



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 |
|-----------------------|--------------|

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 |
| Arm title | 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

| | |
|------------------|---------------------|
| Arm title | ARM B (TAF/FTC+DTG) |
|------------------|---------------------|

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 | |
| Arm title | ARM C (TAF/FTC+DRV/c+DTG) |
| 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 |
| 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 | |
| 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 | |

| 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 | 20 |
| 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 from baseline to W48 is 0.912 in ARM A, 0.267 in ARM B and 0.988 in ARM C. No differences between Arms. Multivariate analysis, change of HIV-DNA was significantly associated to CD4 increase and 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 ₁₀ (copies/10 ⁶ 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 comparison |
| 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 | ≤ 0.05 |
| Method | Chi-squared |
| Parameter estimate | Odds ratio (OR) |

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

48 weeks

| | |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

Dictionary used

| | |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|----|
| Dictionary version | 21 |
|--------------------|----|

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

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

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported