Clinical trial results:
The Central Nervous System Effects of Two Different HIV-Integrase Inhibitor Containing Antiretroviral Regimens.

Summary

EudraCT number	2014-003710-84
Trial protocol	GB
Global end of trial date	02 August 2016

Results information

Result version number	v1 (current)
This version publication date	28 October 2019
First version publication date	28 October 2019

Trial information

Trial identification

Sponsor protocol code	CIIS

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Imperial College London
Sponsor organisation address	South Kensingston Campus, London, United Kingdom, SW7 2AZ
Public contact	Prof Alan Winston, Imperial College London, +44 020 3312 1603, a.winston@imperial.ac.uk
Scientific contact	Prof Alan Winston, Imperial College London, +44 020 3312 1603, a.winston@imperial.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	31 August 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 August 2016
Global end of trial reached?	Yes
Global end of trial date	02 August 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of the study is to compare cerebral function parameters in HIV-infected subjects receiving two different integrase-inhibitor containing antiretroviral regimens by assessing the following questions:

-Principal research question:

- Changes in neurocognitive function between study treatment arms.

Protection of trial subjects:

None

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 January 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: 22
Worldwide total number of subjects	22
EEA total number of subjects	22

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)	20
From 65 to 84 years	2

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study was conducted at St. Mary's Hospital (Imperial College Healthcare NHS Trust, London, UK) from July 2015 to August 2016.

Pre-assignment

Screening details:

Of 28 participants screened, 22 were randomised and 20 completed study.
Individuals were randomised on a 2:1 basis to either switch integrase inhibitor from raltegravir to dolutegravir 50 mg once daily (Switch Arm) or to remain on raltegravir (Control Arm).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Switch Arm

Arm description:

Switch integrase inhibitor from Raltegravir to Dolutegravir 50 mg once daily

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

Dosage and administration details:

50 mg once daily

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

Dosage and administration details:

tenofovir/emtricitabine 245/200 mg

Arm title	Control Arm

Arm description:

Remain on raltegravir treatment

Arm type	Active comparator
Investigational medicinal product name	Raltegravir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

400 mg twice daily

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

Dosage and administration details:
tenofovir/emtricitabine 245/200 mg

Number of subjects in period 1	Switch Arm	Control Arm
Started	13	9
Completed	12	8
Not completed	1	1
Consent withdrawn by subject	-	1
Death not related to drug	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Switch Arm
Reporting group description:	
Switch integrase inhibitor from Raltegravir to Dolutegravir 50 mg once daily	
Reporting group title	Control Arm
Reporting group description:	
Remain on raltegravir treatment	

Reporting group values	Switch Arm	Control Arm	Total
Number of subjects	13	9	22
Age categorical Units: Subjects			
Adults (18-64 years)	12	8	20
From 65-84 years	1	1	2
Age continuous Units: years			
geometric mean	43	39.5	
inter-quartile range (Q1-Q3)	30 to 56	24 to 55	-
Gender categorical Units: Subjects			
Female	0	2	2
Male	13	7	20
BMI Units: kg/m2			
geometric mean	27.4	25.4	
standard deviation	± 3.4	± 2.9	-
Baseline absolute CD4+ count Units: cells/µL			
geometric mean	736	688	
standard deviation	± 237	± 395	-

End points

End points reporting groups

Reporting group title	Switch Arm
Reporting group description: Switch integrase inhibitor from Raltegravir to Dolutegravir 50 mg once daily	
Reporting group title	Control Arm
Reporting group description: Remain on raltegravir treatment	

Primary: Change in PHQ-9 questionnaires score from baseline

End point title	Change in PHQ-9 questionnaires score from baseline
End point description:	
End point type	Primary
End point timeframe: 120 days	

End point values	Switch Arm	Control Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	8		
Units: score				
median (full range (min-max))	-0.5 (-5 to 3)	0 (-5 to 1)		

Statistical analyses

Statistical analysis title	PHQ-9
Comparison groups	Switch Arm v Control Arm
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.57
Method	Wilcoxon (Mann-Whitney)

Primary: Change in Beck’s depression questionnaire score from baseline

End point title	Change in Beck’s depression questionnaire score from baseline
End point description:	
End point type	Primary

End point timeframe: 120 days

End point values	Switch Arm	Control Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	8		
Units: score				
median (full range (min-max))	-1 (-15 to 9)	-1.5 (-10 to 2)		

Statistical analyses

Statistical analysis title	Beck’s depression questionnaire
Comparison groups	Switch Arm v Control Arm
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.38
Method	Wilcoxon (Mann-Whitney)

Primary: Change in cognitive function from baseline
End point title: Change in cognitive function from baseline
End point description:
End point type: Primary
End point timeframe: 120 days

End point values	Switch Arm	Control Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	8		
Units: score				
geometric mean (standard deviation)	0.14 (± 0.4)	0.14 (± 0.37)		

Statistical analyses

Statistical analysis title	Cognitive Function
Comparison groups	Switch Arm v Control Arm

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.98
Method	t-test, 2-sided

Primary: Change in cerebral metabolite from baseline (NAA/Cr frontal grey matter)

End point title	Change in cerebral metabolite from baseline (NAA/Cr frontal grey matter)

End point description:

End point type	Primary

End point timeframe:

120 days

End point values	Switch Arm	Control Arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	8		
Units: ng/mL				
geometric mean (standard deviation)	0.08 (± 00.14)	-0.06 (± 0.16)		

Statistical analyses

Statistical analysis title	Metabolites
Comparison groups	Switch Arm v Control Arm
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.07
Method	Regression, Linear

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: 120 days	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	10

Reporting groups	
Reporting group title	Switch group
Reporting group description: -	
Reporting group title	Control group
Reporting group description: -	

Serious adverse events	Switch group	Control group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	
number of deaths (all causes)	1	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	Switch group	Control group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 13 (0.00%)	0 / 8 (0.00%)	

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: No study related non serious AE

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported