Clinical trial results:
A randomised trial of dolutegravir (DTG)-based antiretroviral therapy vs. standard of care (SOC) in children with HIV infection starting first-line or switching to second-line ART

Summary

EudraCT number	2014-002632-14
Trial protocol	ES DE PT FR
Global end of trial date	07 December 2023

Results information

Result version number	v1 (current)
This version publication date	20 June 2024
First version publication date	20 June 2024

Trial information

Trial identification

Sponsor protocol code	ODYSSEY (PENTA20)

Additional study identifiers

ISRCTN number	ISRCTN91737921
ClinicalTrials.gov id (NCT number)	NCT02259127
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Paediatric European Network for Treatment of AIDS (PENTA) Foundation
Sponsor organisation address	Corso Stati Uniti 4, Padova, Italy, 35127
Public contact	Pablo Rojo, Hospital doce de Octubre / PENTA , 0034 913908569, pablo.rojo@salud.madrid.org
Scientific contact	Pablo Rojo, Hospital doce de Octubre / PENTA , 0034 913908569, pablo.rojo@salud.madrid.org

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	28 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 June 2021
Global end of trial reached?	Yes
Global end of trial date	07 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The main objective of the ODYSSEY trial is evaluating the efficacy and safety of once daily DTG-based ART compared with standard of care in children and adolescents starting first- or second-line ART in resource-limited and well-resourced settings.

Protection of trial subjects:

The details this study were reviewed by an independent committee (a Research Ethics Committee) prior to the trials commencement to ensure that, as far as possible, the safety and wellbeing of participants were protected. A second committee (the Independent Data Monitoring Committee) met regularly during the study to review the interim results as they came out and recommend if the study was safe to continue.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 September 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	3 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 8
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	South Africa: 164
Country: Number of subjects enrolled	Spain: 8
Country: Number of subjects enrolled	Thailand: 61
Country: Number of subjects enrolled	Uganda: 374
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Zimbabwe: 168
Worldwide total number of subjects	792
EEA total number of subjects	17

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)	76
Children (2-11 years)	352
Adolescents (12-17 years)	364
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment to the >=14kg cohort took place between 20th September 2016 and 22nd June 2018 in 8 countries (Germany, Portugal, South Africa, Spain, Thailand, Uganda, United Kingdom, and Zimbabwe) across 29 centres. Recruitment to the <14kg cohort took place between 5th July 2018 and 26th August 2019 in the African countries across 7 centres.

Pre-assignment

Screening details:

>=14kg cohort, 819 children were assessed for eligibility. 109 were determined ineligible. Additionally, 3 children in >=14kg cohort were randomised in error.
<14kg cohort, 102 children were assessed for eligibility. 17 were determined ineligible.
See publications for full details.

Period 1

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

Arms

Are arms mutually exclusive?	No
Arm title	Dolutegravir (>=14kg cohort)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Dolutegravir
Investigational medicinal product code	DTG
Other name	
Pharmaceutical forms	Capsule, Chewable/dispersible tablet, Tablet
Routes of administration	Oral use

Dosage and administration details:

Arm title	Standard of Care (>=14kg cohort)

Arm description: -

Arm type	Active comparator
Investigational medicinal product name	Standard of Care
Investigational medicinal product code	SOC
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Arm title	Dolutegravir (<14kg Cohort)

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Dolutegravir
Investigational medicinal product code	DTG
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Arm title	Standard of Care (<14kg cohort)
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Standard of Care
Investigational medicinal product code	SOC
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Arm title	Dolutegravir - ODYSSEY A (>=14kg cohort)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Dolutegravir
Investigational medicinal product code	DTG
Other name	
Pharmaceutical forms	Capsule, Chewable/dispersible tablet, Tablet
Routes of administration	Oral use

Dosage and administration details:

Arm title	Standard of Care - ODYSSEY A (>=14kg cohort)
Arm description: -	
Arm type	Active comparator
Investigational medicinal product name	Standard of Care
Investigational medicinal product code	SOC
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Arm title	Dolutegravir - ODYSSEY B (>=14kg cohort)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Dolutegravir
Investigational medicinal product code	DTG
Other name	
Pharmaceutical forms	Capsule, Chewable/dispersible tablet, Tablet
Routes of administration	Oral use

Dosage and administration details:

Arm title	Standard of Care - ODYSSEY B (>=14kg cohort)
Arm description: -	
Arm type	Active comparator

Investigational medicinal product name	Standard of Care
Investigational medicinal product code	SOC
Other name	
Pharmaceutical forms	Capsule, Tablet
Routes of administration	Oral use

Dosage and administration details:

Number of subjects in period 1	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir (<14kg Cohort)
Started	350	357	42
Completed	350	357	42

Number of subjects in period 1	Standard of Care (<14kg cohort)	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)
Started	43	154	157
Completed	43	154	157

Number of subjects in period 1	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Started	196	200
Completed	196	200

Baseline characteristics

Reporting groups	
Reporting group title	Dolutegravir (>=14kg cohort)
Reporting group description: -	
Reporting group title	Standard of Care (>=14kg cohort)
Reporting group description: -	
Reporting group title	Dolutegravir (<14kg Cohort)
Reporting group description: -	
Reporting group title	Standard of Care (<14kg cohort)
Reporting group description: -	
Reporting group title	Dolutegravir - ODYSSEY A (>=14kg cohort)
Reporting group description: -	
Reporting group title	Standard of Care - ODYSSEY A (>=14kg cohort)
Reporting group description: -	
Reporting group title	Dolutegravir - ODYSSEY B (>=14kg cohort)
Reporting group description: -	
Reporting group title	Standard of Care - ODYSSEY B (>=14kg cohort)
Reporting group description: -	

Reporting group values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir (<14kg Cohort)
Number of subjects	350	357	42
Age categorical Units: Subjects			
<6 months	0	0	11
6 months-<1 year	0	0	5
1-<2 years	0	0	22
2-<6 years	15	11	4
6-<12 years	153	164	0
12-<18 years	182	182	0
Age continuous Units: years			
median	12.2	12.1	1.3
inter-quartile range (Q1-Q3)	9.2 to 15.1	8.8 to 14.7	0.5 to 2.0
Gender categorical Units: Subjects			
Female	174	171	26
Male	176	186	16
ODYSSEY A\B Units: Subjects			
ODYSSEY A (Starting first-line ART)	154	157	35
ODYSSEY B (Switching to second-line ART)	196	200	7
Weight Units: Subjects			
<6kg	0	0	11
6-<10kg	0	0	20
10-<14kg	0	0	11
14-<20kg	39	43	0

20-<25kg	71	64	0
25-<30kg	58	59	0
30-<35kg	38	51	0
35-<40kg	29	32	0
>=40kg	115	108	0
Weight-for-age Units: Subjects			
<-3	4	4	14
-3-<-2	20	12	7
-2-<0	78	83	18
>=0	14	19	3
missing	234	239	0
BMI-for-age Units: Subjects			
<-3	22	11	3
-3-<-2	20	28	6
-2-<0	216	219	20
>=0	92	99	13
missing	0	0	0
CD4% Units: Subjects			
<15%	121	108	7
15-<30%	152	147	22
>=30%	77	102	12
Missing	0	0	1
Viral Load copies/mL Units: Subjects			
<10,000	93	123	4
10,000-<100,000	159	158	13
>=100,000	98	75	25
Missing	0	1	0
History of WHO Staging Units: Subjects			
Stage 1-2	253	265	31
Stage 3	69	60	6
Stage 4	28	32	5
Country Units: Subjects			
Uganda	170	161	22
Zimbabwe	79	67	12
South Africa	61	83	8
Thailand	28	33	0
Europe	12	13	0
CD4 Units: Subjects			
<200 cells/mm^3	88	70	3
200 to <500 cells/mm^3	118	114	2
>=500 cells/mm^3	144	173	36
Missing	0	0	1
Ethnic origin Units: Subjects			

Black African	310	313	41
Asian	28	32	0
White	5	1	0
Other	7	11	1
Age Units: Subjects			
<6 months	0	0	11
6 months-<1 year	0	0	5
1-<2 years	0	0	22
2-<6 years	15	11	4
6-<12 years	153	164	0
12-<18 years	182	182	0
Weight Units: kilogram(s)			
median	30.4	31.0	8.1
inter-quartile range (Q1-Q3)	23.7 to 43.7	23.3 to 42.7	5.6 to 10.0
Weight-for-age Units: z-score			
median	-1.2	-0.9	-2.1
inter-quartile range (Q1-Q3)	-1.9 to -0.2	-1.6 to -0.2	-3.4 to -1.3
BMI-for-age Units: z-score			
median	-0.6	-0.6	-1.1
inter-quartile range (Q1-Q3)	-1.4 to 0.0	-1.4 to 0.1	-1.9 to 0.2
CD4% Units: percent			
median	20	22	24
inter-quartile range (Q1-Q3)	11 to 29	13 to 31	17 to 35
CD4 Units: cells/millimetre			
median	444	486	1639
inter-quartile range (Q1-Q3)	196 to 652	254 to 751	1026 to 2327
Log 10 Viral load copies/mL Units: copies\mL			
median	4.5	4.4	5.2
inter-quartile range (Q1-Q3)	3.9 to 5.1	3.7 to 4.9	4.4 to 5.8

Reporting group values	Standard of Care (<14kg cohort)	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)
Number of subjects	43	154	157
Age categorical Units: Subjects			
<6 months	8	0	0
6 months-<1 year	8	0	0
1-<2 years	22	0	0
2-<6 years	5	7	5
6-<12 years	0	72	84
12-<18 years	0	75	68
Age continuous Units: years			
median	1.5	11.9	11.5

inter-quartile range (Q1-Q3)	0.6 to 2.1	9.2 to 14.9	8.5 to 15.0

Gender categorical Units: Subjects			
Female	18	87	77
Male	25	67	80
ODYSSEY A\B Units: Subjects			
ODYSSEY A (Starting first-line ART)	37	154	157
ODYSSEY B (Switching to second-line ART)	6	0	0
Weight Units: Subjects			
<6kg	12	0	0
6-<10kg	20	0	0
10-<14kg	11	0	0
14-<20kg	0	18	20
20-<25kg	0	33	29
25-<30kg	0	26	32
30-<35kg	0	16	17
35-<40kg	0	12	10
>=40kg	0	49	49
Weight-for-age Units: Subjects			
<-3	13	2	3
-3-<-2	6	8	6
-2-<0	21	39	35
>=0	3	6	11
missing	0	99	102
BMI-for-age Units: Subjects			
<-3	6	8	4
-3-<-2	6	8	16
-2-<0	14	91	87
>=0	17	47	50
missing	0	0	0
CD4% Units: Subjects			
<15%	11	54	56
15-<30%	18	75	69
>=30%	11	25	32
Missing	3	0	0
Viral Load copies/mL Units: Subjects			
<10,000	7	40	48
10,000-<100,000	5	64	57
>=100,000	26	50	51
Missing	5	0	1
History of WHO Staging Units: Subjects			

Stage 1-2	25	116	125
Stage 3	8	25	22
Stage 4	10	13	10
Country Units: Subjects			
Uganda	21	46	53
Zimbabwe	10	39	28
South Africa	12	36	41
Thailand	0	24	26
Europe	0	9	9
CD4 Units: Subjects			
<200 cells/mm^3	4	37	38
200 to <500 cells/mm^3	3	48	56
>=500 cells/mm^3	33	69	63
Missing	3	0	0
Ethnic origin Units: Subjects			
Black African	42	123	126
Asian	0	24	26
White	0	5	0
Other	1	2	5
Age Units: Subjects			
<6 months	8	0	0
6 months-<1 year	8	0	0
1-<2 years	22	0	0
2-<6 years	5	7	5
6-<12 years	0	72	84
12-<18 years	0	75	68
Weight Units: kilogram(s)			
median	8.2	30.0	29.6
inter-quartile range (Q1-Q3)	5.2 to 10.3	23.4 to 45.0	22.8 to 44.8
Weight-for-age Units: z-score			
median	-1.8	-1.2	-0.6
inter-quartile range (Q1-Q3)	-3.7 to -0.8	-1.6 to -0.3	-1.2 to -0.1
BMI-for-age Units: z-score			
median	-0.7	-0.5	-0.6
inter-quartile range (Q1-Q3)	-2.2 to 0.3	-1.2 to -.2	-1.5 to 0.4
CD4% Units: percent			
median	23	19	19
inter-quartile range (Q1-Q3)	14 to 30	12 to 28	10 to 28
CD4 Units: cells/millimetre			
median	1221	453	435
inter-quartile range (Q1-Q3)	633 to 1870	210 to 623	225 to 707
Log 10 Viral load copies/mL			

Units: copies\mL			
median	5.4	4.6	4.6
inter-quartile range (Q1-Q3)	4.8 to 5.9	4.0 to 5.2	3.8 to 5.1

Reporting group values	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)	Total
Number of subjects	196	200	792
Age categorical Units: Subjects			
<6 months	0	0	19
6 months-<1 year	0	0	13
1-<2 years	0	0	44
2-<6 years	8	6	35
6-<12 years	81	80	317
12-<18 years	107	114	364
Age continuous Units: years			
median	12.9	12.5	
inter-quartile range (Q1-Q3)	9.2 to 15.3	9.4 to 14.6	-
Gender categorical Units: Subjects			
Female	87	94	403
Male	109	106	389
ODYSSEY A\B Units: Subjects			
ODYSSEY A (Starting first-line ART)	0	0	383
ODYSSEY B (Switching to second-line ART)	196	200	409
Weight Units: Subjects			
<6kg	0	0	23
6-<10kg	0	0	40
10-<14kg	0	0	22
14-<20kg	21	23	82
20-<25kg	38	35	135
25-<30kg	32	27	117
30-<35kg	22	34	89
35-<40kg	17	22	61
>=40kg	66	59	223
Weight-for-age Units: Subjects			
<-3	2	1	35
-3-<-2	12	6	45
-2-<0	39	48	200
>=0	8	8	39
missing	135	137	473
BMI-for-age Units: Subjects			
<-3	14	7	42
-3-<-2	12	12	60
-2-<0	125	132	469

>=0	45	49	221
missing	0	0	0
CD4% Units: Subjects			
<15%	67	52	247
15-<30%	77	78	339
>=30%	52	70	202
Missing	0	0	4
Viral Load copies/mL Units: Subjects			
<10,000	53	75	227
10,000-<100,000	95	101	335
>=100,000	48	24	224
Missing	0	0	6
History of WHO Staging Units: Subjects			
Stage 1-2	137	140	574
Stage 3	44	38	143
Stage 4	15	22	75
Country Units: Subjects			
Uganda	124	108	374
Zimbabwe	40	39	168
South Africa	25	42	164
Thailand	4	7	61
Europe	3	4	25
CD4 Units: Subjects			
<200 cells/mm^3	51	32	165
200 to <500 cells/mm^3	70	58	237
>=500 cells/mm^3	75	110	386
Missing	0	0	4
Ethnic origin Units: Subjects			
Black African	187	187	706
Asian	4	6	60
White	0	1	6
Other	5	6	20
Age Units: Subjects			
<6 months	0	0	19
6 months-<1 year	0	0	13
1-<2 years	0	0	44
2-<6 years	8	6	35
6-<12 years	81	80	317
12-<18 years	107	114	364
Weight Units: kilogram(s)			
median	30.4	31.9	
inter-quartile range (Q1-Q3)	23.8 to 42.6	23.4 to 41.3	-
Weight-for-age			

Units: z-score			
median	-1.2	-1.1	
inter-quartile range (Q1-Q3)	-1.9 to -0.2	-1.6 to -0.5	-
BMI-for-age			
Units: z-score			
median	-0.8	-0.6	
inter-quartile range (Q1-Q3)	-1.5 to -0.1	-1.3 to 0	-
CD4%			
Units: percent			
median	21	25	
inter-quartile range (Q1-Q3)	10 to 32	15 to 33	-
CD4			
Units: cells/millimetre			
median	439	554	
inter-quartile range (Q1-Q3)	193 to 716	285 to 790	-
Log 10 Viral load copies/mL			
Units: copies\mL			
median	4.4	4.2	
inter-quartile range (Q1-Q3)	3.9 to 5.0	3.7 to 4.7	-

End points

End points reporting groups

Reporting group title	Dolutegravir (>=14kg cohort)
Reporting group description: -	
Reporting group title	Standard of Care (>=14kg cohort)
Reporting group description: -	
Reporting group title	Dolutegravir (<14kg Cohort)
Reporting group description: -	
Reporting group title	Standard of Care (<14kg cohort)
Reporting group description: -	
Reporting group title	Dolutegravir - ODYSSEY A (>=14kg cohort)
Reporting group description: -	
Reporting group title	Standard of Care - ODYSSEY A (>=14kg cohort)
Reporting group description: -	
Reporting group title	Dolutegravir - ODYSSEY B (>=14kg cohort)
Reporting group description: -	
Reporting group title	Standard of Care - ODYSSEY B (>=14kg cohort)
Reporting group description: -	

Primary: Treatment failure by 96 weeks

End point title	Treatment failure by 96 weeks
End point description:	

End point type	Primary
End point timeframe:	
96 weeks post randomisation	

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir (<14kg Cohort)	Standard of Care (<14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	350	357	42	43
Units: participants				
Insufficient virological response	0	3	0	0
Confirmed VL>=400 copies/mL	40	64	9	16
Severe WHO 3	0	1	0	0
WHO 4	7	5	1	1
Death	0	2	2	4

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg

		cohort)		cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	154	157	196	200
Units: participants				
Insufficient virological response	0	2	0	1
Confirmed VL>=400 copies/mL	10	26	30	38
Severe WHO 3	0	0	0	1
WHO 4	5	5	2	0
Death	0	1	0	1

Statistical analyses

Statistical analysis title	Primary: Diff in adj. KM estimates (>=14kg)
Comparison groups	Standard of Care (>=14kg cohort) v Dolutegravir (>=14kg cohort)
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.004
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	-0.03

Statistical analysis title	Diff in adj. KM estimates (Frequentist <14kg)
Comparison groups	Standard of Care (<14kg cohort) v Dolutegravir (<14kg Cohort)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.057
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.36
upper limit	0.02

Statistical analysis title	Primary:diff in adj. KM estimates (Bayesian <14kg)
Comparison groups	Dolutegravir (<14kg Cohort) v Standard of Care (<14kg cohort)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
P-value	= 0.02
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.19
upper limit	-0.02

Notes:

[1] - Bayesian estimation was used for the primary analysis of the difference in treatment failure by 96 weeks by arm in <14kg cohort. An informative prior distribution was used based on the treatment effect observed in >=14kg cohort, with relative weight defined by clinical opinion, solicited prior to the main trial results.

Statistical analysis title	Diff in adj. KM estimates (ODYSSEY A>=14kg)
Comparison groups	Standard of Care - ODYSSEY A (>=14kg cohort) v Dolutegravir - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003
Method	bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	-0.04

Statistical analysis title	Diff in adj. KM estimates (ODYSSEY B >=14kg)
Comparison groups	Dolutegravir - ODYSSEY B (>=14kg cohort) v Standard of Care - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.22
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.03

Secondary: HIV-1 RNA <50c/ml at 96 weeks

End point title	HIV-1 RNA <50c/ml at 96 weeks[2]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Please see publication on <14kg results.

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	335	330	146	140
Units: participants				
HIV-1 RNA <50c/mL at 96 weeks	270	252	117	113

End point values	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	189	192		
Units: participants				
HIV-1 RNA <50c/mL at 96 weeks	153	139		

Statistical analyses

Statistical analysis title	Adjusted Difference (>=14kg)
Comparison groups	Dolutegravir (>=14kg cohort) v Standard of Care (>=14kg cohort)

Number of subjects included in analysis	665
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1377
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	11

Statistical analysis title	Adjusted Difference (ODYSSEY A >=14kg)
Comparison groups	Dolutegravir - ODYSSEY A (>=14kg cohort) v Standard of Care - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8895
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	-1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10
upper limit	8

Statistical analysis title	Adjusted Difference (ODYSSEY B >=14kg)
Comparison groups	Dolutegravir - ODYSSEY B (>=14kg cohort) v Standard of Care - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	381
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0435
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	17

Secondary: HIV-1 RNA <400c/ml at 96 weeks

End point title	HIV-1 RNA <400c/ml at 96 weeks[3]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	337	333	146	140
Units: participants				
HIV-1 RNA <400c/mL at 96 weeks	299	285	129	124

End point values	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	191	193		
Units: participants				
HIV-1 RNA <400c/mL at 96 weeks	170	161		

Statistical analyses

Statistical analysis title	Adjusted Difference (>=14kg)
Comparison groups	Dolutegravir (>=14kg cohort) v Standard of Care (>=14kg cohort)
Number of subjects included in analysis	670
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2256
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2
upper limit	8

Statistical analysis title	Adjusted Difference (ODYSSEY A >=14kg)
Comparison groups	Dolutegravir - ODYSSEY A (>=14kg cohort) v Standard of Care - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	286
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9536
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8
upper limit	7

Statistical analysis title	Adjusted Difference (ODYSSEY B >=14kg)
Comparison groups	Dolutegravir - ODYSSEY B (>=14kg cohort) v Standard of Care - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	384
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1104
Method	Regression, Logistic
Parameter estimate	Risk difference (RD)
Point estimate	6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1
upper limit	12

Secondary: Mean change in CD4 count from baseline to week 96	
End point title	Mean change in CD4 count from baseline to week 96[4]
End point description:	
Reporting mean change from the global baseline value (across both arms).	
End point type	Secondary
End point timeframe:	
96 weeks post randomisation	

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Please see publication on <14kg results.

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	350	357	154	157
Units: cells/mm^3				
arithmetic mean (standard error)	265 (± 17)	230 (± 17)	311 (± 23)	267 (± 24)

End point values	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	200		
Units: cells/mm^3				
arithmetic mean (standard error)	228 (± 24)	202 (± 24)		

Statistical analyses

Statistical analysis title	Adjusted Difference (>=14kg)
Statistical analysis description:	
Linear regression of CD4 at week 96, adjusting for randomised arm, baseline CD4 and stratification factors. Presenting mean difference between arms.	
Comparison groups	Dolutegravir (>=14kg cohort) v Standard of Care (>=14kg cohort)
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.144
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12
upper limit	82

Statistical analysis title	Adjusted Difference (ODYSSEY A >=14kg)
Statistical analysis description:	
Linear regression of CD4 at week 96, adjusting for randomised arm, baseline CD4 and stratification factors. Presenting mean difference between arms.	
Comparison groups	Dolutegravir - ODYSSEY A (>=14kg cohort) v Standard of Care - ODYSSEY A (>=14kg cohort)

Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.185
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-21
upper limit	109

Statistical analysis title	Adjusted Difference (ODYSSEY B >=14kg)
Statistical analysis description:	
Linear regression of CD4 at week 96, adjusting for randomised arm, baseline CD4 and stratification factors. Presenting mean difference between arms.	
Comparison groups	Dolutegravir - ODYSSEY B (>=14kg cohort) v Standard of Care - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.427
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-39
upper limit	93

Secondary: Mean change in total cholesterol from baseline to week 96	
End point title	Mean change in total cholesterol from baseline to week 96
End point description:	
Reporting mean change from the global baseline value (across both arms).	
End point type	Secondary
End point timeframe:	
96 weeks post randomisation	

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir (<14kg Cohort)	Standard of Care (<14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	350	357	42	43
Units: mg/dl				
arithmetic mean (standard error)	-5.0 (± 1.5)	9.9 (± 1.5)	4.5 (± 5.6)	29.6 (± 5.9)

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	154	157	196	200
Units: mg/dl				
arithmetic mean (standard error)	2.1 (± 2.3)	19.6 (± 2.3)	-10.5 (± 1.8)	2.8 (± 1.8)

Statistical analyses

Statistical analysis title	Adjusted Difference (>=14kg)

Statistical analysis description:

Linear regression of total cholesterol at week 96, adjusting for randomised arm, baseline total cholesterol and stratification factors. Presenting mean difference between arms.

Comparison groups	Dolutegravir (>=14kg cohort) v Standard of Care (>=14kg cohort)
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-15.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19
upper limit	-11.1

Statistical analysis title	Adjusted Difference (<14kg)

Statistical analysis description:

Linear regression of total cholesterol at week 96, adjusting for randomised arm, baseline total cholesterol and stratification factors. Presenting mean difference between arms.

Comparison groups	Dolutegravir (<14kg Cohort) v Standard of Care (<14kg cohort)

Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0032
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-24.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-40.3
upper limit	-8.5

Statistical analysis title	Adjusted Difference (ODYSSEY A >=14kg)
Statistical analysis description:	
Linear regression of total cholesterol at week 96, adjusting for randomised arm, baseline total cholesterol and stratification factors. Presenting mean difference between arms.	
Comparison groups	Dolutegravir - ODYSSEY A (>=14kg cohort) v Standard of Care - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-17.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.9
upper limit	-11.1

Statistical analysis title	Adjusted Difference (ODYSSEY B >=14kg)
Statistical analysis description:	
Linear regression of total cholesterol at week 96, adjusting for randomised arm, baseline total cholesterol and stratification factors. Presenting mean difference between arms.	
Comparison groups	Dolutegravir - ODYSSEY B (>=14kg cohort) v Standard of Care - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	-13.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.5
upper limit	-8.4

Secondary: Serious Adverse Events

End point title	Serious Adverse Events

End point description:

End point type	Secondary

End point timeframe:

Randomised phase

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir (<14kg Cohort)	Standard of Care (<14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	350	357	42	43
Units: number of participants with events	35	40	11	11

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	154	157	196	200
Units: number of participants with events	23	27	12	13

Statistical analyses

Statistical analysis title	Adjusted time to first event (>=14kg)
Comparison groups	Dolutegravir (>=14kg cohort) v Standard of Care (>=14kg cohort)
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.53
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	1.36

Statistical analysis title	Adjusted time to first event (<14kg)
Comparison groups	Standard of Care (<14kg cohort) v Dolutegravir (<14kg Cohort)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	2.49

Statistical analysis title	Adjusted time to first event (ODYSSEY A >=14kg)
Comparison groups	Dolutegravir - ODYSSEY A (>=14kg cohort) v Standard of Care - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.52
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.48
upper limit	1.46

Statistical analysis title	Adjusted time to first event (ODYSSEY B >=14kg)
Comparison groups	Standard of Care - ODYSSEY B (>=14kg cohort) v Dolutegravir - ODYSSEY B (>=14kg cohort)

Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.42
upper limit	2.04

Secondary: Grade 3 or above clinical and laboratory adverse events

End point title	Grade 3 or above clinical and laboratory adverse events
End point description:	

End point type	Secondary
End point timeframe:	
Randomised phase	

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir (<14kg Cohort)	Standard of Care (<14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	350	357	42	43
Units: number of participants with events	73	86	19	21

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	154	157	196	200
Units: number of participants with events	48	43	25	43

Statistical analyses

Statistical analysis title	Adjusted time to first event (>=14kg)
Comparison groups	Dolutegravir (>=14kg cohort) v Standard of Care (>=14kg cohort)

Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.24
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.61
upper limit	1.13

Statistical analysis title	Adjusted time to first event (<14kg)
Comparison groups	Dolutegravir (<14kg Cohort) v Standard of Care (<14kg cohort)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.83
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.74

Statistical analysis title	Adjusted time to first event (ODYSSEY A >=14kg)
Comparison groups	Dolutegravir - ODYSSEY A (>=14kg cohort) v Standard of Care - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.57
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.7

Statistical analysis title	Adjusted time to first event (ODYSSEY B >=14kg)
Comparison groups	Standard of Care - ODYSSEY B (>=14kg cohort) v Dolutegravir - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	0.88

Secondary: Adverse events leading to ART modification any grade

End point title	Adverse events leading to ART modification any grade
End point description:	
End point type	Secondary
End point timeframe:	
Randomised phase	

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir (<14kg Cohort)	Standard of Care (<14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	350	357	42	43
Units: number of participants with events	5	17	0	2

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	154	157	196	200
Units: number of participants with events	3	8	2	9

Statistical analyses

Statistical analysis title	Adjusted time to first event (>=14kg)
Comparison groups	Dolutegravir (>=14kg cohort) v Standard of Care (>=14kg cohort)
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	0.77

Statistical analysis title	Adjusted time to first event (ODYSSEY A >=14kg)
Comparison groups	Dolutegravir - ODYSSEY A (>=14kg cohort) v Standard of Care - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.13
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.09
upper limit	1.33

Statistical analysis title	Adjusted time to first event (ODYSSEY B >=14kg)
Comparison groups	Dolutegravir - ODYSSEY B (>=14kg cohort) v Standard of Care - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.055
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	1.03

Secondary: Treatment failure by 48 weeks

End point title	Treatment failure by 48 weeks[5]

End point description:

End point type	Secondary

End point timeframe:

48 weeks post randomisation

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	350	357	154	157
Units: Participants				
Insufficient virologic response	0	3	0	2
Confirmed viral load>400c/mL	13	31	4	12
Severe WHO stage 3	0	1	0	0
WHO stage 4	7	5	5	5
Death	0	2	0	1

End point values	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	200		
Units: Participants				
Insufficient virologic response	0	1		
Confirmed viral load>400c/mL	9	19		
Severe WHO stage 3	0	1		
WHO stage 4	2	0		
Death	0	1		

Statistical analyses

Statistical analysis title	Diff in adj. KM estimates (>=14kg)

Statistical analysis description:

Difference in adjusted (for stratification factors) Kaplan-Meier survival function estimates at 48 weeks after randomisation.

Comparison groups	Dolutegravir (>=14kg cohort) v Standard of Care (>=14kg cohort)
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	-0.02

Statistical analysis title	Diff in adj. KM estimates (ODYSSEY A >=14kg)
Statistical analysis description:	
Difference in adjusted (for stratification factors) Kaplan-Meier survival function estimates at 48 weeks after randomisation.	
Comparison groups	Standard of Care - ODYSSEY A (>=14kg cohort) v Dolutegravir - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.035
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.13
upper limit	-0.01

Statistical analysis title	Diff in adj. KM estimates (ODYSSEY B >=14kg)
Statistical analysis description:	
Difference in adjusted (for stratification factors) Kaplan-Meier survival function estimates at 48 weeks after randomisation.	
Comparison groups	Dolutegravir - ODYSSEY B (>=14kg cohort) v Standard of Care - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.039
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.05

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.11
upper limit	-0.004

Secondary: Treatment failure by 144 weeks

End point title	Treatment failure by 144 weeks[6]

End point description:

End point type	Secondary

End point timeframe:

144 week post randomisation

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Please see publication on <14kg results.

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	350	357	154	157
Units: Participants				
Insufficient virologic response	0	3	0	2
Confirmed viral load>400c/mL	48	76	13	28
Severe WHO stage 3	0	1	0	0
WHO stage 4	8	5	6	5
Death	0	2	0	1

End point values	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	200		
Units: Participants				
Insufficient virologic response	0	1		
Confirmed viral load>400c/mL	35	48		
Severe WHO stage 3	0	1		
WHO stage 4	2	0		
Death	0	1		

Statistical analyses

Statistical analysis title	Diff in adj. KM estimates (>=14kg)
Statistical analysis description:	
Difference in adjusted (for stratification factors) Kaplan-Meier survival function estimates at 144 weeks after randomisation.	
Comparison groups	Dolutegravir (>=14kg cohort) v Standard of Care (>=14kg cohort)
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.003
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	-0.04

Statistical analysis title	Diff in adj. KM estimates (ODYSSEY A >=14kg)
Statistical analysis description:	
Difference in adjusted (for stratification factors) Kaplan-Meier survival function estimates at 144 weeks after randomisation.	
Comparison groups	Dolutegravir - ODYSSEY A (>=14kg cohort) v Standard of Care - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.009
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	-0.03

Statistical analysis title	Diff in adj. KM estimates (ODYSSEY B >=14kg)
Statistical analysis description:	
Difference in adjusted (for stratification factors) Kaplan-Meier survival function estimates at 144 weeks after randomisation.	
Comparison groups	Dolutegravir - ODYSSEY B (>=14kg cohort) v Standard of Care - ODYSSEY B (>=14kg cohort)

Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.079
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.16
upper limit	0.01

Secondary: WHO 4, severe WHO 3 and death

End point title	WHO 4, severe WHO 3 and death
End point description:	

End point type	Secondary
End point timeframe:	
Randomised phase	

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir (<14kg Cohort)	Standard of Care (<14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	350	357	42	43
Units: number of participants with events	8	8	3	6

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	154	157	196	200
Units: number of participants with events	6	6	2	2

Statistical analyses

Statistical analysis title	Adjusted time to first event (>=14kg)
Comparison groups	Dolutegravir (>=14kg cohort) v Standard of Care (>=14kg cohort)

Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.993
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	2.68

Statistical analysis title	Adjusted time to first event (<14kg)
Comparison groups	Dolutegravir (<14kg Cohort) v Standard of Care (<14kg cohort)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.33
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	2

Statistical analysis title	Adjusted time to first event (ODYSSEY A >=14kg)
Comparison groups	Dolutegravir - ODYSSEY A (>=14kg cohort) v Standard of Care - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.991
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.32
upper limit	3.12

Statistical analysis title	Adjusted time to first event (ODYSSEY B >=14kg)
Comparison groups	Standard of Care - ODYSSEY B (>=14kg cohort) v Dolutegravir - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.997
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	7.13

Secondary: Per protocol: treatment failure by 96 weeks

End point title	Per protocol: treatment failure by 96 weeks
End point description:	
End point type	Secondary
End point timeframe:	
96 weeks post randomisation	

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir (<14kg Cohort)	Standard of Care (<14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	340	337	42	43
Units: Participants	44	62	12	20

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	150	145	190	192
Units: Participants	13	28	31	34

Statistical analyses

Statistical analysis title	Diff in adj. KM estimates (>=14kg)
Statistical analysis description:	
Difference in adjusted (for stratification factors) Kaplan-Meier survival function estimates at 96 weeks after randomisation.	
Comparison groups	Dolutegravir (>=14kg cohort) v Standard of Care (>=14kg cohort)
Number of subjects included in analysis	677
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.015
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	-0.01

Statistical analysis title	Adjusted Difference (frequentist <14kg)
Statistical analysis description:	
Difference in adjusted (for stratification factors) Kaplan-Meier survival function estimates at 96 weeks after randomisation.	
Comparison groups	Dolutegravir (<14kg Cohort) v Standard of Care (<14kg cohort)
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.075
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.172
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.362
upper limit	0.029

Statistical analysis title	Adjusted Difference (ODYSSEY A >=14kg)
Statistical analysis description:	
Difference in adjusted (for stratification factors) Kaplan-Meier survival function estimates at 96 weeks after randomisation.	
Comparison groups	Dolutegravir - ODYSSEY A (>=14kg cohort) v Standard of Care - ODYSSEY A (>=14kg cohort)

Number of subjects included in analysis	295
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.004
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.126
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	-0.036

Statistical analysis title	Adjusted Difference (ODYSSEY B >=14kg)

Statistical analysis description:

Difference in adjusted (for stratification factors) Kaplan-Meier survival function estimates at 96 weeks after randomisation.

Comparison groups	Dolutegravir - ODYSSEY B (>=14kg cohort) v Standard of Care - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	382
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	= 0.547
Method	Bootstrap method
Parameter estimate	Mean difference (final values)
Point estimate	-0.023
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.096
upper limit	0.056

Secondary: Any drug class resistance after virologic failure

End point title	Any drug class resistance after virologic failure[7]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	29	29	40
Units: Participants	0	28	23	36

Statistical analyses

No statistical analyses for this end point

Secondary: NRTI resistance after virologic failure

End point title	NRTI resistance after virologic failure[8]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	29	29	40
Units: Participants	0	18	21	31

Statistical analyses

No statistical analyses for this end point

Secondary: NNRTI resistance after virologic failure

End point title	NNRTI resistance after virologic failure[9]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	29	29	40
Units: Participants	0	27	22	36

Statistical analyses

No statistical analyses for this end point

Secondary: PI resistance after virologic failure

End point title	PI resistance after virologic failure[10]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	11	29	29	40
Units: Participants	0	0	2	3

Statistical analyses

No statistical analyses for this end point

Secondary: INSTI resistance after virologic failure

End point title	INSTI resistance after virologic failure[11]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Please see publication on <14kg results.

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	11	22		
Units: Participants	0	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Any drug class emerging resistance after virologic failure

End point title	Any drug class emerging resistance after virologic failure[12]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[13]	21	6	6
Units: Percent				
number (not applicable)		97	22	19

Notes:

[13] - 0 participants had resistance to INSTI post failure

Statistical analyses

No statistical analyses for this end point

Secondary: NRTI emerging resistance after virologic failure

End point title	NRTI emerging resistance after virologic failure[14]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	0[15]	13	2	3
Units: percent				
number (not applicable)		62	8	10

Notes:

[15] - 0 participants had resistance post failure

Statistical analyses

No statistical analyses for this end point

Secondary: NNRTI emerging resistance after virologic failure

End point title	NNRTI emerging resistance after virologic failure[16]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Standard of Care - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	2		
Units: percent				
number (not applicable)	88	100		

Statistical analyses

No statistical analyses for this end point

Secondary: PI emerging resistance after virologic failure

End point title	PI emerging resistance after virologic failure[17]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Standard of Care - ODYSSEY B (>=14kg cohort)			
Subject group type	Reporting group			
Number of subjects analysed	2			
Units: Perc				
number (not applicable)	5			

Statistical analyses

No statistical analyses for this end point

Secondary: INSTI emerging resistance after virologic failure

End point title	INSTI emerging resistance after virologic failure[18]

End point description:

End point type	Secondary

End point timeframe:

96 weeks post randomisation

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Dolutegravir - ODYSSEY A (>=14kg cohort)	Dolutegravir - ODYSSEY B (>=14kg cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	0[19]	4		
Units: percent				
number (not applicable)		18		

Notes:

[19] - 0 participants had resistance post failure

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Mean change in weight from baseline to week 96	
End point title	Mean change in weight from baseline to week 96[20]
End point description:	
Reporting mean change from the global baseline value (across both arms).	
End point type	Other pre-specified
End point timeframe:	
96 weeks post randomisation	

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	350	357	154	157
Units: kg				
arithmetic mean (standard error)	7.1 (± 0.3)	6.1 (± 0.3)	7.8 (± 0.4)	6.5 (± 0.4)

End point values	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	200		
Units: kg				
arithmetic mean (standard error)	6.7 (± 0.3)	5.9 (± 0.3)		

Statistical analyses

Statistical analysis title	Adjusted Difference (>=14kg)
Comparison groups	Standard of Care (>=14kg cohort) v Dolutegravir (>=14kg cohort)
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	1

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.3
upper limit	1.7

Statistical analysis title	Adjusted Difference (ODYSSEY A >=14kg)
Statistical analysis description:	
Linear regression of weight at week 96, adjusting for randomised arm, baseline weight and stratification factors. Presenting mean difference between arms.	
Comparison groups	Standard of Care - ODYSSEY A (>=14kg cohort) v Dolutegravir - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.024
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	1.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	2.5

Statistical analysis title	Adjusted Difference (ODYSSEY B >=14kg)
Statistical analysis description:	
Linear regression of weight at week 96, adjusting for randomised arm, baseline weight and stratification factors. Presenting mean difference between arms.	
Comparison groups	Dolutegravir - ODYSSEY B (>=14kg cohort) v Standard of Care - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.075
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.1
upper limit	1.6

Other pre-specified: Mean change in BMI-for-age from baseline to week 96

End point title	Mean change in BMI-for-age from baseline to week 96[21]

End point description:

Reporting mean change from the global baseline value (across both arms).

End point type	Other pre-specified

End point timeframe:

96 weeks post randomisation

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Please see publication on <14kg results.

End point values	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir - ODYSSEY A (>=14kg cohort)	Standard of Care - ODYSSEY A (>=14kg cohort)
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	350	357	154	157
Units: Z-score				
arithmetic mean (standard error)	0.24 (± 0.04)	0.11 (± 0.04)	0.36 (± 0.07)	0.20 (± 0.07)

End point values	Dolutegravir - ODYSSEY B (>=14kg cohort)	Standard of Care - ODYSSEY B (>=14kg cohort)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	196	200		
Units: Z-score				
arithmetic mean (standard error)	0.14 (± 0.05)	0.04 (± 0.05)		

Statistical analyses

Statistical analysis title	Adjusted Difference (>=14kg)

Statistical analysis description:

Linear regression of BMI-for-age at week 96, adjusting for randomised arm, baseline BMI-for-age and stratification factors. Presenting mean difference between arms.

Comparison groups	Standard of Care (>=14kg cohort) v Dolutegravir (>=14kg cohort)
Number of subjects included in analysis	707
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.036
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.13

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.01
upper limit	0.25

Statistical analysis title	Adjusted Difference (ODYSSEY A >=14kg)

Statistical analysis description:

Linear regression of BMI-for-age at week 96, adjusting for randomised arm, baseline BMI-for-age and stratification factors. Presenting mean difference between arms.

Comparison groups	Dolutegravir - ODYSSEY A (>=14kg cohort) v Standard of Care - ODYSSEY A (>=14kg cohort)
Number of subjects included in analysis	311
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.092
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.36

Statistical analysis title	Adjusted Difference (ODYSSEY B >=14kg)

Statistical analysis description:

Linear regression of BMI-for-age at week 96, adjusting for randomised arm, baseline BMI-for-age and stratification factors. Presenting mean difference between arms.

Comparison groups	Dolutegravir - ODYSSEY B (>=14kg cohort) v Standard of Care - ODYSSEY B (>=14kg cohort)
Number of subjects included in analysis	396
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.176
Method	Regression, Linear
Parameter estimate	Mean difference (final values)
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.05
upper limit	0.25

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Randomised phase

Adverse event reporting additional description:

Non-serious AEs:There was no single diagnosis reported for 5% or more of participants. Details of all AEs are reported in the supplementary materials of the >=14kg cohort paper (https://www.nejm.org/doi/full/10.1056/NEJMoa2108793) and the <14kg cohort paper (https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00163-1/fulltext)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	3.0

Reporting groups

Reporting group title	Dolutegravir (>=14kg cohort)

Reporting group description:

Non-serious AEs:There was no single diagnosis reported for 5% or more of participants. Details of all AEs are reported in the supplementary materials of the >=14kg cohort paper https://www.nejm.org/doi/full/10.1056/NEJMoa2108793) and the <14kg cohort paper (https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00163-1/fulltext)

Reporting group title	Standard of Care (>=14kg cohort)

Reporting group description:

Non-serious AEs:There was no single diagnosis reported for 5% or more of participants. Details of all AEs are reported in the supplementary materials of the >=14kg cohort paper https://www.nejm.org/doi/full/10.1056/NEJMoa2108793) and the <14kg cohort paper (https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00163-1/fulltext)

Reporting group title	Dolutegravir (<14kg Cohort)

Reporting group description:

Non-serious AEs:There was no single diagnosis reported for 5% or more of participants. Details of all AEs are reported in the supplementary materials of the >=14kg cohort paper https://www.nejm.org/doi/full/10.1056/NEJMoa2108793) and the <14kg cohort paper (https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00163-1/fulltext)

Reporting group title	Standard of Care (<14kg cohort)

Reporting group description:

Non-serious AEs:There was no single diagnosis reported for 5% or more of participants. Details of all AEs are reported in the supplementary materials of the >=14kg cohort paper https://www.nejm.org/doi/full/10.1056/NEJMoa2108793) and the <14kg cohort paper (https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00163-1/fulltext)

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 AEs:There was no single diagnosis reported for 5% or more of participants. Details of all AEs are reported in the supplementary materials of the >=14kg cohort paper https://www.nejm.org/doi/full/10.1056/NEJMoa2108793) and the <14kg cohort paper (https://www.thelancet.com/journals/lanhiv/article/PIIS2352-3018(22)00163-1/fulltext)

Serious adverse events	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir (<14kg Cohort)
Total subjects affected by serious adverse events			
subjects affected / exposed	35 / 350 (10.00%)	40 / 357 (11.20%)	11 / 42 (26.19%)
number of deaths (all causes)	2	3	2
number of deaths resulting from adverse events	2	3	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Neoplasms benign, malignant and unspecified (incl cysts and polyps): serious adverse events			
subjects affected / exposed	1 / 350 (0.29%)	2 / 357 (0.56%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Vascular disorders			
Vascular disorders: serious adverse events			
subjects affected / exposed	1 / 350 (0.29%)	0 / 357 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Pregnancy, puerperium and perinatal conditions: serious adverse events			
subjects affected / exposed	0 / 350 (0.00%)	1 / 357 (0.28%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
General disorders and administration site conditions: serious adverse events			
subjects affected / exposed	0 / 350 (0.00%)	1 / 357 (0.28%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Immune system disorders: serious adverse events			
subjects affected / exposed	1 / 350 (0.29%)	0 / 357 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders: serious adverse events			
subjects affected / exposed	0 / 350 (0.00%)	1 / 357 (0.28%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			

Psychiatric disorders: serious adverse events			
subjects affected / exposed	2 / 350 (0.57%)	2 / 357 (0.56%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	2 / 3	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Investigations: serious adverse events			
subjects affected / exposed	2 / 350 (0.57%)	0 / 357 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications: serious adverse events			
subjects affected / exposed	0 / 350 (0.00%)	2 / 357 (0.56%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Cardiac disorders			
Cardiac disorders: serious adverse events			
subjects affected / exposed	1 / 350 (0.29%)	0 / 357 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Nervous system disorders: serious adverse events			
subjects affected / exposed	3 / 350 (0.86%)	4 / 357 (1.12%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Blood and lymphatic system disorders: serious adverse events			
subjects affected / exposed	3 / 350 (0.86%)	3 / 357 (0.84%)	1 / 42 (2.38%)
occurrences causally related to treatment / all	0 / 12	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastrointestinal disorders: serious adverse events			

subjects affected / exposed	0 / 350 (0.00%)	1 / 357 (0.28%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatobiliary disorders: serious adverse events			
subjects affected / exposed	1 / 350 (0.29%)	0 / 357 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders: serious adverse events			
subjects affected / exposed	2 / 350 (0.57%)	1 / 357 (0.28%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 2	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Renal and urinary disorders: serious adverse events			
subjects affected / exposed	2 / 350 (0.57%)	0 / 357 (0.00%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders: serious adverse events			
subjects affected / exposed	2 / 350 (0.57%)	2 / 357 (0.56%)	0 / 42 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Infections and infestations: serious adverse events			
subjects affected / exposed	25 / 350 (7.14%)	23 / 357 (6.44%)	9 / 42 (21.43%)
occurrences causally related to treatment / all	0 / 30	0 / 24	0 / 11
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Metabolism and nutrition disorders			
Metabolism and nutrition disorders: serious adverse events			

subjects affected / exposed	1 / 350 (0.29%)	0 / 357 (0.00%)	2 / 42 (4.76%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

Serious adverse events	Standard of Care (<14kg cohort)		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 43 (25.58%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	4		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasms benign, malignant and unspecified (incl cysts and polyps): serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Vascular disorders: serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Pregnancy, puerperium and perinatal conditions: serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General disorders and administration site conditions: serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Immune system disorders: serious adverse events			

subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders: serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Psychiatric disorders: serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Investigations: serious adverse events			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications: serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac disorders: serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Nervous system disorders: serious adverse events			

subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Blood and lymphatic system disorders: serious adverse events			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Gastrointestinal disorders: serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatobiliary disorders: serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders: serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal and urinary disorders: serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders: serious adverse events			

subjects affected / exposed	0 / 43 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infections and infestations: serious adverse events			
subjects affected / exposed	9 / 43 (20.93%)		
occurrences causally related to treatment / all	0 / 16		
deaths causally related to treatment / all	0 / 3		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders: serious adverse events			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Dolutegravir (>=14kg cohort)	Standard of Care (>=14kg cohort)	Dolutegravir (<14kg Cohort)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 350 (0.00%)	0 / 357 (0.00%)	0 / 42 (0.00%)

Non-serious adverse events	Standard of Care (<14kg cohort)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 43 (0.00%)		

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