Clinical trial results:
A randomized, open, parallel design study to evaluate the effect on liver fat, adipose tissue and metabolic parameters when switching a protease inhibitor or efavirenz to once daily raltegravir in HIV-infected patients with body mass index over 25 kg/m2 and with at least one metabolic syndrome component.

Summary

EudraCT number	2017-003430-85
Trial protocol	FI
Global end of trial date	02 November 2019

Results information

Result version number	v1 (current)
This version publication date	26 August 2021
First version publication date	26 August 2021

Trial information

Trial identification

Sponsor protocol code	OBERAL

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Helsinki University Hospital Infectious Disease Clinic
Sponsor organisation address	Kolmiosairaala Haartmaninkatu 4, Helsinki, Finland, 00290
Public contact	Dr. Jussi Sutinen, Helsinki University Hospital, jussi.sutinen@hus.fi
Scientific contact	Dr. Jussi Sutinen, Helsinki University Hospital, 358 407480437, jussi.sutinen@hus.fi

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	30 September 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	02 November 2019
Global end of trial reached?	Yes
Global end of trial date	02 November 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the effect of switching from a protease inhibitor or efavirenz to raltegravir on liver fat content.

Protection of trial subjects:

Subjects had direct phone numbers to the investigators and could contact them 24/7. Local anesthesia was used with invasive procedures.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 December 2017
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	Finland: 45
Worldwide total number of subjects	45
EEA total number of subjects	45

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)	43
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

All subjects were recruited from Finland during the period of Oct 2017 - April 2019.

Pre-assignment

Screening details:

HIV-infected patients who were overweight or obese and had at least one metabolic syndrome component, or who had fatty liver diagnosed by imaging studies .

Pre-assignment period milestones

Number of subjects started	45
Number of subjects completed	45

Period 1

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

Blinding implementation details:

This is an open label randomized controlled study.

Arms

Are arms mutually exclusive?	Yes
Arm title	Raltegravir

Arm description:

Those subjects who switched their earlier protease inhibitor or efavirenz to raltegravir.

Arm type	Experimental
Investigational medicinal product name	raltegravir
Investigational medicinal product code	J05AJ01
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Raltegravir was taken 1200 mg once a day.

Arm title	Control

Arm description:

Subjects who continued their protease inhibitor or efavirenz containing antiretroviral regimen unchanged.

Arm type	Active comparator
Investigational medicinal product name	efavirenz
Investigational medicinal product code	J05AG03
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

The control subjects continued their efavirenz (600mg QD) or protease inhibitor containing regimen unchanged.

Number of subjects in period 1	Raltegravir	Control
Started	21	24
Completed	19	23
Not completed	2	1
Consent withdrawn by subject	2	-
Adverse event, non-fatal	-	1

Baseline characteristics

End points

End points reporting groups

Reporting group title	Raltegravir
Reporting group description:	
Those subjects who switched their earlier protease inhibitor or efavirenz to raltegravir.	
Reporting group title	Control
Reporting group description:	
Subjects who continued their protease inhibitor or efavirenz containing antiretroviral regimen unchanged.	

Primary: Change in liver fat content from baseline to 24 weeks.

End point title	Change in liver fat content from baseline to 24 weeks.
End point description:	
End point type	Primary
End point timeframe:	
The change in liver fat between baseline and 24 weeks.	

End point values	Raltegravir	Control		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	21		
Units: liver fat fraction (%)				
median (inter-quartile range (Q1-Q3))	0.6 (-0.3 to 1.6)	0.3 (-0.5 to 2.7)		

Statistical analyses

Statistical analysis title	Comparison
Statistical analysis description:	
The change from baseline and 24 weeks within the study groups and between the study groups were analyzed	
Comparison groups	Raltegravir v Control
Number of subjects included in analysis	39
Analysis specification	Pre-specified
Analysis type	other[1]
P-value	> 0.05 [2]
Method	Wilcoxon (Mann-Whitney)
Parameter estimate	Median difference (net)

Notes:

[1] - Within group changes were analyzed using Wilcoxon signed rank test and differences between the groups were analyzed Mann-Whitney test.
[2] - non significant in all comparisons

Adverse events

Adverse events information	
Timeframe for reporting adverse events: 8 Feb 2018 - 2 Nov 2019.	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.0
Reporting groups	
Reporting group title	Raltegravir
Reporting group description: -	
Reporting group title	Control
Reporting group description: -	

Serious adverse events	Raltegravir	Control	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events		0	
Gastrointestinal disorders			
Pancreatitis			
subjects affected / exposed	0 / 19 (0.00%)	1 / 24 (4.17%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Raltegravir	Control	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 19 (84.21%)	20 / 24 (83.33%)	
Nervous system disorders			
dizzyness			
subjects affected / exposed	5 / 19 (26.32%)	8 / 24 (33.33%)	
occurrences (all)	16	20	
Headache			
subjects affected / exposed	9 / 19 (47.37%)	8 / 24 (33.33%)	
occurrences (all)	16	20	

Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all)	 9 / 19 (47.37%) 16	 7 / 24 (29.17%) 20	

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