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
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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	41		
inter-quartile range (Q1-Q3)	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 particiopants				
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