Clinical trial results:
Immune reconstitution in severely immunosuppressed antiretroviral-naive HIV-1?infected patients (<100 CD4+ T cells/?L) taking antiretroviral regimens based on dolutegravir or ritonavir-boosted darunavir (the AdvanZ-4 Trial).

Summary

EudraCT number	2014-002281-70
Trial protocol	ES
Global end of trial date	28 July 2020

Results information

Result version number	v1 (current)
This version publication date	21 October 2026
First version publication date	21 October 2026

Trial information

Trial identification

Sponsor protocol code	2014-002281-70

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02337322
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Fundacio Recerca Clinic Barcelona - Institut d'Investigacions Biomediques August Pi i Sunyer (FRCB-IDIBAPS)
Sponsor organisation address	C/ Villarroel 170, Barcelona, Spain,
Public contact	Judit Pich, CTU Clinic (Clinical Trial Unit), jpich@recerca.clinic.cat
Scientific contact	Judit Pich, CTU Clinic (Clinical Trial Unit), jpich@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	28 July 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 July 2020
Global end of trial reached?	Yes
Global end of trial date	28 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

-Compare the change in the absolute number of CD4 in peripheral blood to 48 to 96 weeks of initiating treatment.

Protection of trial subjects:

All subjects provided written informed consent before participation. The study protocol was approved by the Institutional Review Boards/Ethics Committees of all participating centres and by the Spanish Regulatory Authorities (AEMPS). The trial was conducted in accordance with the Declaration of Helsinki and applicable data protection regulations. Patient safety was monitored throughout the study, including adverse event and serious adverse event reporting procedures, predefined treatment discontinuation criteria, pregnancy reporting, and regular safety assessments.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2015
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: 104
Worldwide total number of subjects	104
EEA total number of subjects	104

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)	104
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 149 subjects were screened for eligibility between December 2014 and July 2018. Eligible participants were antiretroviral-naïve HIV-1 infected adults with CD4+ cell counts <100 cells/µL. Subjects were excluded if they did not meet inclusion/exclusion criteria, including positive HLA-B*5701 status or a confirmatory CD4+ count >100 cells/µ

Pre-assignment

Screening details:

A total of 149 subjects were screened for participation. Forty-five subjects were excluded during screening and were not randomised. A total of 104 eligible subjects were randomised into the study.

Period 1

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

Blinding implementation details:

Open-label trial. Participants and investigators were aware of treatment allocation after enrolment. Randomization was centralized and computer-generated (1:1), stratified by AIDS diagnosis. Investigators remained blinded only until patient inclusion/allocation. No blinding of participants, treating physicians, outcome assessors, or data collection procedures was reported.

Arms

Are arms mutually exclusive?	Yes
Arm title	DTG arm

Arm description:

Participants randomized to receive once-daily dolutegravir-based triple antiretroviral therapy consisting of dolutegravir 50 mg, abacavir 600 mg, and lamivudine 300 mg (Triumeq®) for the treatment of antiretroviral-naïve adults with advanced HIV-1 infection and CD4+ cell counts <100 cells/µL.

Arm type	Experimental
Investigational medicinal product name	Triumeq
Investigational medicinal product code	
Other name	Dolutegravir/Abacavir/Lamivudine, DTG/ABC/3TC
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Triumeq: 300mg 3TC/LAmivudina + 600mg ABC/Abacavir + 50mg DGT/Doultegrvir
1 tablet once per day.

Arm title	DRV/c arm

Arm description:

Participants randomized to receive once-daily darunavir/ritonavir-based triple antiretroviral therapy consisting of darunavir 800 mg plus ritonavir 100 mg, combined with abacavir 600 mg and lamivudine 300 mg. Participants enrolled after the protocol amendment received darunavir/cobicistat (Rezolsta®) instead of darunavir/ritonavir.

Arm type	Active comparator
Investigational medicinal product name	Rezolsta
Investigational medicinal product code	
Other name	Darunavir/Cobicistat, DRV/c
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Rezolsta:Darunavir 800 mg/Cobicistat 150 mg (Rezolsta®), one film-coated tablet orally once daily.

Investigational medicinal product name	Kivexa
Investigational medicinal product code	
Other name	Abacavir/Lamivudine, ABC/3TC
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Abacavir 600 mg/Lamivudine 300 mg (Kivexa®), one film-coated tablet orally once daily.

Number of subjects in period 1	DTG arm	DRV/c arm
Started	52	52
Completed	48	37
Not completed	4	15
Adverse event, serious fatal	-	1
Virologic failure	1	-
Adverse event, non-fatal	-	5
New AIDS event / disease progression	-	1
Randomised but did not receive allocated treatment	-	3
Lost to follow-up	1	2
New AIDS events	2	-
Lack of efficacy	-	3

Baseline characteristics

Reporting groups	
Reporting group title	DTG arm
Reporting group description:	
Participants randomized to receive once-daily dolutegravir-based triple antiretroviral therapy consisting of dolutegravir 50 mg, abacavir 600 mg, and lamivudine 300 mg (Triumeq®) for the treatment of antiretroviral-naïve adults with advanced HIV-1 infection and CD4+ cell counts <100 cells/µL.	
Reporting group title	DRV/c arm
Reporting group description:	
Participants randomized to receive once-daily darunavir/ritonavir-based triple antiretroviral therapy consisting of darunavir 800 mg plus ritonavir 100 mg, combined with abacavir 600 mg and lamivudine 300 mg. Participants enrolled after the protocol amendment received darunavir/cobicistat (Rezolsta®) instead of darunavir/ritonavir.	

Reporting group values	DTG arm	DRV/c arm	Total
Number of subjects	52	52	104
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	40	42	
inter-quartile range (Q1-Q3)	30 to 48.5	34.5 to 47	-
Gender categorical			
Units: Subjects			
Female	8	6	14
Male	44	46	90

End points

End points reporting groups

Reporting group title	DTG arm
Reporting group description:	
Participants randomized to receive once-daily dolutegravir-based triple antiretroviral therapy consisting of dolutegravir 50 mg, abacavir 600 mg, and lamivudine 300 mg (Triumeq®) for the treatment of antiretroviral-naïve adults with advanced HIV-1 infection and CD4+ cell counts <100 cells/µL.	
Reporting group title	DRV/c arm
Reporting group description:	
Participants randomized to receive once-daily darunavir/ritonavir-based triple antiretroviral therapy consisting of darunavir 800 mg plus ritonavir 100 mg, combined with abacavir 600 mg and lamivudine 300 mg. Participants enrolled after the protocol amendment received darunavir/cobicistat (Rezolsta®) instead of darunavir/ritonavir.	

Primary: Change in the absolute number of CD4+ cells in peripherial blood 48 weeks after treatment start

End point title	Change in the absolute number of CD4+ cells in peripherial blood 48 weeks after treatment start
End point description:	
End point type	Primary
End point timeframe:	
48 weeks	

End point values	DTG arm	DRV/c arm		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	52	49		
Units: cells/microlitre				
median (inter-quartile range (Q1-Q3))	206.5 (154.4 to 2310.5)	180.0 (89.4 to 314.0)		

Statistical analyses

Statistical analysis title	Comparison of change in CD4+ cell count at Week 48
Statistical analysis description:	
Comparison of the change from baseline in absolute CD4+ cell count in peripheral blood at Week 48 between the DTG and DRV/r arms in the modified intention-to-treat population.	
Comparison groups	DTG arm v DRV/c arm

Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4299
Method	Wilcoxon (Mann-Whitney)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

48 weeks

Adverse event reporting additional description:

Adverse events were assessed throughout the 48-week treatment period in all patients who received at least one dose of study treatment (safety population).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	DTG arm

Reporting group description:

Participants randomized to receive once-daily dolutegravir-based triple antiretroviral therapy consisting of dolutegravir 50 mg, abacavir 600 mg, and lamivudine 300 mg (Triumeq®) for the treatment of antiretroviral-naïve adults with advanced HIV-1 infection and CD4+ cell counts <100 cells/µL.

Reporting group title	DRV/c arm

Reporting group description:

Participants randomized to receive once-daily darunavir/ritonavir-based triple antiretroviral therapy consisting of darunavir 800 mg plus ritonavir 100 mg, combined with abacavir 600 mg and lamivudine 300 mg. Participants enrolled after the protocol amendment received darunavir/cobicistat (Rezolsta®) instead of darunavir/ritonavir.

Serious adverse events	DTG arm	DRV/c arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	12 / 52 (23.08%)	11 / 51 (21.57%)	
number of deaths (all causes)	0	1	
number of deaths resulting from adverse events	0	1	
General disorders and administration site conditions			
Total SAEs	Additional description: Reported serious adverse events included severe allergic reactions, neurocognitive/behavioural disorders, pharmacokinetic interactions with anti-tuberculosis medication, and one sudden cardiovascular death.		
subjects affected / exposed	12 / 52 (23.08%)	11 / 51 (21.57%)	
occurrences causally related to treatment / all	0 / 19	5 / 18	
deaths causally related to treatment / all	0 / 0	0 / 1	

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

Non-serious adverse events	DTG arm	DRV/c arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	12 / 52 (23.08%)	10 / 51 (19.61%)	
General disorders and administration site conditions			
Any AE Grade 3 and 4			
subjects affected / exposed	12 / 52 (23.08%)	10 / 51 (19.61%)	
occurrences (all)	12	10	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 May 2016	Substantial Modification Number 2: Harmonisation of microbiome sampling procedures, addition of DEXA assessments as a secondary objective, extension of the randomisation period by 12 months, and inclusion of CMV testing (IgG, IgM, PCR and QuantiFERON) as secondary objectives.
15 June 2018	Substantial Modification Number 3: Modification of Arm B treatment regimen, inclusion of interim efficacy analyses, and extension of the recruitment period.

Notes:

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.

The open-label design may have contributed to treatment discontinuation decisions, particularly in the DRV/r arm. Additionally, the sample size was relatively small.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/41083105