



## Clinical trial results:

**A Single-Dose, Open-Label, Randomized, Replicate Crossover Pivotal Bioequivalence Study in Healthy Adult Participants to Assess the Bioequivalence of Darunavir 675 mg, Emtricitabine 200 mg, and Tenofovir Alafenamide 10 mg in the Presence of Cobicistat 150 mg when Administered as a Fixed Dose Combination (Darunavir/Cobicistat/Emtricitabine/Tenofovir Alafenamide) Compared to the Co-administration of the Separate Agents (Darunavir, Cobicistat, and Emtricitabine/Tenofovir Alafenamide), Under Fed Conditions**

### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2020-003396-18 |
| Trial protocol           | NL             |
| Global end of trial date | 23 July 2021   |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 03 July 2022 |
| First version publication date | 03 July 2022 |

### Trial information

#### Trial identification

|                       |                  |
|-----------------------|------------------|
| Sponsor protocol code | TMC114FD2HTX1007 |
|-----------------------|------------------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT04661397 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |                                                                                            |
|------------------------------|--------------------------------------------------------------------------------------------|
| Sponsor organisation name    | Janssen-Cilag International N.V.                                                           |
| Sponsor organisation address | Turnhoutseweg 30, Beerse, Belgium, B-2340                                                  |
| Public contact               | Clinical Registry Group, Janssen-Cilag International N.V.,<br>ClinicalTrialsEU@its.jnj.com |
| Scientific contact           | Clinical Registry Group, Janssen-Cilag International N.V.,<br>ClinicalTrialsEU@its.jnj.com |

Notes:

### Paediatric regulatory details

|                                                                      |                     |
|----------------------------------------------------------------------|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP)       | Yes                 |
| EMA paediatric investigation plan number(s)                          | EMA-001280-PIP01-12 |
| 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                       | 23 July 2021 |
| Is this the analysis of the primary completion data? | No           |
| Global end of trial reached?                         | Yes          |
| Global end of trial date                             | 23 July 2021 |
| Was the trial ended prematurely?                     | No           |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this study was to evaluate the single-dose pharmacokinetic (PK) and pivotal bioequivalence of 3 compounds (darunavir [DRV/D] 675 milligrams (mg), emtricitabine [FTC/F] 200 mg, and tenofovir alafenamide [TAF] 10 mg) in the presence of cobicistat (COBI/C) 150 mg when administered together as a fixed dose combination (FDC) tablet (D/C/F/TAF) compared to the co-administration as the separate commercial formulations (DRV 1\*600 mg and 1\*75 mg tablet and F/TAF 1\*200 mg/10 mg tablet, and COBI 1\*150 mg tablet), under fed conditions, in healthy adult subjects.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices and applicable regulatory requirements. Safety evaluations were based upon the incidence of adverse events reported throughout the study, and on clinical laboratory tests, electrocardiogram (ECG), vital signs, and physical examination.

Background therapy: -

Evidence for comparator: -

|                                                           |                 |
|-----------------------------------------------------------|-----------------|
| Actual start date of recruitment                          | 05 January 2021 |
| 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 | Netherlands: 37 |
| Worldwide total number of subjects   | 37              |
| EEA total number of subjects         | 37              |

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)      | 37 |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

A total of 37 healthy subjects were randomized and treated (19 subjects in treatment sequence ABBA and 18 subjects in treatment sequence BAAB). Of these, 32 subjects completed the study.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (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>             | Treatment Sequence ABBA |

Arm description:

Subjects received a single oral dose of Darunavir (675 milligrams [mg])/Cobicistat (150 mg)/Emtricitabine (200 mg)/Tenofovir Alafenamide (10 mg) as one fixed dose combination (FDC) tablet (D/C/F/TAF) under fed conditions (Treatment A, test) on Day 1 of Period 1 followed by a single oral dose of Darunavir (DRV) 600 mg and 75 mg tablet, Emtricitabine 200 mg/Tenofovir Alafenamide 10 mg (F/TAF) and Cobicistat (COBI) 150 mg tablet under fed conditions (Treatment B, reference) on Day 1 of Period 2 followed by Treatment B again on Day 1 of Period 3 and, then Treatment A on Day 1 of Period 4. Each period was separated by a washout period of at least 7 days.

|                                        |                                                                                                       |
|----------------------------------------|-------------------------------------------------------------------------------------------------------|
| Arm type                               | Experimental                                                                                          |
| Investigational medicinal product name | Darunavir 675 mg/Cobicistat 150 mg/Emtricitabine 200 mg/Tenofovir Alafenamide (10 mg) (D/C/F/TAF) FDC |
| Investigational medicinal product code |                                                                                                       |
| Other name                             | TMC114/JNJ-48763364/JNJ-35807551/JNJ-63625328                                                         |
| Pharmaceutical forms                   | Tablet                                                                                                |
| Routes of administration               | Oral use                                                                                              |

Dosage and administration details:

Subjects received a single dose of D/C/F/TAF 675/150/200/10 mg FDC tablet orally as Treatment A on Day 1 as per assigned treatment sequences.

|                                        |                                                          |
|----------------------------------------|----------------------------------------------------------|
| Investigational medicinal product name | Emtricitabine 200 mg/Tenofovir Alafenamide 10 mg (F/TAF) |
| Investigational medicinal product code |                                                          |
| Other name                             | JNJ-35807551/JNJ-63625328                                |
| Pharmaceutical forms                   | Tablet                                                   |
| Routes of administration               | Oral use                                                 |

Dosage and administration details:

Subjects received a single dose of E/TAF 200/10mg tablet orally as a component of Treatment B on Day 1 as per assigned treatment sequences.

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Cobicistat (COBI) 150 mg |
| Investigational medicinal product code |                          |
| Other name                             | JNJ-48763364             |
| Pharmaceutical forms                   | Tablet                   |
| Routes of administration               | Oral use                 |

Dosage and administration details:

Subjects received a single dose of COBI 150 mg tablet orally as a component of Treatment B on Day 1 as per assigned treatment sequences.

|                                        |                                  |
|----------------------------------------|----------------------------------|
| Investigational medicinal product name | Darunavir (DRV) 600 mg and 75 mg |
| Investigational medicinal product code |                                  |
| Other name                             | TMC114                           |
| Pharmaceutical forms                   | Tablet                           |
| Routes of administration               | Oral use                         |

**Dosage and administration details:**

Subjects received a single dose of DRV 600 mg and 75 mg tablet orally as a component of Treatment B on Day 1 as per assigned treatment sequences.

|                  |                         |
|------------------|-------------------------|
| <b>Arm title</b> | Treatment Sequence BAAB |
|------------------|-------------------------|

**Arm description:**

Subjects received a single oral dose of DRV 600 mg and 75 mg tablet, F/TAF 200/10 mg and COBI 150 mg tablet under fed conditions (Treatment B, reference) on Day 1 of Period 1 followed by a single oral dose D/C/F/TAF 675/150/200/10 mg as one fixed dose combination (FDC) tablet under fed conditions (Treatment A, test) on Day 1 of Period 2 followed by Treatment A on Day 1 of Period 3 and, then Treatment B on Day 1 of Period 4. Each period was separated by a washout period of at least 7 days.

|                                        |                                  |
|----------------------------------------|----------------------------------|
| Arm type                               | Experimental                     |
| Investigational medicinal product name | Darunavir (DRV) 600 mg and 75 mg |
| Investigational medicinal product code |                                  |
| Other name                             | TMC114                           |
| Pharmaceutical forms                   | Tablet                           |
| Routes of administration               | Oral use                         |

**Dosage and administration details:**

Subjects received a single dose of DRV 600 mg and 75 mg tablet orally as a component of Treatment B on Day 1 as per assigned treatment sequences.

|                                        |                                                          |
|----------------------------------------|----------------------------------------------------------|
| Investigational medicinal product name | Emtricitabine 200 mg/Tenofovir Alafenamide 10 mg (F/TAF) |
| Investigational medicinal product code |                                                          |
| Other name                             | JNJ-35807551/JNJ-63625328                                |
| Pharmaceutical forms                   | Tablet                                                   |
| Routes of administration               | Oral use                                                 |

**Dosage and administration details:**

Subjects received a single dose of E/TAF 200/10mg tablet orally as a component of Treatment B on Day 1 as per assigned treatment sequences.

|                                        |                          |
|----------------------------------------|--------------------------|
| Investigational medicinal product name | Cobicistat (COBI) 150 mg |
| Investigational medicinal product code |                          |
| Other name                             | JNJ-48763364             |
| Pharmaceutical forms                   | Tablet                   |
| Routes of administration               | Oral use                 |

**Dosage and administration details:**

Subjects received a single dose of COBI 150 mg tablet orally as a component of Treatment B on Day 1 as per assigned treatment sequences.

|                                        |                                                                                                       |
|----------------------------------------|-------------------------------------------------------------------------------------------------------|
| Investigational medicinal product name | Darunavir 675 mg/Cobicistat 150 mg/Emtricitabine 200 mg/Tenofovir Alafenamide (10 mg) (D/C/F/TAF) FDC |
| Investigational medicinal product code |                                                                                                       |
| Other name                             | TMC114/JNJ-48763364/JNJ-35807551/JNJ-63625328                                                         |
| Pharmaceutical forms                   | Tablet                                                                                                |
| Routes of administration               | Oral use                                                                                              |

**Dosage and administration details:**

Subjects received a single dose of D/C/F/TAF 675/150/200/10 mg FDC tablet orally as Treatment A on Day 1 as per assigned treatment sequences.

| <b>Number of subjects in period 1</b> | Treatment Sequence<br>ABBA | Treatment Sequence<br>BAAB |
|---------------------------------------|----------------------------|----------------------------|
| Started                               | 19                         | 18                         |
| Completed                             | 16                         | 16                         |
| Not completed                         | 3                          | 2                          |
| Adverse event                         | 1                          | -                          |
| Unspecified                           | 1                          | 1                          |
| Withdrawal by subject                 | 1                          | 1                          |

## Baseline characteristics

### Reporting groups

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Treatment Sequence ABBA |
|-----------------------|-------------------------|

Reporting group description:

Subjects received a single oral dose of Darunavir (675 milligrams [mg])/Cobicistat (150 mg)/Emtricitabine (200 mg)/Tenofovir Alafenamide (10 mg) as one fixed dose combination (FDC) tablet (D/C/F/TAF) under fed conditions (Treatment A, test) on Day 1 of Period 1 followed by a single oral dose of Darunavir (DRV) 600 mg and 75 mg tablet, Emtricitabine 200 mg/Tenofovir Alafenamide 10 mg (F/TAF) and Cobicistat (COBI) 150 mg tablet under fed conditions (Treatment B, reference) on Day 1 of Period 2 followed by Treatment B again on Day 1 of Period 3 and, then Treatment A on Day 1 of Period 4. Each period was separated by a washout period of at least 7 days.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Treatment Sequence BAAB |
|-----------------------|-------------------------|

Reporting group description:

Subjects received a single oral dose of DRV 600 mg and 75 mg tablet, F/TAF 200/10 mg and COBI 150 mg tablet under fed conditions (Treatment B, reference) on Day 1 of Period 1 followed by a single oral dose D/C/F/TAF 675/150/200/10 mg as one fixed dose combination (FDC) tablet under fed conditions (Treatment A, test) on Day 1 of Period 2 followed by Treatment A on Day 1 of Period 3 and, then Treatment B on Day 1 of Period 4. Each period was separated by a washout period of at least 7 days.

| Reporting group values                      | Treatment Sequence ABBA | Treatment Sequence BAAB | Total |
|---------------------------------------------|-------------------------|-------------------------|-------|
| Number of subjects                          | 19                      | 18                      | 37    |
| Title for AgeCategorical<br>Units: subjects |                         |                         |       |
| Children (2-11 years)                       | 0                       | 0                       | 0     |
| Adolescents (12-17 years)                   | 0                       | 0                       | 0     |
| Adults (18-64 years)                        | 19                      | 18                      | 37    |
| From 65 to 84 years                         | 0                       | 0                       | 0     |
| 85 years and over                           | 0                       | 0                       | 0     |
| Title for AgeContinuous<br>Units: years     |                         |                         |       |
| median                                      | 26                      | 27.5                    |       |
| full range (min-max)                        | 18 to 54                | 19 to 55                | -     |
| Title for Gender<br>Units: subjects         |                         |                         |       |
| Female                                      | 8                       | 5                       | 13    |
| Male                                        | 11                      | 13                      | 24    |

## End points

### End points reporting groups

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Treatment Sequence ABBA |
|-----------------------|-------------------------|

Reporting group description:

Subjects received a single oral dose of Darunavir (675 milligrams [mg])/Cobicistat (150 mg)/Emtricitabine (200 mg)/Tenofovir Alafenamide (10 mg) as one fixed dose combination (FDC) tablet (D/C/F/TAF) under fed conditions (Treatment A, test) on Day 1 of Period 1 followed by a single oral dose of Darunavir (DRV) 600 mg and 75 mg tablet, Emtricitabine 200 mg/Tenofovir Alafenamide 10 mg (F/TAF) and Cobicistat (COBI) 150 mg tablet under fed conditions (Treatment B, reference) on Day 1 of Period 2 followed by Treatment B again on Day 1 of Period 3 and, then Treatment A on Day 1 of Period 4. Each period was separated by a washout period of at least 7 days.

|                       |                         |
|-----------------------|-------------------------|
| Reporting group title | Treatment Sequence BAAB |
|-----------------------|-------------------------|

Reporting group description:

Subjects received a single oral dose of DRV 600 mg and 75 mg tablet, F/TAF 200/10 mg and COBI 150 mg tablet under fed conditions (Treatment B, reference) on Day 1 of Period 1 followed by a single oral dose D/C/F/TAF 675/150/200/10 mg as one fixed dose combination (FDC) tablet under fed conditions (Treatment A, test) on Day 1 of Period 2 followed by Treatment A on Day 1 of Period 3 and, then Treatment B on Day 1 of Period 4. Each period was separated by a washout period of at least 7 days.

|                            |             |
|----------------------------|-------------|
| Subject analysis set title | Treatment A |
|----------------------------|-------------|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Subjects received a single oral dose of Darunavir (675 milligrams [mg])/Cobicistat (150 mg)/Emtricitabine (200 mg)/Tenofovir Alafenamide (10 mg) as one fixed dose combination (FDC) tablet (D/C/F/TAF) under fed conditions (Treatment A, test) on Day 1 of Period 1.

|                            |             |
|----------------------------|-------------|
| Subject analysis set title | Treatment B |
|----------------------------|-------------|

|                           |                 |
|---------------------------|-----------------|
| Subject analysis set type | Safety analysis |
|---------------------------|-----------------|

Subject analysis set description:

Subjects received a single oral dose of DRV 600 mg and 75 mg tablet, F/TAF 200/10 mg and COBI 150 mg tablet under fed conditions (Treatment B, reference) on Day 1 of Period 1.

### Primary: Maximum Observed Plasma Concentration (C<sub>max</sub>) of Darunavir (DRV)

|                 |                                                                              |
|-----------------|------------------------------------------------------------------------------|
| End point title | Maximum Observed Plasma Concentration (C <sub>max</sub> ) of Darunavir (DRV) |
|-----------------|------------------------------------------------------------------------------|

End point description:

C<sub>max</sub> was defined as the maximum observed plasma concentration of Darunavir. Pharmacokinetic (PK) data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre dose and 1, 2, 3, 4, 5, 6, 8, 12, 18, 24, 36, 48, 72 hours post dose

| End point values                        | Treatment A          | Treatment B          |  |  |
|-----------------------------------------|----------------------|----------------------|--|--|
| Subject group type                      | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed             | 33                   | 32                   |  |  |
| Units: nanograms per millilitre (ng/mL) |                      |                      |  |  |
| arithmetic mean (standard deviation)    | 6363 (± 1449)        | 6426 (± 1277)        |  |  |

### Statistical analyses

|                                                                                                                                                                                                                                                                                                                |                                |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                                              | Treatment B Versus Treatment A |
| Statistical analysis description:<br>Log transformed pharmacokinetic (PK) parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm. |                                |
| Comparison groups                                                                                                                                                                                                                                                                                              | Treatment A v Treatment B      |
| Number of subjects included in analysis                                                                                                                                                                                                                                                                        | 65                             |
| Analysis specification                                                                                                                                                                                                                                                                                         | Pre-specified                  |
| Analysis type                                                                                                                                                                                                                                                                                                  | equivalence <sup>[1]</sup>     |
| Parameter estimate                                                                                                                                                                                                                                                                                             | Geometric Mean Ratio           |
| Point estimate                                                                                                                                                                                                                                                                                                 | 98.06                          |
| Confidence interval                                                                                                                                                                                                                                                                                            |                                |
| level                                                                                                                                                                                                                                                                                                          | 90 %                           |
| sides                                                                                                                                                                                                                                                                                                          | 2-sided                        |
| lower limit                                                                                                                                                                                                                                                                                                    | 94.1                           |
| upper limit                                                                                                                                                                                                                                                                                                    | 102.18                         |

Notes:

[1] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 32. Pre-defined bioequivalence limits were 80 to 125 percent (%).

### Primary: Maximum Observed Plasma Concentration (Cmax) of Emtricitabine (FTC)

|                 |                                                                     |
|-----------------|---------------------------------------------------------------------|
| End point title | Maximum Observed Plasma Concentration (Cmax) of Emtricitabine (FTC) |
|-----------------|---------------------------------------------------------------------|

End point description:

Cmax was the maximum observed plasma concentration of FTC. PK data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre dose and 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 12, 24, 48, 72 hours post dose

| End point values                     | Treatment A          | Treatment B          |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 33                   | 32                   |  |  |
| Units: ng/mL                         |                      |                      |  |  |
| arithmetic mean (standard deviation) | 1806 (± 385)         | 1835 (± 366)         |  |  |

### Statistical analyses

|                                                                                                                                                                                                                                                                                              |                                |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| <b>Statistical analysis title</b>                                                                                                                                                                                                                                                            | Treatment B Versus Treatment A |
| Statistical analysis description:<br>Log transformed PK parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm. |                                |
| Comparison groups                                                                                                                                                                                                                                                                            | Treatment A v Treatment B      |

|                                         |                            |
|-----------------------------------------|----------------------------|
| Number of subjects included in analysis | 65                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | equivalence <sup>[2]</sup> |
| Parameter estimate                      | Geometric Mean Ratio       |
| Point estimate                          | 98.64                      |
| Confidence interval                     |                            |
| level                                   | 90 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 93.66                      |
| upper limit                             | 103.89                     |

Notes:

[2] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 32. Pre-defined bioequivalence limits were 80 to 125%.

### Primary: Maximum Observed Plasma Concentration (C<sub>max</sub>) of Tenofovir Alafenamide (TAF)

|                 |                                                                                          |
|-----------------|------------------------------------------------------------------------------------------|
| End point title | Maximum Observed Plasma Concentration (C <sub>max</sub> ) of Tenofovir Alafenamide (TAF) |
|-----------------|------------------------------------------------------------------------------------------|

End point description:

C<sub>max</sub> was the maximum observed plasma concentration of TAF. PK data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre dose and 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8 hours post dose

| End point values                     | Treatment A          | Treatment B          |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 33                   | 32                   |  |  |
| Units: ng/mL                         |                      |                      |  |  |
| arithmetic mean (standard deviation) | 144 (± 86.8)         | 134 (± 78.8)         |  |  |

### Statistical analyses

|                            |                                |
|----------------------------|--------------------------------|
| Statistical analysis title | Treatment B Versus Treatment A |
|----------------------------|--------------------------------|

Statistical analysis description:

Log transformed PK parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm.

|                                         |                            |
|-----------------------------------------|----------------------------|
| Comparison groups                       | Treatment A v Treatment B  |
| Number of subjects included in analysis | 65                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | equivalence <sup>[3]</sup> |
| Parameter estimate                      | Geometric Mean Ratio       |
| Point estimate                          | 105.23                     |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 90 %    |
| sides               | 2-sided |
| lower limit         | 90.86   |
| upper limit         | 121.87  |

Notes:

[3] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 32. Pre-defined bioequivalence limits were 80 to 125%.

**Primary: Area Under the Plasma Concentration-time Curve From Time Zero to Time of Last Measurable (Non-below Quantification Limit [non-BQL]) Concentration (AUC[0-last]) of Darunavir (DRV)**

|                 |                                                                                                                                                                                    |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Area Under the Plasma Concentration-time Curve From Time Zero to Time of Last Measurable (Non-below Quantification Limit [non-BQL]) Concentration (AUC[0-last]) of Darunavir (DRV) |
|-----------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

AUC(0-last) was area under the plasma concentration-time curve from time zero to the time of the last measurable (non-BQL) concentration, calculated by linear-linear trapezoidal summation. PK data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre dose and 1, 2, 3, 4, 5, 6, 8, 12, 18, 24, 36, 48, 72 hours post dose

| End point values                              | Treatment A          | Treatment B          |  |  |
|-----------------------------------------------|----------------------|----------------------|--|--|
| Subject group type                            | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed                   | 33                   | 32                   |  |  |
| Units: hour*nanogram per millilitre (h*ng/mL) |                      |                      |  |  |
| arithmetic mean (standard deviation)          | 74698 (± 23915)      | 72380 (± 22435)      |  |  |

**Statistical analyses**

|                            |                                |
|----------------------------|--------------------------------|
| Statistical analysis title | Treatment B Versus Treatment A |
|----------------------------|--------------------------------|

Statistical analysis description:

Log transformed PK parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm.

|                                         |                            |
|-----------------------------------------|----------------------------|
| Comparison groups                       | Treatment A v Treatment B  |
| Number of subjects included in analysis | 65                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | equivalence <sup>[4]</sup> |
| Parameter estimate                      | Geometric Mean Ratio       |
| Point estimate                          | 102.74                     |

|                     |         |
|---------------------|---------|
| Confidence interval |         |
| level               | 90 %    |
| sides               | 2-sided |
| lower limit         | 98.11   |
| upper limit         | 107.6   |

Notes:

[4] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 32. Pre-defined bioequivalence limits were 80 to 125%.

### Primary: Area Under the Plasma Concentration-time Curve From Time Zero to Time of Last Measurable (non-BQL) Concentration (AUC[0-last]) of Emtricitabine (FTC)

|                 |                                                                                                                                                       |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Area Under the Plasma Concentration-time Curve From Time Zero to Time of Last Measurable (non-BQL) Concentration (AUC[0-last]) of Emtricitabine (FTC) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

AUC(0-last) was area under the plasma concentration-time curve from time zero to the time of the last measurable non-BQL concentration, calculated by linear-linear trapezoidal summation. PK data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre dose and 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 12, 24, 48, 72 hours post dose

| End point values                     | Treatment A          | Treatment B          |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 33                   | 32                   |  |  |
| Units: h*ng/mL                       |                      |                      |  |  |
| arithmetic mean (standard deviation) | 9967 (± 1854)        | 9995 (± 1802)        |  |  |

### Statistical analyses

|                            |                                |
|----------------------------|--------------------------------|
| Statistical analysis title | Treatment B Versus Treatment A |
|----------------------------|--------------------------------|

Statistical analysis description:

Log transformed PK parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm.

|                                         |                            |
|-----------------------------------------|----------------------------|
| Comparison groups                       | Treatment A v Treatment B  |
| Number of subjects included in analysis | 65                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | equivalence <sup>[5]</sup> |
| Parameter estimate                      | Geometric Mean Ratio       |
| Point estimate                          | 100.6                      |
| Confidence interval                     |                            |
| level                                   | 90 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 98.83                      |
| upper limit                             | 102.4                      |

Notes:

[5] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 32. Pre-defined bioequivalence limits were 80 to 125%.

### **Primary: Area Under the Plasma Concentration-time Curve From Time Zero to Time of Last Measurable (non-BQL) Concentration (AUC[0-last]) of Tenofovir Alafenamide (TAF)**

|                 |                                                                                                                                                               |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|
| End point title | Area Under the Plasma Concentration-time Curve From Time Zero to Time of Last Measurable (non-BQL) Concentration (AUC[0-last]) of Tenofovir Alafenamide (TAF) |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------|

End point description:

AUC(0-last) was area under the plasma concentration-time curve from time zero to the time of the last measurable non-BQL concentration, calculated by linear-linear trapezoidal summation. PK data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Pre dose and 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8 hours post dose

| End point values                     | Treatment A          | Treatment B          |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 33                   | 32                   |  |  |
| Units: h*ng/mL                       |                      |                      |  |  |
| arithmetic mean (standard deviation) | 124 ( $\pm$ 36.7)    | 113 ( $\pm$ 44.1)    |  |  |

### **Statistical analyses**

|                            |                                |
|----------------------------|--------------------------------|
| Statistical analysis title | Treatment B Versus Treatment A |
|----------------------------|--------------------------------|

Statistical analysis description:

Log transformed PK parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm.

|                                         |                            |
|-----------------------------------------|----------------------------|
| Comparison groups                       | Treatment A v Treatment B  |
| Number of subjects included in analysis | 65                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | equivalence <sup>[6]</sup> |
| Parameter estimate                      | Geometric Mean Ratio       |
| Point estimate                          | 113.41                     |
| Confidence interval                     |                            |
| level                                   | 90 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 106.82                     |
| upper limit                             | 120.41                     |

Notes:

[6] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 32. Pre-defined bioequivalence limits were 80 to 125%.

### **Secondary: Area Under the Plasma was Concentration-time Curve From Time Zero to**

**Infinite Time (AUC[0-infinity]) of Darunavir**

|                 |                                                                                                                   |
|-----------------|-------------------------------------------------------------------------------------------------------------------|
| End point title | Area Under the Plasma was Concentration-time Curve From Time Zero to Infinite Time (AUC[0-infinity]) of Darunavir |
|-----------------|-------------------------------------------------------------------------------------------------------------------|

End point description:

The AUC (0-infinity) was the area under the plasma concentration-time curve from time zero to infinite time, calculated as the sum of AUC(last) and C(last)/lambda(z); wherein AUC(last) is area under the plasma concentration-time curve from time zero to last quantifiable time, C(last) is the last observed quantifiable concentration, and lambda(z) is elimination rate constant. PK data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre dose and 1, 2, 3, 4, 5, 6, 8, 12, 18, 24, 36, 48, 72 hours post dose

| End point values                     | Treatment A          | Treatment B          |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 33                   | 32                   |  |  |
| Units: h*ng/mL                       |                      |                      |  |  |
| arithmetic mean (standard deviation) | 74891 (± 23974)      | 72564 (± 22502)      |  |  |

**Statistical analyses**

|                            |                                |
|----------------------------|--------------------------------|
| Statistical analysis title | Treatment B Versus Treatment A |
|----------------------------|--------------------------------|

Statistical analysis description:

Log transformed PK parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm.

|                                         |                            |
|-----------------------------------------|----------------------------|
| Comparison groups                       | Treatment A v Treatment B  |
| Number of subjects included in analysis | 65                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | equivalence <sup>[7]</sup> |
| Parameter estimate                      | Geometric Mean Ratio       |
| Point estimate                          | 102.73                     |
| Confidence interval                     |                            |
| level                                   | 90 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 98.1                       |
| upper limit                             | 107.58                     |

Notes:

[7] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 32. Pre-defined bioequivalence limits were 80 to 125%.

**Secondary: Area Under the Plasma Concentration-time Curve From Time Zero to Infinite Time (AUC[0-infinity]) of Cobicistat**

|                 |                                                                                                                |
|-----------------|----------------------------------------------------------------------------------------------------------------|
| End point title | Area Under the Plasma Concentration-time Curve From Time Zero to Infinite Time (AUC[0-infinity]) of Cobicistat |
|-----------------|----------------------------------------------------------------------------------------------------------------|

End point description:

The AUC (0-infinity) was the area under the plasma concentration-time curve from time zero to infinite

time, calculated as the sum of AUC(last) and C(last)/lambda(z); wherein AUC(last) is area under the plasma concentration-time curve from time zero to last quantifiable time, C(last) is the last observed quantifiable concentration, and lambda(z) is elimination rate constant. PK data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods.

|                                                                          |           |
|--------------------------------------------------------------------------|-----------|
| End point type                                                           | Secondary |
| End point timeframe:                                                     |           |
| Pre dose and 1, 2, 3, 4, 5, 6, 8, 12, 18, 24, 36, 48, 72 hours post dose |           |

| End point values                     | Treatment A          | Treatment B          |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 33                   | 32                   |  |  |
| Units: h*ng/mL                       |                      |                      |  |  |
| arithmetic mean (standard deviation) | 6276 (± 2169)        | 6476 (± 2190)        |  |  |

## Statistical analyses

|                            |                                |
|----------------------------|--------------------------------|
| Statistical analysis title | Treatment B Versus Treatment A |
|----------------------------|--------------------------------|

Statistical analysis description:

Log transformed PK parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm.

|                                         |                            |
|-----------------------------------------|----------------------------|
| Comparison groups                       | Treatment A v Treatment B  |
| Number of subjects included in analysis | 65                         |
| Analysis specification                  | Pre-specified              |
| Analysis type                           | equivalence <sup>[8]</sup> |
| Parameter estimate                      | Geometric Mean Ratio       |
| Point estimate                          | 97.68                      |
| Confidence interval                     |                            |
| level                                   | 90 %                       |
| sides                                   | 2-sided                    |
| lower limit                             | 93.44                      |
| upper limit                             | 102.1                      |

Notes:

[8] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 32. Pre-defined bioequivalence limits were 80 to 125%.

## Secondary: Area Under the Plasma Concentration-time Curve From Time Zero to Infinite Time (AUC[0-infinity]) of Emtricitabine (FTC)

|                 |                                                                                                                         |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|
| End point title | Area Under the Plasma Concentration-time Curve From Time Zero to Infinite Time (AUC[0-infinity]) of Emtricitabine (FTC) |
|-----------------|-------------------------------------------------------------------------------------------------------------------------|

End point description:

The AUC (0-infinity) was the area under the plasma concentration-time curve from time zero to plasma time, calculated as the sum of AUC(last) and C(last)/lambda(z); wherein AUC(last) is area under the plasma concentration-time curve from time zero to last quantifiable time, C(last) is the last observed quantifiable concentration, and lambda(z) is elimination rate constant. PK data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods. Here, N (Number of Subjects Analysed) signifies number of subjects evaluable for this endpoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre dose and 0.5, 1, 1.5, 2, 3, 4, 5, 6, 8, 12, 24, 48, 72 hours post dose

| End point values                     | Treatment A          | Treatment B          |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 30                   | 28                   |  |  |
| Units: h*ng/mL                       |                      |                      |  |  |
| arithmetic mean (standard deviation) | 10174 ( $\pm$ 1900)  | 10199 ( $\pm$ 1791)  |  |  |

## Statistical analyses

| Statistical analysis title                                                                                                                                                                                                                                                                   | Treatment B Versus Treatment A |
|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Statistical analysis description:<br>Log transformed PK parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm. |                                |
| Comparison groups                                                                                                                                                                                                                                                                            | Treatment A v Treatment B      |
| Number of subjects included in analysis                                                                                                                                                                                                                                                      | 58                             |
| Analysis specification                                                                                                                                                                                                                                                                       | Pre-specified                  |
| Analysis type                                                                                                                                                                                                                                                                                | equivalence <sup>[9]</sup>     |
| Parameter estimate                                                                                                                                                                                                                                                                           | Geometric Mean Ratio           |
| Point estimate                                                                                                                                                                                                                                                                               | 101.26                         |
| Confidence interval                                                                                                                                                                                                                                                                          |                                |
| level                                                                                                                                                                                                                                                                                        | 90 %                           |
| sides                                                                                                                                                                                                                                                                                        | 2-sided                        |
| lower limit                                                                                                                                                                                                                                                                                  | 99.31                          |
| upper limit                                                                                                                                                                                                                                                                                  | 103.24                         |

Notes:

[9] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 25. Pre-defined bioequivalence limits were 80 to 125%.

## Secondary: Area Under the Plasma Concentration-time Curve From Time Zero to Infinite Time (AUC[0-infinity]) of Tenofovir Alafenamide (TAF)

|                 |                                                                                                                                 |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|
| End point title | Area Under the Plasma Concentration-time Curve From Time Zero to Infinite Time (AUC[0-infinity]) of Tenofovir Alafenamide (TAF) |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------|

End point description:

The AUC (0-infinity) was the area under the plasma concentration-time curve from time zero to infinite time, calculated as the sum of AUC(last) and C(last)/lambda(z); wherein AUC(last) is area under the plasma concentration-time curve from time zero to last quantifiable time, C(last) is the last observed quantifiable concentration, and lambda(z) is elimination rate constant. PK data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods. Here, N (Number of Subjects Analysed) signifies number of subjects evaluable for this endpoint.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Pre dose and 0.25, 0.5, 0.75, 1, 1.5, 2, 2.5, 3, 3.5, 4, 5, 6, 8 hours post dose

| End point values                     | Treatment A          | Treatment B          |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 25                   | 25                   |  |  |
| Units: h*ng/mL                       |                      |                      |  |  |
| arithmetic mean (standard deviation) | 127 (± 38.4)         | 116 (± 43.8)         |  |  |

## Statistical analyses

| Statistical analysis title                                                                                                                                                                                                                              | Treatment B Versus Treatment A |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                       |                                |
| Log transformed PK parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm. |                                |
| Comparison groups                                                                                                                                                                                                                                       | Treatment A v Treatment B      |
| Number of subjects included in analysis                                                                                                                                                                                                                 | 50                             |
| Analysis specification                                                                                                                                                                                                                                  | Pre-specified                  |
| Analysis type                                                                                                                                                                                                                                           | equivalence <sup>[10]</sup>    |
| Parameter estimate                                                                                                                                                                                                                                      | Geometric Mean Ratio           |
| Point estimate                                                                                                                                                                                                                                          | 115.01                         |
| Confidence interval                                                                                                                                                                                                                                     |                                |
| level                                                                                                                                                                                                                                                   | 90 %                           |
| sides                                                                                                                                                                                                                                                   | 2-sided                        |
| lower limit                                                                                                                                                                                                                                             | 107.31                         |
| upper limit                                                                                                                                                                                                                                             | 123.25                         |

Notes:

[10] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 19. Pre-defined bioequivalence limits were 80 to 125%.

## Secondary: Maximum Observed Plasma Concentration (Cmax) of Cobicistat

| End point title                                                                                                                                                                                                                      | Maximum Observed Plasma Concentration (Cmax) of Cobicistat |
|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------|
| End point description:                                                                                                                                                                                                               |                                                            |
| Cmax was the maximum observed plasma concentration of Cobicistat. PK data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods. |                                                            |
| End point type                                                                                                                                                                                                                       | Secondary                                                  |
| End point timeframe:                                                                                                                                                                                                                 |                                                            |
| Pre dose and 1, 2, 3, 4, 5, 6, 8, 12, 18, 24, 36, 48, 72 hours post dose                                                                                                                                                             |                                                            |

| End point values                     | Treatment A          | Treatment B          |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 33                   | 32                   |  |  |
| Units: ng/mL                         |                      |                      |  |  |
| arithmetic mean (standard deviation) | 842 ( $\pm$ 206)     | 898 ( $\pm$ 202)     |  |  |

## Statistical analyses

| Statistical analysis title                                                                                                                                                                                                                              | Treatment B Versus Treatment A |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                       |                                |
| Log transformed PK parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm. |                                |
| Comparison groups                                                                                                                                                                                                                                       | Treatment A v Treatment B      |
| Number of subjects included in analysis                                                                                                                                                                                                                 | 65                             |
| Analysis specification                                                                                                                                                                                                                                  | Pre-specified                  |
| Analysis type                                                                                                                                                                                                                                           | equivalence <sup>[11]</sup>    |
| Parameter estimate                                                                                                                                                                                                                                      | Geometric Mean Ratio           |
| Point estimate                                                                                                                                                                                                                                          | 93.67                          |
| Confidence interval                                                                                                                                                                                                                                     |                                |
| level                                                                                                                                                                                                                                                   | 90 %                           |
| sides                                                                                                                                                                                                                                                   | 2-sided                        |
| lower limit                                                                                                                                                                                                                                             | 89.63                          |
| upper limit                                                                                                                                                                                                                                             | 97.9                           |

Notes:

[11] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 32. Pre-defined bioequivalence limits were 80 to 125%.

## Secondary: Area Under the Plasma Concentration-time Curve From Time Zero to Time of Last Measurable (non-BQL) Concentration (AUC[0-last]) of Cobicistat

|                                                                                                                                                                                                                                                                                                                                                            |                                                                                                                                              |
|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|
| End point title                                                                                                                                                                                                                                                                                                                                            | Area Under the Plasma Concentration-time Curve From Time Zero to Time of Last Measurable (non-BQL) Concentration (AUC[0-last]) of Cobicistat |
| End point description:                                                                                                                                                                                                                                                                                                                                     |                                                                                                                                              |
| AUC(0-last) was area under the plasma concentration-time curve from time 0 to the time of the last measurable non-BQL concentration, calculated by linear-linear trapezoidal summation. PK data analysis set included all subjects who completed all treatment periods and for which an evaluable PK parameter could be obtained in all treatment periods. |                                                                                                                                              |
| End point type                                                                                                                                                                                                                                                                                                                                             | Secondary                                                                                                                                    |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                       |                                                                                                                                              |
| Pre dose and 1, 2, 3, 4, 5, 6, 8, 12, 18, 24, 36, 48, 72 hours post dose                                                                                                                                                                                                                                                                                   |                                                                                                                                              |

| End point values                     | Treatment A          | Treatment B          |  |  |
|--------------------------------------|----------------------|----------------------|--|--|
| Subject group type                   | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed          | 33                   | 32                   |  |  |
| Units: h*ng/mL                       |                      |                      |  |  |
| arithmetic mean (standard deviation) | 6160 (± 2116)        | 6366 (± 2113)        |  |  |

## Statistical analyses

| Statistical analysis title                                                                                                                                                                                                                              | Treatment B Versus Treatment A |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| Statistical analysis description:                                                                                                                                                                                                                       |                                |
| Log transformed PK parameters were analyzed by mixed model analysis of variance with period, treatment, treatment sequence as fixed effects, and subject within-sequence as a random effect and the results were back-transformed using anti-logarithm. |                                |
| Comparison groups                                                                                                                                                                                                                                       | Treatment A v Treatment B      |
| Number of subjects included in analysis                                                                                                                                                                                                                 | 65                             |
| Analysis specification                                                                                                                                                                                                                                  | Pre-specified                  |
| Analysis type                                                                                                                                                                                                                                           | equivalence <sup>[12]</sup>    |
| Parameter estimate                                                                                                                                                                                                                                      | Geometric Mean Ratio           |
| Point estimate                                                                                                                                                                                                                                          | 97.45                          |
| Confidence interval                                                                                                                                                                                                                                     |                                |
| level                                                                                                                                                                                                                                                   | 90 %                           |
| sides                                                                                                                                                                                                                                                   | 2-sided                        |
| lower limit                                                                                                                                                                                                                                             | 93.18                          |
| upper limit                                                                                                                                                                                                                                             | 101.91                         |

Notes:

[12] - Subjects analysed for statistical analysis in both the treatments (in each Treatment A and Treatment B) as per assigned treatment sequence were 32. Pre-defined bioequivalence limits were 80 to 125%.

## Secondary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

| End point title                                                                                                                                                                                                                                                                                                                                                                                                                             | Number of Subjects With Treatment-emergent Adverse Events (TEAEs) |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|
| End point description:                                                                                                                                                                                                                                                                                                                                                                                                                      |                                                                   |
| An adverse event is any untoward medical event that occurs in a subject administered an investigational product, and it does not necessarily indicate only events with clear causal relationship with the relevant investigational product. TEAEs are defined as AEs with onset or worsening on or after date of first dose of study treatment. Safety analysis set included all subjects who received at least one dose of the study drug. |                                                                   |
| End point type                                                                                                                                                                                                                                                                                                                                                                                                                              | Secondary                                                         |
| End point timeframe:                                                                                                                                                                                                                                                                                                                                                                                                                        |                                                                   |
| Up to 5 weeks                                                                                                                                                                                                                                                                                                                                                                                                                               |                                                                   |

| End point values            | Treatment A          | Treatment B          |  |  |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type          | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed | 36                   | 36                   |  |  |
| Units: Subjects             | 20                   | 26                   |  |  |

## **Statistical analyses**

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From signing of the Informed consent form (ICF) till the last study-related activity (up to 9 weeks)

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 24.0 |
|--------------------|------|

### Reporting groups

|                       |             |
|-----------------------|-------------|
| Reporting group title | Treatment B |
|-----------------------|-------------|

Reporting group description:

Subjects received a single oral dose of DRV 600 mg and 75 mg tablet, F/TAF 200/10 mg and COBI 150 mg tablet under fed conditions (Treatment B, reference) on Day 1 of Period 1 followed by a single oral dose D/C/F/TAF 675/150/200/10 mg as one fixed dose combination (FDC) tablet under fed conditions (Treatment A, test) on Day 1 of Period 2 followed by Treatment A on Day 1 of Period 3 and, then Treatment B on Day 1 of Period 4. Each period was separated by a washout period of at least 7 days.

|                       |             |
|-----------------------|-------------|
| Reporting group title | Treatment A |
|-----------------------|-------------|

Reporting group description:

Subjects received a single oral dose of Darunavir (675 milligrams [mg])/Cobicistat (150 mg)/Emtricitabine (200 mg)/Tenofovir Alafenamide (10 mg) as one fixed dose combination (FDC) tablet (D/C/F/TAF) under fed conditions (Treatment A, test) on Day 1 of Period 1 followed by a single oral dose of Darunavir (DRV) 600 mg and 75 mg tablet, Emtricitabine 200 mg/Tenofovir Alafenamide 10 mg (F/TAF) and Cobicistat (COBI) 150 mg tablet under fed conditions (Treatment B, reference) on Day 1 of Period 2 followed by Treatment B again on Day 1 of Period 3 and, then Treatment A on Day 1 of Period 4. Each period was separated by a washout period of at least 7 days.

| Serious adverse events                            | Treatment B    | Treatment A    |  |
|---------------------------------------------------|----------------|----------------|--|
| Total subjects affected by serious adverse events |                |                |  |
| subjects affected / exposed                       | 0 / 36 (0.00%) | 0 / 36 (0.00%) |  |
| number of deaths (all causes)                     | 0              | 0              |  |
| number of deaths resulting from adverse events    |                |                |  |

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

| Non-serious adverse events                            | Treatment B      | Treatment A      |  |
|-------------------------------------------------------|------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                  |                  |  |
| subjects affected / exposed                           | 21 / 36 (58.33%) | 20 / 36 (55.56%) |  |
| Nervous system disorders                              |                  |                  |  |
| Dizziness                                             |                  |                  |  |
| subjects affected / exposed                           | 2 / 36 (5.56%)   | 2 / 36 (5.56%)   |  |
| occurrences (all)                                     | 2                | 3                |  |
| Headache                                              |                  |                  |  |

|                                                                                    |                        |                       |  |
|------------------------------------------------------------------------------------|------------------------|-----------------------|--|
| subjects affected / exposed<br>occurrences (all)                                   | 5 / 36 (13.89%)<br>6   | 6 / 36 (16.67%)<br>9  |  |
| General disorders and administration<br>site conditions                            |                        |                       |  |
| Catheter Site Bruise<br>subjects affected / exposed<br>occurrences (all)           | 1 / 36 (2.78%)<br>1    | 2 / 36 (5.56%)<br>3   |  |
| Fatigue<br>subjects affected / exposed<br>occurrences (all)                        | 3 / 36 (8.33%)<br>4    | 4 / 36 (11.11%)<br>4  |  |
| Catheter Site Related Reaction<br>subjects affected / exposed<br>occurrences (all) | 7 / 36 (19.44%)<br>9   | 6 / 36 (16.67%)<br>7  |  |
| Vessel Puncture Site Reaction<br>subjects affected / exposed<br>occurrences (all)  | 0 / 36 (0.00%)<br>0    | 2 / 36 (5.56%)<br>3   |  |
| Gastrointestinal disorders                                                         |                        |                       |  |
| Abdominal Pain Upper<br>subjects affected / exposed<br>occurrences (all)           | 2 / 36 (5.56%)<br>2    | 1 / 36 (2.78%)<br>1   |  |
| Abdominal Discomfort<br>subjects affected / exposed<br>occurrences (all)           | 2 / 36 (5.56%)<br>2    | 3 / 36 (8.33%)<br>4   |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)                      | 3 / 36 (8.33%)<br>3    | 2 / 36 (5.56%)<br>2   |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)                         | 13 / 36 (36.11%)<br>19 | 8 / 36 (22.22%)<br>11 |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)                       | 3 / 36 (8.33%)<br>3    | 1 / 36 (2.78%)<br>1   |  |
| Respiratory, thoracic and mediastinal<br>disorders                                 |                        |                       |  |
| Epistaxis<br>subjects affected / exposed<br>occurrences (all)                      | 0 / 36 (0.00%)<br>0    | 2 / 36 (5.56%)<br>2   |  |
| Oropharyngeal Pain                                                                 |                        |                       |  |

|                                                                                                                                                                                     |                                                |                                                |  |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------------------------------|------------------------------------------------|--|
| subjects affected / exposed<br>occurrences (all)                                                                                                                                    | 1 / 36 (2.78%)<br>1                            | 2 / 36 (5.56%)<br>3                            |  |
| Skin and subcutaneous tissue disorders<br>Dry Skin<br>subjects affected / exposed<br>occurrences (all)                                                                              | 1 / 36 (2.78%)<br>1                            | 2 / 36 (5.56%)<br>2                            |  |
| Musculoskeletal and connective tissue disorders<br>Back Pain<br>subjects affected / exposed<br>occurrences (all)<br><br>Myalgia<br>subjects affected / exposed<br>occurrences (all) | 2 / 36 (5.56%)<br>2<br><br>1 / 36 (2.78%)<br>1 | 0 / 36 (0.00%)<br>0<br><br>2 / 36 (5.56%)<br>3 |  |
| Metabolism and nutrition disorders<br>Decreased Appetite<br>subjects affected / exposed<br>occurrences (all)                                                                        | 2 / 36 (5.56%)<br>2                            | 4 / 36 (11.11%)<br>4                           |  |

## **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