Clinical trial results:
Exploratory, open-label, randomized clinical trial to assess the efficacy of first-line dual vs. triple antiretroviral therapy (art) in HIV-1 reservoir and in peripheral compartments in HIV-infected patients.

Summary

EudraCT number	2019-002733-10
Trial protocol	ES
Global end of trial date	22 September 2022

Results information

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

Trial information

Trial identification

Sponsor protocol code	Dual-Triple-ART

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Fundació Lluita contra les Infeccions
Sponsor organisation address	Carretera de Canyet s/n, Badalona, Spain, 08916
Public contact	CRO, Fundació Lluita contra les Infeccions, +34 93497 8414, info@scienhub.org
Scientific contact	CRO, Fundació Lluita contra les Infeccions, +34 93497 8414, info@scienhub.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	31 October 2022
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	22 September 2022
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare changes in the HIV-1 reservoir (proviral HIV-1 DNA in CD4+ T cells) from baseline to week 48 between first-line treatment with DTG+3TC versus DTG +FTC/TAF.

Protection of trial subjects:

The processing of the data to be compiled by the study sponsor during the study will be participant to current legislation as regards data protection (LOPD, The Organic Law 3/2018 of 5 December on the Protection of Personal Data and the Guarantee of Digital Rights complementary to the Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016, on the protection of natural persons about the processing of personal data and on the free movement of such data). The corresponding unique code number will identify the participant in the records. The participant is guaranteed anonymity and informed that all communication will take place between him/her and the investigator, not the sponsor of the study.

The

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 November 2019
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Spain: 44
Worldwide total number of subjects	44
EEA total number of subjects	44

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)	44
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Adults infected by HIV-1 without prior ART experience. The participants were recruited at Hospital U. Germans Trias i Pujol.

Pre-assignment

Screening details:

Age ≥18 years, Documented HIV-1 infection (confirmed by a NAT/PCR test), Naïve to cART, willing and able to be adherent to antiretroviral therapy for the duration of the study and follow protocol requirements.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Triple ART Group

Arm description:

Dolutegravir (Tivicay) 50 mg every 24 hours.
Emtricitabine/Tenofovir alafenamide fumarate (Descovy) 200/25 mg every 24 hours.
Patients will be advised to take antiretroviral medication orally.
Commercial medication will be used.

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

Dosage and administration details:

50 mg every 24 hours

Investigational medicinal product name	Emtricitabine/Tenofovir alafenamide fumarate
Investigational medicinal product code	
Other name	Descovy
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Emtricitabine/Tenofovir alafenamide fumarate (Descovy) 200/25 mg every 24 hours

Arm title	Dual ART Group

Arm description:

Dolutegravir (Tivicay) 50 mg every 24 hours.
Lamivudine (Lamivudine EFG) 300 mg every 24 hours.
Patients will be advised to take antiretroviral medication orally.
Commercial medication will be used.

Arm type	Active comparator
Investigational medicinal product name	Dolutegravir
Investigational medicinal product code	
Other name	Tivicay
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details: Dolutegravir (Tivicay) 50 mg every 24 hours.	
Investigational medicinal product name	Lamivudine
Investigational medicinal product code	
Other name	Lamivudine EFG
Pharmaceutical forms	Coated tablet
Routes of administration	Oral use

Dosage and administration details:

Lamivudine (Lamivudine EFG) 300 mg every 24 hours.

Number of subjects in period 1	Triple ART Group	Dual ART Group
Started	22	22
Completed	21	20
Not completed	1	2
Consent withdrawn by subject	-	1
Lost to follow-up	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Triple ART Group
Reporting group description:	
Dolutegravir (Tivicay) 50 mg every 24 hours. Emtricitabine/Tenofovir alafenamide fumarate (Descovy) 200/25 mg every 24 hours. Patients will be advised to take antiretroviral medication orally. Commercial medication will be used.	
Reporting group title	Dual ART Group
Reporting group description:	
Dolutegravir (Tivicay) 50 mg every 24 hours. Lamivudine (Lamivudine EFG) 300 mg every 24 hours. Patients will be advised to take antiretroviral medication orally. Commercial medication will be used.	

Reporting group values	Triple ART Group	Dual ART Group	Total
Number of subjects	22	22	44
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	22	22	44
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
median	30.8	33.5	
inter-quartile range (Q1-Q3)	27.7 to 35.2	27.5 to 35.3	-
Gender categorical			
Units: Subjects			
Female	0	0	0
Male	22	22	44

End points

End points reporting groups

Reporting group title	Triple ART Group
Reporting group description:	
Dolutegravir (Tivicay) 50 mg every 24 hours. Emtricitabine/Tenofovir alafenamide fumarate (Descovy) 200/25 mg every 24 hours. Patients will be advised to take antiretroviral medication orally. Commercial medication will be used.	
Reporting group title	Dual ART Group
Reporting group description:	
Dolutegravir (Tivicay) 50 mg every 24 hours. Lamivudine (Lamivudine EFG) 300 mg every 24 hours. Patients will be advised to take antiretroviral medication orally. Commercial medication will be used.	

Primary: Change in proviral HIV-1 DNA in CD4+ Tcells from baseline to week 48.

End point title	Change in proviral HIV-1 DNA in CD4+ Tcells from baseline to week 48.
End point description:	
At week 48, the GMR (95%CI) from baseline in total HIV-1 DNA was 0.21 (0.17 - 0.26) in the 2DR group and 0.18 (0.15 - 0.21) in the 3DR group (MMRM, p=0.325).	
End point type	Primary
End point timeframe:	
From baseline to week 48	

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: Copies/10^6 CD4+ Tcells				
geometric mean (confidence interval 95%)	0.18 (0.15 to 0.21)	0.21 (0.17 to 0.26)		

Statistical analyses

Statistical analysis title	Mixed-model for repeated measures (MMRM)
Statistical analysis description:	
Due to wide interindividual variability, reservoir parameters were described using the geometric mean (GM) and its SD, and longitudinal changes were assessed employing the GM ratio (GMR) and its 95% confidence interval (95% CI). A mixed-model for repeated measures (MMRM) was used to assess the endpoint on log10 scale for each arm. In each model, the interaction between visit (weeks) and study arm was included as a fixed effect, and the participant was considered as a random effect.	
Comparison groups	Triple ART Group v Dual ART Group

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	equivalence[1]
P-value	= 0.325
Method	Mixed models analysis

Notes:

[1] - A mixed-model for repeated measures (MMRM) was used to assess the endpoint on log10 scale for each arm. In each model, the interaction between visit (weeks) and study arm was included as a fixed effect, and the participant was considered as a random effect. An unstructured covariance matrix was used to model the within-subject error and the Kenward-Roger approximation was employed to estimate the degrees of freedom.

Secondary: Changes in intact proviral HIV-1 DNA

End point title	Changes in intact proviral HIV-1 DNA

End point description:

At week 48, the GMR (95%CI) from baseline intact proviral HIV-1 DNA was 0.19(0.15 - 0.25) in the 2DR group and 0.18 (0.13 - 0.25) in the 3DR group (MMRM, p=0.838).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18	18		
Units: copies/106 CD4+ T cells				
geometric mean (confidence interval 95%)	0.18 (0.13 to 0.25)	0.19 (0.15 to 0.25)		

Statistical analyses

Statistical analysis title	Mixed-model for repeated measures (MMRM)

Statistical analysis description:

A mixed-model for repeated measures (MMRM) was used to assess the endpoint on log10 scale for each arm. In each model, the interaction between visit (weeks) and study arm was included as a fixed effect, and the participant was considered as a random effect.

Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.838 [2]
Method	Mixed models analysis

Notes:

[2] - Mixed-model for repeated measures including week and arm as fixed effects and subjects as random effect

Secondary: Changes in cell-associated RNA (ca-RNA)

End point title	Changes in cell-associated RNA (ca-RNA)

End point description:

At week 48, the GMR (95%CI) from baseline in cell-associated RNA (ca-RNA) was 0.06(0.03 - 0.15) in

the 2DR group and 0.07 (0.03 - 0.16) in the 3DR group (MMRM, p=0.8764).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	10[3]	16[4]		
Units: Copies/10^3 copies TBP				
geometric mean (confidence interval 95%)	0.07 (0.03 to 0.16)	0.06 (0.03 to 0.15)		

Notes:

[3] - Analyzed samples based on availability of cryopreserved PBMC

[4] - Analyzed samples based on availability of cryopreserved PBMCs

Statistical analyses

Statistical analysis title	Mixed-model for repeated measures (MMRM)
Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	26
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.8764
Method	Mixed models analysis

Secondary: Changes in inductible reservoir in CD4+ T cells

End point title	Changes in inductible reservoir in CD4+ T cells

End point description:

At week 48, the GMR (95%CI) from baseline in inductible reservoir in CD4+ T cells was 0.03(0.01 - 0.05) in the 2DR group and 0.03 (0.01 - 0.06) in the 3DR group (MMRM, p=0.3907).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	15[5]	17[6]		
Units: HAP cells /10^6 CD4*T cell				
geometric mean (confidence interval 95%)	0.03 (0.01 to 0.06)	0.03 (0.01 to 0.05)		

Notes:

[5] - Analyzed samples based on availability of cryopreserved PBMCs

[6] - Analyzed samples based on availability of cryopreserved PBMCs

Statistical analyses

Statistical analysis title	Mixed-model for repeated measures (MMRM)
Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	32
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3907
Method	Mixed models analysis

Secondary: Changes in CD4+ T cell counts

End point title	Changes in CD4+ T cell counts

End point description:

At week 48, the median (IQR) from baseline in inducible reservoir CD4+ T cell counts241 (90 to 315) in the 2DR group and 196 (14 to 319) in the 3DR group (MMRM, p=0.3907).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: cells/mm3				
median (inter-quartile range (Q1-Q3))	196 (14 to 319)	241 (90 to 315)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.3157
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in CD4/CD8 ratio

End point title	Changes in CD4/CD8 ratio

End point description:

At week 48, the changes in CD4/CD8 ratio was equal in both groups

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: Ratio				
number (not applicable)	0.5	0.5		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.954
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in plasma levels of soluble inflammatory biomarkers (SCD14)

End point title	Changes in plasma levels of soluble inflammatory biomarkers (SCD14)

End point description:

The median (IQR) ratio w48/baseline in plasma levels of soluble inflammatory biomarkers (SCD14) are 0.70(0.51 - 1.00) in the 2DR group and 0.70 (0.42 - 0.85) in the 3DR group (MMRM, p=0.7034).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: mg/mL				
median (inter-quartile range (Q1-Q3))	0.70 (0.42 to 0.85)	0.70 (0.51 to 1.00)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.7034
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in plasma levels of soluble inflammatory biomarkers (FABP2)

End point title	Changes in plasma levels of soluble inflammatory biomarkers (FABP2)

End point description:

The median (IQR) ratio w48/baseline in plasma levels of soluble inflammatory biomarkers (FABP2) are 0.41 (0.44 - 1.66) in the 2DR group and 0.73(0.78 - 2.53) in the 3DR group (MMRM, p=0.0864).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: ng/mL				
median (inter-quartile range (Q1-Q3))	0.73 (0.44 to 1.66)	1.41 (0.78 to 2.53)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.0864
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in plasma levels of soluble inflammatory biomarkers (TRAIL)

End point title	Changes in plasma levels of soluble inflammatory biomarkers (TRAIL)

End point description:

The median (IQR) ratio w48/baseline in plasma levels of soluble inflammatory biomarkers (TRAIL) are 0.77(0.49 - 1.04) in the 2DR group and 0.93 (0.44 - 1.45) in the 3DR group (MMRM, p=0.6468).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))	0.93 (0.44 to 1.45)	0.77 (0.49 to 1.04)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group

Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.6468
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in plasma levels of soluble inflammatory biomarkers (IP-10))

End point title	Changes in plasma levels of soluble inflammatory biomarkers (IP-10))

End point description:

The median (IQR) ratio w48/baseline in plasma levels of soluble inflammatory biomarkers ((IP-10) are 0.69(0.50 - 0.95) in the 2DR group and 0.80 (0.48 - 1.19) in the 3DR group (MMRM, p=0.8821).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))	0.80 (0.48 to 1.19)	0.69 (0.50 to 0.95)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.8821
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in plasma levels of soluble inflammatory biomarkers (IL-6)

End point title	Changes in plasma levels of soluble inflammatory biomarkers (IL-6)

End point description:

The median (IQR) ratio w48/baseline in plasma levels of soluble inflammatory biomarkers (IL-6) are 1.09 (0.86 - 1.41) in the 2DR group and 1.28 (0.94 - 1.53) in the 3DR group (MMRM, p=0.4042).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: pg/mL				
median (inter-quartile range (Q1-Q3))	1.28 (0.94 to 1.53)	1.09 (0.86 to 1.41)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.4042
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in plasma levels of soluble inflammatory biomarkers (CRP)

End point title	Changes in plasma levels of soluble inflammatory biomarkers (CRP)

End point description:

The median (IQR) ratio w48/baseline in plasma levels of soluble inflammatory biomarkers (CRP) are 0.92 (0.63 - 1.27) in the 2DR group and 0.83(0.51 - 5.11) in the 3DR group (MMRM, p=0.7722).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: ng/mL				
median (inter-quartile range (Q1-Q3))	0.83 (0.51 to 5.11)	0.92 (0.63 to 1.27)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.7722
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in plasma levels of soluble inflammatory biomarkers (D-Dimer))

End point title	Changes in plasma levels of soluble inflammatory biomarkers (D-Dimer))

End point description:

The median (IQR) ratio w48/baseline in plasma levels of soluble inflammatory biomarkers (D-Dimer) are 0.99 (0.73 - 1.32) in the 2DR group and 1.13 (0.88 - 1.57) in the 3DR group (MMRM, p=0.4224).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	20	20		
Units: mg/mL				
median (inter-quartile range (Q1-Q3))	1.13 (0.88 to 1.57)	0.99 (0.73 to 1.32)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group

Number of subjects included in analysis	40
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.4224
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in Surface markers of immune activation: CD4+/HLA-DR+/CD38+

End point title	Changes in Surface markers of immune activation: CD4+/HLA-DR+/CD38+

End point description:

The median (IQR) ratio w48/baseline in Surface markers of immune activation: CD4+/HLA-DR+/CD38+ is 0.56(0.39 - 0.75) in the 2DR group and 0.58 (0.38 - 0.90) in the 3DR group (MMRM, p=0.633).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: %				
median (inter-quartile range (Q1-Q3))	0.58 (0.38 to 0.90)	0.56 (0.39 to 0.75)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.633
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in Surface markers of immune activation: CD8+/HLA-DR+/CD38+

End point title	Changes in Surface markers of immune activation: CD8+/HLA-DR+/CD38+

End point description:

The median (IQR) ratio w48/baseline in Surface markers of immune activation: CD8+/HLA-DR+/CD38+ is 0.26 (0.15 - 0.60) in the 2DR group and 0.34 (0.25 - 0.63) in the 3DR group (MMRM, p=0.1812).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: %				
median (inter-quartile range (Q1-Q3))	0.34 (0.25 to 0.63)	0.26 (0.15 to 0.60)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.1812
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in Surface markers of T cell exhaustion: CD4+/PD-1+/TIGIT+

End point title	Changes in Surface markers of T cell exhaustion: CD4+/PD-1+/TIGIT+

End point description:

The median (IQR) ratio w48/baseline in Surface markers of immune activation: CD4+/PD-1+/TIGIT+ is 0.94 (0.62 - 1.04) in the 2DR group and 0.81 (0.68 - 0.99) in the 3DR group (MMRM, p=0.5612).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: %				
median (inter-quartile range (Q1-Q3))	0.81 (0.68 to 0.99)	0.94 (0.62 to 1.04)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5612
Method	Wilcoxon (Mann-Whitney)

Secondary: Changes in Surface markers of T cell exhaustion: CD8+/PD-1+/TIGIT+

End point title	Changes in Surface markers of T cell exhaustion: CD8+/PD-1+/TIGIT+

End point description:

The median (IQR) ratio w48/baseline in Surface markers of immune activation: CD8+/PD-1+/TIGIT+ is 0.44 (0.22 - 0.76) in the 2DR group and 0.35 (0.21 - 0.51) in the 3DR group (MMRM, p=0.5101).

End point type	Secondary

End point timeframe:

From baseline to week 48

End point values	Triple ART Group	Dual ART Group		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	20		
Units: %				
median (inter-quartile range (Q1-Q3))	0.35 (0.21 to 0.51)	0.44 (0.22 to 0.76)		

Statistical analyses

Statistical analysis title	Mann-Whitney test

Statistical analysis description:

Comparisons between groups at each timepoint were performed by the Mann-Whitney test non adjusted

for multiple comparisons.

Comparison groups	Triple ART Group v Dual ART Group
Number of subjects included in analysis	41
Analysis specification	Pre-specified
Analysis type	equivalence
P-value	= 0.5101
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs have been reported from baseline until week 48.

Adverse event reporting additional description:

The SAE reports subject to the above reporting provisions occur following the first dose and through to 28 days after discontinuation of the study medication.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups

Reporting group title	Triple ART Group

Reporting group description:

Dolutegravir (Tivicay) 50 mg every 24 hours.
Emtricitabine/Tenofovir alafenamide fumarate (Descovy) 200/25 mg every 24 hours.
Patients will be advised to take antiretroviral medication orally.
Commercial medication will be used.

Reporting group title	Dual ART Group

Reporting group description:

Dolutegravir (Tivicay) 50 mg every 24 hours.
Lamivudine (Lamivudine EFG) 300 mg every 24 hours.
Patients will be advised to take antiretroviral medication orally.
Commercial medication will be used.

Serious adverse events	Triple ART Group	Dual ART Group	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Blood and lymphatic system disorders			
Burkitt's lymphoma			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (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: 5 %

Non-serious adverse events	Triple ART Group	Dual ART Group	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 22 (68.18%)	18 / 22 (81.82%)	

Vascular disorders Haemorrhoids subjects affected / exposed occurrences (all)	0 / 22 (0.00%) 0	1 / 22 (4.55%) 1	
Nervous system disorders Headache subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1 1 / 22 (4.55%) 1	1 / 22 (4.55%) 1 0 / 22 (0.00%) 0	
Blood and lymphatic system disorders Seroma subjects affected / exposed occurrences (all) Tonsillitis bacterial subjects affected / exposed occurrences (all)	2 / 22 (9.09%) 2 0 / 22 (0.00%) 0	5 / 22 (22.73%) 5 1 / 22 (4.55%) 1	
Gastrointestinal disorders Odynophagia subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Epigastric discomfort subjects affected / exposed occurrences (all) Pinworm infection subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all)	1 / 22 (4.55%) 1 1 / 22 (4.55%) 1 0 / 22 (0.00%) 0 1 / 22 (4.55%) 1 0 / 22 (0.00%) 0 0 / 22 (0.00%) 0	1 / 22 (4.55%) 1 0 / 22 (0.00%) 0 1 / 22 (4.55%) 1 0 / 22 (0.00%) 0 1 / 22 (4.55%) 1 1 / 22 (4.55%) 1	

rectorrhagia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Flatulence			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	1 / 22 (4.55%)	1 / 22 (4.55%)	
occurrences (all)	1	1	
Respiratory, thoracic and mediastinal disorders			
Upper respiratory tract infection			
subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
allergic rhinitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Seborrhoeic dermatitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Scab			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Acne			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Folliculitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Molluscum contagiosum			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Proctitis			

subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Urethritis			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Post-traumatic stress disorder			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypoglycemia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Buttock injury			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
Pain			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Omalgia			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences (all)	1	0	
tendinitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Infections and infestations			
Genital infection viral			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Genital herpes			
subjects affected / exposed	2 / 22 (9.09%)	0 / 22 (0.00%)	
occurrences (all)	4	0	
Anal LSIL			
subjects affected / exposed	1 / 22 (4.55%)	0 / 22 (0.00%)	
occurrences (all)	1	0	

Neisseria infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Syphilis			
subjects affected / exposed	2 / 22 (9.09%)	2 / 22 (9.09%)	
occurrences (all)	2	2	
Cutaneous infection			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
COVID-19			
subjects affected / exposed	4 / 22 (18.18%)	2 / 22 (9.09%)	
occurrences (all)	4	2	
Wound drainage			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	
Chlamydial infection			
subjects affected / exposed	0 / 22 (0.00%)	2 / 22 (9.09%)	
occurrences (all)	0	2	
Orchitis			
subjects affected / exposed	0 / 22 (0.00%)	1 / 22 (4.55%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 July 2020	Extension of the recruitment period: Due to the interruption of participant recruitment during the COVID-19 crisis in Spain and the complexity of the participant selection criteria, it has been decided to extend the recruitment period by 9 months to reach the total planned number of participants.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported