



Clinical trial results:

Doravirine concentrations and antiviral activity in Cerebrospinal fluid in HIV-1 Infected individuals

Summary

EudraCT number	2018-003915-24
Trial protocol	ES
Global end of trial date	31 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	DORACeNeS
-----------------------	-----------

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04079452
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	31 August 2020
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	31 August 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To assess Doravirine concentrations in CSF and to estimate penetration into The CNS.
- To evaluate antiviral activity of a combination of TAF/FTC+Doravirine in CSF.

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: 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:

Subjects who met inclusion criteria and accepted to sign the informed consent to participate will be cited for a screening visit. A total of 15 HIV-infected patients were selected at the screening phase.

Recruitment was started 18-feb-2020 and the last patient recruited was 21-may-2020.

Pre-assignment

Screening details:

15 patients were screened

Pre-assignment period milestones

Number of subjects started	15
Number of subjects completed	15

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	15
Completed	15

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	15	15	
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	47		
inter-quartile range (Q1-Q3)	27 to 65	-	
Gender categorical			
Units: Subjects			
Female	2	2	
Male	13	13	

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.	

Reporting group values	Overall analysis		
Number of subjects	15		
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)			
Gender categorical Units: Subjects			
Female	2		
Male	13		

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.	

Primary: Total Doravirine Concentrations in Cerebrospinal Fluid

End point title	Total Doravirine Concentrations in Cerebrospinal Fluid ^[1]
End point description:	

End point type	Primary
End point timeframe: 4 Weeks	

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 total Doravirine concentration in CSF

End point values	DOR/TAF+FTC	Overall analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	58.6 (23.2 to 127.3)	58.6 (23.2 to 127.3)		

Statistical analyses

No statistical analyses for this end point

Primary: Total Doravirine Concentrations in Blood Plasma

End point title	Total Doravirine Concentrations in Blood Plasma ^[2]
End point description:	

End point type	Primary
End point timeframe: 4 Weeks	

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: Data reported has been a descriptive analysis.

End point values	DOR/TAF+FTC	Overall analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: ng/ml				
median (inter-quartile range (Q1-Q3))	417.6 (169.5 to 942.2)	417.6 (169.5 to 942.2)		

Statistical analyses

No statistical analyses for this end point

Primary: Total Doravirine Concentration CSF/Plasma Ratio

End point title	Total Doravirine Concentration CSF/Plasma Ratio ^[3]
-----------------	--

End point description:

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

End point timeframe:

4 weeks

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: Data reported has been a descriptive analysis.

End point values	DOR/TAF+FTC	Overall analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: ratio				
median (inter-quartile range (Q1-Q3))	0.13 (0.09 to 0.19)	0.13 (0.09 to 0.19)		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With HIV-1 RNA cerebrospinal fluid <40 Copies/mL

End point title	Number of Participants With HIV-1 RNA cerebrospinal fluid <40 Copies/mL ^[4]
-----------------	--

End point description:

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

End point timeframe:

4 weeks

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.

End point values	DOR/TAF+FTC	Overall analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: Count of participants				
number (not applicable)	13	13		

Statistical analyses

No statistical analyses for this end point

Primary: Number of patients with HIV-1 RNA in blood plasma <40 copies/ml

End point title	Number of patients with HIV-1 RNA in blood plasma <40 copies/ml ^[5]
-----------------	--

End point description:

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

End point timeframe:

4 weeks

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: Data reported has been a descriptive analysis.

End point values	DOR/TAF+FTC	Overall analysis		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: Count of participants				
number (not applicable)	14	14		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

6 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 6 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