Clinical trial results:
HIV-1 RNA suppression and drug concentrations in semen, cervicovaginal fluid and rectum in HIV-1 infected individuals receiving intramuscular long-acting cabotegravir plus rilpivirine (“CAR-GR Study)

Summary

EudraCT number	2021-006779-41
Trial protocol	ES
Global end of trial date	05 April 2024

Results information

Result version number	v1 (current)
This version publication date	11 June 2025
First version publication date	11 June 2025

Trial information

Trial identification

Sponsor protocol code	CAR-GR

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	Hospital Germans Trias i Pujol S/N Canyet, Badalona, Spain, 08916
Public contact	Arkaitz Imaz Vacas, Hospital Universitari de Bellvitge, +34 932607667, aimaz@bellvitgehospital.cat
Scientific contact	Arkaitz Imaz Vacas, Hospital Universitari de Bellvitge, +34 932607667, aimaz@bellvitgehospital.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	05 April 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	05 April 2024
Global end of trial reached?	Yes
Global end of trial date	05 April 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To determine Cabotegravir and Rilpivirine concentrations in seminal plasma, rectal tissue and cervicovaginal fluid (CVF) in male and female individuals living with HIV receiving IM Cabotegravir and Rilpivirine LA every 2 months.

Protection of trial subjects:

Investigators provided participants with a comprehensive explanation of the informed consent process and all study-related procedures. Study medication was administered by highly qualified nursing personnel in a controlled, quiet, and private clinical setting to ensure participant comfort and protocol adherence.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2022
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: 31
Worldwide total number of subjects	31
EEA total number of subjects	31

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)	30
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The final recruitment period lasted 9 months. The first subject signed the informed consent in March 2023, and the last one in November 2023.

Pre-assignment

Screening details:

Inclusion criteria: cisgender adults with HIV-1 on stable ART ≥6 months with virologic suppression. Exclusion: resistance to CAB/RPV, virologic failure to InSTI/NNRTIs, HBV co-infection, pregnancy, severe hepatic/renal issues, grade 4 labs, malignancies, anticoagulants, or bleeding disorders.

Period 1

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

Arms

Arm title	Cabotegravir+Rilpivirine

Arm description:

Single Arm, Open-Label

Arm type	Experimental
Investigational medicinal product name	Cabotegravir
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet, Suspension for injection
Routes of administration	Intramuscular use, Oral use

Dosage and administration details:

Cabotegravir Oral use: 30 mg 1 tablet once daily for 28 days.
Cabotegravir Intramuscular Use: 600 mg suspension every 2 months.

Investigational medicinal product name	Rilpivirine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Suspension for injection, Tablet
Routes of administration	Intramuscular use, Oral use

Dosage and administration details:

Rilpivirine Oral use: 25 mg 1 tablet once daily for 28 days.
Rilpivirine Intramuscular Use: 900 mg suspension every 2 months.

Number of subjects in period 1	Cabotegravir+Rilpivirine
Started	31
Completed	31

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description: -

Reporting group values	Overall Trial	Total	
Number of subjects	31	31	
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)	30	30	
From 65-84 years	1	1	
85 years and over	0	0	
Age continuous Units: years			
median	43		
full range (min-max)	28 to 66	-	
Gender categorical Units: Subjects			
Female	15	15	
Male	16	16	

End points

End points reporting groups

Reporting group title	Cabotegravir+Rilpivirine
Reporting group description: Single Arm, Open-Label	
Subject analysis set title	Cisgender Female
Subject analysis set type	Per protocol
Subject analysis set description: Cisgender Female	
Subject analysis set title	Cisgender Male Seminal Plasma
Subject analysis set type	Per protocol
Subject analysis set description: Cisgender Male Seminal Plasma	
Subject analysis set title	Cisgender Male Rectal Tissue
Subject analysis set type	Per protocol
Subject analysis set description: Cisgender Male Rectal Tissue	

Primary: Total concentrations of Cabotegravir and Rilpivirine

End point title	Total concentrations of Cabotegravir and Rilpivirine[1]
End point description:	
End point type	Primary
End point timeframe: 2 months after cabotegravir and rilpivirine LA IM second dose	

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: Quantitative data were summarized as median and range; qualitative data as counts and percentages. Interindividual variability of CAB and RPV in plasma, genital fluids, and rectal tissue was assessed using the coefficient of variation. Correlations were evaluated via Spearman's rho with bootstrapped confidence intervals. Analyses were conducted using R software (v4.4.1)

End point values	Cisgender Female	Cisgender Male Seminal Plasma	Cisgender Male Rectal Tissue	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	16	16	
Units: ng/mL				
median (full range (min-max))				
Cabotegravir	15.63 (0.89 to 428.23)	23.30 (10.10 to 130.00)	90.02 (54.35 to 138.77)	
Rilpivirine	21.41 (0.07 to 47.77)	2.66 (1.47 to 9.37)	38.57 (19.68 to 79.64)	

Attachments (see zip file)	Supplementary Material/Supplementary Material.pdf

Statistical analyses

No statistical analyses for this end point

Secondary: Protein unbound fraction of Cabotegravir and Rilpivirine

End point title	Protein unbound fraction of Cabotegravir and Rilpivirine

End point description:

End point type	Secondary

End point timeframe:

months after cabotegravir and rilpivirine LA IM second dose

End point values	Cisgender Female	Cisgender Male Seminal Plasma	Cisgender Male Rectal Tissue	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	14	16	
Units: %				
median (full range (min-max))				
Cabotegravir	31.86 (12.86 to 50.73)	56.56 (44.08 to 77.17)	71.66 (46.04 to 78.44)	
Rilpivirine	94.92 (46.84 to 97.86)	97.03 (94.49 to 99.19)	93.68 (80.27 to 96.86)	

Statistical analyses

No statistical analyses for this end point

Secondary: Estimated unbound concentrations of Cabotegravir and Rilpivirine

End point title	Estimated unbound concentrations of Cabotegravir and Rilpivirine

End point description:

End point type	Secondary

End point timeframe:

2 months after cabotegravir and rilpivirine LA IM second dose

End point values	Cisgender Female	Cisgender Male Seminal Plasma	Cisgender Male Rectal Tissue	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	12	14	16	
Units: ng/mL				
median (full range (min-max))				
Cabotegravir	13.73 (2.60 to 283.11)	9.01 (5.20 to 16.43)	27.10 (13.47 to 59.50)	
Rilpivirine	0.81 (0.14 to 13.22)	0.08 (0.04 to 0.19)	2.69 (1.41 to 5.51)	

Statistical analyses

No statistical analyses for this end point

Secondary: HIV-1 RNA

End point title	HIV-1 RNA

End point description:

End point type	Secondary

End point timeframe:

2 months after second cabotegravir and rilpivirine LA IM dose

End point values	Cisgender Female	Cisgender Male Seminal Plasma	Cisgender Male Rectal Tissue	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	15	16	16	
Units: copies/mL	0	0	0	

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse events are reported from the date of informed consent signature until the subject's last visit in the study.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.1

Reporting groups	
Reporting group title	Cabotegravir+Rilpivirine
Reporting group description: Single Arm, Open-Label	

Serious adverse events	Cabotegravir+Rilpivirine		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 31 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Cabotegravir+Rilpivirine		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	31 / 31 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Angioma surgery			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
General disorders and administration site conditions			
Injection site pain	Additional description: Likely related to the study treatment		
alternative assessment type: Non-systematic			
subjects affected / exposed	28 / 31 (90.32%)		
occurrences (all)	53		
Injection site nodule	Additional description: Likely related to the study treatment		
alternative assessment type: Non-			

systematic			
subjects affected / exposed	4 / 31 (12.90%)		
occurrences (all)	4		
Injection site injury	Additional description: Likely related to the study treatment		
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Hematoma injection site	Additional description: Likely related to the study treatment		
alternative assessment type: Non-systematic			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
Asthenia			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Caries dental	Additional description: Dental and oral disorders		
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Dizziness			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Fainting			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Fever			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
General discomfort			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Injection site discomfort			
subjects affected / exposed	5 / 31 (16.13%)		
occurrences (all)	6		
Injection site induration			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Odontalgia	Additional description: Dental and oral disorders		

subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Periodontitis	Additional description: Dental and oral disorders		
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Reproductive system and breast disorders			
Menstrual flooding			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Vaginal discharge abnormality			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Abscess Bartholin's			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Amenorrhea			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Endocervical polyp			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Bronchitis acute			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Asthmatic attack			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Cold			
subjects affected / exposed	3 / 31 (9.68%)		
occurrences (all)	3		
COVID-19			
subjects affected / exposed	2 / 31 (6.45%)		
occurrences (all)	2		
Pain pharynx			

subjects affected / exposed occurrences (all) Pharyngitis subjects affected / exposed occurrences (all) Tonsillitis subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1 1 / 31 (3.23%) 1 1 / 31 (3.23%) 1		
Psychiatric disorders Anxiety disorder aggravated subjects affected / exposed occurrences (all) Anxiety state subjects affected / exposed occurrences (all)	 1 / 31 (3.23%) 1 2 / 31 (6.45%) 2		
Nervous system disorders Omalgia subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all) Epicondylitis subjects affected / exposed occurrences (all) Odynophagia subjects affected / exposed occurrences (all)	 1 / 31 (3.23%) 1 3 / 31 (9.68%) 3 1 / 31 (3.23%) 1 1 / 31 (3.23%) 1		
Blood and lymphatic system disorders Lymphadenopathy cervical subjects affected / exposed occurrences (all)	 1 / 31 (3.23%) 1		
Ear and labyrinth disorders Otitis externa subjects affected / exposed occurrences (all)	 1 / 31 (3.23%) 1		
Gastrointestinal disorders			

Lower abdominal pain subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Fructose intolerance subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Fecal incontinence subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Abnormal stools subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Acute gastritis subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Flatus increased subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Heartburn subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Nausea subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Hepatobiliary disorders			
Hemangioma of liver subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Hepatomegaly subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Transaminitis subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Renal and urinary disorders			

Cystitis, unspecified subjects affected / exposed occurrences (all)	1 / 31 (3.23%) 1		
Musculoskeletal and connective tissue disorders Acute lumbago subjects affected / exposed occurrences (all) Fasciitis plantar subjects affected / exposed occurrences (all) Fracture subjects affected / exposed occurrences (all) Neck pain subjects affected / exposed occurrences (all) Spondyloarthropathy subjects affected / exposed occurrences (all)	 3 / 31 (9.68%) 3 1 / 31 (3.23%) 1 1 / 31 (3.23%) 1 2 / 31 (6.45%) 2 1 / 31 (3.23%) 1		
Infections and infestations Herpes infection subjects affected / exposed occurrences (all) Axillary abscess subjects affected / exposed occurrences (all) Chlamydia trachomatis infection of lower genitourinary sites subjects affected / exposed occurrences (all) Chlamydial proctitis subjects affected / exposed occurrences (all) Condyloma subjects affected / exposed occurrences (all) Conjunctivitis	 2 / 31 (6.45%) 2 1 / 31 (3.23%) 1 1 / 31 (3.23%) 1 1 / 31 (3.23%) 1 1 / 31 (3.23%) 1		

subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Gonorrhoea of anus			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Latent syphilis			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Oral gonorrhea			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Papilloma viral infection			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Parasitic infection intestinal			
subjects affected / exposed	1 / 31 (3.23%)		
occurrences (all)	1		
Scabies			
subjects affected / exposed	1 / 31 (3.23%)		
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.

This study has limitations, including lack of intraindividual variability due to single sampling. Drug levels were assessed 3 months post-switch, before steady state. Still, plasma levels matched expectations from phase 3 trials.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/24521854

http://www.ncbi.nlm.nih.gov/pubmed/28449051

http://www.ncbi.nlm.nih.gov/pubmed/35986671

http://www.ncbi.nlm.nih.gov/pubmed/33830459