



Clinical trial results:

An Open-Label Study with TMC278 25 mg q.d. in Combination with a Background Regimen Containing 2 Nucleoside/Nucleotide Reverse Transcriptase Inhibitors in HIV-1 Infected Subjects, Who Participated in TMC278 clinical studies

Summary

| | |
|--------------------------|----------------------------|
| EudraCT number | 2010-021209-18 |
| Trial protocol | BE DE GB SE ES IT DK AT NL |
| Global end of trial date | 28 February 2020 |

Results information

| | |
|--------------------------------|------------------|
| Result version number | v1 (current) |
| This version publication date | 26 February 2021 |
| First version publication date | 26 February 2021 |

Trial information

Trial identification

| | |
|-----------------------|-------------------|
| Sponsor protocol code | TMC278-TiDP6-C222 |
|-----------------------|-------------------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01266902 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | Janssen Research & Development, LLC |
| Sponsor organisation address | 920 Route 202, Raritan, United States, NJ 08869 |
| Public contact | Janssen Research & Development, LLC, Clinical Registry group, ClinicalTrialsEU@its.jnj.com |
| Scientific contact | Janssen Research & Development, LLC, Clinical Registry group, ClinicalTrialsEU@its.jnj.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|------------------|
| Analysis stage | Final |
| Date of interim/final analysis | 28 February 2020 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|------------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 28 February 2020 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The objective of this study was to provide continued access to rilpivirine (RPV) for subjects who were randomized and treated with RPV in the Phase 2b (TMC278-C204 [C204]) or Phase 3 studies (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]), and who, at the time of roll-over, experienced and were expected to continue experiencing clinical benefit from RPV treatment.

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 Practice (GCP) and applicable regulatory requirements. Serious Adverse Events (SAEs), Adverse events (AEs) leading to discontinuation, any grade 3/4 events of rash (irrespective of causality), AEs considered at least possibly related to RPV, human immunodeficiency virus (HIV)-related AEs, and pregnancies were collected from signing of the informed consent form (ICF) until the data cut-off date and were followed up by the investigator.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 25 February 2011 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Efficacy, Safety |
| Long term follow-up duration | 9 Years |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | Argentina: 35 |
| Country: Number of subjects enrolled | Australia: 11 |
| Country: Number of subjects enrolled | Austria: 8 |
| Country: Number of subjects enrolled | Belgium: 13 |
| Country: Number of subjects enrolled | Canada: 21 |
| Country: Number of subjects enrolled | Chile: 12 |
| Country: Number of subjects enrolled | China: 26 |
| Country: Number of subjects enrolled | Germany: 27 |
| Country: Number of subjects enrolled | Denmark: 5 |
| Country: Number of subjects enrolled | Spain: 14 |
| Country: Number of subjects enrolled | France: 20 |
| Country: Number of subjects enrolled | United Kingdom: 25 |
| Country: Number of subjects enrolled | Italy: 10 |
| Country: Number of subjects enrolled | Netherlands: 3 |

| | |
|--------------------------------------|------------------------|
| Country: Number of subjects enrolled | Puerto Rico: 7 |
| Country: Number of subjects enrolled | Romania: 4 |
| Country: Number of subjects enrolled | Russian Federation: 38 |
| Country: Number of subjects enrolled | Sweden: 3 |
| Country: Number of subjects enrolled | Thailand: 65 |
| Country: Number of subjects enrolled | Taiwan: 2 |
| Country: Number of subjects enrolled | United States: 85 |
| Country: Number of subjects enrolled | South Africa: 48 |
| Worldwide total number of subjects | 482 |
| EEA total number of subjects | 107 |

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) | 479 |
| From 65 to 84 years | 3 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Total of 482 subjects were treated and 437 discontinued at data cut-off date (8 Feb 2018): 371 switched to commercially available RPV and 6 discontinued as they reached a virologic endpoint. At last visit of last subject (28 February 2020), out of 45 subjects 37 switched to commercially available RPV and 6 lost to follow-up.

Period 1

| | |
|------------------------------|-----------------------------|
| Period 1 title | Period 1 (Main Study) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

Blinding implementation details:

Not Applicable

Arms

| | |
|------------------------------|-----|
| Are arms mutually exclusive? | Yes |
|------------------------------|-----|

| | |
|------------------|--|
| Arm title | Rilpivirine (RPV) (TMC278-C204 [C204]) |
|------------------|--|

Arm description:

Subjects who rolled over from trial C204 continued to receive RPV 25 milligrams (mg) once daily (qd) in combination with an investigator-selected background regimen consisting of 2 nucleos(t)ide reverse transcriptase inhibitors (N[t]RTIs) starting Day 1.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Rilpivirine |
| Investigational medicinal product code | |
| Other name | TMC278 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

RPV 25 mg oral tablets were administered orally.

| | |
|--|--|
| Investigational medicinal product name | Nucleos(t)ide Reverse Transcriptase Inhibitors |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Two N(t)RTIs were administered as the investigator-selected background regimen.

| | |
|------------------|---|
| Arm title | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) |
|------------------|---|

Arm description:

Subjects who rolled over from trial C209 and C215 continued to receive RPV 25 mg qd in combination with an investigator-selected background regimen consisting of 2 N(t)RTIs starting Day 1. In trial C209, the background regimen was fixed to tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) and in trial C215, the background regimen was selected by the investigator and contained either abacavir (ABC)/lamivudine (3TC), zidovudine (AZT)/3TC, or TDF/FTC.

| | |
|----------|--------------|
| Arm type | Experimental |
|----------|--------------|

| | |
|---|--|
| Investigational medicinal product name | Nucleos(t)ide Reverse Transcriptase Inhibitors |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| Two N(t)RTIs were administered as the investigator-selected background regimen. | |
| Investigational medicinal product name | Rilpivirine |
| Investigational medicinal product code | |
| Other name | TMC278 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |
| Dosage and administration details: | |
| RPV 25 mg oral tablets were administered orally. | |

| Number of subjects in period 1 | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6- C209 [C209] and TMC278-TiDP6-C215 [C215]) |
|-----------------------------------|--|---|
| Started | 119 | 363 |
| Completed | 89 | 282 |
| Not completed | 30 | 81 |
| Consent withdrawn by subject | 2 | 12 |
| Adverse events | 3 | 11 |
| Continued to RPV treatment | 11 | 34 |
| Investigator's/Subject's decision | 2 | 3 |
| Subject non-compliant | 3 | 7 |
| Lost to follow-up | 5 | 12 |
| Lack of efficacy | 4 | 2 |

| | |
|----------------------------------|---------------------------------------|
| Period 2 | |
| Period 2 title | Period 2 (After Protocol Amendment 3) |
| Is this the baseline period? | No |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |
| Blinding implementation details: | |
| Not Applicable | |

Arms

| | |
|--|--|
| Arm title | RPV 25 mg (After Protocol Amendment 3) |
| Arm description: All subjects who were continued under a simplified study setting with only a minimum of study-related activities, as per Protocol Amendment 3 continued to receive RPV 25 mg and followed up for safety. | |
| Arm type | Experimental |
| Investigational medicinal product name | Rilpivirine |
| Investigational medicinal product code | |
| Other name | TMC278 |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

RPV 25 mg oral tablets were administered orally.

| Number of subjects in period 2^[1] | RPV 25 mg (After Protocol Amendment 3) |
|---|--|
| Started | 45 |
| Completed | 37 |
| Not completed | 8 |
| Consent withdrawn by subject | 1 |
| Adverse event, non-fatal | 1 |
| Lost to follow-up | 6 |

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Only 45 subjects continued Rilpivirine (RPV) treatment per Protocol Amendment 3.

Baseline characteristics

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Rilpivirine (RPV) (TMC278-C204 [C204]) |
|-----------------------|--|

Reporting group description:

Subjects who rolled over from trial C204 continued to receive RPV 25 milligrams (mg) once daily (qd) in combination with an investigator-selected background regimen consisting of 2 nucleos(t)ide reverse transcriptase inhibitors (N[t]RTI)s starting Day 1.

| | |
|-----------------------|---|
| Reporting group title | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) |
|-----------------------|---|

Reporting group description:

Subjects who rolled over from trial C209 and C215 continued to receive RPV 25 mg qd in combination with an investigator-selected background regimen consisting of 2 N(t)RTIs starting Day 1. In trial C209, the background regimen was fixed to tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) and in trial C215, the background regimen was selected by the investigator and contained either abacavir (ABC)/lamivudine (3TC), zidovudine (AZT)/3TC, or TDF/FTC.

| Reporting group values | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6- C209 [C209] and TMC278-TiDP6-C215 [C215]) | Total |
|---|--|---|-------|
| Number of subjects | 119 | 363 | 482 |
| Title for AgeCategorical Units: subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Adults (18-64 years) | 118 | 361 | 479 |
| From 65 to 84 years | 1 | 2 | 3 |
| 85 years and over | 0 | 0 | 0 |
| Title for AgeContinuous Units: years | | | |
| median | 40 | 39 | |
| full range (min-max) | 28 to 66 | 22 to 69 | - |
| Title for Gender Units: subjects | | | |
| Female | 41 | 84 | 125 |
| Male | 78 | 279 | 357 |

End points

End points reporting groups

| | |
|--|---|
| Reporting group title | Rilpivirine (RPV) (TMC278-C204 [C204]) |
| Reporting group description: Subjects who rolled over from trial C204 continued to receive RPV 25 milligrams (mg) once daily (qd) in combination with an investigator-selected background regimen consisting of 2 nucleos(t)ide reverse transcriptase inhibitors (N[t]RTIs) starting Day 1. | |
| Reporting group title | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) |
| Reporting group description: Subjects who rolled over from trial C209 and C215 continued to receive RPV 25 mg qd in combination with an investigator-selected background regimen consisting of 2 N(t)RTIs starting Day 1. In trial C209, the background regimen was fixed to tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) and in trial C215, the background regimen was selected by the investigator and contained either abacavir (ABC)/lamivudine (3TC), zidovudine (AZT)/3TC, or TDF/FTC. | |
| Reporting group title | RPV 25 mg (After Protocol Amendment 3) |
| Reporting group description: All subjects who were continued under a simplified study setting with only a minimum of study-related activities, as per Protocol Amendment 3 continued to receive RPV 25 mg and followed up for safety. | |

Primary: Number of Subjects with Adverse Events (AEs)

| | |
|--|---|
| End point title | Number of Subjects with Adverse Events (AEs) ^[1] |
| End point description: An AE can be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal (investigational or non investigational) product, whether or not related to that medicinal (investigational or non investigational) product. The intent-to-treat (ITT) population included all subjects who have taken at least 1 dose of rilpivirine (RPV), regardless of their compliance with the protocol and adherence to the dosing regimen. | |
| End point type | Primary |
| End point timeframe: Up to 7 years | |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No Inferential statistical analysis was planned for the Primary Endpoint.

| End point values | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 363 | | |
| Units: Subjects | 32 | 70 | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Grade 3/4 Events of Rash irrespective of

Causality

| | |
|-----------------|---|
| End point title | Number of Subjects with Grade 3/4 Events of Rash irrespective of Causality ^[2] |
|-----------------|---|

End point description:

Subjects with grade 3/4 events of rash irrespective of causality were assessed. A grade 3 rash defined as diffuse macular, maculopapular or morbilliform rash with vesicles or limited number of bullae or; rash with superficial ulcerations of mucous membranes limited to 1 anatomical site or; rash with at least one of following: elevations in aspartate aminotransferase (AST)/alanine aminotransferase (ALT) more than 2*baseline value and at least 5 times upper limit of normal; fever greater than (>) 38 degree celsius or 100 degree fahrenheit; eosinophils > 1000/millimeter (mm)³; serum sickness-like reaction. A grade 4 rash defined as following: extensive or generalized bullous lesions or; Stevens-Johnsons Syndrome (SJS) or ulceration of mucous membrane involving 2 or more distinct mucosal sites or toxic epidermal necrolysis. The ITT population included all subjects who have taken at least 1 dose of RPV, regardless of their compliance with the protocol and adherence to the dosing regimen.

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

End point timeframe:

Up to 7 years

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No Inferential statistical analysis was planned for the Primary Endpoint.

| | | | | |
|-----------------------------|--|---|--|--|
| End point values | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) | | |
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 363 | | |
| Units: Subjects | 0 | 0 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Virologic Rebound

| | |
|-----------------|---------------------------|
| End point title | Time to Virologic Rebound |
|-----------------|---------------------------|

End point description:

Time to virologic rebound was time to (first) human immunodeficiency virus type 1 (HIV-1) ribonucleic acid (RNA) greater than or equal to (\geq) 50 or \geq 200 copies/milliliter (copies/mL). The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time. The ITT population included all subjects who have taken at least 1 dose of RPV, regardless of their compliance with the protocol and adherence to the dosing regimen.

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

End point timeframe:

Up to Week 360

| End point values | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) | | |
|----------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 363 | | |
| Units: days | | | | |
| arithmetic mean (standard error) | | | | |
| >= 50 copies/mL | 1670.6 (± 51.32) | 1939.3 (± 52.43) | | |
| >= 200 copies/mL | 1901.3 (± 47.19) | 1877.3 (± 25.93) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Time To Treatment Failure

| | |
|--|---------------------------|
| End point title | Time To Treatment Failure |
| End point description: | |
| Time to treatment failure was defined as time to virologic rebound (time to first HIV-1 RNA >= 50 or >= 200 copies/mL) or discontinuation for reason other than RPV having become commercially available in the participating country, whichever came first, calculated as the time (in days) from baseline until treatment failure. The mean survival time and its standard error were underestimated because the largest observation was censored and the estimation was restricted to the largest event time. The ITT population included all subjects who have taken at least 1 dose of RPV, regardless of their compliance with the protocol and adherence to the dosing regimen. | |
| End point type | Secondary |
| End point timeframe: | |
| Up to Week 360 | |

| End point values | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) | | |
|----------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 363 | | |
| Units: days | | | | |
| arithmetic mean (standard error) | | | | |
| >= 50 copies/mL | 1795.7 (± 70.03) | 1694.1 (± 59.42) | | |
| >= 200 copies/mL | 1868.7 (± 63.29) | 1637.5 (± 42.42) | | |

Statistical analyses

Secondary: Change from Baseline in Cluster of Differentiation 4 (CD4+) Cell Count for Observed Case Approach until Week 336

| | |
|-----------------|--|
| End point title | Change from Baseline in Cluster of Differentiation 4 (CD4+) Cell Count for Observed Case Approach until Week 336 |
|-----------------|--|

End point description:

Change from baseline in CD4+ cell count were reported for observed case approach. The immunologic assessment was determined by changes in Cluster of CD4+ cell count for observed case approach. The ITT population included all subjects who have taken at least 1 dose of RPV, regardless of their compliance with the protocol and adherence to the dosing regimen. Here 'n' (number analyzed) included all subjects who were evaluable for specified time point categories.

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

End point timeframe:

Baseline up to Weeks 96, 192, 288, 336

| End point values | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) | | |
|--------------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 363 | | |
| Units: cells/microliter (cells/mL) | | | | |
| arithmetic mean (standard error) | | | | |
| Week 96: Observed Case (n= 74, 149) | 72.63 (± 20.581) | 55.91 (± 13.425) | | |
| Week 192: Observed Case (n= 68, 100) | 148.76 (± 24.111) | 132.73 (± 21.989) | | |
| Week 288: Observed Case (n= 45, 89) | 122.29 (± 29.628) | 101.50 (± 24.108) | | |
| Week 336: Observed Case (n= 12, 30) | 161.73 (± 39.851) | 76.49 (± 40.484) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+ Cell Count for Non-Completer Equals Failure (NC=F) Approach until Week 336

| | |
|-----------------|---|
| End point title | Change from Baseline in CD4+ Cell Count for Non-Completer Equals Failure (NC=F) Approach until Week 336 |
|-----------------|---|

End point description:

Change from baseline in CD4+ cell count were reported for NC=F approach (subjects who discontinued because RPV became commercially available or could be accessed through another source or because the subjects switched to other local [RPV-based] treatment options or local standard of care, were censored at that time; other subjects after discontinuation had their CD4+ values imputed with baseline value. Intermittently missing values were imputed with a last observation carried-forward approach). The ITT population included all subjects who have taken at least 1 dose of RPV, regardless of their compliance with the protocol and adherence to the dosing regime. Here 'n' (number analyzed) included all subjects who were evaluable for specified time point categories.

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

End point timeframe:

Baseline up to weeks 96, 192, 288, 336

| End point values | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) | | |
|----------------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 363 | | |
| Units: cells/mcL | | | | |
| arithmetic mean (standard error) | | | | |
| Week 96 (n= 79, 196) | 69.76 (± 19.372) | 42.19 (± 11.525) | | |
| Week 192 (n= 77, 153) | 133.56 (± 21.906) | 91.69 (± 15.563) | | |
| Week 288 (n= 61, 134) | 92.12 (± 22.809) | 63.33 (± 17.132) | | |
| Week 336 (n= 27, 86) | 70.69 (± 23.558) | 49.24 (± 16.688) | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Serious Adverse Events (SAEs)

| | |
|---|---|
| End point title | Number of Subjects with Serious Adverse Events (SAEs) |
| End point description: A SAE is any untoward medical occurrence that at any dose: results in death; is life threatening; requires inpatient hospitalization or prolongation of existing hospitalization; results in persistent or significant disability/incapacity; is a congenital anomaly/birth defect. The ITT population included all subjects who have taken at least 1 dose of RPV, regardless of their compliance with the protocol and adherence to the dosing regimen. | |
| End point type | Secondary |
| End point timeframe: Up to 7 years | |

| End point values | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 363 | | |
| Units: Subjects | 9 | 14 | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with AEs related to Rilpivirine (RPV)

| | |
|-----------------|--|
| End point title | Number of Subjects with AEs related to Rilpivirine (RPV) |
|-----------------|--|

End point description:

Number of subjects with AEs related to RPV were assessed. An AE can be any unfavorable and unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of a medicinal (investigational or non investigational) product, whether or not related to that medicinal (investigational or non investigational) product. The ITT population included all subjects who have taken at least 1 dose of RPV, regardless of their compliance with the protocol and adherence to the dosing regimen.

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

End point timeframe:

Up to 7 years

| End point values | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) | | |
|-----------------------------|--|---|--|--|
| Subject group type | Reporting group | Reporting group | | |
| Number of subjects analysed | 119 | 363 | | |
| Units: Subjects | 7 | 16 | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 7 years

Adverse event reporting additional description:

The safety analysis set included all subjects who have taken at least 1 dose of rilpivirine (RPV), regardless of their compliance with the protocol and adherence to the dosing regimen.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 14.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--|
| Reporting group title | Rilpivirine (RPV) (TMC278-C204 [C204]) |
|-----------------------|--|

Reporting group description:

Subjects who rolled over from trial C204 continued to receive RPV 25 milligrams (mg) once daily (qd) in combination with an investigator-selected background regimen consisting of 2 nucleos(t)ide reverse transcriptase inhibitors (N[t]RTI)s starting Day 1.

| | |
|-----------------------|---|
| Reporting group title | RPV (TMC278-TiDP6-C209 [C209] and TMC278-TiDP6-C215 [C215]) |
|-----------------------|---|

Reporting group description:

Subjects who rolled over from trial C209 and C215 continued to receive RPV 25 mg qd in combination with an investigator-selected background regimen consisting of 2 N(t)RTIs starting Day 1. In trial C209, the background regimen was fixed to tenofovir disoproxil fumarate (TDF)/emtricitabine (FTC) and in trial C215, the background regimen was selected by the investigator and contained either abacavir (ABC)/lamivudine (3TC), zidovudine (AZT)/3TC, or TDF/FTC.

| Serious adverse events | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6- C209 [C209] and TMC278-TiDP6-C215 [C215]) | |
|---|--|---|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 119 (7.56%) | 14 / 363 (3.86%) | |
| number of deaths (all causes) | 0 | 2 | |
| number of deaths resulting from adverse events | | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Adrenal Adenoma | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Colon Cancer | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|--|-----------------|-----------------|--|
| Gastric Cancer | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 1 | |
| Vascular disorders | | | |
| Thrombophlebitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Varicose Vein | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| General disorders and administration site conditions | | | |
| Chest Pain | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Death | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 1 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 1 / 1 | |
| Reproductive system and breast disorders | | | |
| Benign Prostatic Hyperplasia | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Psychiatric disorders | | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Investigations | | | |
| Blood Glucose Increased | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Injury, poisoning and procedural complications | | | |
| Foot Fracture | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hand Fracture | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Limb Injury | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Stab Wound | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Cardiac disorders | | | |
| Cardiac Hypertrophy | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Coronary Artery Disease | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Nervous system disorders | | | |
| Cerebrovascular Accident | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

| | | | |
|---|-----------------|-----------------|--|
| Ischaemic Stroke | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Sciatica | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Blood and lymphatic system disorders | | | |
| Haemolytic Anaemia | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrointestinal disorders | | | |
| Abdominal Discomfort | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Abdominal Pain | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Gastrooesophageal Reflux Disease | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Rectal Haemorrhage | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Hepatobiliary disorders | | | |
| Cholelithiasis | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Renal and urinary disorders | | | |
| Renal Failure | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Infections and infestations | | | |
| Bronchitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Dengue Fever | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Liver Abscess | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Lung Infection | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |
| Syphilis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | |

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

| Non-serious adverse events | Rilpivirine (RPV) (TMC278-C204 [C204]) | RPV (TMC278-TiDP6- C209 [C209] and TMC278-TiDP6-C215 [C215]) | |
|---|--|---|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 24 / 119 (20.17%) | 61 / 363 (16.80%) | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Anogenital Warts | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Vascular disorders | | | |
| Arteriosclerosis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 119 (1.68%) | 0 / 363 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pregnancy, puerperium and perinatal conditions | | | |
| Pregnancy | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 7 / 363 (1.93%) | |
| occurrences (all) | 0 | 7 | |
| General disorders and administration site conditions | | | |
| Chest Discomfort | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 363 (0.28%) | |
| occurrences (all) | 1 | 1 | |
| Chest Pain | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Feeling Hot | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Nodule | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Oedema Peripheral | | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 119 (0.84%) 1 | 0 / 363 (0.00%) 0 | |
| Pyrexia subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Immune system disorders Seasonal Allergy subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 2 | |
| Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 2 / 363 (0.55%) 2 | |
| Epistaxis subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Nasal Congestion subjects affected / exposed occurrences (all) | 1 / 119 (0.84%) 1 | 0 / 363 (0.00%) 0 | |
| Oropharyngeal Pain subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 3 / 363 (0.83%) 3 | |
| Productive Cough subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Psychiatric disorders Abnormal Dreams subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Anxiety subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 2 / 363 (0.55%) 2 | |
| Depression | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Insomnia | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 3 / 363 (0.83%) | |
| occurrences (all) | 0 | 3 | |
| Investigations | | | |
| Alanine Aminotransferase Increased | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 3 / 363 (0.83%) | |
| occurrences (all) | 1 | 4 | |
| Aspartate Aminotransferase Increased | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 2 | |
| Blood Cholesterol Increased | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 363 (0.55%) | |
| occurrences (all) | 0 | 2 | |
| Blood Creatine Phosphokinase Increased | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Blood Creatinine Increased | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 363 (0.55%) | |
| occurrences (all) | 0 | 2 | |
| Blood Lactic Acid Increased | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Blood Triglycerides Increased | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 3 / 363 (0.83%) | |
| occurrences (all) | 0 | 3 | |
| Liver Function Test Abnormal | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Injury, poisoning and procedural complications | | | |
| Bone Fissure | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Injury | | | |

| | | | |
|---|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 1 / 119 (0.84%) 1 | 0 / 363 (0.00%) 0 | |
| Joint Injury subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Laceration subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Skin Injury subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Cardiac disorders Palpitations subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Nervous system disorders Carpal Tunnel Syndrome subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Cluster Headache subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Disturbance in Attention subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Headache subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 4 / 363 (1.10%) 4 | |
| Paraesthesia subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Blood and lymphatic system disorders Lymphadenopathy subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Eye disorders | | | |

| | | | |
|-----------------------------|-----------------|-----------------|--|
| Conjunctivitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Eye Pain | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Gastrointestinal disorders | | | |
| Abdominal Distension | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Abdominal Pain | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Abdominal Pain Lower | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Abdominal Pain Upper | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 2 / 363 (0.55%) | |
| occurrences (all) | 1 | 3 | |
| Anal Pruritus | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Cheilitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Constipation | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 363 (0.55%) | |
| occurrences (all) | 0 | 2 | |
| Diarrhoea | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 363 (0.55%) | |
| occurrences (all) | 0 | 2 | |
| Enteritis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Gastritis | | | |

| | | | |
|--|-----------------|-----------------|--|
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 363 (0.28%) | |
| occurrences (all) | 1 | 1 | |
| Gingivitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Nausea | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Oesophagitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Hepatobiliary disorders | | | |
| Cholecystitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Skin and subcutaneous tissue disorders | | | |
| Acne | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Alopecia | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Dermal Cyst | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Dermatitis Allergic | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 3 | |
| Dyshidrosis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Erythema | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Facial Wasting | | | |

| | | | |
|---|-----------------|-----------------|--|
| subjects affected / exposed | 2 / 119 (1.68%) | 0 / 363 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Lipoatrophy | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 363 (0.28%) | |
| occurrences (all) | 1 | 1 | |
| Lipodystrophy Acquired | | | |
| subjects affected / exposed | 2 / 119 (1.68%) | 0 / 363 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Pruritus | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Rash | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Seborrhoeic Dermatitis | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Skin Plaque | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Musculoskeletal and connective tissue disorders | | | |
| Back Pain | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 363 (0.55%) | |
| occurrences (all) | 0 | 2 | |
| Osteopenia | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Tendonitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Trismus | | | |

| | | | |
|--|----------------------|----------------------|--|
| subjects affected / exposed occurrences (all) | 0 / 119 (0.00%) 0 | 1 / 363 (0.28%) 1 | |
| Infections and infestations | | | |
| Body Tinea | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Bronchitis | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Chlamydial Infection | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 363 (0.28%) | |
| occurrences (all) | 1 | 1 | |
| Dengue Fever | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Eye Infection Toxoplasmal | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Fungal Infection | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Genital Herpes | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Hepatitis C | | | |
| subjects affected / exposed | 2 / 119 (1.68%) | 0 / 363 (0.00%) | |
| occurrences (all) | 2 | 0 | |
| Herpes Simplex | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 363 (0.28%) | |
| occurrences (all) | 1 | 1 | |
| Herpes Zoster | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 2 / 363 (0.55%) | |
| occurrences (all) | 2 | 2 | |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |

| | | |
|-----------------------------------|-----------------|-----------------|
| Influenza | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 363 (0.55%) |
| occurrences (all) | 0 | 2 |
| Latent Tuberculosis | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) |
| occurrences (all) | 0 | 1 |
| Lymph Node Tuberculosis | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) |
| occurrences (all) | 1 | 0 |
| Nasopharyngitis | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 2 / 363 (0.55%) |
| occurrences (all) | 0 | 2 |
| Oral Herpes | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) |
| occurrences (all) | 1 | 0 |
| Otitis Externa | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) |
| occurrences (all) | 0 | 1 |
| Otitis Media | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) |
| occurrences (all) | 0 | 1 |
| Perineal Abscess | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) |
| occurrences (all) | 1 | 0 |
| Periorbital Cellulitis | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) |
| occurrences (all) | 0 | 1 |
| Pharyngitis | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) |
| occurrences (all) | 0 | 1 |
| Respiratory Tract Infection Viral | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) |
| occurrences (all) | 0 | 1 |
| Syphilis | | |
| subjects affected / exposed | 2 / 119 (1.68%) | 2 / 363 (0.55%) |
| occurrences (all) | 3 | 2 |

| | | | |
|------------------------------------|-----------------|-----------------|--|
| Tonsillitis | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Upper Respiratory Tract Infection | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 3 / 363 (0.83%) | |
| occurrences (all) | 0 | 3 | |
| Urinary Tract Infection | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Metabolism and nutrition disorders | | | |
| Decreased Appetite | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Diabetes Mellitus | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 0 / 363 (0.00%) | |
| occurrences (all) | 1 | 0 | |
| Hypercholesterolaemia | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 363 (0.28%) | |
| occurrences (all) | 3 | 3 | |
| Hyperglycaemia | | | |
| subjects affected / exposed | 1 / 119 (0.84%) | 1 / 363 (0.28%) | |
| occurrences (all) | 1 | 3 | |
| Hyperuricaemia | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |
| Vitamin D Deficiency | | | |
| subjects affected / exposed | 0 / 119 (0.00%) | 1 / 363 (0.28%) | |
| occurrences (all) | 0 | 1 | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 05 May 2011 | Amendment 1, issued on 5 May 2011, was considered substantial and the overall reason for the amendment was to replace the serum pregnancy test by a urine pregnancy test, add a reminder for the human leukocyte antigen (HLA)-B*5701 allele testing and viral genotype determination, switching of background nucleos(t)ide reverse transcriptase inhibitors [N(t)RTI]s from the roll-over visit onwards was allowed, effective methods of birth control for male and female subjects were updated and the withdrawal criteria were updated. |
| 28 November 2016 | Amendment 3, issued on 28 November 2016 (with country-specific amendments in South Africa and Chile [25 July 2017]), was considered substantial and the overall reason for the amendment was the simplification of the study and the reduction of study-related activities to a minimum for the limited number of subjects remaining in this study. The main component of the study remained to allow subjects who experienced and were expected to continue experiencing clinical benefit from rilpivirine (RPV) treatment to have continued access to RPV in a simplified study setting or to be switched to local (RPV-based) treatment options or local standard of care, as appropriate. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Not all AEs were collected; AEs considered related to RPV, leading to discontinuations, SAEs, or grade 3/4 events of rash regardless of causality were collected; discontinuation rate was > 90 percent which makes interpretation of results difficult.

Notes: