# 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<br>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<br>Units: years | | | |
| median | 31.6 | 34.2 | |
| inter-quartile range (Q1-Q3) | 26.1 to 39.1 | 31.8 to 38.9 | - |
| Gender categorical<br>Units: Subjects | | | |
| Female | 0 | 0 | 0 |
| Male | 15 | 15 | 30 |

## End points

### End points reporting groups

| | |
|---|---|
| Reporting group title | Control arm |
| Reporting group description:<br>tenofovir/emtricitabine/raltegravir | |
| Reporting group title | Intensifying HAART group (+MVC group) |
| Reporting group description:<br>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:<br>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:<br>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<br>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