



Clinical trial results:

Pilot singlearm clinical trial to evaluate the efficacy, PK interactions and safety of dolutegravir plus 2 NRTIs in HIV1infected solid organ transplant patients

Summary

EudraCT number	2017-000469-62
Trial protocol	ES
Global end of trial date	21 May 2020

Results information

Result version number	v1 (current)
This version publication date	21 August 2025
First version publication date	21 August 2025

Trial information

Trial identification

Sponsor protocol code	DTG-SOT
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03360682
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundació Clínic per a la Recerca Biomèdica
Sponsor organisation address	C/ Rosselló, 149-153, Barcelona, Spain, 08036
Public contact	CTU, CTU Clinic (Clinical Trial Unit), +34 9322754009838, acruceta@recerca.clinic.cat
Scientific contact	CTU, CTU Clinic (Clinical Trial Unit), +34 9322754009838, acruceta@recerca.clinic.cat

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	21 May 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 May 2020
Global end of trial reached?	Yes
Global end of trial date	21 May 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The aims of this study are to obtain pharmacokinetic data on interactions between DTG and immunosuppressant drugs (Cyclosporine A, Tacrolimus, Syrolimus and Mycophenolic acid) in SOT recipients To provide proof of principle data that DTG plus 2 NUCs is safe and effective in HIVinfected SOT recipients.

Protection of trial subjects:

The study was conducted in accordance with the Royal Decree 1090/2015 (Spain), ICH-GCP (International Conference on Harmonisation – Good Clinical Practice) and The Declaration of Helsinki (latest version, Fortaleza 2013). Before initiation, the following approvals were required: Ethics Committee approval, Authorization from the Spanish Medicines Agency (AEMPS), Institutional approval and

Acceptance by the sponsor and coordinating investigator.

All participants had to provide signed and dated informed consent before any study procedures; Received written and verbal information about the study's nature, duration, purpose, and potential risks; Have the right to withdraw at any time without penalty; Had guaranteed continuous medical and nursing supervision throughout the study. The protocol also follows UNAIDS Good Participatory Practice Guidelines, involving community representatives in the design of the protocol and patient information materials.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 April 2018
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: 19
Worldwide total number of subjects	19
EEA total number of subjects	19

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)	19
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

HIV-1-infected adults (>18) with kidney, liver, or heart transplant, on stable ART ≥6 months, HIV RNA <50 c/mL for 12 months, no major resistance mutations, and HLA-B*5701 negative. Excluded: ART failure, contraindicated meds, active infections, cancer, pregnancy, or drug intolerance.

Period 1

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

Arms

Arm title	DTG + 2 NRTIs
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Arm description:

Dolutegravir plus 2 NRTIs in HIV-1-infected solid organ transplant recipients

Arm type	Experimental
Investigational medicinal product name	Dolutegravir/ Abacavir/ Lamivudina (DTG/ABC/3TC)
Investigational medicinal product code	
Other name	Triumeq®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dolutegravir 50mg + Abacavir 600 mg + Lamivudina 300 mg + (1 tablet once daily)

Investigational medicinal product name	Dolutegravir (DTG) + Emtricitabina/ Tenofovir (FTC/TDF)
Investigational medicinal product code	
Other name	Truvada® + Tivicay®
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Emtricitabina 200 mg/ Tenofovir 245 mg (Truvada®, 1 tablet once daily)

Dolutegravir 50 mg (Tivicay®, 1 tablet once daily)

Number of subjects in period 1	DTG + 2 NRTIs
Started	19
Completed	16
Not completed	3
Adverse event, non-fatal	3

Baseline characteristics

Reporting groups

Reporting group title

Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	19	19	
Age categorical			
Units: Subjects			
In utero		0	
Preterm newborn infants (gestational age < 37 wks)		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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous			
Units: years			
median	57		
inter-quartile range (Q1-Q3)	51 to 60	-	
Gender categorical			
Units: Subjects			
Female	8	8	
Male	11	11	

End points

End points reporting groups

Reporting group title	DTG + 2 NRTIs
Reporting group description: Dolutegravir plus 2 NRTIs in HIV-1-infected solid organ transplant recipients	
Subject analysis set title	Pharmacokinetic (PK) subset before ART change
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants who underwent pharmacokinetic sampling before switching to DTG-based ART (n = 9).	
Subject analysis set title	Pharmacokinetic (PK) subset after 2wk ART change
Subject analysis set type	Sub-group analysis
Subject analysis set description: Participants who underwent pharmacokinetic sampling after 2 weeks switching to DTG-based ART (n = 9).	

Primary: Change in pharmacokinetic parameters (Cmax, Cmin, T, AUC) of CsA immunosuppressant

End point title	Change in pharmacokinetic parameters (Cmax, Cmin, T, AUC) of CsA immunosuppressant ^[1]
End point description: Change in pharmacokinetic parameters (Cmax, Cmin, T, AUC) of immunosuppressant Cyclosporine A (CsA)	
End point type	Primary
End point timeframe: 2 weeks after switching from raltegravir-based ART to dolutegravir-based ART	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The change in CsA pharmacokinetic parameters was analyzed using the Wilcoxon signed-rank test for paired samples. This non-parametric test was selected due to the small sample size (n = 2) and non-normal distribution of the data. Results were reported as median and interquartile range (IQR), and a two-tailed p-value < 0.05 was considered statistically significant.

End point values	Pharmacokinetic (PK) subset before ART change	Pharmacokinetic (PK) subset after 2wk ART change		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	2	2		
Units: ng/mL				
median (inter-quartile range (Q1-Q3))				
Cmax	825 (686 to 946)	299 (120 to 478)		
Cmin	86.5 (83 to 90)	98.5 (65 to 132)		
T (h)	1 (1 to 1)	0.75 (0.5 to 1)		
AUC	2649.55 (2307.30 to 2991.80)	1407.50 (900.10 to 1914.90)		

Statistical analyses

No statistical analyses for this end point

Primary: Change in pharmacokinetic parameters (Cmax, Cmin, T, AUC) of MPA immunosuppressant

End point title	Change in pharmacokinetic parameters (Cmax, Cmin, T, AUC) of MPA immunosuppressant ^[2]
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End point description:

Change in pharmacokinetic parameters (Cmax, Cmin, T, AUC) of immunosuppressant Mycophenolic Acid (MPA).

End point type	Primary
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End point timeframe:

2 weeks after switching from raltegravir-based ART to dolutegravir-based ART

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The change in MPA pharmacokinetic parameters was analyzed using the Wilcoxon signed-rank test for paired samples. This non-parametric test was selected due to the small sample size (n = 7) and non-normal distribution of the data. Results were reported as median and interquartile range (IQR), and a two-tailed p-value < 0.05 was considered statistically significant.

End point values	Pharmacokinetic (PK) subset before ART change	Pharmacokinetic (PK) subset after 2wk ART change		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	7		
Units: µg/mL				
median (inter-quartile range (Q1-Q3))				
Cmax	6.3 (3.8 to 10.7)	10.3 (5.3 to 12.9)		
Cmin	1.9 (1.5 to 2.5)	2.9 (1.7 to 4)		
T (h)	2 (0.5 to 4)	1 (0.5 to 2)		
AUC	35.8 (23.7 to 43.9)	41.4 (33.9 to 47.7)		

Statistical analyses

No statistical analyses for this end point

Primary: Change in pharmacokinetic parameters (Cmax, Cmin, T, AUC) of Tacrolimus immunosuppressant

End point title	Change in pharmacokinetic parameters (Cmax, Cmin, T, AUC) of Tacrolimus immunosuppressant ^[3]
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End point description:

End point type	Primary
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End point timeframe:

2 weeks after switching from raltegravir-based ART to dolutegravir-based ART

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: The change in Tacrolimus pharmacokinetic parameters was analyzed using the Wilcoxon signed-rank test for paired samples. This non-parametric test was selected due to the small sample size (n = 2) and non-normal distribution of the data. Results were reported as median and interquartile

range (IQR), and a two-tailed p-value < 0.05 was considered statistically significant.

End point values	Pharmacokinetic (PK) subset before ART change	Pharmacokinetic (PK) subset after 2wk ART change		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	7	7		
Units: ng/mL				
median (inter-quartile range (Q1-Q3))				
C _{max}	14.4 (10.8 to 18.3)	16.4 (12.1 to 18.7)		
C _{min}	6.2 (5.2 to 8.9)	4.4 (4.3 to 8.5)		
T _{max} (h)	2 (1 to 2)	2 (1 to 2)		
AUC	113 (78.6 to 166.3)	103 (59.2 to 171.1)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

All AEs will be recorded by the Investigator from the time the subject signs informed consent until the last study visit or to 28 days after the last dose of IMP in case of early withdrawal while patient is receiving IMP.

Adverse event reporting additional description:

Only adverse events leading to treatment discontinuation or considered clinically relevant are reported individually. All other AEs occurred with low frequency and were not considered related to treatment.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	28.0
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Reporting groups

Reporting group title	DTG plus 2NRTIs
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Reporting group description: -

Serious adverse events	DTG plus 2NRTIs		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 19 (5.26%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Infections and infestations			
Cytomegalovirus infection	Additional description: Unrelated to treatment		
subjects affected / exposed	1 / 19 (5.26%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	DTG plus 2NRTIs		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	15 / 19 (78.95%)		
Nervous system disorders			
Insomnia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Tremor			

subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
Anxiety symptoms			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		
General disorders and administration site conditions			
Other			
subjects affected / exposed	10 / 19 (52.63%)		
occurrences (all)	10		
Gastrointestinal disorders			
Diarrhea			
subjects affected / exposed	3 / 19 (15.79%)		
occurrences (all)	3		
Endocrine disorders			
Hyperglycemia			
subjects affected / exposed	1 / 19 (5.26%)		
occurrences (all)	1		

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

DTG plus 2 NRTIs: lack clinically significant drug–drug interactions with calcineurin inhibitors (tacrolimus) and MPA in PHIV SOT recipients. Sample size for the PK analysis of CsA (n = 2): insufficient to draw robust conclusions.
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Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/40256046>