



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/mm ³ | | | | |
| 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/mm ³ | | | | |
| 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 | 1 / 30 (3.33%) | | |
| occurrences (all) | 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