

**Clinical trial results:****AN OPEN-LABEL, MULTICENTER, MULTIPLE-DOSE PHARMACOKINETIC AND 48-WEEK SAFETY AND EFFICACY TRIAL OF MARAVIROC IN COMBINATION WITH OPTIMIZED BACKGROUND THERAPY FOR THE TREATMENT OF ANTIRETROVIRAL-EXPERIENCED CCR5-TROPIC HIV-1 INFECTED CHILDREN 2-18 YEARS OF AGE****Summary**

| | |
|--------------------------|-------------------------------|
| EudraCT number | 2008-006873-33 |
| Trial protocol | ES PT IT GB FR Outside EU/EEA |
| Global end of trial date | |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 |
| This version publication date | 14 April 2016 |
| First version publication date | 14 April 2016 |

Trial information**Trial identification**

| | |
|-----------------------|----------|
| Sponsor protocol code | A4001031 |
|-----------------------|----------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00791700 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | ViiV Healthcare |
| Sponsor organisation address | 980 Great West Road, Brentford, Middlesex, United Kingdom, TW8 9GS |
| Public contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc, +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |
| Scientific contact | Pfizer ClinicalTrials.gov Call Center, Pfizer, Inc, +1 8007181021, ClinicalTrials.gov_Inquiries@pfizer.com |

Notes:

Paediatric regulatory details

| | |
|--|---------------------|
| Is trial part of an agreed paediatric investigation plan (PIP) | Yes |
| EMA paediatric investigation plan number(s) | EMA-000020-PIP01-07 |
| 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? | Yes |

Notes:

Results analysis stage

| | |
|--|-------------------|
| Analysis stage | Interim |
| Date of interim/final analysis | 17 September 2015 |
| Is this the analysis of the primary completion data? | Yes |
| Primary completion date | 14 April 2015 |
| Global end of trial reached? | No |

Notes:

General information about the trial

Main objective of the trial:

This study aimed to:

Primary objectives:

- determine the PK profile(s) and dosing schedule(s) for MVC in treatment experienced HIV infected children and adolescents on different background therapies;
- determine the safety and tolerability of MVC in HIV infected children and adolescents.

Secondary objectives:

- describe the efficacy of multiple dose administration of MVC in treatment experienced children infected with R5 HIV 1;
 - describe tropism changes over time
-

Protection of trial subjects:

This study was designed and monitored in accordance with Pfizer standard operating procedures (SOPs), until transition to the Contract Research Organization (CRO) PAREXEL in November 2012, after which the study was monitored in accordance with CRO SOPs. Both Pfizer and CRO SOPs complied with the ethical principles of Good Clinical Practice (GCP) as required by the major regulatory authorities, and in accordance with the Declaration of Helsinki as amended by legal and regulatory requirements, as well as the general principles set forth in the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences 2002), Guidelines for GCP (International Conference on Harmonization 1996), and the Declaration of Helsinki (World Medical Association 2008). In addition, the study was conducted in accordance with the CSP, the International Conference on Harmonization guideline on GCP, and applicable local regulatory requirements and laws.

Background therapy:

Optimized background treatment (OBT), consisting of 3 to 5 commercially available Anti-retroviral (ARV) agents were selected by the investigator and approved by Pfizer, on the basis of resistance testing, treatment history and safety considerations. Participants with toxicity due to drugs in the OBT regimen were able to substitute a drug of the same class during the study in consultation with the medical monitor. All concomitant medications were recorded on the CRF. Although no other ARV agents for HIV infection were allowed while on study drug, intravenous immunoglobulin (IVIG) for the management of immune deficiency/prevention of opportunistic infections was allowed. ARV agents comprising the OBT regimen were taken according to the manufacturer product labeling or local guidelines.

Dose adjustments to Maraviroc (MVC) were made in subjects taking concomitant medications that significantly inhibit and/or induce CYP3A4. This is because MVC is a substrate for CYP3A4.

Medications such as analgesics, antiinflammatory agents, antibiotics, and nutritional supplements other than those contraindicated (list below), could be used as needed.

Contraindicated medications included but not limited to were immunomodulators (except interferon or IVIG), grapefruit or grapefruit related citrus fruits (eg, Seville oranges, pomelos) and St.John's Wort or other herbal therapies.

The use of rifampin for the treatment mycobacterial infection for participants in Stage 2 was allowed on a case-by-case basis with the approval of the study team. Rifampin was not allowed for participants in Stage 1. Co administration of isoniazid was allowed on an individual basis upon discussion with and approval of the study team.

Evidence for comparator: -

| | |
|---|---------------|
| Actual start date of recruitment | 22 April 2009 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety |
| Long term follow-up duration | 5 Years |
| Independent data monitoring committee (IDMC) involvement? | Yes |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | Brazil: 6 |
| Country: Number of subjects enrolled | Italy: 1 |
| Country: Number of subjects enrolled | Portugal: 4 |
| Country: Number of subjects enrolled | Puerto Rico: 1 |
| Country: Number of subjects enrolled | South Africa: 62 |
| Country: Number of subjects enrolled | Spain: 6 |
| Country: Number of subjects enrolled | Thailand: 11 |
| Country: Number of subjects enrolled | United States: 12 |
| Worldwide total number of subjects | 103 |
| EEA total number of subjects | 11 |

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) | 61 |
| Adolescents (12-17 years) | 42 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

This open-label, multicenter, multiple dose pharmacokinetic, safety and efficacy study enrolled 103 participants at 24 sites in 8 countries.

Pre-assignment

Screening details:

Criteria such as the following were considered: HIV-1 infected treatment-experienced children and adolescents who were failing current ARV therapy or have failed their most recent ARV regimen, defined by plasma HIV-1 RNA \geq 1000 copies/mL, infected with only R5 HIV-1, and have ARV experience/intolerance of 6 months with at least 2 ARV drug classes.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Blinding implementation details:

Open-label study

Arms

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

| | |
|------------------|----------|
| Arm title | Cohort 1 |
|------------------|----------|

Arm description:

\geq 2 - <6 years of age, MVC liquid formulation

| | |
|--|---------------|
| Arm type | Experimental |
| Investigational medicinal product name | Maraviroc |
| Investigational medicinal product code | UK-427,857 |
| Other name | |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |

Dosage and administration details:

MVC liquid formulation (20 mg/ml)

| | |
|------------------|----------|
| Arm title | Cohort 2 |
|------------------|----------|

Arm description:

\geq 6 - <12 years of age, MVC tablet formulation

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Maraviroc |
| Investigational medicinal product code | UK-427,857 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

MVC tablet formulation (25 mg, 75 mg, 150 mg)

| | |
|------------------|----------|
| Arm title | Cohort 3 |
|------------------|----------|

Arm description:

\geq 6 - <12 years of age, MVC liquid formulation

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

| | |
|---|---------------|
| Investigational medicinal product name | Maraviroc |
| Investigational medicinal product code | UK-427,857 |
| Other name | |
| Pharmaceutical forms | Oral solution |
| Routes of administration | Oral use |
| Dosage and administration details: MVC liquid formulation (20 mg/ml) | |
| Arm title | Cohort 4 |

Arm description:

>=12 - <18 years of age, MVC tablet formulation

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Maraviroc |
| Investigational medicinal product code | UK-427,857 |
| Other name | |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

MVC tablet formulation (25 mg, 75 mg, 150 mg)

| Number of subjects in period 1 | Cohort 1 | Cohort 2 | Cohort 3 |
|--|----------|----------|----------|
| Started | 16 | 31 | 13 |
| Completed | 12 | 26 | 9 |
| Not completed | 4 | 5 | 4 |
| Blood sampling not done before Stage 1 | - | - | - |
| Non-compliance with study treatment | 1 | - | - |
| Adverse event | - | - | 1 |
| No longer willing to participate | - | 1 | - |
| Insufficient clinical response | 3 | 4 | 3 |

| Number of subjects in period 1 | Cohort 4 |
|--|----------|
| Started | 43 |
| Completed | 25 |
| Not completed | 18 |
| Blood sampling not done before Stage 1 | 1 |
| Non-compliance with study treatment | 2 |
| Adverse event | 1 |
| No longer willing to participate | 1 |
| Insufficient clinical response | 13 |

Baseline characteristics

Reporting groups

| | |
|---|----------|
| Reporting group title | Cohort 1 |
| Reporting group description: >=2 - <6 years of age, MVC liquid formulation | |
| Reporting group title | Cohort 2 |
| Reporting group description: >=6 - <12 years of age, MVC tablet formulation | |
| Reporting group title | Cohort 3 |
| Reporting group description: >=6 - <12 years of age, MVC liquid formulation | |
| Reporting group title | Cohort 4 |
| Reporting group description: >=12 - <18 years of age, MVC tablet formulation | |

| Reporting group values | Cohort 1 | Cohort 2 | Cohort 3 |
|--|----------|----------|----------|
| Number of subjects | 16 | 31 | 13 |
| Age categorical Units: Subjects | | | |
| Children (2-11 years) | 16 | 31 | 13 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 3.4 | 9.1 | 8.9 |
| standard deviation | ± 0.9 | ± 1.7 | ± 2 |
| Gender, Male/Female Units: participants | | | |
| Female | 5 | 16 | 6 |
| Male | 11 | 15 | 7 |

| Reporting group values | Cohort 4 | Total | |
|--|----------|-------|--|
| Number of subjects | 43 | 103 | |
| Age categorical Units: Subjects | | | |
| Children (2-11 years) | 1 | 61 | |
| Adolescents (12-17 years) | 42 | 42 | |
| Age Continuous Units: years | | | |
| arithmetic mean | 14 | | |
| standard deviation | ± 1.6 | - | |
| Gender, Male/Female Units: participants | | | |
| Female | 27 | 54 | |
| Male | 16 | 49 | |

Subject analysis sets

| | |
|--|-------------------------|
| Subject analysis set title | Response |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants with plasma HIV-1 RNA <48 copies/mL at Week 48 using Missing, Switch, Discontinuation'=Failure (MSDF) algorithm. | |
| Subject analysis set title | PDVF |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants with protocol-defined virologic failure | |
| Subject analysis set title | Other Failure/Remainder |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants who discontinued due to other reasons. | |
| Subject analysis set title | Cohort 1 (Grade 3) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=2 - <6 years of age, MVC liquid formulation | |
| Subject analysis set title | Cohort 1 (Grade 4) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=2 - <6 years of age, MVC liquid formulation | |
| Subject analysis set title | Cohort 2 (Grade 3) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=6 - <12 years of age, MVC tablet formulation | |
| Subject analysis set title | Cohort 2 (Grade 4) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=6 - <12 years of age, MVC tablet formulation | |
| Subject analysis set title | Cohort 3 (Grade 3) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=6 - <12 years of age, MVC liquid formulation | |
| Subject analysis set title | Cohort 3 (Grade 4) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=6- <12years of age, MVC liquid formulation | |
| Subject analysis set title | Cohort 4 (Grade 3) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=12 - <18 years of age, MVC tablet formulation | |
| Subject analysis set title | Cohort 4 (Grade 4) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=12 - <18 years of age, MVC tablet formulation | |

| Reporting group values | Response | PDVF | Other Failure/Remainder |
|------------------------|----------|------|-------------------------|
| Number of subjects | 44 | 23 | 30 |

| | | | |
|--|-----|-----|-----|
| Age categorical Units: Subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 0 | 0 | 0 |
| standard deviation | ± 0 | ± 0 | ± 0 |
| Gender, Male/Female Units: participants | | | |
| Female | 0 | 0 | 0 |
| Male | 0 | 0 | 0 |

| | | | |
|--|--------------------|--------------------|--------------------|
| Reporting group values | Cohort 1 (Grade 3) | Cohort 1 (Grade 4) | Cohort 2 (Grade 3) |
| Number of subjects | 16 | 16 | 31 |
| Age categorical Units: Subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 0 | 0 | 0 |
| standard deviation | ± 0 | ± 0 | ± 0 |
| Gender, Male/Female Units: participants | | | |
| Female | 0 | 0 | 0 |
| Male | 0 | 0 | 0 |

| | | | |
|--|--------------------|--------------------|--------------------|
| Reporting group values | Cohort 2 (Grade 4) | Cohort 3 (Grade 3) | Cohort 3 (Grade 4) |
| Number of subjects | 31 | 13 | 13 |
| Age categorical Units: Subjects | | | |
| Children (2-11 years) | 0 | 0 | 0 |
| Adolescents (12-17 years) | 0 | 0 | 0 |
| Age Continuous Units: years | | | |
| arithmetic mean | 0 | 0 | 0 |
| standard deviation | ± 0 | ± 0 | ± 0 |
| Gender, Male/Female Units: participants | | | |
| Female | 0 | 0 | 0 |
| Male | 0 | 0 | 0 |

| | | | |
|------------------------------------|--------------------|--------------------|--|
| Reporting group values | Cohort 4 (Grade 3) | Cohort 4 (Grade 4) | |
| Number of subjects | 43 | 43 | |
| Age categorical Units: Subjects | | | |
| Children (2-11 years) | 0 | 0 | |
| Adolescents (12-17 years) | 0 | 0 | |

| | | | |
|---------------------|-----|-----|--|
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 0 | 0 | |
| standard deviation | ± 0 | ± 0 | |
| Gender, Male/Female | | | |
| Units: participants | | | |
| Female | 0 | 0 | |
| Male | 0 | 0 | |

End points

End points reporting groups

| | |
|--|-------------------------|
| Reporting group title | Cohort 1 |
| Reporting group description: >=2 - <6 years of age, MVC liquid formulation | |
| Reporting group title | Cohort 2 |
| Reporting group description: >=6 - <12 years of age, MVC tablet formulation | |
| Reporting group title | Cohort 3 |
| Reporting group description: >=6 - <12 years of age, MVC liquid formulation | |
| Reporting group title | Cohort 4 |
| Reporting group description: >=12 - <18 years of age, MVC tablet formulation | |
| Subject analysis set title | Response |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants with plasma HIV-1 RNA <48 copies/mL at Week 48 using Missing, Switch, Discontinuation'=Failure (MSDF) algorithm. | |
| Subject analysis set title | PDVF |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants with protocol-defined virologic failure | |
| Subject analysis set title | Other Failure/Remainder |
| Subject analysis set type | Full analysis |
| Subject analysis set description: Participants who discontinued due to other reasons. | |
| Subject analysis set title | Cohort 1 (Grade 3) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=2 - <6 years of age, MVC liquid formulation | |
| Subject analysis set title | Cohort 1 (Grade 4) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=2 - <6 years of age, MVC liquid formulation | |
| Subject analysis set title | Cohort 2 (Grade 3) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=6 - <12 years of age, MVC tablet formulation | |
| Subject analysis set title | Cohort 2 (Grade 4) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=6 - <12 years of age, MVC tablet formulation | |
| Subject analysis set title | Cohort 3 (Grade 3) |
| Subject analysis set type | Safety analysis |
| Subject analysis set description: >=6 - <12 years of age, MVC liquid formulation | |
| Subject analysis set title | Cohort 3 (Grade 4) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

>=6- <12years of age, MVC liquid formulation

| | |
|----------------------------|--------------------|
| Subject analysis set title | Cohort 4 (Grade 3) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

>=12 - <18 years of age, MVC tablet formulation

| | |
|----------------------------|--------------------|
| Subject analysis set title | Cohort 4 (Grade 4) |
| Subject analysis set type | Safety analysis |

Subject analysis set description:

>=12 - <18 years of age, MVC tablet formulation

Primary: Pharmacokinetic (PK) Parameters for participants with data in Stage 1 enrolled in Stage 2 – Week 2 and Week 48

| | |
|-----------------|---|
| End point title | Pharmacokinetic (PK) Parameters for participants with data in Stage 1 enrolled in Stage 2 – Week 2 and Week 48 ^[1] |
|-----------------|---|

End point description:

A PK analysis was performed using PK data from participants that participated in Stage 1 (PK Populations 2 and 3) where intensive MVC PK data were available at Week 2. The primary aim of this analysis was to describe and summarize MVC PK parameters at Week 2 and Week 48 by cohort and OBT group. Geometric Coefficient of Variation is defined as the geometric standard deviation to the power of the reciprocal of the geometric mean. PK analysis was also performed for Population 2 (subset of APS 1) consisting of all Stage 1 participants who had a Week 2 full PK profile; and for Population 3 (subset of APS 1) consisting of all Stage 1 participants who had an approved dose for Stage 2 / met the PK target.

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

End point timeframe:

Week 2 and Week 48 (0, 1, 2, 4, 6, 8, 12 hours post-dose)

Notes:

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

Justification: No statistical analyses were done.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|---|------------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 8 | 8 | 12 |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| Cavg-Week2 | 237.34 (± 63) | 260.65 (± 43) | 264.45 (± 62) | 239.85 (± 67) |
| Cavg-Week 48 | 163.73 (± 146) | 289.69 (± 50) | 168.62 (± 117) | 199.12 (± 78) |
| Cmax-Week2 | 581.47 (± 69) | 546.8 (± 51) | 444.37 (± 61) | 530.8 (± 62) |
| Cmax-Week 48 | 334.68 (± 156) | 593.68 (± 25) | 284.96 (± 128) | 423.32 (± 48) |
| Cmin-Week2 | 18.97 (± 202208) | 100.02 (± 39) | 115.84 (± 90) | 56.17 (± 145) |
| Cmin-Week 48 | 48.11 (± 180) | 82.21 (± 120) | 60.03 (± 245) | 66.51 (± 140) |

Statistical analyses

No statistical analyses for this end point

Primary: PK Parameters for Stage 1 participants Enrolled in Stage 2 – Week 2 and Week 48 Results for Stage 2 doses - AUCtau (Area under the curve at steady state)

| | |
|-----------------|--|
| End point title | PK Parameters for Stage 1 participants Enrolled in Stage 2 – |
|-----------------|--|

End point description:

A PK analysis was performed using PK data from participants that participated in Stage 1 (PK Populations 2 and 3) where intensive MVC PK data were available at Week 2. The primary aim of this analysis was to describe and summarize MVC PK parameters (AUCtau) at Week 2 and Week 48 by cohort and OBT group. Correlations between MVC PK and efficacy as well as compliance were also assessed. PK analysis was also performed for Population 2 (subset of APS 1) consisting of all Stage 1 participants who had a Week 2 full PK profile; and for Population 3 (subset of APS 1) consisting of all Stage 1 participants who had an approved dose for Stage 2 / met the PK target.

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

End point timeframe:

Week 2 and Week 48 (0, 1, 2, 4, 6, 8, 12 hours post-dose)

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 statistical analyses were done.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|---|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 8 | 8 | 12 |
| Units: ng*hr/mL | | | | |
| geometric mean (geometric coefficient of variation) | | | | |
| AUCtau - Week 2 | 2848.1 (± 63) | 3127.7 (± 43) | 3173.4 (± 62) | 2878.2 (± 67) |
| AUCtau - Week 48 | 1964.7 (± 146) | 3476.3 (± 50) | 2023.5 (± 117) | 2389.4 (± 78) |

Statistical analyses

No statistical analyses for this end point

Primary: PK Parameters for Stage 1 participants Enrolled in Stage 2 – Week 2 and Week 48 Results for Stage 2 doses - Tmax (Time at maximum concentration)

| | |
|-----------------|---|
| End point title | PK Parameters for Stage 1 participants Enrolled in Stage 2 – Week 2 and Week 48 Results for Stage 2 doses - Tmax (Time at maximum concentration) ^[3] |
|-----------------|---|

End point description:

A PK analysis was performed using PK data from participants that participated in Stage 1 (PK Populations 2 and 3) where intensive MVC PK data were available at Week 2. The primary aim of this analysis was to describe and summarize MVC PK parameters (Tmax) at Week 2 and Week 48 by cohort and OBT group. Correlations between MVC PK and efficacy as well as compliance were also assessed. PK analysis was also performed for Population 2 (subset of APS 1) consisting of all Stage 1 participants who had a Week 2 full PK profile; and for Population 3 (subset of APS 1) consisting of all Stage 1 participants who had an approved dose for Stage 2 / met the PK target.

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

End point timeframe:

Week 2 and Week 48 (0, 1, 2, 4, 6, 8, 12 hours post-dose)

Notes:

[3] - 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 statistical analyses were done.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|-------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 9 | 8 | 8 | 12 |
| Units: hour | | | | |
| median (full range (min-max)) | | | | |
| Tmax - Week 2 | 2 (0.97 to 6) | 4 (0.75 to 6) | 2 (1 to 4) | 2 (1 to 4) |
| Tmax - Week 48 | 2 (0 to 6.03) | 2 (1 to 8) | 3 (0 to 6) | 2 (1 to 4) |

Statistical analyses

No statistical analyses for this end point

Primary: Incidence and Severity of Grade 3 and Grade 4 Treatment-Emergent Adverse Events (All Causality)

| | |
|-----------------|--|
| End point title | Incidence and Severity of Grade 3 and Grade 4 Treatment-Emergent Adverse Events (All Causality) ^[4] |
|-----------------|--|

End point description:

Safety analysis was performed on all participants who received at least 1 dose of study drug. It was assessed by spontaneous reports, physical examination and laboratory test results in all participants who received at least 1 dose of study drug. The investigator used the Division of AIDS (DAIDS) version 4 Table for Grading the Severity of Adult and Pediatric AEs.

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

End point timeframe:

48 weeks

Notes:

[4] - 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 statistical analyses were done.

| End point values | Cohort 1 (Grade 3) | Cohort 1 (Grade 4) | Cohort 2 (Grade 3) | Cohort 2 (Grade 4) |
|--|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 16 | 16 | 31 | 31 |
| Units: Number of events | | | | |
| Gastrointestinal disorders - Vomiting | 1 | 0 | 0 | 0 |
| Hepat. disorders - Drug-induced liver injury | 0 | 0 | 0 | 0 |
| Infections and infestations - H1N1 influenza | 0 | 0 | 0 | 0 |
| Infections and infestations - Pneumonia | 0 | 0 | 0 | 0 |
| Investigations - Lipase increased | 0 | 1 | 0 | 0 |
| Psychiatric disorder - Bipolar disorder | 0 | 0 | 1 | 0 |

| End point values | Cohort 3 (Grade 3) | Cohort 3 (Grade 4) | Cohort 4 (Grade 3) | Cohort 4 (Grade 4) |
|---------------------------------------|----------------------|----------------------|----------------------|----------------------|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | Subject analysis set |
| Number of subjects analysed | 13 | 13 | 43 | 43 |
| Units: Number of events | | | | |
| Gastrointestinal disorders - Vomiting | 0 | 0 | 0 | 0 |

| | | | | |
|--|---|---|---|---|
| Hepat. disorders - Drug-induced liver injury | 0 | 0 | 0 | 1 |
| Infections and infestations - H1N1 influenza | 0 | 0 | 1 | 0 |
| Infections and infestations - Pneumonia | 1 | 0 | 1 | 0 |
| Investigations - Lipase increased | 0 | 0 | 0 | 0 |
| Pyschiatric disorder - Bipolar disorder | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Primary: Treatment discontinuation secondary to Serious Adverse Event (SAE) related to study drug

| | |
|-----------------|---|
| End point title | Treatment discontinuation secondary to Serious Adverse Event (SAE) related to study drug ^[5] |
|-----------------|---|

End point description:

The primary reason for a participant discontinuing from study drug or the clinical study was recorded in the source documents as well as the case report form. A discontinuation had to be reported immediately to the study medical monitor or his/her designated representative if it was due to an SAE. Safety analysis was performed on all participants who received at least 1 dose of study drug. In this study, there was no treatment discontinuation secondary to Serious Adverse Event (SAE) related to study drug.

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

End point timeframe:

Week 48

Notes:

[5] - 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 statistical analyses were done.

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|-----------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 16 | 31 | 13 | 43 |
| Units: participants | 0 | 0 | 0 | 0 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV1 RNA <400 copies/mL through Week 48 (MSDF)

| | |
|-----------------|--|
| End point title | Percentage of participants with HIV1 RNA <400 copies/mL through Week 48 (MSDF) |
|-----------------|--|

End point description:

The proportion of participants who achieved HIV-1 RNA <400 copies/mL at week 24 or 48 was assessed according to Food and Drug Administration's (FDA's) MSDF Snapshot algorithm. The algorithm uses the plasma HIV-1 RNA in the Week 24 or 48 visit window, follows the "virology-first principle" and considers a participant who has a missing plasma HIV-1 RNA, or switches to prohibited ARV regimen or discontinues from the study or study drug for any reason, or dies, as a failure. The percentage of participants is reported below.

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

End point timeframe:
Week 24 and Week 48 post-treatment

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 16 | 31 | 13 | 43 |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 68.8 | 90.3 | 69.2 | 62.8 |
| Week 48 | 75 | 77.4 | 69.2 | 51.2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV1 RNA <48 copies/mL through Week 48 (MSDF)

| | |
|-----------------|---|
| End point title | Percentage of participants with HIV1 RNA <48 copies/mL through Week 48 (MSDF) |
|-----------------|---|

End point description:

The proportion of participants who achieved HIV-1 RNA <48 copies/mL at week 24 or 48 was assessed according to Food and Drug Administration's (FDA's) MSDF Snapshot algorithm. The algorithm uses the plasma HIV-1 RNA in the Week 24 or 48 visit window, follows the "virology-first principle" and considers a participant who has a missing plasma HIV-1 RNA, or switches to prohibited ARV regimen or discontinues from the study or study drug for any reason, or dies, as a failure. The percentage of participants is reported below. The FAS consisted of all participants who received at least 1 dose of study drug.

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

End point timeframe:
Week 24 and Week 48 post-treatment

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 16 | 31 | 13 | 43 |
| Units: percentage of participants | | | | |
| number (not applicable) | | | | |
| Week 24 | 18.75 | 64.5 | 61.5 | 48.8 |
| Week 48 | 50 | 51.6 | 61.5 | 39.5 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HIV-1 RNA Levels <400 copies/mL at Weeks 24 and 48 using Missing, Discontinuation = Failure (MD=F) Approach

| | |
|-----------------|---|
| End point title | Percentage of Participants with HIV-1 RNA Levels <400 copies/mL at Weeks 24 and 48 using Missing, Discontinuation = Failure (MD=F) Approach |
|-----------------|---|

End point description:

Participants who have been discontinued from the study, have been lost to follow-up, or have missing HIV-1 RNA data prior to the time point of interest were considered to have HIV-1 RNA levels > lower limit of quantification (LLOQ) . This will be referred to as [non-completer = failure; NC=F] or [missing, discontinuation = failure; MD=F]. The proportion of participants (100*n/N) is reported below. The FAS consisted of all participants who received at least 1 dose of study drug.

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

End point timeframe:

Week 24 and Week 48 post-treatment

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|-----------------------------------|---------------------|---------------------|---------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 16 | 31 | 13 | 43 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 24 (n=10, 27, 8, 27) | 62.5 (38.8 to 86.2) | 87.1 (75.3 to 98.9) | 69.2 (44.1 to 94.3) | 62.8 (48.3 to 77.2) |
| Week 48 (n=12, 23, 9, 22) | 75 (53.8 to 96.2) | 74.2 (58.8 to 89.6) | 69.2 (44.1 to 94.3) | 51.2 (36.2 to 66.1) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with HIV-1 RNA Levels < 48 copies/mL at Weeks 24 and 48 using MD=F Approach

| | |
|-----------------|--|
| End point title | Percentage of Participants with HIV-1 RNA Levels < 48 copies/mL at Weeks 24 and 48 using MD=F Approach |
|-----------------|--|

End point description:

Participants who have been discontinued from the study, have been lost to follow-up, or have missing HIV-1 RNA data prior to the time point of interest were considered to have HIV-1 RNA levels > lower limit of quantification (LLOQ) . This will be referred to as [non-completer = failure; NC=F] or [missing, discontinuation = failure; MD=F]. The proportion of participants (100*n/N) is reported below. The FAS consisted of all participants who received at least 1 dose of study drug.

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

End point timeframe:

Week 24 and Week 48 post-treatment

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|-----------------------------------|-------------------|---------------------|-------------------|---------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 16 | 31 | 13 | 43 |
| Units: Percentage of Participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 24 (n=3, 20, 8, 21) | 18.8 (0 to 37.9) | 64.5 (47.7 to 81.4) | 61.5 (35.1 to 89) | 48.8 (33.9 to 63.8) |
| Week 48 (n=8, 16, 8, 17) | 50 (25.5 to 74.5) | 51.6 (34 to 69.2) | 61.5 (35.1 to 89) | 39.5 (24.9 to 54.2) |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with HIV-1 RNA < 400 copies/mL and <48 copies/mL using the time to loss of virologic response algorithm (TLOVR) at Week 48

| | |
|------------------------|---|
| End point title | Percentage of participants with HIV-1 RNA < 400 copies/mL and <48 copies/mL using the time to loss of virologic response algorithm (TLOVR) at Week 48 |
| End point description: | TLOVR is defined as the time from first dose of study medication (Day 1) until the time of virologic failure using the a TLOVR algorithm. The FAS consisted of all participants who received at least 1 dose of study drug. |
| End point type | Secondary |
| End point timeframe: | Week 48 |

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|-----------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 16 | 31 | 13 | 43 |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| <400 copies/mL; TLOVR Responder | 62.5 | 74.2 | 69.2 | 48.8 |
| <48 copies/mL; TLOVR Responder | 43.8 | 54.8 | 46.2 | 44.2 |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants with $\geq 1.0 \log_{10}$ reduction in HIV-1RNA concentration from baseline to Week 24 and Week 48

| | |
|------------------------|---|
| End point title | Percentage of Participants with $\geq 1.0 \log_{10}$ reduction in HIV-1RNA concentration from baseline to Week 24 and Week 48 |
| End point description: | Percentage of participants with at least a $1.0 \log_{10}$ reduction in HIV-1 RNA from baseline to Week 24 |

and Week 48 were tabulated and is presented below. The number of participants with an observation at specified time points were used to calculate the percentage.

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

End point timeframe:

Week 24 and Week 48 post-treatment

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|-----------------------------------|----------------------|----------------------|------------------|----------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 16 | 31 | 13 | 43 |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | | | | |
| Week 24 | 92.3 (77.8 to 106.8) | 100 (100 to 100) | 100 (100 to 100) | 93.1 (83.9 to 102.3) |
| Week 48 | 100 (100 to 100) | 96.2 (88.8 to 103.6) | 100 (100 to 100) | 88 (75.3 to 100.7) |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Change from Baseline in HIV-1 RNA (Original) by Visit

| | |
|-----------------|--|
| End point title | Summary of Change from Baseline in HIV-1 RNA (Original) by Visit |
|-----------------|--|

End point description:

Plasma HIV-1 RNA was determined using the Roche COBAS AmpliPrep/COBAS TaqMan HIV-1 Test (lower limit of quantification [LLOQ] <48 copies/mL). Blood samples were taken at the time points indicated in the participant evaluation schedule. Screening HIV-1 RNA >1000 copies/ml was used to determine eligibility for the study. The FAS consisted of all participants who received at least 1 dose of study drug. LOCF was used to impute missing values.

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

End point timeframe:

Week 24 and Week 48 post-treatment

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|---|-------------------------|----------------------|-----------------------|------------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 15 | 31 | 12 | 39 |
| Units: copies/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change from Baseline - Original - Week 24 | -271974.6 (± 391843.59) | -38764 (± 63688.93) | -58081 (± 79720.33) | -57325.7 (± 172108.62) |
| Change from Baseline - Original - Week 48 | -267834.2 (± 378896.88) | -34787.7 (± 60222.6) | -56351.7 (± 76231.03) | -55321.1 (± 173840.55) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in cluster of differentiation 4 (CD4+) cell count at weeks 24 and 48

| | |
|-----------------|---|
| End point title | Change from Baseline in cluster of differentiation 4 (CD4+) cell count at weeks 24 and 48 |
|-----------------|---|

End point description:

Change from baseline in CD4 cell count to Week 24 and Week 48 were tabulated in aggregated and broken down by age cohort using summary statistics. The FAS consisted of all participants who received at least 1 dose of study drug. LOCF was used to impute missing values.

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

End point timeframe:

Week 24 and Week 48 post-treatment

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 15 | 30 | 12 | 39 |
| Units: cells/mm ³ | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 | 232.7 (± 381.6) | 355.8 (± 294) | 213.9 (± 166.4) | 173.6 (± 203.6) |
| Week 48 | 275.9 (± 363.4) | 362.7 (± 373.5) | 167.3 (± 150.9) | 168.6 (± 211) |

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in CD4+ % at weeks 24 and 48

| | |
|-----------------|---|
| End point title | Change from Baseline in CD4+ % at weeks 24 and 48 |
|-----------------|---|

End point description:

Change from baseline in CD4 % to Week 24 and Week 48 were tabulated in aggregated and broken down by age cohort using summary statistics. The FAS consisted of all participants who received at least 1 dose of study drug. LOCF was used to impute missing values.

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

End point timeframe:

Week 24 and Week 48 post-treatment

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|--------------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 15 | 31 | 12 | 39 |
| Units: percentage of CD4+ cells | | | | |
| arithmetic mean (standard deviation) | | | | |
| Week 24 (n=15, 31, 12, 39) | 7.3 (± 5) | 3.8 (± 7.4) | 3.5 (± 4) | 3.8 (± 6.1) |
| Week 48 (n=15, 31, 12, 39) | 7.5 (± 7.6) | 6 (± 6.8) | 2.5 (± 4.2) | 4.6 (± 6.5) |

Statistical analyses

No statistical analyses for this end point

Secondary: Protocol Defined Virologic Failure

| | |
|---|------------------------------------|
| End point title | Protocol Defined Virologic Failure |
| End point description: | |
| <p>The occurrence of any one of the following criteria would constitute Virologic failure: A=Decrease from Baseline plasma HIV-1 RNA <1 log₁₀ and plasma HIV-1 RNA >400 copies/mL starting at Week 12 and confirmed at consecutive Week 16; B=Decrease from Baseline plasma HIV-1 RNA <2.0 log₁₀ and plasma HIV-1 RNA >400 copies/mL at Week 24 OR plasma HIV-1 RNA >10,000 copies/mL on and after Week 24, and confirmed within 14 to 21 days; C=Increase from nadir plasma HIV-1 RNA of ≥1 log₁₀ (≥1,000 copies/mL if nadir plasma HIV-1 RNA <48 copies/mL) at any time, and confirmed within 14 to 21 days. The FAS consisted of all participants who received at least 1 dose of study drug.</p> | |
| End point type | Secondary |
| End point timeframe: | |
| Week 48 | |

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|-------------------------------|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 16 | 31 | 13 | 43 |
| Units: Number of participants | | | | |
| A (measure description above) | 0 | 2 | 1 | 5 |
| B (measure description above) | 0 | 0 | 0 | 0 |
| C (measure description above) | 3 | 3 | 2 | 8 |
| Number of PDVF | 3 | 5 | 3 | 13 |

Statistical analyses

No statistical analyses for this end point

Secondary: Shift Table of Viral Tropism between Screening and Confirmed PDVF Prior to Week 48

| | |
|--|--|
| End point title | Shift Table of Viral Tropism between Screening and Confirmed PDVF Prior to Week 48 |
| End point description: | |
| <p>Virus tropism was determined using the Monogram Biosciences Trofile™ viral tropism assay. A shift table of the change in detected tropism from screening to the time of failure was produced in the aggregate</p> | |

and also broken down by age cohort. Participants who experienced confirmed PDVF through Week 48 with sufficient plasma HIV-1 RNA for virology analysis while receiving MVC. One participant was excluded from summary tables as classified as MSDF response; one participant was analyzed after stopping treatment.

| | |
|-----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| Screening and Week 48 | |

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|--|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 4 | 3 | 12 |
| Units: Number of participants | | | | |
| With valid on-treatment results | 2 | 4 | 3 | 11 |
| Tropism at Confirmed PDVF R5 | 2 | 3 | 2 | 9 |
| Tropism at Confirmed PDVF DM | 0 | 1 | 1 | 2 |
| Tropism at Confirmed PDVF X4 | 0 | 0 | 0 | 0 |
| Tropism at Confirmed PDVF Not Reportable | 1 | 0 | 0 | 1 |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of the Emergence of reverse transcriptase inhibitor (RTI) and protease inhibitor (PI) resistance associated mutations (RAMs) Between Screening and On-Treatment Confirmed PDVF: Total and by Cohort Prior to Week 48

| | |
|-----------------|--|
| End point title | Summary of the Emergence of reverse transcriptase inhibitor (RTI) and protease inhibitor (PI) resistance associated mutations (RAMs) Between Screening and On-Treatment Confirmed PDVF: Total and by Cohort Prior to Week 48 |
|-----------------|--|

End point description:

Phenotypic and genotypic susceptibility to reverse transcriptase and protease inhibitors was evaluated at screening using the Monogram Biosciences PhenoSense™ GT (PSGT) assay. Samples from a confirmatory PDVF visit or early termination of MVC were planned to be analyzed if the plasma HIV-1 RNA was ≥ 400 copies/mL. Participants with more than one mutation are counted more than once. One participant was excluded from summary tables as classified as MSDF response; one participant was analyzed after stopping treatment.

| | |
|----------------------|-----------|
| End point type | Secondary |
| End point timeframe: | |
| 48 weeks | |

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|--|-----------------|-----------------|-----------------|-----------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 3 | 4 | 3 | 12 |
| Units: Number of participants | | | | |
| With valid on-treatment results | 2 | 4 | 3 | 11 |
| PI Minor (L10L/F, L89L/I/M, V77V/I and K20K/R) | 0 | 0 | 2 | 3 |
| PI Major | 0 | 0 | 0 | 0 |
| NNRTI (K103K/N and K103N) | 0 | 1 | 1 | 1 |
| NRTI M184V | 0 | 0 | 1 | 0 |
| Total with emergence | 0 | 1 | 3 | 4 |

Statistical analyses

No statistical analyses for this end point

Secondary: Optimized Background Treatment (OBT) Susceptibility Scores (Net/Overall) by Outcome

| | |
|-----------------|---|
| End point title | Optimized Background Treatment (OBT) Susceptibility Scores (Net/Overall) by Outcome |
|-----------------|---|

End point description:

Outcome (Response, PDVF or other/remainder) was summarized by the total ARV activity of the background regimen using simple and weighted totals (TOBT and p-wTOBTss, respectively) in the aggregate, categorized as 0, 1, ≥ 2 (TOBT) and 0 0.5, 1 1.5 and ≥ 2 (p-wOBTss) respectively, as well as by screening genotype. Six participants (Response: n=5; Other failure: n=1) failed to have successful PhenoSense GT analysis at screening, and so a net susceptibility score was not generated. One more participant was not included in the wOBTss analysis due to failed phenotype analysis. However, net susceptibility scores were imputed for simple analysis based on genotype. The FAS consisted of all participants who received at least 1 dose of study drug. Susceptibility scores indicate the level resistance to the study medication. Scores include: 1 = susceptible and potential low-level resistance; 0.5 = low and intermediate-level resistance; 0 = high-level resistance.

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

End point timeframe:

48 weeks

| End point values | Response | PDVF | Other Failure/Remainder | |
|-----------------------------------|----------------------|----------------------|-------------------------|--|
| Subject group type | Subject analysis set | Subject analysis set | Subject analysis set | |
| Number of subjects analysed | 49 | 23 | 31 | |
| Units: Percentage of participants | | | | |
| number (not applicable) | | | | |
| Simple score 0 | 0 | 0 | 0 | |
| Simple score 1.0 | 8.2 | 4.3 | 0 | |
| Simple score ≥ 2.0 | 81.6 | 95.7 | 96.8 | |
| Weighted score 0-0.5 | 6.1 | 30.4 | 29 | |
| Weighted score 1.0-1.5 | 53.1 | 65.2 | 29 | |
| Weighted score ≥ 2.0 | 28.6 | 4.3 | 38.7 | |

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Change from Baseline in HIV-1 RNA (Log10 copies/mL) by Visit

| | |
|------------------------|--|
| End point title | Summary of Change from Baseline in HIV-1 RNA (Log10 copies/mL) by Visit |
| End point description: | Plasma HIV-1 RNA was determined using the Roche COBAS AmpliPrep/COBAS TaqMan HIV-1 Test (lower limit of quantification [LLOQ] <48 copies/mL). Blood samples were taken at the time points indicated in the participant evaluation schedule. Screening HIV-1 RNA >1000 copies/ml was used to determine eligibility for the study. |
| End point type | Secondary |
| End point timeframe: | Week 24 and Week 48 post-treatment |

| End point values | Cohort 1 | Cohort 2 | Cohort 3 | Cohort 4 |
|--|--------------------|--------------------|--------------------|--------------------|
| Subject group type | Reporting group | Reporting group | Reporting group | Reporting group |
| Number of subjects analysed | 15 | 31 | 12 | 39 |
| Units: Log10 Copies/mL | | | | |
| arithmetic mean (standard deviation) | | | | |
| Change from Baseline - Log10 - Week 24 | -2.4853 (± 1.1421) | -2.2324 (± 0.8668) | -2.1756 (± 1.1854) | -1.6482 (± 1.3806) |
| Change from Baseline - Log10 - Week 48 | -2.5831 (± 1.2148) | -1.9579 (± 1.0861) | -2.0549 (± 1.2125) | -1.4591 (± 1.4477) |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From the day the informed consent form was signed up to 30 days after last dose was administered.

Adverse event reporting additional description:

The same event may appear as both an AE and a SAE. However, what is presented are distinct events. An event may be categorized as serious in one participant and as non-serious in another participant, or one participant may have experienced both a serious and non-serious event during the study.

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

Dictionary used

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

| | |
|--------------------|------|
| Dictionary version | 18.0 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|----------|
| Reporting group title | Cohort 1 |
|-----------------------|----------|

Reporting group description:

>=2 - <6 years of age, MVC liquid formulation

| | |
|-----------------------|----------|
| Reporting group title | Cohort 2 |
|-----------------------|----------|

Reporting group description:

>=6 - <12 years of age, MVC tablet formulation

| | |
|-----------------------|----------|
| Reporting group title | Cohort 3 |
|-----------------------|----------|

Reporting group description:

>=6 - <12 years of age, MVC liquid formulation

| | |
|-----------------------|----------|
| Reporting group title | Cohort 4 |
|-----------------------|----------|

Reporting group description:

>=12 - <18 years of age, MVC tablet formulation

| Serious adverse events | Cohort 1 | Cohort 2 | Cohort 3 |
|---|-----------------|-----------------|-----------------|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 5 / 31 (16.13%) | 3 / 13 (23.08%) |
| number of deaths (all causes) | 0 | 0 | 0 |
| number of deaths resulting from adverse events | 0 | 0 | 0 |
| Investigations | | | |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| | | | |
|---|----------------|----------------|----------------|
| Gastrointestinal disorders | | | |
| Gastric fistula | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Gastritis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Vomiting | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Hepatobiliary disorders | | | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Respiratory, thoracic and mediastinal disorders | | | |
| Hyperventilation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Skin and subcutaneous tissue disorders | | | |
| Prurigo | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Psychiatric disorders | | | |
| Bipolar disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Musculoskeletal and connective tissue disorders | | | |

| | | | |
|---|----------------|----------------|----------------|
| Osteopenia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 1 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tendon disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Infections and infestations | | | |
| Abscess oral | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 1 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Cellulitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| H1N1 influenza | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pelvic inflammatory disease | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pneumonia | | | |

| | | | |
|---|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 1 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 1 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |
| deaths causally related to treatment / all | 0 / 0 | 0 / 0 | 0 / 0 |

| Serious adverse events | Cohort 4 | | |
|--|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 9 / 43 (20.93%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Investigations | | | |
| Transaminases increased | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Gastric fistula | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastritis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hepatobiliary disorders | | | |
| Drug-induced liver injury | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Hyperventilation | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Skin and subcutaneous tissue disorders | | | |
| Prurigo | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Bipolar disorder | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Osteopenia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tendon disorder | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Abscess oral | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Bronchopneumonia | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cellulitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| H1N1 influenza | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pelvic inflammatory disease | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences causally related to treatment / all | 0 / 4 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pulmonary tuberculosis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences causally related to treatment / all | 0 / 0 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

Frequency threshold for reporting non-serious adverse events: 2 %

| Non-serious adverse events | Cohort 1 | Cohort 2 | Cohort 3 |
|--|------------------|------------------|------------------|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 11 / 16 (68.75%) | 22 / 31 (70.97%) | 10 / 13 (76.92%) |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) | | | |
| Skin papilloma | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Fatigue | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Influenza like illness | | | |

| | | | |
|--|----------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Malaise subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 2 | 0 / 13 (0.00%) 0 |
| Pyrexia subjects affected / exposed occurrences (all) | 2 / 16 (12.50%) 3 | 1 / 31 (3.23%) 1 | 2 / 13 (15.38%) 2 |
| Immune system disorders Allergy to arthropod bite subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Reproductive system and breast disorders Amenorrhoea subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 2 | 0 / 13 (0.00%) 0 |
| Breast enlargement subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Breast mass subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Breast pain subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Dysmenorrhoea subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Vaginal discharge subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 2 | 0 / 13 (0.00%) 0 |
| Bronchospasm | | | |

| | | | |
|-----------------------------|----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Catarrh | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Cough | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 6 / 31 (19.35%) | 2 / 13 (15.38%) |
| occurrences (all) | 2 | 12 | 3 |
| Epistaxis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Hyperventilation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Nasal congestion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 1 | 1 |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Pharyngeal disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Productive cough | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Respiratory disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis allergic | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 31 (6.45%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Rhinorrhoea | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 31 (6.45%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 5 | 2 |
| Rhonchi | | | |

| | | | |
|--|--|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Psychiatric disorders | | | |
| Attention deficit/hyperactivity disorder | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Depression | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Hallucination | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Insomnia | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Nightmare | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Panic disorder | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Investigations | | | |
| Blood HIV RNA increased | Additional description: From informed consent to 30 days after last MVC dose and within a frequency threshold of 2%. | | |
| subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Blood alkaline phosphatase increased | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Blood creatine phosphokinase increased | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Blood iron decreased | | | |
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Blood phosphorus decreased | | | |

| | | | |
|--|--|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Cardiac murmur | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Hepatic enzyme abnormal | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Hepatic enzyme increased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 1 | 0 | 2 |
| Lipase increased | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Neutrophil count decreased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral load increased | Additional description: From informed consent to 30 days after last MVC dose and within a frequency threshold of 2%. | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Weight decreased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Weight increased | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Injury, poisoning and procedural complications | | | |
| Accidental exposure to product | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropod bite | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Arthropod sting | | | |

| | | | |
|-----------------------------|----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Contusion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 31 (6.45%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Fall | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Head injury | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Injury | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Limb injury | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Muscle strain | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Overdose | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Skin abrasion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Thermal burn | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Underdose | | | |

| | | | |
|---|---------------------|---------------------|----------------------|
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Wound subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Cardiac disorders Cardiac disorder subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Epilepsy subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Generalised tonic-clonic seizure subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 3 | 0 / 13 (0.00%) 0 |
| Headache subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 2 / 13 (15.38%) 2 |
| Lethargy subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 1 / 13 (7.69%) 1 |
| Mental retardation subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 2 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Somnolence subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Tension headache subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| Anaemia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Iron deficiency anaemia subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Lymphadenitis subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Lymphadenopathy subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Ear and labyrinth disorders Deafness subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Eye disorders Conjunctival pallor subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 2 | 0 / 13 (0.00%) 0 |
| Conjunctivitis allergic subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 2 / 31 (6.45%) 2 | 0 / 13 (0.00%) 0 |
| Hypermetropia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Refraction disorder subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Abdominal pain subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 1 / 13 (7.69%) 1 |
| Abdominal pain lower | | | |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Abdominal pain upper | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Anal pruritus | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Cheilitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Constipation | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Dental caries | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 1 | 2 |
| Diarrhoea | | | |
| subjects affected / exposed | 6 / 16 (37.50%) | 3 / 31 (9.68%) | 3 / 13 (23.08%) |
| occurrences (all) | 11 | 3 | 3 |
| Dyspepsia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Flatulence | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gingival swelling | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Mouth ulceration | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 1 | 0 | 1 |
| Nausea | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 3 / 31 (9.68%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Odynophagia | | | |

| | | | |
|--|-----------------|-----------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Proctitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Salivary gland mucocoele | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tongue disorder | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Toothache | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Vomiting | | | |
| subjects affected / exposed | 5 / 16 (31.25%) | 8 / 31 (25.81%) | 3 / 13 (23.08%) |
| occurrences (all) | 14 | 9 | 4 |
| Hepatobiliary disorders | | | |
| Hepatotoxicity | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Skin and subcutaneous tissue disorders | | | |
| Acanthosis nigricans | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acne | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Dermatitis allergic | | | |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Dermatitis diaper | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Dry skin | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Ecchymosis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Eczema | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Papule | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Prurigo | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Rash | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 1 / 31 (3.23%) | 1 / 13 (7.69%) |
| occurrences (all) | 4 | 3 | 1 |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 2 / 13 (15.38%) |
| occurrences (all) | 0 | 0 | 2 |
| Urticaria | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Urticaria papular | | | |

| | | | |
|--|---------------------|---------------------|---------------------|
| subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 31 (6.45%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Back pain | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bone swelling | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bursitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Joint swelling | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Musculoskeletal discomfort | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Myofascial pain syndrome | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Osteoporosis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Pain in extremity | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 1 | 1 |
| Infections and infestations | | | |
| Abscess | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Acarodermatitis | | | |

| | | | |
|-----------------------------|-----------------|----------------|-----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Acute tonsillitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Bacterial vaginosis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Bronchitis | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 3 / 31 (9.68%) | 0 / 13 (0.00%) |
| occurrences (all) | 8 | 12 | 0 |
| Bullous impetigo | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Conjunctivitis | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Cystitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Ear infection | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Gastroenteritis | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 0 / 31 (0.00%) | 2 / 13 (15.38%) |
| occurrences (all) | 3 | 0 | 2 |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Gingivitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Herpes virus infection | | | |

| | | | |
|-----------------------------|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Impetigo | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Influenza | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 31 (3.23%) | 3 / 13 (23.08%) |
| occurrences (all) | 1 | 1 | 3 |
| Latent tuberculosis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Lice infestation | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 31 (6.45%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 4 / 31 (12.90%) | 0 / 13 (0.00%) |
| occurrences (all) | 5 | 5 | 0 |
| Oral herpes | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 2 / 31 (6.45%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 3 | 0 |
| Otitis externa | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Otitis media | | | |
| subjects affected / exposed | 5 / 16 (31.25%) | 1 / 31 (3.23%) | 1 / 13 (7.69%) |
| occurrences (all) | 7 | 1 | 1 |
| Otitis media acute | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 2 / 31 (6.45%) | 0 / 13 (0.00%) |
| occurrences (all) | 9 | 2 | 0 |
| Otitis media chronic | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 0 | 0 |
| Paronychia | | | |

| | | | |
|-----------------------------|-----------------|----------------|----------------|
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Parotitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Oropharyngeal candidiasis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Pneumonia | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 3 / 31 (9.68%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 3 | 0 |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Rhinitis | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 5 | 1 | 0 |
| Sinobronchitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 2 / 31 (6.45%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 2 | 0 |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 1 | 0 |
| Tinea capitis | | | |
| subjects affected / exposed | 2 / 16 (12.50%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 2 | 1 | 0 |
| Tinea faciei | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Tinea infection | | | |

| | | | |
|---|-----------------|-----------------|-----------------|
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 2 / 31 (6.45%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 2 | 0 |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 1 / 13 (7.69%) |
| occurrences (all) | 0 | 0 | 1 |
| Tracheitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Tuberculosis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 5 / 16 (31.25%) | 7 / 31 (22.58%) | 2 / 13 (15.38%) |
| occurrences (all) | 18 | 9 | 2 |
| Varicella | | | |
| subjects affected / exposed | 1 / 16 (6.25%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 1 | 0 | 0 |
| Viral infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 3 / 16 (18.75%) | 2 / 31 (6.45%) | 3 / 13 (23.08%) |
| occurrences (all) | 4 | 2 | 4 |
| Vulvovaginitis | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Wound infection | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 0 / 31 (0.00%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 0 | 0 |
| Lipodystrophy acquired | | | |
| subjects affected / exposed | 0 / 16 (0.00%) | 1 / 31 (3.23%) | 0 / 13 (0.00%) |
| occurrences (all) | 0 | 1 | 0 |
| Metabolism and nutrition disorders | | | |

| | | | |
|---|---------------------|---------------------|---------------------|
| Decreased appetite subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Dehydration subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Hypertriglyceridaemia subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 2 | 0 / 13 (0.00%) 0 |
| Hypokalaemia subjects affected / exposed occurrences (all) | 1 / 16 (6.25%) 1 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |
| Insulin resistance subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 1 / 31 (3.23%) 1 | 0 / 13 (0.00%) 0 |
| Vitamin D deficiency subjects affected / exposed occurrences (all) | 0 / 16 (0.00%) 0 | 0 / 31 (0.00%) 0 | 0 / 13 (0.00%) 0 |

| Non-serious adverse events | Cohort 4 | | |
|---|---------------------|--|--|
| Total subjects affected by non-serious adverse events subjects affected / exposed | 34 / 43 (79.07%) | | |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) Skin papilloma subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | | |
| General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Fatigue subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |

| | | | |
|---|----------------------|--|--|
| Influenza like illness subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Malaise subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Pyrexia subjects affected / exposed occurrences (all) | 5 / 43 (11.63%) 7 | | |
| Immune system disorders Allergy to arthropod bite subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Reproductive system and breast disorders Amenorrhoea subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Breast enlargement subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Breast mass subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Breast pain subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Dysmenorrhoea subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Vaginal discharge subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Respiratory, thoracic and mediastinal disorders Asthma subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |

| | | | |
|-----------------------------|----------------|--|--|
| Bronchospasm | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Catarrh | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cough | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 4 | | |
| Epistaxis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hyperventilation | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Nasal congestion | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Oropharyngeal pain | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Pharyngeal disorder | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Productive cough | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Respiratory disorder | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis allergic | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Rhinorrhoea | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences (all) | 2 | | |

| | | | |
|--|---------------------|--|--|
| Rhonchi subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Psychiatric disorders | | | |
| Attention deficit/hyperactivity disorder subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Depression subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | | |
| Hallucination subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Insomnia subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Nightmare subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Panic disorder subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Investigations | | | |
| Blood HIV RNA increased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | Additional description: From informed consent to 30 days after last MVC dose and within a frequency threshold of 2%. | |
| Blood alkaline phosphatase increased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Blood creatine phosphokinase increased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Blood iron decreased subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |

| | | | |
|--|---------------------|--|--|
| Blood phosphorus decreased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Cardiac murmur subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Hepatic enzyme abnormal subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Hepatic enzyme increased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Lipase increased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Neutrophil count decreased subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 3 | | |
| Viral load increased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | Additional description: From informed consent to 30 days after last MVC dose and within a frequency threshold of 2%. | |
| Weight decreased subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Weight increased subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Injury, poisoning and procedural complications | | | |
| Accidental exposure to product subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Arthropod bite subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Arthropod sting | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Contusion | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Fall | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Foot fracture | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Head injury | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Injury | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ligament sprain | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Limb injury | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Muscle strain | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Overdose | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Skin abrasion | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Thermal burn | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Underdose | | | |

| | | | |
|---|-----------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Wound subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Cardiac disorders Cardiac disorder subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Nervous system disorders Dizziness subjects affected / exposed occurrences (all) | 3 / 43 (6.98%) 4 | | |
| Epilepsy subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Generalised tonic-clonic seizure subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Headache subjects affected / exposed occurrences (all) | 7 / 43 (16.28%) 10 | | |
| Lethargy subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Mental retardation subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Somnolence subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Tension headache subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 8 | | |
| Blood and lymphatic system disorders | | | |

| | | | |
|--|----------------------|--|--|
| Anaemia subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 3 | | |
| Iron deficiency anaemia subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Lymphadenitis subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Lymphadenopathy subjects affected / exposed occurrences (all) | 5 / 43 (11.63%) 5 | | |
| Ear and labyrinth disorders Deafness subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Eye disorders Conjunctival pallor subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Conjunctivitis allergic subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Hypermetropia subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Refraction disorder subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Gastrointestinal disorders Abdominal discomfort subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Abdominal pain subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 5 | | |
| Abdominal pain lower | | | |

| | | | |
|-----------------------------|------------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Anal pruritus | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Cheilitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Constipation | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences (all) | 3 | | |
| Dental caries | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 10 / 43 (23.26%) | | |
| occurrences (all) | 12 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 2 | | |
| Flatulence | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gingival swelling | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Mouth ulceration | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Nausea | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | | |
| occurrences (all) | 5 | | |
| Odynophagia | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Proctitis | | | |
| subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Salivary gland mucocoele | | | |
| subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Tongue disorder | | | |
| subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Toothache | | | |
| subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Vomiting | | | |
| subjects affected / exposed occurrences (all) | 4 / 43 (9.30%) 7 | | |
| Hepatobiliary disorders | | | |
| Hepatotoxicity | | | |
| subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | | |
| Skin and subcutaneous tissue disorders | | | |
| Acanthosis nigricans | | | |
| subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Acne | | | |
| subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | | |
| Dermatitis | | | |
| subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | | |
| Dermatitis allergic | | | |

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|-----------------------------|----------------|--|--|
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Dermatitis contact | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dermatitis diaper | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Dry skin | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Ecchymosis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Eczema | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Papule | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Prurigo | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rash | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Rash pruritic | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Skin lesion | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urticaria | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Urticaria papular | | | |

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|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | | |
| Back pain subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Bone swelling subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Bursitis subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Joint swelling subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Musculoskeletal discomfort subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Myofascial pain syndrome subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Osteoporosis subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Infections and infestations | | | |
| Abscess subjects affected / exposed occurrences (all) | 2 / 43 (4.65%) 2 | | |
| Acarodermatitis | | | |

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|-----------------------------|-----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Acute tonsillitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Bacterial vaginosis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Bronchitis | | | |
| subjects affected / exposed | 6 / 43 (13.95%) | | |
| occurrences (all) | 7 | | |
| Bullous impetigo | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Conjunctivitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Cystitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Ear infection | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Fungal skin infection | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gastroenteritis | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences (all) | 2 | | |
| Gastroenteritis viral | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Gingivitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Herpes virus infection | | | |

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|-----------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Hordeolum | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Impetigo | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Influenza | | | |
| subjects affected / exposed | 4 / 43 (9.30%) | | |
| occurrences (all) | 4 | | |
| Latent tuberculosis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Lice infestation | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 4 | | |
| Oral herpes | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otitis externa | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences (all) | 2 | | |
| Otitis media | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otitis media acute | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Otitis media chronic | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Paronychia | | | |

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|----------------------------------|----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Parotitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Pharyngitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Oropharyngeal candidiasis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Pharyngotonsillitis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Pneumonia bacterial | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Rhinitis | | | |
| subjects affected / exposed | 3 / 43 (6.98%) | | |
| occurrences (all) | 5 | | |
| Sinobronchitis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Sinusitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Tinea capitis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tinea faciei | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tinea infection | | | |

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|---|-----------------|--|--|
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tonsillitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Tooth abscess | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Tracheitis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Tuberculosis | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 1 | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 5 / 43 (11.63%) | | |
| occurrences (all) | 5 | | |
| Varicella | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Viral infection | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 3 | | |
| Viral upper respiratory tract infection | | | |
| subjects affected / exposed | 1 / 43 (2.33%) | | |
| occurrences (all) | 2 | | |
| Vulvovaginitis | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Wound infection | | | |
| subjects affected / exposed | 2 / 43 (4.65%) | | |
| occurrences (all) | 2 | | |
| Lipodystrophy acquired | | | |
| subjects affected / exposed | 0 / 43 (0.00%) | | |
| occurrences (all) | 0 | | |
| Metabolism and nutrition disorders | | | |

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|---|---------------------|--|--|
| Decreased appetite subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Dehydration subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Hyperglycaemia subjects affected / exposed occurrences (all) | 0 / 43 (0.00%) 0 | | |
| Hypertriglyceridaemia subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Hypokalaemia subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Insulin resistance subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |
| Vitamin D deficiency subjects affected / exposed occurrences (all) | 1 / 43 (2.33%) 1 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|------------------|---|
| 22 October 2009 | Amendment 1: Cut-off value for HIV RNA was assay added. Complete abstinence was added as an acceptable form of contraception. Grapefruit-related citrus fruits such as Seville oranges and pomelos were added to the list of concomitant medications to ensure MVC PK was not affected. Instructions for stringent liver function test monitoring were added. |
| 16 August 2010 | Amendment 2: ViiV Healthcare was added as the new Sponsor. Sparse PK Sampling was removed at the Early Termination Visits. It was clarified that confirmation virologic failure visit to be conducted 14-21 Days after participant withdrawal. Visit window for Isod visits changed to 1 month. Exclusion criteria for creatinine clearance was mentioned as <90 ml/min. Reference to "Sterilization" and "Post-Menopausal" was deleted. Supply of OBT was clarified. It was clarified that Isoniazid may be allowed on an individual basis and that rifampin was only allowed during Stage 2. It was clarified that an alternate method to Trofile assay could be performed if Trofile assay was not reportable. It was added that an alternate method to PhenoSense GT if result is not reportable. It was clarified that virus susceptibility to MVC would be done at the same time points as the virus susceptibility to OBT. |
| 03 December 2010 | Amendment 3: (Country Specific: Kenya and Uganda): It was clarified that local labs may be used for safety testing for sites in Kenya and Uganda. New safety language was added to the AE section. |
| 25 February 2011 | Amendment 4: (Country Specific: Brazil): It was clarified that the Sponsor would cover the cost of OBTs if not covered under the Brazil National Program. New safety language was added to the AE section. |
| 01 June 2011 | Amendment 5: Information was added to the "Subject Withdrawal" section. Exposure in Utero was renamed Exposure during pregnancy and more instructions were added. Additional details were added to the "Communication of Results by Sponsor" section. The Schedule of Activities section was updated to state that the Screening Period ended on Day 1 and that the follow up period window was increased up to 1 month (this was also done elsewhere it was mentioned in the protocol). It was clarified that in the subjects who had X4 or dual/mixed tropic virus at time of failure, HIV-1 RNA and tropism would be collected at the first ISOD Follow Up visit. It was clarified that the screening BSA will be utilized for initial MVC dose. The objectives of the population PK analyses were clarified. |
| 10 June 2012 | Amendment 6: (Country Specific: Brazil): It was clarified that the Sponsor would cover the cost of OBTs if not covered under the Brazil National Program. |
| 09 August 2012 | Amendment 7: Appendix 1 was modified (Liver enzyme monitoring to be the same as other ongoing MVC studies). Appendix 5 was added (Rationale for initial MVC dose change for participants not on potent CYP3A4 inhibitors). Appendix 6 was added (Specific for sites in Brazil). Appendix 7 was added (Division of AIDS Table for Grading the Severity of Adult and Pediatric Adverse Events). Changes made were aligned with CT-3: a. Reported medication error as adverse events regardless of whether it is accompanied by an AE. b. AE reporting section was updated. |
| 30 December 2013 | Amendment 8: The protocol was amended to extend and ensure the continued supply of the study drug beyond 5 years to participants benefitting from therapy. It was clarified that the Sponsor would cover the cost of OBTs if it was not covered under the Brazil National Program. |

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| 19 May 2014 | Amendment 9: In "Schedule of Activities" section and wherever applicable, it was a.) added that at the End of Study visit and follow-up contact, unused medications had to be returned. b.) clarified that study visits in the follow-up period would be up to Week 261. Follow up Visit 9 was added in the Schedule of Activities. The rationale was that the protocol used 52 weeks to equate to a year, however IMPALA drug management system used 48 weeks to equate to a year, resulting in a 5 month gap at the end of 5 years of follow up. c.) clarified that the window in follow-up period was updated to 14days. The rationale was to be consistent with IMPALA drug management system. d.) added that "Contraception Check" would be done at all study visits, per new protocol template. e.) added that creatinine phosphokinase, lipid profile, free T4, TSH and Hepatitis C Virus RNA from Early Termination, were done to be consistent with follow-up period. |
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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.

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| The Participant Flow section, mentioning "Overall Study" has data only for participant discontinuations up to Week 48, as the study is ongoing. The planned enrollment per protocol was 125 participants, however, 103 participants enrolled in the study. |
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Notes: