Clinical trial results:
PILOT STUDY TO ASSESS THE ROLE OF IMMUNE ACTIVATION AND APOPTOSIS AS A MARKER FOR TREATMENT INTENSIFICATION WITH RALTEGRAVIR IN HIV-INFECTED PATIENTS ON ANTIRETROVIRAL THERAPY WITH LONG-TERM VIRAL SUPPRESSION AND UNFAVOURABLE IMMUNOLOGIC RESPONSE (DISCORDANT PATIENTS: V+I-).

Summary

EudraCT number	2008-005473-35
Trial protocol	ES
Global end of trial date	18 May 2011

Results information

Result version number	v1 (current)
This version publication date	09 August 2017
First version publication date	09 August 2017

Trial information

Trial identification

Sponsor protocol code	DISCOR-RAL

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00773708
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	18 May 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 May 2011
Global end of trial reached?	Yes
Global end of trial date	18 May 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess whether the intensification with Raltegravir affect the immune recovery in "discordant" patients with high level of CD8+HLADR+CD38+.

Protection of trial subjects:

not specific

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 March 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: 44
Worldwide total number of subjects	44
EEA total number of subjects	44

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)	44
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

We enrolled 49 HIV-1-infected subjects on suppressive HAART for at least 96 weeks.

Pre-assignment

Screening details:

The final sample comprised 44 patients: 30 in the intensified arm and 14 in the control arm.

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	Intensified arm (RAL arm)

Arm description:

Intensification of previous therapy with Raltegravir

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

Dosage and administration details:

400 mg/12h

Arm title	control arm

Arm description:

Continue with the same antiretroviral therapy

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Intensified arm (RAL arm)	control arm
Started	30	14
Completed	25	14
Not completed	5	0
Consent withdrawn by subject	1	-
Adverse event, non-fatal	3	-
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Intensified arm (RAL arm)
Reporting group description:	
Intensification of previous therapy with Raltegravir	
Reporting group title	control arm
Reporting group description:	
Continue with the same antiretroviral therapy	

Reporting group values	Intensified arm (RAL arm)	control arm	Total
Number of subjects	30	14	44
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)	30	14	44
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
median	48.5	45.5	
inter-quartile range (Q1-Q3)	44 to 53.4	41.8 to 50.8	-
Gender categorical Units: Subjects			
Female	4	2	6
Male	26	12	38

End points

End points reporting groups	
Reporting group title	Intensified arm (RAL arm)
Reporting group description: Intensification of previous therapy with Raltegravir	
Reporting group title	control arm
Reporting group description: Continue with the same antiretroviral therapy	

Primary: Impact of raltegravir intensification on CD4 T cell counts	
End point title	Impact of raltegravir intensification on CD4 T cell counts
End point description:	
End point type	Primary
End point timeframe: from baseline to week 48	

End point values	Intensified arm (RAL arm)	control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	14		
Units: cells/mm3				
median (inter-quartile range (Q1-Q3))				
baseline	253 (208 to 301)	242 (188 to 292)		
week 48	281 (230 to 320)	247 (212 to 411)		

Statistical analyses

Statistical analysis title	Comparing medians between groups
Comparison groups	Intensified arm (RAL arm) v control arm
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.668
Method	Wilcoxon (Mann-Whitney)

Primary: Percentage CD4 T cell counts	
End point title	Percentage CD4 T cell counts

End point description:

End point type	Primary

End point timeframe:
from baseline to week 48

End point values	Intensified arm (RAL arm)	control arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	30	14		
Units: cells/mm3				
median (inter-quartile range (Q1-Q3))				
baseline	19 (14 to 22)	19 (15 to 21)		
week 48	19 (15 to 22)	18 (17 to 23)		

Statistical analyses

Statistical analysis title	Comparing medians between groups
Comparison groups	Intensified arm (RAL arm) v control arm
Number of subjects included in analysis	44
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.761
Method	Wilcoxon (Mann-Whitney)

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	Intensified arm (RAL arm)

Reporting group description: -

Serious adverse events	Intensified arm (RAL arm)		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 30 (6.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Epilepsy			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Bowel obstruction			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Intensified arm (RAL arm)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 30 (3.33%)		
Gastrointestinal disorders			
Diarrhoea			

subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 January 2009	Protocol modified (wk 2 visit added + safety analysis added)
16 April 2009	Second phase added + information sheet form modified
29 May 2009	protocol modified (substudy included) and information sheet form modified

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported