Clinical trial results:
HERB-DRUG INTERACTION BETWEEN ECHINACEA PURPUREA AND DARUNAVIR-RITONAVIR IN HIV-INFECTED PATIENTS

Summary

EudraCT number	2009-013265-26
Trial protocol	ES
Global end of trial date	30 April 2010

Results information

Result version number	v1 (current)
This version publication date	05 January 2018
First version publication date	05 January 2018

Trial information

Trial identification

Sponsor protocol code	EQUIDAR

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01046890
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, jtoro@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	30 April 2010
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 April 2010
Global end of trial reached?	Yes
Global end of trial date	30 April 2010
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To investigate the potential of Echinacea purpurea, a commonly used botanical supplement, to interact with the boosted protease inhibitor darunavir-ritonavir.

Protection of trial subjects:

not specific

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 January 2010
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: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Fifteen HIV-infected patients who were receiving antiretroviral therapy with darunavir-ritonavir at a dosage of 600/100 mg twice daily for at least 4 weeks and whose HIV-1 RNA load in plasma was <50 copies/ml were included.

Period 1

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

Arms

Arm title	Experimental group

Arm description:

darunavir-ritonavir plus capsules containing E. purpurea root extract

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:

600/100 mg twice daily

Investigational medicinal product name	Arkocapsulas Echinacea
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

500 mg every 6 h from days 1 to 14.

Number of subjects in period 1	Experimental group
Started	15
Completed	15

Baseline characteristics

Reporting groups	
Reporting group title	overall

Reporting group description: -

Reporting group values	overall	Total	
Number of subjects	15	15	
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)	15	15	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	49		
inter-quartile range (Q1-Q3)	43 to 67	-	
Gender categorical Units: Subjects			
Female	1	1	
Male	14	14	

End points

End points reporting groups

Reporting group title	Experimental group
Reporting group description: darunavir-ritonavir plus capsules containing E. purpurea root extract	

Primary: Comparison of darunavir pharmacokinetic : concentration at the end of the dosing interval

End point title	Comparison of darunavir pharmacokinetic : concentration at the end of the dosing interval[1]
End point description:	
End point type	Primary
End point timeframe: day 14	

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: one single arm study

End point values	Experimental group			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mg/liter				
geometric mean (confidence interval 90%)				
after administration of DRV/r	2.1 (1.7 to 2.6)			
after administration of DRV/r + echinacea	1.7 (1.4 to 2.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Comparison of darunavir pharmacokinetic: area under the time-concentration curve

End point title	Comparison of darunavir pharmacokinetic: area under the time-concentration curve[2]
End point description:	
End point type	Primary
End point timeframe: day 14	

Notes:

[2] - 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: one single arm study

End point values	Experimental group			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mg*h/l				
geometric mean (confidence interval 90%)				
after administration of DRV/r	46.2 (40.1 to 53.1)			
after administration of DRV/r+echinacea+	41.6 (36.1 to 47.8)			

Statistical analyses

No statistical analyses for this end point

Primary: Comparison of darunavir pharmacokinetic: maximum concentration

End point title	Comparison of darunavir pharmacokinetic: maximum concentration[3]

End point description:

End point type	Primary

End point timeframe:

day 14

Notes:

[3] - 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: one single arm study

End point values	Experimental group			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mg/liter				
geometric mean (confidence interval 90%)				
after administration DRV/r	6.4 (5.6 to 7.2)			
after administration DRV/r+echinacea	6.2 (5.5 to 7.1)			

Statistical analyses

No statistical analyses for this end point

Primary: Comparison of ritonavir pharmacokinetic: concentration at the end of the dosing interval

End point title	Comparison of ritonavir pharmacokinetic: concentration at the end of the dosing interval[4]

End point description:

End point type	Primary

End point timeframe:

day 14

Notes:

[4] - 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: one single arm study

End point values	Experimental group			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mg/liter				
geometric mean (confidence interval 90%)				
after administration of DRV/r	0.21 (0.17 to 0.26)			
after administration of DRV/r+echinacea	0.22 (0.18 to 0.27)			

Statistical analyses

No statistical analyses for this end point

Primary: Comparison of ritonavir pharmacokinetic: area under the time-concentration curve

End point title	Comparison of ritonavir pharmacokinetic: area under the time-concentration curve[5]

End point description:

End point type	Primary

End point timeframe:

day 14

Notes:

[5] - 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: one single arm study

End point values	Experimental group			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mg*h/l				
geometric mean (confidence interval 90%)				
after administration of DRV/r	6.16 (5.03 to 7.55)			
after administration of DRV/r+echinacea	6.44 (5.26 to 7.89)			

Statistical analyses

No statistical analyses for this end point

Primary: Comparison of ritonavir pharmacokinetic: maximum concentration

End point title	Comparison of ritonavir pharmacokinetic: maximum concentration[6]

End point description:

End point type	Primary

End point timeframe:

day 14

Notes:

[6] - 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: one single arm study

End point values	Experimental group			
Subject group type	Reporting group			
Number of subjects analysed	15			
Units: mg/l				
geometric mean (confidence interval 90%)				
after adminitration of DRV/r	0.86 (0.69 to 1.08)			
after administration of DRV/r+echinacea	1.01 (0.81 to 1.27)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: from baseline to week 4	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	DAIDS AE GRADING TAB
Dictionary version	1.0

Reporting groups	
Reporting group title	experimental group

Reporting group description: -

Serious adverse events	experimental group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 15 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	experimental group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 15 (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: In this clinical trial neither non-serious adverse avents nor serious adverse events occured.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 September 2009	protocol and patient information sheet modified

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported