



Clinical trial results: Doravirine concentrations and antiviral activity in genital fluids in HIV-1 infected individuals.

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2018-003921-27 |
| Trial protocol | ES |
| Global end of trial date | 24 August 2020 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 21 December 2023 |
| First version publication date | 21 December 2023 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | DORAGEN |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04097925 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Fundación FLS de Lucha Contra el Sida, las Enfermedades Infecciosas y la Promoción de la Salud y la Ciencia |
| Sponsor organisation address | Ctra. de Canyet s/n, Badalona, Spain, 08916 |
| Public contact | Antonio Navarro, Fundación FLS de Lucha Contra el Sida, las Enfermedades Infecciosas y la Promoción de la Salud y la, +34 675335888, anavarro@irsicaixa.es |
| Scientific contact | Antonio Navarro, Fundación FLS de Lucha Contra el Sida, las Enfermedades Infecciosas y la Promoción de la Salud y la, +34 675335888, anavarro@irsicaixa.es |

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 | 24 August 2020 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 24 August 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

Determine Doravirine concentrations in seminal plasma and cervicovaginal fluid in HIV-1 infected male and female individuals receiving ART with Doravirine plus TAF/FTC.

Protection of trial subjects:

Although assessed treatment is approved and is used in routine care, the sponsor contracted an insurance as a mandatory aspect defined in the legal framework of the country site due a different procedures performed during the clinical trial out of routine clinical practice.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 18 February 2020 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | Yes |

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:

Subjects who met inclusion criteria and accepted to sign the informed consent to participate will be cited for a screening visit. A total of 30 HIV-infected patients were selected at the screening phase.

Recruitment was started 18-feb-2020 and the last patient recruited was 28-may-2020.

Pre-assignment

Screening details:

30 patient were screened.

Pre-assignment period milestones

| | |
|------------------------------|----|
| Number of subjects started | 30 |
| Number of subjects completed | 30 |

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall trial (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|-------------|
| Arm title | DOR/TAF+FTC |
|-----------|-------------|

Arm description:

Doravirine administered orally once daily in combination with Tenofovir alafenamide (TAF) and emtricitabine (FTC)

co-formulated as single tablet (Descovy® TAF/FTC) and administered orally once daily

| | |
|--|---|
| Arm type | Experimental |
| Investigational medicinal product name | Doravirine/Emtricitabine/Tenofovir alafenamide fumarate |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Doravirine 100 mg table + Tenofovir alafenamide 25 mg / emtricitabine 200 mg tablet

| Number of subjects in period 1 | DOR/TAF+FTC |
|--------------------------------|-------------|
| Started | 30 |
| Completed | 29 |
| Not completed | 1 |
| Consent withdrawn by subject | 1 |

Baseline characteristics

Reporting groups

| | |
|---|--------------------------------|
| Reporting group title | Overall trial (overall period) |
| Reporting group description: | |
| Doravirine (MK-1439) 100 mg administered orally once daily in combination with Tenofovir alafenamide (TAF) and emtricitabine (FTC) co-formulated as single tablet (Descovy® TAF/FTC 25/200 mg) and administered orally once daily during 16 weeks | |
| Doravirine: Doravirine 100 mg tablet | |
| Descovy: Tenofovir alafenamide 25 mg / emtricitabine 200 mg tablet | |

| Reporting group values | Overall trial (overall period) | Total | |
|--|--------------------------------|-------|--|
| Number of subjects | 30 | 30 | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | | 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) | | 0 | |
| From 65-84 years | | 0 | |
| 85 years and over | | 0 | |
| Age continuous | | | |
| Units: years | | | |
| median | 41 | | |
| inter-quartile range (Q1-Q3) | 23 to 62 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 15 | 15 | |
| Male | 15 | 15 | |

Subject analysis sets

| | |
|---|------------------|
| Subject analysis set title | Overall analysis |
| Subject analysis set type | Full analysis |
| Subject analysis set description: | |
| All patients were included in this analysis. Full analysis assessed the differences in viral suppression efficacy on the different reservoirs evaluated | |

| Reporting group values | Overall analysis | | |
|------------------------|------------------|--|--|
| Number of subjects | 29 | | |
| Age categorical | | | |
| Units: Subjects | | | |
| In utero | | | |

| | | | |
|--|----------------|--|--|
| Preterm newborn infants (gestational age < 37 wks) Newborns (0-27 days) Infants and toddlers (28 days-23 months) Children (2-11 years) Adolescents (12-17 years) Adults (18-64 years) From 65-84 years 85 years and over | | | |
| Age continuous Units: years median inter-quartile range (Q1-Q3) | 41 23 to 62 | | |
| Gender categorical Units: Subjects | | | |
| Female | 15 | | |
| Male | 14 | | |

End points

End points reporting groups

| | |
|---|------------------|
| Reporting group title | DOR/TAF+FTC |
| Reporting group description: Doravirine administered orally once daily in combination with Tenofovir alafenamide (TAF) and emtricitabine (FTC) co-formulated as single tablet (Descovy® TAF/FTC) and administered orally once daily | |
| Subject analysis set title | Overall analysis |
| Subject analysis set type | Full analysis |
| Subject analysis set description: All patients were included in this analysis. Full analysis assessed the differences in viral suppression efficacy on the different reservoirs evaluated | |

Primary: Concentration of Doravirine in Seminal Plasma Fluid

| | |
|--|--|
| End point title | Concentration of Doravirine in Seminal Plasma Fluid ^[1] |
| End point description: | |
| End point type | Primary |
| End point timeframe: 8 weeks after switching (from baseline visit) to Doravirine plus TAF/FTC | |
| 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: Data reported has been a descriptive analysis, which shows the Doravirine concentration in different anatomical reservoirs | |

| End point values | DOR/TAF+FTC | Overall analysis | | |
|---------------------------------------|-------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 15 ^[2] | 15 ^[3] | | |
| Units: ng/ml | | | | |
| median (inter-quartile range (Q1-Q3)) | 127 (31.2 to 272) | 127 (31.2 to 272) | | |

Notes:
[2] - Only male participants were assessed on this endpoint
[3] - Only male participants were assessed on this endpoint

Statistical analyses

No statistical analyses for this end point

Primary: Concentration of Doravirine in Cervicovaginal Fluid

| | |
|--|--|
| End point title | Concentration of Doravirine in Cervicovaginal Fluid ^[4] |
| End point description: | |
| End point type | Primary |
| End point timeframe: 8 weeks after switching to Doravirine plus TAF/FTC | |
| 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: Data reported has been a descriptive analysis, which shows the Doravirine concentration in different anatomical reservoirs | |

| End point values | DOR/TAF+FTC | Overall analysis | | |
|---------------------------------------|------------------------|------------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 14 ^[5] | 14 ^[6] | | |
| Units: ng/ml | | | | |
| median (inter-quartile range (Q1-Q3)) | 505.8 (199.8 to 960.8) | 505.8 (199.8 to 960.8) | | |

Notes:

[5] - Only female participants were assessed on this endpoint

[6] - Only female participants were assessed on this endpoint

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With HIV-1 RNA Seminal Plasma <40 Copies/mL

| | |
|-----------------|---|
| End point title | Number of Participants With HIV-1 RNA Seminal Plasma <40 Copies/mL ^[7] |
|-----------------|---|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

8 weeks after switching (from baseline visit) to Doravirine plus TAF/FTC

Notes:

[7] - 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: Data reported has been a descriptive analysis, which shows the number of participants with HIV-2 RNA

<40 copies/mL in different anatomical reservoirs

| End point values | DOR/TAF+FTC | Overall analysis | | |
|-------------------------------|-------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 15 ^[8] | 15 ^[9] | | |
| Units: Number of participants | | | | |
| number (not applicable) | 15 | 15 | | |

Notes:

[8] - Only male participants were assessed on this endpoint

[9] - Only male participants were assessed on this endpoint

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With HIV-1 RNA Cervicovaginal Fluid <40 Copies/mL

| | |
|-----------------|--|
| End point title | Number of Participants With HIV-1 RNA Cervicovaginal Fluid <40 Copies/mL ^[10] |
|-----------------|--|

End point description:

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

8 weeks after switching (from baseline visit) to Doravirine plus TAF/FTC

Notes:

[10] - 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: Data reported has been a descriptive analysis, which shows the number of participants with HIV-2 RNA

<40 copies/mL in different anatomical reservoirs

| End point values | DOR/TAF+FTC | Overall analysis | | |
|-------------------------------|--------------------|----------------------|--|--|
| Subject group type | Reporting group | Subject analysis set | | |
| Number of subjects analysed | 14 ^[11] | 14 ^[12] | | |
| Units: Number of participants | | | | |
| number (not applicable) | 14 | 14 | | |

Notes:

[11] - Only female participants were assessed on this endpoint

[12] - Only female participants were assessed on this endpoint

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

16 weeks

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|--------------------|--------|
| Dictionary name | MedDRA |
| Dictionary version | 17.1 |

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

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: Non-serious adverse event were reported during the 16 weeks of follow up

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported