Clinical trial results:
EFFICACY OF TREATMENT INTENSIFICATION WITH MARAVIROC ON HIV-1 VIRAL LATENCY IN RECENTLY INFECTED HIV-1 NAÏVE PATIENTS STARTING RALTEGRAVIR PLUS TENOFOVIR/EMTRICITABINE. (EFICACIA DE LA INTENSIFICACIÓN DE TRATAMIENTO CON MARAVIROC EN LA LATENCIA VIRAL DEL VIH-1 EN PACIENTES NAIVES RECIENTEMENTE INFECTADOS QUE INICIAN RALTEGRAVIR MÁS TENOFOVIR/EMTRICITABINA)

Summary

EudraCT number	2008-006065-87
Trial protocol	ES
Global end of trial date	16 May 2011

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	MARAVIBOOST

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00808002
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	16 May 2011
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 May 2011
Global end of trial reached?	Yes
Global end of trial date	16 May 2011
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Change at 48 weeks in the slope of decay of integrated and unintegrated viral DNA in PBMCs.

Protection of trial subjects:

not specific

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 February 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: 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:

We screened 44 HIV-1-positive treatment-naïve patients with documented seroconversion in the previous 6 months.

Pre-assignment

Screening details:

A total of 30 HIV-1-positive patients with documented seroconversion in the previous 6 months and screened for CCR5-tropic viruses were 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	Control arm

Arm description:

tenofovir/emtricitabine/raltegravir

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

Dosage and administration details:

300/200 mg QD

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 BiD

Arm title	Intensifying HAART group (+MVC group)

Arm description:

tenofovir/emtricitabine/raltegravir plus maraviroc

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

Dosage and administration details:

300/200 mg QD

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 BiD

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

Dosage and administration details:
300mg BiD

Number of subjects in period 1	Control arm	Intensifying HAART group (+MVC group)
Started	15	15
Completed	15	15

Baseline characteristics

Reporting groups	
Reporting group title	Control arm
Reporting group description: tenofovir/emtricitabine/raltegravir	
Reporting group title	Intensifying HAART group (+MVC group)
Reporting group description: tenofovir/emtricitabine/raltegravir plus maraviroc	

Reporting group values	Control arm	Intensifying HAART group (+MVC 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	31.6	34.2	
inter-quartile range (Q1-Q3)	26.1 to 39.1	31.8 to 38.9	-
Gender categorical Units: Subjects			
Female	0	0	0
Male	15	15	30

End points

End points reporting groups

Reporting group title	Control arm
Reporting group description: tenofovir/emtricitabine/raltegravir	
Reporting group title	Intensifying HAART group (+MVC group)
Reporting group description: tenofovir/emtricitabine/raltegravir plus maraviroc	

Primary: changes in total VIH-1 DNA

End point title	changes in total VIH-1 DNA
End point description:	
End point type	Primary
End point timeframe: from baseline to week 48	

End point values	Control arm	Intensifying HAART group (+MVC group)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: copies per million PBMCs				
median (inter-quartile range (Q1-Q3))				
baseline	560 (305 to 1082)	325 (138 to 893)		
week 48	73 (39 to 118)	60 (16 to 87)		

Statistical analyses

Statistical analysis title	Comparing medians between groups
Statistical analysis description: Baseline	
Comparison groups	Intensifying HAART group (+MVC group) v Control arm
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.93
Method	Wilcoxon (Mann-Whitney)

Primary: changes in 2-LTR circles

End point title	changes in 2-LTR circles

End point description:

End point type	Primary

End point timeframe:
from baseline to week 48

End point values	Control arm	Intensifying HAART group (+MVC group)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: copies per million PBMCs				
median (inter-quartile range (Q1-Q3))				
baseline	35.4 (25.2 to 76.5)	52 (6.5 to 83.4)		
week 48	6.4 (0.1 to 20.6)	9.2 (0 to 18.4)		

Statistical analyses

Statistical analysis title	Comparing medians between groups

Statistical analysis description:
Comparison were made in baseline

Comparison groups	Control arm v Intensifying HAART group (+MVC group)
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.88
Method	Wilcoxon (Mann-Whitney)

Secondary: number of patients who had isolated blips in plasma viremia

End point title	number of patients who had isolated blips in plasma viremia

End point description:

End point type	Secondary

End point timeframe:
week 48

End point values	Control arm	Intensifying HAART group (+MVC group)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: patients				
number (not applicable)	1	3		

Statistical analyses

No statistical analyses for this end point

Secondary: number of patients with undetectable plasma viral load

End point title	number of patients with undetectable plasma viral load

End point description:

End point type	Secondary

End point timeframe:

week 48

End point values	Control arm	Intensifying HAART group (+MVC group)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: patients				
number (not applicable)	15	15		

Statistical analyses

No statistical analyses for this end point

Secondary: change in the lymphocyte activation marker HLADR+CD38+ (% of CD4+)

End point title	change in the lymphocyte activation marker HLADR+CD38+ (% of CD4+)

End point description:

End point type	Secondary

End point timeframe:

from baseline to week 48

End point values	Control arm	Intensifying HAART group (+MVC group)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: % of CD4+				
median (inter-quartile range (Q1-Q3))				
baseline	14.2 (11.3 to 20.7)	17.1 (14.1 to 19.8)		
week 48	4.5 (3.4 to 7.1)	5.85 (5 to 6.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: change in the lymphocyte activation marker HLADR+CD38+ (% of CD8+)

End point title	change in the lymphocyte activation marker HLADR+CD38+ (% of CD8+)

End point description:

End point type	Secondary

End point timeframe:

from baeline to week 48

End point values	Control arm	Intensifying HAART group (+MVC group)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15	15		
Units: % of CD8+				
median (inter-quartile range (Q1-Q3))				
baseline	56.3 (40.7 to 60.1)	53 (48.8 to 59.5)		
week 48	15 (10.4 to 18.6)	14.6 (10.9 to 16.8)		

Statistical analyses

No statistical analyses for this end point

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	Control group
Reporting group description: -	
Reporting group title	Intensifying HAART group (+MVC group)
Reporting group description: -	

Serious adverse events	Control group	Intensifying HAART group (+MVC 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: 0 %

Non-serious adverse events	Control group	Intensifying HAART group (+MVC group)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 15 (20.00%)	10 / 15 (66.67%)	
Nervous system disorders			
Syphilis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Genital herpes			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
heartburn			

subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Sinusitis			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	2 / 15 (13.33%)	0 / 15 (0.00%)	
occurrences (all)	2	0	
odynophagia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Endocrine disorders			
hypertransaminasemia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
neck strain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Cervical vertebral fracture (c5-c6)			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Infections and infestations			
urinary infection			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gonococcia			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Gonorrhoea			
subjects affected / exposed	0 / 15 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 September 2009	secondary objective added in the protocol
19 November 2009	1. number of patients enrolled increased and recruitment period extended 2. lymphocyte subsets and immune activation performed in week 24 added
30 March 2010	number of patients enrolled increased
28 July 2010	two substudies added
22 December 2010	ileum biopsy substudy added

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported