Clinical trial results:
Changes in weight, body composition and metabolic parameters after switch to dolutegravir/lamuvidine compared to continued treatment with dolutegravir/abacavir/lamuvidine for virologically suppressed HIV infection: A randomized open-label superiority trial. The AVERTAS-1 trial

Summary

EudraCT number	2019-004999-19
Trial protocol	DK
Global end of trial date	06 November 2023

Results information

Result version number	v1 (current)
This version publication date	12 April 2025
First version publication date	12 April 2025

Trial information

Trial identification

Sponsor protocol code	191001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Department of Infectious Diseaess, Copenhagen University Hospital - Amager and Hvidovre
Sponsor organisation address	Kettegaard Alle 30, Hvidovre, Denmark, 2650
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Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	02 January 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 November 2023
Global end of trial reached?	Yes
Global end of trial date	06 November 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aim of this study is to investigate if discontinuing abacavir by switching from a 3 drug regimen with with dolutegravir /abacavir/lamivudine to a 2 drug regimen with dolutegravir/lamivudine will cause changes in weight, and in metabolic and cardiac parameters in individuals infected with HIV.

Protection of trial subjects:

Plasma HIV-RNA

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 October 2020
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	Denmark: 81
Worldwide total number of subjects	81
EEA total number of subjects	81

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	77
From 65 to 84 years	4
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Participants were screened and recruited from the outpatient clinics at the Departments of Infectious Diseases at Copenhagen University Hospital - Amager and Hvidovre and Rigshospitalet from October 2020 to November 2022.

Pre-assignment

Screening details:

Inclusion cirteria: ≥ 18 years; DTG/ABC/3TC treatment for at least 6 months; Female participant: Contraception during study period
Exclusion criteria: pre-existing resistance to 3TC or DTG, hepatitis B antigen (HBsAg) or HBV DNA, cancer within the past five years, unstable cardiovascular disease or diabetes, pregnancy/breastfeeding.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	DTG/3TC

Arm description:

Intervention arm, switched treatment to dolutegravir (DTG) + lamivudine (3TC)

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

Dosage and administration details:

co-formulated DTG 50 mg and 3TC 300 mg administrated once daily

Arm title	DTG/ABC/3TC

Arm description:

Continued treatment with dolutegravir (DTG)/abacavir(ABC)/lamivudine(3TC)

Arm type	Active comparator
Investigational medicinal product name	dolutegravir/abacavir/lamivudine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

co-formulated dolutegravir 50 mg, abacavir 600 mg, and lamivudine 300 mg administrated once daily.

Number of subjects in period 1	DTG/3TC	DTG/ABC/3TC
Started	55	26
Completed	52	24
Not completed	3	2
Consent withdrawn by subject	1	1
Physician decision	1	-
Lost to follow-up	-	1
Protocol deviation	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	81	81	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	77	77	
From 65-84 years	4	4	
85 years and over	0	0	
18-64	0	0	
Age continuous Units: years			
arithmetic mean	45.3		
standard deviation	± 17.1	-	
Gender categorical Units: Subjects			
Female	11	11	
Male	70	70	
Smoking Units: Subjects			
Current	19	19	
Previous	20	20	
No smoking	42	42	
Hypertension Units: Subjects			
Yes	7	7	
No	74	74	
Hypercholesterolemia Units: Subjects			
Yes	8	8	
No	73	73	
Diabetes Units: Subjects			
Yes	4	4	
No	77	77	
Chronic obstructive pulmonary disease (COPD) Units: Subjects			

Yes	1	1	
No	80	80	
Asthma			
Units: Subjects			
Yes	4	4	
No	77	77	
BMI			
(kg/m2)			
Units: Subjects			
Underweight	1	1	
Normal	29	29	
Overweight	37	37	
Obese	14	14	
CD4 cell count			
Units: copies/mL			
arithmetic mean	699		
standard deviation	± 217	-	
Nadir CD4 cell count			
Units: copies/mL			
arithmetic mean	287		
standard deviation	± 199	-	
Visceral/subcutaneous fat ratio (VAT/SAT			
Units: ratio			
median	0.6		
inter-quartile range (Q1-Q3)	0.4 to 1.5	-	
P-hsCRP			
Units: mg/L			
arithmetic mean	2.1		
standard deviation	± 2.9	-	
P-LDL			
plasma low density lipoprotein			
Units: mmol/L			
arithmetic mean	3.0		
standard deviation	± 0.8	-	

End points

End points reporting groups	
Reporting group title	DTG/3TC
Reporting group description:	
Intervention arm, switched treatment to dolutegravir (DTG) + lamivudine (3TC)	
Reporting group title	DTG/ABC/3TC
Reporting group description:	
Continued treatment with dolutegravir (DTG)/abacavir(ABC)/lamivudine(3TC)	

Primary: Body weight	
End point title	Body weight
End point description:	
Difference in mean weight from baseline to week 48 between treatment arms	
End point type	Primary
End point timeframe:	
Baseline to week 48	

End point values	DTG/3TC	DTG/ABC/3TC		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	24		
Units: kg				
arithmetic mean (standard deviation)	0.9 (± 3.6)	0.9 (± 3.2)		

Statistical analyses

Statistical analysis title	Primary endpoint
Statistical analysis description:	
To analyse repeated measurements, a linear mixed model was employed, comparing changes in weight across treatment arms from baseline to week 24 and week 48, assuming a linear relationship over time.	
Comparison groups	DTG/ABC/3TC v DTG/3TC
Number of subjects included in analysis	76
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	> 0.05
Method	Regression, Linear
Parameter estimate	Mean difference (final values)

Adverse events

Adverse events information	
Timeframe for reporting adverse events: October 2020 to november 2023	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	NA

Reporting groups	
Reporting group title	DTG/3TC
Reporting group description: Intervention arm, switched treatment to dolutegravir (DTG) + lamivudine (3TC)	
Reporting group title	DTG/ABC/3TC
Reporting group description: Continued treatment with dolutegravir (DTG)/abacavir(ABC)/lamivudine(3TC)	

Serious adverse events	DTG/3TC	DTG/ABC/3TC	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 55 (1.82%)	1 / 26 (3.85%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Shoulder surgery	Additional description: Shoulder surgery after contusion of right shoulder		
subjects affected / exposed	0 / 55 (0.00%)	1 / 26 (3.85%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Myocardial infarction	Additional description: Silent myocardial infarction. Was randomly found during study regular cardiac MRI scan in the study		
subjects affected / exposed	1 / 55 (1.82%)	0 / 26 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	DTG/3TC	DTG/ABC/3TC	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 55 (0.00%)	1 / 26 (3.85%)	
Gastrointestinal disorders			
Gastroenteritis	Additional description: Gastroenteritis after eating oisters		
subjects affected / exposed	0 / 55 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 September 2020	• HIV-RNA and CD4 cell count control changed from to week 1, 4, 24 and 48 (instead of week 1, 4, 12, 24, 36, 48) • Plasma erythrocyte volume fraction added to blood tests, because it was used in the cardiac MRI analysis • The questions about adverse effects omitted from questionnaire, because low risk of adverse effects are expected since the participants either continue usual treatment or a reduced regimen with the same drugs. • 24-hour EKG-monitoring added to the cardiac MR sub study to evaluate potential cardiac arrhythmia
12 February 2021	• 24-hour EKG-monitoring added to the cardiac MR sub study to evaluate potential cardiac arrhythmia
23 April 2021	• Enrolment of healthy controls added to the cardiac MR sub study project • Specification of cardiac MR sub study outcomes
24 August 2023	• Specification of primary endpoint to difference in change from baseline to week 48 between the intervention arm and the control arm (continuous outcome) - Previous wording could be interpret as I binary outcome • Sample size changed from 95 to 70 participants by downsizing from 90-80%: Due to limited eligible participants in the two study sites

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported