



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 administration 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 events nor serious adverse events occurred.

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