



## Clinical trial results:

### Implication for strategies of long term control of viral replication in patient with primary HIV infection (PHI) treated with multitarget antiviral therapy (MT-ART)

#### Summary

EudraCT number	2017-000554-19
Trial protocol	IT
Global end of trial date	11 February 2021

#### Results information

Result version number	v1 (current)
This version publication date	27 April 2022
First version publication date	27 April 2022

#### Trial information

##### Trial identification

Sponsor protocol code	P25-INACTION
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04225325
WHO universal trial number (UTN)	-
Other trial identifiers	P25-INACTION : P25-INACTION

Notes:

##### Sponsors

Sponsor organisation name	IRCCS Ospedale San Raffaele
Sponsor organisation address	Via Olgettina, 60, Milano, Italy, 20132
Public contact	Silvia Nozza, Department of Infectious Disease, 0039 0226437934, nozza.silvia@hsr.it
Scientific contact	Silvia Nozza, Department of Infectious Disease, 0039 0226437934, nozza.silvia@hsr.it

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	10 January 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	11 February 2020
Global end of trial reached?	Yes
Global end of trial date	11 February 2021
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

The aim of the study is to compare the virological efficacy of an intensive four-drug antiretroviral regimen against a standard regimen (chosen as the best one between an integrase-based or a protease inhibitor-based three drugs regimen) in HIV-1 subjects with Primary HIV Infection (PHI). In addition, we wish to evaluate changes in immunological and safety laboratory parameters, in viral reservoirs and to determine drugs concentrations in plasma, cerebrospinal fluid, lymph nodes and GALT

Protection of trial subjects:

Approval by the local Ethics Committee was obtained before the beginning of the study and written informed consent was obtained from all patients at time of enrolment. Sponsor has stipulated an insurance to cover damages related to the study.

Background therapy: -

Evidence for comparator:

Approved by Antiretroviral Therapy Guidelines

Actual start date of recruitment	03 May 2018
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy, Scientific research
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Italy: 78
Worldwide total number of subjects	78
EEA total number of subjects	78

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)	78
From 65 to 84 years	0
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

This Multicenter, parallel group, randomised, open label, study involved 78 patients (between 18 and 65 years) with PHI never treated among those attending the outpatient Clinic of Infectious Diseases, Ospedale San Raffaele and other Italian centres, involved in the INACTION network. Patients were enrolled between 2018 and 2020.

### Pre-assignment

Screening details:

Subjects with active opportunistic infection or malignancy, positive for Hepatitis B, with unstable liver disease or cirrhosis, with any clinically significant condition or situation that would interfere with the study evaluations or optimal participation, with allergy/sensitivity to drugs or its excipients were excluded

### Period 1

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

### Arms

Are arms mutually exclusive?	Yes
<b>Arm title</b>	ARM A (TAF/FTC+DRV/c)

Arm description:

TAF/FTC 10 mg/200 mg single tablet QD + DRV /cobicistat 800 mg /150 mg single tablet QD (standard regimen)

Arm type	Active comparator
Investigational medicinal product name	TAF/FTC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

10 mg/200 mg single tablet QD

Investigational medicinal product name	DRV/cobicistato
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

800 mg /150 mg single tablet QD

<b>Arm title</b>	ARM B (TAF/FTC+DTG)
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Arm description:

TAF/FTC 25 mg/200 mg single tablet QD + DTG 50 mg QD (standard regimen)

Arm type	Active comparator
Investigational medicinal product name	TAF/FTC
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

25 mg/200 mg single tablet QD

Investigational medicinal product name	DTG
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

50 mg QD

<b>Arm title</b>	ARM C (TAF/FTC+DRV/c+DTG)
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Arm description:

TAF/FTC 10 mg/200 mg single tablet QD + DRV/cobicistat 800 mg /150 mg single tablet QD + DTG 50 mg QD (experimental regimen).

Arm type	Experimental
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Investigational medicinal product name	TAF/FTC
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

10 mg/200 mg single tablet QD

Investigational medicinal product name	DRV/cobicistato
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

800 mg /150 mg single tablet QD

Investigational medicinal product name	DTG
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Investigational medicinal product code	
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Other name	
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Pharmaceutical forms	Tablet
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Routes of administration	Oral use
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Dosage and administration details:

50 mg QD

Number of subjects in period 1	ARM A (TAF/FTC+DRV/c)	ARM B (TAF/FTC+DTG)	ARM C (TAF/FTC+DRV/c+DTG)
	Started	30	28
Completed	26	27	19
Not completed	4	1	1
Consent withdrawn by subject	4	1	1

## Baseline characteristics

### Reporting groups

Reporting group title	ARM A (TAF/FTC+DRV/c)
Reporting group description:	TAF/FTC 10 mg/200 mg single tablet QD + DRV /cobicistat 800 mg /150 mg single tablet QD (standard regimen)
Reporting group title	ARM B (TAF/FTC+DTG)
Reporting group description:	TAF/FTC 25 mg/200 mg single tablet QD + DTG 50 mg QD (standard regimen)
Reporting group title	ARM C (TAF/FTC+DRV/c+DTG)
Reporting group description:	TAF/FTC 10 mg/200 mg single tablet QD + DRV/cobicistat 800 mg /150 mg single tablet QD + DTG 50 mg QD (experimental regimen).

Reporting group values	ARM A (TAF/FTC+DRV/c)	ARM B (TAF/FTC+DTG)	ARM C (TAF/FTC+DRV/c+DTG)
Number of subjects	30	28	20
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)	0	0	0
From 65-84 years	30	28	20
85 years and over	0	0	0
Gender categorical			
Units: Subjects			
Female	3	0	1
Male	27	28	19

Reporting group values	Total		
Number of subjects	78		
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	78		
85 years and over	0		

Gender categorical			
Units: Subjects			
Female	4		
Male	74		

## End points

### End points reporting groups

Reporting group title	ARM A (TAF/FTC+DRV/c)
Reporting group description:	TAF/FTC 10 mg/200 mg single tablet QD + DRV /cobicistat 800 mg /150 mg single tablet QD (standard regimen)
Reporting group title	ARM B (TAF/FTC+DTG)
Reporting group description:	TAF/FTC 25 mg/200 mg single tablet QD + DTG 50 mg QD (standard regimen)
Reporting group title	ARM C (TAF/FTC+DRV/c+DTG)
Reporting group description:	TAF/FTC 10 mg/200 mg single tablet QD + DRV/cobicistat 800 mg /150 mg single tablet QD + DTG 50 mg QD (experimental regimen).

### Primary: HIV-DNA level

End point title	HIV-DNA level
End point description:	The primary end point is the change in total HIV-DNA level from baseline to 48 weeks. HIV-DNA change form baseline to W48 is 0.912 in ARMA A, 0.267 in ARM B and 0.988 in ARM C. No differences between Amrs. Multivariate analysis, change of HIV-DNA was significantly associated to CD4 increase an not to Treatment ARM, Age, Fiebig STage, CD4/CD8 Ratio or HIV-RNA.
End point type	Primary
End point timeframe:	48 weeks post treatment

End point values	ARM A (TAF/FTC+DRV /c)	ARM B (TAF/FTC+DTG )	ARM C (TAF/FTC+DRV /c+DTG)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	30	28	20	
Units: log <sub>10</sub> (copies/10 <sup>6</sup> PBMCs)				
log mean (inter-quartile range (Q1-Q3))	3.79 (3.30 to 4.34)	3.95 (3.46 to 4.36)	4.09 (3.57 to 4.24)	

### Statistical analyses

Statistical analysis title	Treatment comparation
Comparison groups	ARM A (TAF/FTC+DRV/c) v ARM B (TAF/FTC+DTG) v ARM C (TAF/FTC+DRV/c+DTG)

Number of subjects included in analysis	78
Analysis specification	Post-hoc
Analysis type	non-inferiority
P-value	$\leq 0.05$
Method	Chi-squared
Parameter estimate	Odds ratio (OR)

## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

48 weeks

Assessment type	Systematic
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### Dictionary used

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Dictionary name	MedDRA
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Dictionary version	21
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Frequency threshold for reporting non-serious adverse events: 5 %

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Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: No non-serious adverse event associated to IMPs were recorded.

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported