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)	EMEA-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>=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:

>=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:

>=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:

>=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 –

	Week 2 and Week 48 Results for Stage 2 doses - AUCtau (Area under the curve at steady state)[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
Pyschiatric 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 >= 1.0 log10 reduction in HIV-1RNA concentration from baseline to Week 24 and Week 48

End point title	Percentage of Participants with >= 1.0 log10 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 log10 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:

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.

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:

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

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; oneparticipant 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	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Malaise			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Pyrexia			
subjects affected / exposed	2 / 16 (12.50%)	1 / 31 (3.23%)	2 / 13 (15.38%)
occurrences (all)	3	1	2
Immune system disorders			
Allergy to arthropod bite			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Amenorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Breast enlargement			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Breast mass			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Breast pain			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Dysmenorrhoea			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Vaginal discharge			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	2	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	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Depression			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Hallucination			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Nightmare			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Panic disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	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	1 / 16 (6.25%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Blood iron decreased			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	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	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Wound			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Epilepsy			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	3	0
Headache			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	2 / 13 (15.38%)
occurrences (all)	0	1	2
Lethargy			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	1 / 13 (7.69%)
occurrences (all)	0	0	1
Mental retardation			
subjects affected / exposed	1 / 16 (6.25%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	2	0	0
Somnolence			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Tension headache			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	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 (all)	0	0	0
Iron deficiency anaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Lymphadenitis			
subjects affected / exposed	1 / 16 (6.25%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Lymphadenopathy			
subjects affected / exposed	1 / 16 (6.25%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Conjunctival pallor			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Conjunctivitis allergic			
subjects affected / exposed	1 / 16 (6.25%)	2 / 31 (6.45%)	0 / 13 (0.00%)
occurrences (all)	1	2	0
Hypermetropia			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Refraction disorder			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	1 / 13 (7.69%)
occurrences (all)	0	1	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	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	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	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Hypertriglyceridaemia			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	2	0
Hypokalaemia			
subjects affected / exposed	1 / 16 (6.25%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	1	0	0
Insulin resistance			
subjects affected / exposed	0 / 16 (0.00%)	1 / 31 (3.23%)	0 / 13 (0.00%)
occurrences (all)	0	1	0
Vitamin D deficiency			
subjects affected / exposed	0 / 16 (0.00%)	0 / 31 (0.00%)	0 / 13 (0.00%)
occurrences (all)	0	0	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	2 / 43 (4.65%)		
occurrences (all)	2		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Fatigue			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	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	1 / 43 (2.33%)		
occurrences (all)	1		
Psychiatric disorders			
Attention deficit/hyperactivity disorder			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	2		
Hallucination			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Nightmare			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Panic disorder			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
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	0 / 43 (0.00%)		
occurrences (all)	0		
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Blood iron decreased			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		

Blood phosphorus decreased			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Cardiac murmur			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Hepatic enzyme abnormal			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Hepatic enzyme increased			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Lipase increased			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Neutrophil count decreased			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	3		
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 / 43 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Weight increased			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Injury, poisoning and procedural complications			
Accidental exposure to product			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Arthropod bite			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	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	1 / 43 (2.33%)		
occurrences (all)	1		
Wound			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 43 (6.98%)		
occurrences (all)	4		
Epilepsy			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	7 / 43 (16.28%)		
occurrences (all)	10		
Lethargy			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Mental retardation			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Tension headache			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	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	1 / 43 (2.33%)		
occurrences (all)	1		
Proctitis			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Salivary gland mucocoele			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Tongue disorder			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Toothache			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	4 / 43 (9.30%)		
occurrences (all)	7		
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Hyperbilirubinaemia			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Acanthosis nigricans			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Acne			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	2		
Dermatitis			
subjects affected / exposed	2 / 43 (4.65%)		
occurrences (all)	2		
Dermatitis allergic			

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				

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

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				

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				

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				

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			

Decreased appetite			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Dehydration			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 43 (0.00%)		
occurrences (all)	0		
Hypertriglyceridaemia			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Hypokalaemia			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Insulin resistance			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	1		
Vitamin D deficiency			
subjects affected / exposed	1 / 43 (2.33%)		
occurrences (all)	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 addded 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 addded to the AE section.
01 June 2011	Amendment 5: Information was added to the "Subject Withdrawal" section. Exposure in Utero was renames 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.

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.

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.

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.

Notes: