Clinical trial results:
MULTICENTRE STUDY TO ASSESS CHANGES IN BONE MINERAL DENSITY OF THE SWITCH FROM PROTEASE INHIBITORS TO DOLUTEGRAVIR IN HIV-1-INFECTED SUBJECTS WITH LOW BONE MINERAL DENSITY

Summary

EudraCT number	2013-000547-85
Trial protocol	ES
Global end of trial date	28 October 2015

Results information

Result version number	v1 (current)
This version publication date	19 March 2017
First version publication date	19 March 2017

Trial information

Trial identification

Sponsor protocol code	OSTEODOLU

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02577042
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundació Lluita contra la SIDA
Sponsor organisation address	Crta de Canyet s/n, Badalona, Spain, 08916
Public contact	Clinical Research Associates, Fundació Lluita contra la SIDA, +34 93497 84 14, jtoro@fls-rs.com
Scientific contact	Clinical Research Associates, Fundació Lluita contra la SIDA, +34 93497 84 14, jtoro@fls-rs.com

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	14 March 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate changes in BMD 48 weeks after the switch from a PI to dolutegravir in HIV-infected patients with low bone mineral density.

Protection of trial subjects:

not specific

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2013
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	Spain: 73
Worldwide total number of subjects	73
EEA total number of subjects	73

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)	73
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Candidates were HIV-infected adults who had been receiving a stable antiretroviral combination including abacavir/lamivudine (Kivexa) plus a ritonavir-boosted PI for at least 6 months.

Pre-assignment

Screening details:

Seventy-five subjects were screened.

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	PI group

Arm description:

ritonavir-boosted PI plus co-formulated lamivudine/abacavir (Kivexa)

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

Dosage and administration details:

daily

Investigational medicinal product name	ATV/r
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

daily

Investigational medicinal product name	DRV/r
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

800/100mg once daily in all patients but one, who received 600/100mg every 12 h.

Investigational medicinal product name	FosAPV/r
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

daily

Investigational medicinal product name	abacavir/ lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:
600mg/300mg once daily

Arm title	DOLU group

Arm description:
dolutegravir 50mg plus co-formulated lamivudine/abacavir (Kivexa) every 24h

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

Dosage and administration details:
600mg/300mg every 24h

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

Dosage and administration details:
50mg every 24h

Number of subjects in period 1	PI group	DOLU group
Started	36	37
Completed	33	36
Not completed	3	1
Consent withdrawn by subject	-	1
Adverse event, non-fatal	1	-
Lost to follow-up	2	-

Baseline characteristics

Reporting groups	
Reporting group title	PI group
Reporting group description: ritonavir-boosted PI plus co-formulated lamivudine/abacavir (Kivexa)	
Reporting group title	DOLU group
Reporting group description: dolutegravir 50mg plus co-formulated lamivudine/abacavir (Kivexa) every 24h	

Reporting group values	PI group	DOLU group	Total
Number of subjects	36	37	73
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	36	37	73
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	49.2	46.8	
inter-quartile range (Q1-Q3)	45.7 to 53.9	39.3 to 53.8	-
Gender categorical Units: Subjects			
Female	4	7	11
Male	32	30	62

End points

End points reporting groups

Reporting group title	PI group
Reporting group description: ritonavir-boosted PI plus co-formulated lamivudine/abacavir (Kivexa)	
Reporting group title	DOLU group
Reporting group description: dolutegravir 50mg plus co-formulated lamivudine/abacavir (Kivexa) every 24h	

Primary: evaluate the effect on BMD of switching from a ritonavir-boosted PI to dolutegravir in HIV-infected patients with osteopenia or osteoporosis (Femoral neck BMD)

End point title	evaluate the effect on BMD of switching from a ritonavir-boosted PI to dolutegravir in HIV-infected patients with osteopenia or osteoporosis (Femoral neck BMD)
End point description:	
End point type	Primary
End point timeframe: from baseline to wk48	

End point values	PI group	DOLU group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	37		
Units: Percentage change in BMD				
median (inter-quartile range (Q1-Q3))	-0.66 (-2.94 to 1.38)	-0.11 (-1.47 to 2.64)		

Statistical analyses

Statistical analysis title	Comparing medians
Comparison groups	PI group v DOLU group
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.29
Method	Wilcoxon (Mann-Whitney)

Primary: evaluate the effect on BMD of switching from a ritonavir-boosted PI to dolutegravir in HIV-infected patients with osteopenia or osteoporosis (Trochanter BMD)

End point title	evaluate the effect on BMD of switching from a ritonavir-boosted PI to dolutegravir in HIV-infected patients with osteopenia or osteoporosis (Trochanter BMD)

End point description:

End point type	Primary

End point timeframe:

from baseline to week 48

End point values	PI group	DOLU group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	37		
Units: Percentage change in BMD				
median (inter-quartile range (Q1-Q3))	0.5 (-1.71 to 2.41)	0.46 (-1.25 to 3.32)		

Statistical analyses

Statistical analysis title	Comparing medians
Comparison groups	PI group v DOLU group
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.63
Method	Wilcoxon (Mann-Whitney)

Primary: evaluate the effect on BMD of switching from a ritonavirboosted PI to dolutegravir in HIV-infected patients with osteopenia or osteoporosis (Total femur BMD)

End point title	evaluate the effect on BMD of switching from a ritonavirboosted PI to dolutegravir in HIV-infected patients with osteopenia or osteoporosis (Total femur BMD)

End point description:

End point type	Primary

End point timeframe:

from baseline to week 48

End point values	PI group	DOLU group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	37		
Units: Percentage change in BMD				
median (inter-quartile range (Q1-Q3))	0.25 (-1.87 to 1.62)	0.43 (-0.96 to 1.75)		

Statistical analyses

Statistical analysis title	Comparing medians
Comparison groups	PI group v DOLU group
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.56
Method	Wilcoxon (Mann-Whitney)

Primary: evaluate the effect on BMD of switching from a ritonavirboosted PI to dolutegravir in HIV-infected patients with osteopenia or osteoporosis (Lumbar spine BMD)

End point title	evaluate the effect on BMD of switching from a ritonavirboosted PI to dolutegravir in HIV-infected patients with osteopenia or osteoporosis (Lumbar spine BMD)

End point description:

End point type	Primary

End point timeframe:

from baseline to week 48

End point values	PI group	DOLU group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	37		
Units: Percentage change in BMD				
median (inter-quartile range (Q1-Q3))	0.12 (-2.83 to 2.89)	1.43 (-1.36 to 2.92)		

Statistical analyses

Statistical analysis title	Comparing medians
Comparison groups	PI group v DOLU group

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.29
Method	Wilcoxon (Mann-Whitney)

Secondary: assess the antiviral efficacy of the switch

End point title	assess the antiviral efficacy of the switch

End point description:

End point type	Secondary

End point timeframe:
at week 48

End point values	PI group	DOLU group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	37		
Units: snapshot analysis	33	36		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from baseline to wk48	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	DAIDS AE GRADING TAB
Dictionary version	1.0

Reporting groups	
Reporting group title	PI group
Reporting group description: -	
Reporting group title	DOLU group
Reporting group description: -	

Serious adverse events	PI group	DOLU group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Renal and urinary disorders			
nephrolithiasis nephrolithiasis and rupture of the ureter			
subjects affected / exposed	1 / 36 (2.78%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	PI group	DOLU group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 36 (0.00%)	2 / 37 (5.41%)	
Nervous system disorders			
Anxiety			
subjects affected / exposed	0 / 36 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Nausea			

subjects affected / exposed occurrences (all)	0 / 36 (0.00%) 0	1 / 37 (2.70%) 1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
18 September 2013	Changes in the supply, packaging, labeling and storage of the investigational product
04 February 2014	Changes in the Informed Consent Information Sheet

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported