Clinical trial results:
PILOT STUDY ASSESSING TREATMENT SIMPLIFICATION TO DARUNAVIR/RITONAVIR 900/100 mg ONCE DAILY GUIDED BY THE DARUNAVIR INHIBITORY QUOTIENT IN HEAVILY PRETREATED HIV-INFECTED PATIENT

Summary

EudraCT number	2007-005979-34
Trial protocol	ES
Global end of trial date	31 July 2009

Results information

Result version number	v1 (current)
This version publication date	11 August 2017
First version publication date	11 August 2017

Trial information

Trial identification

Sponsor protocol code	DRV 900100 QD

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00611039
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	CRA, Fundació Lluita contra la SIDA, +34 93 497 84 14, rescrig@flsida.org
Scientific contact	CRA, Fundació Lluita contra la SIDA, +34 93 497 84 14,

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 July 2009
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 July 2009
Global end of trial reached?	Yes
Global end of trial date	31 July 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the efficacy and safety to switch from darunavir / ritonavir 900/100 mg once daily in HIV-infected patients who maintain plasma HIV-1 RNA load <50 copies / mL while receiving darunavir / ritonavir 600/100 mg twice daily and who have a DRV vIQ equal to or greater than 2.

Protection of trial subjects:	
not specific	
Background therapy: -	
Evidence for comparator: -	
Actual start date of recruitment	23 January 2008
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: 30
Worldwide total number of subjects	30
EEA total number of subjects	30

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)	30
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

In this clinical trial 45 patients were screened

Pre-assignment

Screening details:

30 participants were finally enrolled

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	QD group

Arm description:

darunavir/ritonavir 900/100 mg qd

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

Dosage and administration details:

3 capsules (900 mg) / 24 hours.

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

Dosage and administration details:

1 tablet (100 mg) / 24 hours

Arm title	BID group

Arm description:

darunavir/ritonavir 600/100 mg bid

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

Dosage and administration details:

2 capsules (600 mg) / 12 hours.

Investigational medicinal product name	ritonavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet

Routes of administration	Oral use

Dosage and administration details:

1 tablet (100 mg) / 12 hours.

Number of subjects in period 1	QD group	BID group
Started	15	15
Completed	13	13
Not completed	2	2
Consent withdrawn by subject	1	-
persistent AE grade 2	-	1
stroke with serious difficulty in swallowing pills	-	1
Adverse event, non-fatal	1	-

Baseline characteristics

Reporting groups	
Reporting group title	QD group
Reporting group description: darunavir/ritonavir 900/100 mg qd	
Reporting group title	BID group
Reporting group description: darunavir/ritonavir 600/100 mg bid	

Reporting group values	QD group	BID group	Total
Number of subjects	15	15	30
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)	15	15	30
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	47	47	
full range (min-max)	39 to 59	40 to 61	-
Gender categorical Units: Subjects			
Female	4	1	5
Male	11	14	25

End points

End points reporting groups

Reporting group title	QD group
Reporting group description: darunavir/ritonavir 900/100 mg qd	
Reporting group title	BID group
Reporting group description: darunavir/ritonavir 600/100 mg bid	

Primary: percentage of patients without therapeutic failure at week 48

End point title	percentage of patients without therapeutic failure at week 48[1]
End point description:	
End point type	Primary
End point timeframe: week 48	

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: No patient developed virologic failure during the follow-up. The proportion of patients without therapeutic failure at week 48 was 13/15 (86.7%) in both study groups together. Nothing to compare

End point values	QD group	BID group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: percentage (%)				
number (not applicable)	86.7	86.7		

Statistical analyses

No statistical analyses for this end point

Secondary: changes in the CD4+ T-cell count

End point title	changes in the CD4+ T-cell count
End point description:	
End point type	Secondary
End point timeframe: from baseline to week 48	

End point values	QD group	BID group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: cells/mm3				
arithmetic mean (standard deviation)				
baseline	546 (± 242)	439 (± 212)		
week 48	584 (± 310)	430 (± 119)		

Statistical analyses

Statistical analysis title	Comparing mean between groups at week 48
Comparison groups	BID group v QD group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.093
Method	t-test, 2-sided

Statistical analysis title	Comparing mean between groups at baseline
Comparison groups	QD group v BID group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.206
Method	t-test, 2-sided

Secondary: changes in lipid profile: Total cholesterol

End point title	changes in lipid profile: Total cholesterol

End point description:

End point type	Secondary

End point timeframe:
from baseline to week 48

End point values	QD group	BID group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: mg/dl				
arithmetic mean (standard deviation)				
baseline	179 (± 34)	185 (± 39)		

week 48	175 (± 34)	189 (± 27)		

Statistical analyses

No statistical analyses for this end point

Secondary: changes in lipid profile: HDL-cholesterol

End point title	changes in lipid profile: HDL-cholesterol

End point description:

End point type	Secondary

End point timeframe:
from baseline to week 48

End point values	QD group	BID group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: mg/dl				
arithmetic mean (standard deviation)				
baseline	40 (± 12)	44 (± 16)		
week 48	40 (± 12)	41 (± 13)		

Statistical analyses

No statistical analyses for this end point

Secondary: changes in lipid profile: LDL-cholesterol

End point title	changes in lipid profile: LDL-cholesterol

End point description:

End point type	Secondary

End point timeframe:
from baseline to week 48

End point values	QD group	BID group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: mg/dl				
arithmetic mean (standard deviation)				
baseline	101 (± 25)	98 (± 32)		
week 48	107 (± 29)	102 (± 22)		

Statistical analyses

No statistical analyses for this end point

Secondary: changes in lipid profile: Triglycerides

End point title	changes in lipid profile: Triglycerides

End point description:

End point type	Secondary

End point timeframe:
from baseline to week 48

End point values	QD group	BID group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: mg/dl				
arithmetic mean (standard deviation)				
baseline	186 (± 101)	227 (± 202)		
week 48	164 (± 115)	238 (± 121)		

Statistical analyses

No statistical analyses for this end point

Secondary: changes in liver enzymes: AST

End point title	changes in liver enzymes: AST

End point description:

End point type	Secondary

End point timeframe:
from baseline to week 48

End point values	QD group	BID group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: IU/l				
median (inter-quartile range (Q1-Q3))				
baseline	23 (18 to 31)	25 (18 to 42)		
week 48	25 (16 to 31)	24 (21 to 25)		

Statistical analyses

No statistical analyses for this end point

Secondary: changes in liver enzymes: ALT

End point title	changes in liver enzymes: ALT

End point description:

End point type	Secondary

End point timeframe:
from baseline to week 48

End point values	QD group	BID group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: IU/l				
median (inter-quartile range (Q1-Q3))				
baseline	26 (16 to 38)	28 (16 to 50)		
week 48	23 (17 to 41)	31 (19 to 88)		

Statistical analyses

No statistical analyses for this end point

Secondary: increase ritonavir Ctrough

End point title	increase ritonavir Ctrough

End point description:

End point type	Secondary

End point timeframe:
week 48

End point values	QD group	BID group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: mg/l				
geometric mean (confidence interval 95%)				
week 48	0.19 (0.1 to 0.36)	1.11 (0.72 to 1.73)		

Statistical analyses

No statistical analyses for this end point

Secondary: increase darunavir Ctrough

End point title	increase darunavir Ctrough

End point description:

End point type	Secondary

End point timeframe:

week 48

End point values	QD group	BID group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: mg/l				
geometric mean (confidence interval 95%)	0.52 (0.37 to 0.73)	1.07 (0.79 to 1.45)		

Statistical analyses

No statistical analyses for this end point

Secondary: patients who remained on the originally assigned dosage

End point title	patients who remained on the originally assigned dosage

End point description:

End point type	Secondary

End point timeframe:

week 48

End point values	QD group	BID group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: percentage (%)				
number (not applicable)	66.7	86.7		

Statistical analyses

Statistical analysis title	Comparing percentages
Comparison groups	QD group v BID group
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.195
Method	Fisher exact

Adverse events

Adverse events information	
Timeframe for reporting adverse events: from baseline to week 48	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	DAIDS AE GRADING TAB
Dictionary version	1.0

Reporting groups	
Reporting group title	QD group
Reporting group description: -	
Reporting group title	BID group
Reporting group description: -	

Serious adverse events	QD group	BID group	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)	0 / 15 (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	QD group	BID group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)	2 / 15 (13.33%)	
Vascular disorders			
stroke with serious difficulty in swallowing pills			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Endocrine disorders			
Cushing's syndrome			

subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 15 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 January 2008	Subject withdrawal criteria redefined
25 March 2008	sample size modified
16 April 2008	treatment follow up changed from 24 to 48 weeks (protocol plus information sheet form modified)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported