.8 (-1.2 to -0.3)
HDL	1.4 (1.2 to 1.6)	1.3 (1.1 to 1.5)	1.3 (1.1 to 1.5)	1.3 (1.1 to 1.5)
HDL change from baseline	0.0 (0.0 to 0.0)	-0.11 (-0.23 to 0.02)	-0.10 (-0.26 to 0.00)	-0.13 (-0.30 to 0.06)
LDL	3.1 (2.4 to 3.5)	2.8 (2.2 to 3.1)	2.5 (2.1 to 3.1)	2.7 (2.1 to 3.3)
LDL change from baseline	0.0 (0.0 to 0.0)	-0.36 (-0.61 to -0.07)	-0.50 (-0.79 to -0.28)	-0.40 (-0.80 to -0.08)
total:HDL ratio	3.6 (3.2 to 4.2)	3.4 (2.8 to 4.2)	3.6 (3.0 to 4.1)	3.5 (2.8 to 4.3)
total:HDL ratio change from baseline	0.0 (0.0 to 0.0)	-0.12 (-0.49 to -0.10)	-0.24 (-0.50 to 0.01)	-0.19 (-0.47 to 0.21)
Triglycerides	1.3 (0.8 to 2.4)	0.9 (0.7 to 1.8)	1.3 (0.6 to 1.6)	0.9 (0.7 to 1.6)
Triglycerides change from baseline	0.0 (0.0 to 0.0)	-0.26 (-0.71 to 0.01)	-0.17 (-0.82 to 0.10)	-0.28 (-0.72 to 0.08)

Statistical analyses

No statistical analyses for this end point

Secondary: Change in quality of life 4, 12 and 24 weeks post switch, as measured by the EuroQOL questionnaire

End point title	Change in quality of life 4, 12 and 24 weeks post switch, as measured by the EuroQOL questionnaire

End point description:

Scores were converted to (/100) to facilitate comparison
Max possible=100 (best imaginable health state)
Min possible=0 (worst imaginable health state)

End point type	Secondary

End point timeframe:

From Baseline to Weeks 4, 12 and 24

End point values	Baseline	Week 4	Week 12	Week 24
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	40	39	39
Units: Score (/100)				
median (inter-quartile range (Q1-Q3))				
Absolute score	80 (75 to 90)	90 (73 to 94)	89 (80 to 90)	90 (75 to 95)
Change from baseline	0 (0 to 0)	-2 (-10 to 0)	-5 (-10 to 0)	-3 (-10 to 0)

Attachments (see zip file)	SSAT058 EQ5d results.pdf

Statistical analyses

Statistical analysis title	Friedman's test
Comparison groups	Week 4 v Baseline v Week 12 v Week 24
Number of subjects included in analysis	159
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.002
Method	Friedman's test

Statistical analysis title	Baseline to week 4
Comparison groups	Baseline v Week 4
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.003
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Baseline to week 12
Comparison groups	Baseline v Week 12
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.007
Method	Wilcoxon (Mann-Whitney)

Statistical analysis title	Baseline to week 24
Comparison groups	Baseline v Week 24
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Wilcoxon (Mann-Whitney)

Secondary: Change in neurocognitive function from baseline to Weeks 4, 12 and 24. As measured by Instrumental Activities of Daily Life questionnaire

End point title	Change in neurocognitive function from baseline to Weeks 4, 12 and 24. As measured by Instrumental Activities of Daily Life questionnaire

End point description:

Scores were converted to (/100) to facilitate comparison
Max possible=100 (best imaginable health state)
Min possible=0 (worst imaginable health state)

End point type	Secondary

End point timeframe:

From Baseline to Weeks 4, 12 and 24

End point values	Baseline	Week 4	Week 12	Week 24
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	41	40	39	39
Units: Score (/100)				
median (inter-quartile range (Q1-Q3))				
Absolute score	100 (100 to 100)	100 (100 to 100)	100 (100 to 100)	100 (100 to 100)
Change from Baseline	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)	0 (0 to 0)

Attachments (see zip file)	SSAT058 IADL Results.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Change in medication adherence from Baseline to Weeks 12 and 24. As measured by the adherence questionnaire

End point title	Change in medication adherence from Baseline to Weeks 12 and 24. As measured by the adherence questionnaire

End point description:

Adherence to study medication as measured by the Modified Medication Adherence Self-Report Inventory (M-MASRI) questionnaire

End point type	Secondary

End point timeframe:

From baseline to Week 12/24

End point values	Week 12	Week 24		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	39	39		
Units: % improvement				
median (inter-quartile range (Q1-Q3))	0 (0 to 1)	0 (0 to 5)		

Attachments (see zip file)	SSAT 058 Analysis v3.3 MMASRI.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Change in cerebral MRI modalities from Baseline to Week 24

End point title	Change in cerebral MRI modalities from Baseline to Week 24

End point description:

Imaging modalities given as absolute values, then as change from baseline (difference)

End point type	Secondary

End point timeframe:

Baseline to Week 24

End point values	Baseline	Week 24		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	11	10		
Units: Ratio				
median (inter-quartile range (Q1-Q3))				

ThalbasNAACr	0.96 (0.70 to 1.08)	1.07 (0.95 to 1.41)		
Difference ThalbasNAACr	0 (0 to 0)	0.19 (-0.11 to 0.44)		
Tha cholCr	0.23 (0.19 to 0.25)	0.23 (0.21 to 0.27)		
Difference Tha cholCr	0 (0 to 0)	0.01 (-0.04 to 0.04)		
Thal GlxCr	0.80 (0.73 to 1.16)	0.98 (0.84 to 1.38)		
Difference Thal GlxCr	0 (0 to 0)	0.22 (-0.28 to 0.65)		
FW NAACr	1.24 (1.07 to 1.33)	1.12 (1.01 to 1.23)		
Difference FW NAACr	0 (0 to 0)	-0.05 (-0.17 to 0.02)		
FW CholCr	0.31 (0.27 to 0.34)	0.27 (0.24 to 0.34)		
Difference FW CholCr	0 (0 to 0)	-0.04 (-0.08 to 0.01)		
FW GlxCr	0.88 (0.62 to 1.00)	0.90 (0.85 to 0.96)		
Difference FW GlxCr	0 (0 to 0)	0.10 (-0.02 to 0.40)		
FW InsCr	0.59 (0.53 to 0.71)	0.61 (0.58 to 0.85)		
Difference FW InsCr	0 (0 to 0)	0.106 (-0.01 to 0.19)		
FG NAACr	1.09 (1.04 to 1.14)	1.06 (0.94 to 1.13)		
Difference FG NAACr	0 (0 to 0)	-0.02 (-0.15 to 0.05)		
FG choCr	0.25 (0.23 to 0.26)	0.22 (0.21 to 0.26)		
Difference FG choCr	0 (0 to 0)	-0.01 (-0.05 to 0.02)		
FG InsCr	0.61 (0.53 to 0.64)	0.62 (0.57 to 0.68)		
Difference FG InsCr	0 (0 to 0)	-0.04 (-0.05 to 0.10)		

Attachments (see zip file)	SSAT058 MR results.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Change in neurocognitive function from baseline to Weeks 4 and 24. As measured by computerised cognitive testing

End point title	Change in neurocognitive function from baseline to Weeks 4 and 24. As measured by computerised cognitive testing

End point description:

CogState cognitive tasks use novel visual and verbal stimuli to ensure assessment is culture-neutral and not limited by a subject or participant’s level of education. All Cogstate tasks are designed for repeated administration with minimal practice or learning effects.

A Cogstate battery comprises a number of individual tasks – each designed to test a specific area of

cognition. When a number of these individual tests are put together to form a test battery, a more complete picture of a person’s cognitive state can be defined.

Each participants score was measured against available normative data, and is shown as a summary below. Individual comparisons for each test are given in the attached table.

End point type	Secondary

End point timeframe:

From Baseline to Weeks 4 and 24.

End point values	Baseline	Week 4	Week 24	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	40	40	39	
Units: Score (/100)				
median (inter-quartile range (Q1-Q3))	-0.01 (-0.71 to 0.80)	-0.06 (-0.71 to 0.72)	-0.15 (-0.62 to 0.78)	

Attachments (see zip file)	SSAT058 Cogstate.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From consent to follow-up (Week 24+30 days)

Adverse event reporting additional description:

Adverse event incidence for laboratory and CNS categories, are further detailed in the endpoints section.

Assessment type	Systematic

Dictionary used

Dictionary name	ACTG Adverse Events
Dictionary version	1.0

Reporting groups

Reporting group title	Experimental Arm

Reporting group description:

Single Arm Study - all patients were switched from tenofovir/emtricitabine/efavirenz (Atripla®) to a fixed dose combination of tenofovir/emtricitabine/rilpivirine (Eviplera®).

Serious adverse events	Experimental Arm		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 40 (5.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Musculoskeletal and connective tissue disorders			
Trauma (foot)	Additional description: Hospitalisation		
alternative assessment type: Non-systematic			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Epiglotitis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Experimental Arm		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 40 (100.00%)		
Nervous system disorders			
Paraesthesia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
General disorders and administration site conditions			
Tiredness			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Ear and labyrinth disorders			
Hayfever			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Toothache	Additional description: including tooth pain		
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Renal and urinary disorders			
Urinary tract infection			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		

Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	6		
Myalgia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Infections and infestations			
Cold			
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Influenza			
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		
Viral infection			
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Gonorrhea			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 October 2015	Principal Investigator change
08 February 2016	Addition of an interim analysis post after all patients had completed their Week 4 visit
07 December 2016	Addition of an interim analysis after all participants had completed the Week 12 visit

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported