Clinical trial results:
A Study to Assess the Acceptability of the Darunavir/Cobicistat (DRV/COBI) Fixed-dose Combination (FDC) Tablet in Human Immunodeficiency Virus (HIV)-1 Infected Children Aged >=3 Years and Weighing >=15 kg to <25 kg

Summary

EudraCT number	2021-000738-32
Trial protocol	ES Outside EU/EEA
Global end of trial date	23 September 2022

Results information

Result version number	v1 (current)
This version publication date	07 April 2023
First version publication date	07 April 2023

Trial information

Trial identification

Sponsor protocol code	TMC114FD1HTX1001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International N.V.
Sponsor organisation address	Turnhoutseweg 30, Beerse, Belgium, B-2340
Public contact	Clinical Registry Group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International N.V., ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001280-PIP01-12
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	23 September 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	23 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Main objective of the trial was to assess, as part of the acceptability, the ability to swallow a single dose of the 600/90 milligrams (mg) DRV/COBI FDC tablet dispersed in water.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 August 2022
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: 5
Country: Number of subjects enrolled	United States: 3
Country: Number of subjects enrolled	South Africa: 4
Worldwide total number of subjects	12
EEA total number of subjects	5

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)	12
Adolescents (12-17 years)	0
Adults (18-64 years)	0
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 12 HIV-1 infected children subjects were enrolled and treated in the study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	DRV/COBI FDC 600/90mg

Arm description:

HIV-infected subjects received a single dose of the DRV 600 mg and COBI 90 mg in a FDC tablet formulation dispersed in water once orally on Day 1.

Arm type	Experimental
Investigational medicinal product name	Cobicistat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered with single fixed dose of Cobicistat (COBI) 90 mg dispersed in water on Day 1.

Investigational medicinal product name	Darunavir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects were administered with single fixed dose of Darunavir (DRV) 600 mg dispersed in water on Day 1.

Number of subjects in period 1	DRV/COBI FDC 600/90mg
Started	12
Completed	12

Baseline characteristics

Reporting groups	
Reporting group title	DRV/COBI FDC 600/90mg
Reporting group description:	
HIV-infected subjects received a single dose of the DRV 600 mg and COBI 90 mg in a FDC tablet formulation dispersed in water once orally on Day 1.	

Reporting group values	DRV/COBI FDC 600/90mg	Total	
Number of subjects	12	12	
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	12	12	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65 to 84 years	0	0	
85 years and over	0	0	
Title for AgeContinuous			
Units: years			
median	5		
full range (min-max)	4 to 8	-	
Title for Gender			
Units: subjects			
Female	9	9	
Male	3	3	

End points

End points reporting groups

Reporting group title	DRV/COBI FDC 600/90mg

Reporting group description:

HIV-infected subjects received a single dose of the DRV 600 mg and COBI 90 mg in a FDC tablet formulation dispersed in water once orally on Day 1.

Primary: Percentage of Subjects With Ability to Swallow the Darunavir/Cobicistat (DRV/COBI) Fixed Dosed Combination (FDC) Tablet Dispersed in Water as Reported by Observer

End point title	Percentage of Subjects With Ability to Swallow the Darunavir/Cobicistat (DRV/COBI) Fixed Dosed Combination (FDC) Tablet Dispersed in Water as Reported by Observer[1]

End point description:

Percentage of subjects with ability to swallow the DRV/COBI FDC tablet dispersed in water as reported by observer were reported. The subject's observer was given an acceptability questionnaire to assess about how the subject had taken the tablet dispersed in water and were asked to respond on the responses "fully", "partially" and "not at all". Only the category in which at least 1 subject had data were reported. Intent to treat (ITT) population included all subjects who were enrolled and received at least partial study intervention.

End point type	Primary

End point timeframe:

Day 1

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: No formal hypothesis testing was planned in this study. The statistical analysis was based upon descriptive statistics.

End point values	DRV/COBI FDC 600/90mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of subjects				
number (confidence interval 95%)	100 (75.75 to 100)			

Statistical analyses

No statistical analyses for this end point

Secondary: Ease of Swallowing of Tablet Dispersed in Water Reported by Subject

End point title	Ease of Swallowing of Tablet Dispersed in Water Reported by Subject

End point description:

An acceptability questionnaire was used to assess the ease of swallowing of tablet dispersed in water by the subject. Subjects were asked to indicate how difficult/easy it was to swallow the tablet dispersed in water on a 5-point hedonic scale: very difficult, difficult, Ok, easy, very easy. Only the category in which at least 1 subject had data were reported. Percentage of subjects with ease of swallowing of tablet dispersed in water were reported. ITT population included all subjects who were enrolled and received at least partial study intervention.

End point type	Secondary

End point timeframe:

Day 1

End point values	DRV/COBI FDC 600/90mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of subjects				
number (not applicable)				
Difficult	16.7			
Okay	8.3			
Easy	16.7			
Very Easy	58.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Ease of Swallowing of Tablet Dispersed in Water by the Subject as Reported by the Caregiver

End point title	Ease of Swallowing of Tablet Dispersed in Water by the Subject as Reported by the Caregiver

End point description:

An acceptability questionnaire was used to assess the ease of swallowing of tablet dispersed in water by the caregiver on the basis of reaction/ facial expression of children. Caregiver were asked to indicate how difficult/easy it was for the subjects to swallow the tablet dispersed in water on a 5-point hedonic scale: very difficult, difficult, Ok, easy, very easy. Only the category in which at least 1 subject had data were reported. Percentage of subjects with ease of swallowing of tablet dispersed in water were reported. ITT population included all subjects who were enrolled and received at least partial study intervention

End point type	Secondary

End point timeframe:

Day 1

End point values	DRV/COBI FDC 600/90mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of subjects				
number (not applicable)				
Very Difficult	8.3			
Difficult	8.3			
Okay	16.7			
Easy	16.7			
Very Easy	50.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Palatability of the Tablet Dispersed in Water Reported by the Subject

End point title	Palatability of the Tablet Dispersed in Water Reported by the Subject

End point description:

An acceptability questionnaire was given to subject to assess palatability of tablet dispersed in water. Subjects were asked to respond on how much they like the taste of the tablet dispersed in water on a 5-point hedonic scale: disliked very much, disliked a little, not sure, liked a little, liked a lot. Only categories with at least 1 subject are reported. ITT population included all subjects who were enrolled and received at least partial study intervention.

End point type	Secondary

End point timeframe:

Day 1

End point values	DRV/COBI FDC 600/90mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of subjects				
number (not applicable)				
Disliked very much	33.3			
Liked a little	33.3			
Liked a lot	33.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Palatability of the Tablet Dispersed in Water by the Subject as Reported by the Caregiver

End point title	Palatability of the Tablet Dispersed in Water by the Subject as Reported by the Caregiver

End point description:

An acceptability questionnaire was given to caregiver to assess palatability of tablet dispersed in water based on reaction/ facial expression of the subject. Subjects were asked to respond on how much they like the taste of the tablet dispersed in water on a 5-point hedonic scale: disliked very much, disliked a little, not sure, liked a little, liked a lot. ITT population included all subjects who were enrolled and received at least partial study intervention.

End point type	Secondary

End point timeframe: Day 1

End point values	DRV/COBI FDC 600/90mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of subjects				
number (not applicable)				
Disliked very much	41.7			
Disliked a little	8.3			
Not sure	8.3			
Liked a little	25.0			
Liked a lot	16.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Ease of Dispersion of the Tablet in Water as Reported by the Caregiver

End point title	Ease of Dispersion of the Tablet in Water as Reported by the Caregiver

End point description:

Ease of dispersion of the tablet in water was reported by the caregiver. An acceptability questionnaire was given to the caregiver to assess how easy it was to disperse the tablet on a 5-point hedonic scale: very difficult, difficult, Ok, easy, very easy. Only categories with at least 1 subject are reported. ITT population included all subjects who were enrolled and received at least partial study intervention.

End point type	Secondary

End point timeframe:

Day 1

End point values	DRV/COBI FDC 600/90mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of subjects				
number (not applicable)				
Difficult	16.7			
Ok	33.3			
Easy	16.7			
Very Easy	33.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability of Taking the Tablet Dispersed in Water Everyday Reported by Subject

End point title	Acceptability of Taking the Tablet Dispersed in Water Everyday Reported by Subject

End point description:

Acceptability of taking the tablet dispersed in water everyday by subject was reported. An acceptability questionnaire was given to subject to assess the acceptability of tablet dispersed in water. Subjects were asked to indicate how difficult/easy it was to take the tablet every day on a 5-point hedonic scale: disliked very much, disliked a little, not sure, liked a little, liked a lot. ITT population included all subjects who were enrolled and received at least partial study intervention.

End point type	Secondary

End point timeframe:

Day 1

End point values	DRV/COBI FDC 600/90mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of subjects				
number (not applicable)				
Disliked very much	8.3			
Disliked a little	16.7			
Not sure	8.3			
Liked a little	16.7			
Liked a Lot	41.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability of Taking the Tablet Dispersed in Water Everyday by the Subject as Reported by the Caregiver

End point title	Acceptability of Taking the Tablet Dispersed in Water Everyday by the Subject as Reported by the Caregiver

End point description:

Acceptability of taking the tablet dispersed in water by the subject everyday was reported by the caregiver on the basis of reaction/ facial expression of children. An acceptability questionnaire was given to caregiver to assess how easy it was to give the tablet dispersed in water to child every day via a 5-point hedonic scale: very difficult, difficult, Ok, easy, very easy. Only categories with at least 1 subject are reported. ITT population included all subjects who were enrolled and received at least partial study intervention. Here N (number of subjects analysed) signifies subjects evaluable for this endpoint.

End point type	Secondary

End point timeframe:

Day 1

End point values	DRV/COBI FDC 600/90mg			
Subject group type	Reporting group			
Number of subjects analysed	11			
Units: Percentage of subject				
number (not applicable)				
Very difficult	8.3			
Okay	50.0			
Very easy	41.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (SAEs)

End point title	Percentage of Subjects With Treatment Emergent Adverse Events (TEAEs) and Treatment Emergent Serious Adverse Events (SAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a clinical investigation where subjects administered a product or medical device; the event needed not necessarily have a causal relationship with the treatment or usage. TEAEs were events between first dose of study and until 11 days after the last dose of study medication. An SAE was any untoward medical occurrence at any dose that: resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, or resulted in congenital anomaly/birth defect. ITT population included all subjects who were enrolled and received at least partial study intervention.

End point type	Secondary

End point timeframe:

Up to Day 11

End point values	DRV/COBI FDC 600/90mg			
Subject group type	Reporting group			
Number of subjects analysed	12			
Units: Percentage of subjects				
number (not applicable)				
TEAE	0			
TESAE	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Up to 32 days

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	DRV/COBI FDC

Reporting group description:

Subjects received DRV 600 mg and COBI 150 mg in a FDC tablet formulation dispersed in water once orally on Day 1.

Serious adverse events	DRV/COBI FDC		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (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	DRV/COBI FDC		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 12 (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: No subject experienced non-serious adverse event during the trial.

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