Clinical trial results:
A Study to Assess the Acceptability of Scored Film-coated Darunavir/Cobicistat/Emtricitabine/Tenofovir alafenamide (D/C/F/TAF) Fixed-dose Combination (FDC) Tablets in HIV-1 Infected Pediatric Participants Aged 6 to <12 years, Using Matching Placebo Tablets

Summary

EudraCT number	2019-001384-68
Trial protocol	ES
Global end of trial date	06 March 2020

Results information

Result version number	v1 (current)
This version publication date	20 June 2021
First version publication date	20 June 2021

Trial information

Trial identification

Sponsor protocol code	TMC114FD2HTX1006

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04006704
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Sciences Ireland UC
Sponsor organisation address	Barnahely, Cork, Ireland, P43 FA46
Public contact	Clinical Registry Group, Janssen Sciences Ireland UC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Sciences Ireland UC, 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-001825-PIP01-15
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	06 March 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 March 2020
Global end of trial reached?	Yes
Global end of trial date	06 March 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the ability to swallow the placebo-matched scored film-coated D/C/F/TAF FDC (fixed-dose combination) tablet, irrespective of the mode of intake.

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. Safety evaluations were based upon the type, incidence, and severity of Treatment-emergent adverse events (TEAEs) reported throughout the study and on changes in physical examination.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 October 2019
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: 14
Country: Number of subjects enrolled	United States: 10
Worldwide total number of subjects	24
EEA total number of subjects	14

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)	24
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 24 participants were enrolled and all participants completed the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo whole then Placebo split

Arm description:

Subjects received scored film-coated FDC matching placebo tablet, swallowed whole on Day 1 in intake Period 1 followed by scored film-coated FDC matching placebo tablet, swallowed as a split tablet on Day 1 in intake Period 2. Both the intakes were separated by at least 15 minutes.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single placebo tablet matching the scored film-coated D/C/F/TAF 675/150/200/10 mg FDC tablets as a whole tablet followed by Scored film-coated placebo tablet, swallowed as a split tablet.

Arm title	Placebo split then Placebo whole

Arm description:

Subjects received scored film-coated FDC matching placebo tablet, swallowed as a split tablet on Day 1 in intake Period 1 followed by scored film-coated FDC matching placebo tablet, swallowed whole on Day 1 in intake Period 2. Both the intakes were separated by at least 15 minutes.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received a single placebo tablet matching the scored film-coated D/C/F/TAF 675/150/200/10 mg FDC tablets as a split tablet followed by Scored film-coated placebo tablet, swallowed whole.

Number of subjects in period 1	Placebo whole then Placebo split	Placebo split then Placebo whole
Started	12	12
Completed	12	12

Baseline characteristics

Reporting groups	
Reporting group title	Placebo whole then Placebo split
Reporting group description:	
Subjects received scored film-coated FDC matching placebo tablet, swallowed whole on Day 1 in intake Period 1 followed by scored film-coated FDC matching placebo tablet, swallowed as a split tablet on Day 1 in intake Period 2. Both the intakes were separated by at least 15 minutes.	
Reporting group title	Placebo split then Placebo whole
Reporting group description:	
Subjects received scored film-coated FDC matching placebo tablet, swallowed as a split tablet on Day 1 in intake Period 1 followed by scored film-coated FDC matching placebo tablet, swallowed whole on Day 1 in intake Period 2. Both the intakes were separated by at least 15 minutes.	

Reporting group values	Placebo whole then Placebo split	Placebo split then Placebo whole	Total
Number of subjects	12	12	24
Title for AgeCategorical Units: subjects			
Children (2-11 years)	12	12	24
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
median	9	9.5	
full range (min-max)	7 to 11	7 to 11	-
Title for Gender Units: subjects			
Female	7	8	15
Male	5	4	9

End points

End points reporting groups

Reporting group title	Placebo whole then Placebo split
Reporting group description:	
Subjects received scored film-coated FDC matching placebo tablet, swallowed whole on Day 1 in intake Period 1 followed by scored film-coated FDC matching placebo tablet, swallowed as a split tablet on Day 1 in intake Period 2. Both the intakes were separated by at least 15 minutes.	
Reporting group title	Placebo split then Placebo whole
Reporting group description:	
Subjects received scored film-coated FDC matching placebo tablet, swallowed as a split tablet on Day 1 in intake Period 1 followed by scored film-coated FDC matching placebo tablet, swallowed whole on Day 1 in intake Period 2. Both the intakes were separated by at least 15 minutes.	
Subject analysis set title	D/C/F/TAF FDC Placebo–Whole
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received scored film-coated D/C/F/TAF FDC matched Placebo tablet as a whole tablet.	
Subject analysis set title	D/C/F/TAF FDC Placebo–Split
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received scored film-coated D/C/F/TAF FDC matched Placebo tablet as a split tablet.	
Subject analysis set title	D/C/F/TAF FDC Placebo (All Subjects)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received D/C/F/TAF FDC Placebo tablets as a whole and split tablet	

Primary: Percentage of Subjects who are Able to Swallow the Scored Film-Coated D/C/F/TAF FDC Tablet Irrespective of Mode of Intake

End point title	Percentage of Subjects who are Able to Swallow the Scored Film-Coated D/C/F/TAF FDC Tablet Irrespective of Mode of Intake[1]
End point description:	
Ability to swallow the scored film-coated tablet irrespective of mode of intake (whole or split tablet) was assessed. The intent-to-treat (ITT) population included all the subjects who were randomized and received at least 1 dose of treatment subsequent to randomization in the study.	
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: Analysis was descriptive in nature, no inferential analysis was done.

End point values	D/C/F/TAF FDC Placebo (All Subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Percentage of Subjects				
number (confidence interval 95%)	95.8 (79.76 to 99.26)			

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability of Intake of the Whole Tablet by the Subject and by the Caregiver

End point title	Acceptability of Intake of the Whole Tablet by the Subject and by the Caregiver

End point description:

Acceptability of intake of whole tablet was assessed based on a 3-point questionnaire indicating how hard/easy it was to swallow the tablet, ('hard', 'neither hard nor easy', 'easy'). The intent-to-treat (ITT) population included all the subjects who were randomized and received at least 1 dose of treatment subsequent to randomization in the study.

End point type	Secondary

End point timeframe:

Day 1

End point values	D/C/F/TAF FDC Placebo–Whole			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Subjects				
By Subject: Hard	3			
By Subject: Neither hard nor easy	1			
By Subject: Easy	20			
By Caregiver: Hard	3			
By Caregiver: Neither hard nor easy	2			
By Caregiver: Easy	19			

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability of Intake of the Split Tablet by the Subject and by the Caregiver

End point title	Acceptability of Intake of the Split Tablet by the Subject and by the Caregiver

End point description:

Acceptability of intake of split tablet was assessed based on a 3-point questionnaire indicating how difficult/easy it was to swallow 2 pieces of the tablet ('hard', 'neither hard or easy', 'easy'). The intent-to-treat (ITT) population included all the subjects who were randomized and received at least 1 dose of treatment subsequent to randomization in the study.

End point type	Secondary

End point timeframe:

Day 1

End point values	D/C/F/TAF FDC Placebo–Split			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Subjects				
By Subject: Hard	4			
By Subject: Neither hard nor easy	6			
By Subject: Easy	14			
By Caregiver (Split 1): Hard	1			
By Caregiver (Split 1): Neither hard nor easy	7			
By Caregiver (Split 1): Easy	16			
By Caregiver (Split 2): Hard	2			
By Caregiver (Split 2): Neither hard nor easy	5			
By Caregiver (Split 2): Easy	17			

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability of Daily Intake of the Whole Tablet by the Subject

End point title	Acceptability of Daily Intake of the Whole Tablet by the Subject

End point description:

Acceptability of whole tablet describing how it would be to take this tablet once daily for a longer period ('Not Acceptable', 'Acceptable', 'Good to take', 'Unable to assess this question') was reported. The intent-to-treat (ITT) population included all the subjects who were randomized and received at least 1 dose of treatment subsequent to randomization in the study.

End point type	Secondary

End point timeframe:

Day 1

End point values	D/C/F/TAF FDC Placebo–Whole			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Subjects				
Not acceptable	4			
Acceptable	2			
Good to take	18			
Unable to assess this question	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Acceptability of Daily Intake of the Split Tablet by the Subject

End point title	Acceptability of Daily Intake of the Split Tablet by the Subject

End point description:

Acceptability of split tablet describing how it would be to take this tablet once daily for a longer period ("Not Acceptable', 'Acceptable', 'Good to take', 'Unable to assess this question') was reported. The intent-to-treat (ITT) population included all the subjects who were randomized and received at least 1 dose of treatment subsequent to randomization in the study.

End point type	Secondary

End point timeframe:

Day 1

End point values	D/C/F/TAF FDC Placebo–Split			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Subjects				
Not acceptable	6			
Acceptable	6			
Good to take	11			
Unable to assess this question	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Ease of Splitting the Tablet by the Subject's Caregiver

End point title	Ease of Splitting the Tablet by the Subject's Caregiver

End point description:

Ease of splitting the tablet by the subject's caregiver was assessed based on a 3- point questionnaire indicating how difficult was it for the subject's caregiver to break the tablet by hand ('hard', 'ok',' easy'). The intent-to-treat (ITT) population included all the subjects who were randomized and received at least 1 dose of treatment subsequent to randomization in the study.

End point type	Secondary

End point timeframe:

Day 1

End point values	D/C/F/TAF FDC Placebo–Split			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Subjects				
Hard	5			
Ok	7			
Easy	12			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Swallowing Difficulties as Reported by the Observer

End point title	Number of Subjects with Swallowing Difficulties as Reported by the Observer

End point description:

Number of subjects with swallowing difficulties as reported by the observer. The intent-to-treat (ITT) population included all the subjects who were randomized and received at least 1 dose of treatment subsequent to randomization in the study.

End point type	Secondary

End point timeframe:

Day 1

End point values	D/C/F/TAF FDC Placebo (All Subjects)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Subjects				
First attempt: Whole Tablet	3			
First attempt: Split 1 Tablet	4			
First attempt: Split 2 Tablet	6			
Second attempt: Whole Tablet	1			
Second attempt: Split 1 Tablet	0			
Second attempt: Split 2 Tablet	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Adverse Events

End point title	Number of Subjects with Adverse Events

End point description:

An adverse event is any untoward medical event that occurs in a participant administered an investigational product, and it does not necessarily indicate only events with clear causal relationship with the relevant investigational product. The intent-to-treat (ITT) population included all the subjects who were randomized and received at least 1 dose of treatment subsequent to randomization in the study.

End point type	Secondary

End point timeframe:

Up to Day 22

End point values	Placebo whole then Placebo split	Placebo split then Placebo whole		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Up to Day 22

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups

Reporting group title	Placebo whole then Placebo split

Reporting group description:

Subjects received scored film-coated FDC matching placebo tablet, swallowed whole on Day 1 in intake Period 1 followed by scored film-coated FDC matching placebo tablet, swallowed as a split tablet on Day 1 in intake Period 2. Both the intakes were separated by at least 15 minutes.

Reporting group title	Placebo split then Placebo whole

Reporting group description:

Subjects received scored film-coated FDC matching placebo tablet, swallowed as a split tablet on Day 1 in intake Period 1 followed by scored film-coated FDC matching placebo tablet, swallowed whole on Day 1 in intake Period 2. Both the intakes were separated by at least 15 minutes.

Serious adverse events	Placebo whole then Placebo split	Placebo split then Placebo whole	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Placebo whole then Placebo split	Placebo split then Placebo whole	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	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 treatment- emergent non serious adverse events were reported.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 July 2019	The protocol is amended to clarify the number of attempts allowed for each half of the split tablet and the inclusion criterion 'willingness to swallow' and to address changes requested by the Agencia Española de Medicamentos y Productos Sanitarios.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported