Clinical trial results:
RANDOMISED AND PROSPECTIVE CLINICAL STUDY TO EVALUATE THE EFFICACY AND SAFETY OF LOPINAVIR/RITONAVIR MONOTHERAPY VS DARUNAVIR/RITONAVIR MONOTHERAPIES AS SIMPLIFICATION SWITCHING STRATEGIES OF PI/NNRTI-TRIPLE THERAPY BASED-REGIMENS.

Summary

EudraCT number	2009-013287-39
Trial protocol	ES
Global end of trial date	25 October 2012

Results information

Result version number	v1 (current)
This version publication date	24 March 2017
First version publication date	24 March 2017

Trial information

Trial identification

Sponsor protocol code	LOPIDAR

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00994344
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,
Public contact	CRA, Fundació lluita contrala SIDA, jtoro@fls-rs.com
Scientific contact	CRA, Fundació lluita contrala SIDA, 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	25 October 2012
Is this the analysis of the primary completion data?	Yes
Primary completion date	25 October 2012
Global end of trial reached?	Yes
Global end of trial date	25 October 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the non-inferiority in the efficacy of DRV/r (900/100 mg) monotherapy at 48 weeks versus LPV/r (400/100 mg) as simplification strategy in subjects with sustained viral suppression on stable PI or NNRTI-antiretroviral regimens.

Protection of trial subjects:

not specific

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	26 October 2009
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:

A total of 75 patients were enrolled. Patients were randomly assigned to receive once-daily DRV/r 800/100 mg or twice-daily LPV/r 400/100mg

Pre-assignment

Screening details:

A total of 75 patients were enrolled. Two patients withdrew consent before initiation of the study medication and were excluded.

Period 1

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

Blinding implementation details:

not blinding

Arms

Are arms mutually exclusive?	Yes
Arm title	DRVr monotherapy

Arm description:

once-daily DRV/r 800/100 mg

Arm type	Experimental
Investigational medicinal product name	Darunavir/ritonavir (DRV/r)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

once-daily DRV/r 800/100 mg

Arm title	LPVr monotherapy

Arm description:

twice-daily LPV/r 400/100mg

Arm type	Experimental
Investigational medicinal product name	lopinavir/ritonavir (LPV/r)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

twice-daily LPV/r 400/100mg

Number of subjects in period 1	DRVr monotherapy	LPVr monotherapy
Started	40	33
Completed	31	22
Not completed	9	11
Consent withdrawn by subject	-	1
Adverse event, non-fatal	6	6
Virological failure	-	2
Lost to follow-up	3	2

Baseline characteristics

Reporting groups	
Reporting group title	overall

Reporting group description: -

Reporting group values	overall	Total	
Number of subjects	73	73	
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)	73	73	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	43		
inter-quartile range (Q1-Q3)	34 to 47	-	
Gender categorical Units: Subjects			
Female	13	13	
Male	60	60	

End points

End points reporting groups	
Reporting group title	DRVr monotherapy
Reporting group description: once-daily DRV/r 800/100 mg	
Reporting group title	LPVr monotherapy
Reporting group description: twice-daily LPV/r 400/100mg	

Primary: patients who maintained virological suppression in plasma	
End point title	patients who maintained virological suppression in plasma
End point description:	
End point type	Primary
End point timeframe: week 48	

End point values	DRVr monotherapy	LPVr monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	33		
Units: percentage				
number (not applicable)	77.5	66.6		

Statistical analyses

Statistical analysis title	Comparing proportions
Statistical analysis description: Comparing percentage of patients without virological failure between groups at week 48 ITT(Missing=Failure)	
Comparison groups	DRVr monotherapy v LPVr monotherapy
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.302
Method	Chi-squared

Secondary: laboratory parameters (creatinine)	
End point title	laboratory parameters (creatinine)

End point description:

End point type	Secondary

End point timeframe:
from baseline to week 48

End point values	DRVr monotherapy	LPVr monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	22		
Units: umol/L				
median (inter-quartile range (Q1-Q3))				
baseline	79.5 (71.3 to 85.5)	76 (65 to 86)		
week 48	79 (65.5 to 85)	70 (55.2 to 83.5)		

Statistical analyses

Statistical analysis title	Comparing medians

Statistical analysis description:
Comparisons between arms at week 48

Comparison groups	LPVr monotherapy v DRVr monotherapy
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.194
Method	Wilcoxon (Mann-Whitney)

Secondary: laboratory parameters cholesterol [HDL]

End point title	laboratory parameters cholesterol [HDL]

End point description:

End point type	Secondary

End point timeframe:
from baseline to week 48

End point values	DRVr monotherapy	LPVr monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	22		
Units: mmol/L				
median (inter-quartile range (Q1-Q3))				
baseline	1.2 (1 to 1.4)	1.3 (1 to 1.5)		
week 48	1.3 (1.1 to 1.5)	1.1 (0.9 to 1.7)		

Statistical analyses

Statistical analysis title	Comparing medians
Statistical analysis description: Comparisons between arms at 48 weeks	
Comparison groups	DRVr monotherapy v LPVr monotherapy
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.746
Method	Wilcoxon (Mann-Whitney)

Secondary: laboratory parameters (CD4+)

End point title	laboratory parameters (CD4+)
End point description:	
End point type	Secondary
End point timeframe: from baseline to week 48	

End point values	DRVr monotherapy	LPVr monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	31	22		
Units: cells/mm3				
median (inter-quartile range (Q1-Q3))				
baseline	629 (448 to 891)	593 (471 to 831)		
week 48	628 (478 to 819)	652 (570 to 887)		

Statistical analyses

Statistical analysis title	Comparing medians
Statistical analysis description: Comparisons between arms at 48 weeks	
Comparison groups	DRVr monotherapy v LPVr monotherapy
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.11
Method	Wilcoxon (Mann-Whitney)

Secondary: percentage of patients who discontinued monotherapy nonserious adverse events

End point title	percentage of patients who discontinued monotherapy nonserious adverse events
End point description:	
End point type	Secondary
End point timeframe: week 48	

End point values	DRVr monotherapy	LPVr monotherapy		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	33		
Units: patients	1	6		

Statistical analyses

Statistical analysis title	comparing proportions
Statistical analysis description: comparing percentages of patient with non serios adverse events	
Comparison groups	LPVr monotherapy v DRVr monotherapy
Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.019
Method	Chi-squared

Statistical analysis title	comparing proportions
Comparison groups	DRVr monotherapy v LPVr monotherapy

Number of subjects included in analysis	73
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.019
Method	Chi-squared

Adverse events

Adverse events information	
Timeframe for reporting adverse events: week 48	
Assessment type	Non-systematic
Dictionary used	
Dictionary name	DAIDS AE GRADING TAB
Dictionary version	1.0
Reporting groups	
Reporting group title	darunavir/ritonavir (DRV/r)
Reporting group description: -	
Reporting group title	lopinavir/ritonavir (LPV/r)
Reporting group description: -	

Serious adverse events	darunavir/ritonavir (DRV/r)	lopinavir/ritonavir (LPV/r)	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 40 (0.00%)	0 / 33 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

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

Non-serious adverse events	darunavir/ritonavir (DRV/r)	lopinavir/ritonavir (LPV/r)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 40 (15.00%)	6 / 33 (18.18%)	
Gastrointestinal disorders			
Gastrointestinal disturbances			
subjects affected / exposed	1 / 40 (2.50%)	6 / 33 (18.18%)	
occurrences (all)	1	6	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 October 2009	protocol, informed sheet form (study and substudy) modification
23 October 2009	subestudy removed from original protocol
20 January 2010	protocol and informed sheet form modification
29 June 2010	Two more sites added
21 June 2011	protocol and informed sheet form modification

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported