Clinical trial results:
A Study of the Comparative Bioavailability of Two Second-Generation Investigational Pediatric Oral Granule Formulations of MK-1439 Compared to the Adult Formulation

Summary

EudraCT number	2016-004656-30
Trial protocol	Outside EU/EEA
Global end of trial date	26 July 2016

Results information

Result version number	v1 (current)
This version publication date	11 August 2017
First version publication date	11 August 2017

Trial information

Trial identification

Sponsor protocol code	1439-052

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Merck Sharp & Dohme Corp.
Sponsor organisation address	2000 Galloping Hill Road, Kenilworth, NJ, United States, 07033
Public contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com
Scientific contact	Clinical Trials Disclosure, Merck Sharp & Dohme Corp., ClinicalTrialsDisclosure@merck.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-001676-PIP01-14
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 July 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 July 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of the study are as follows: 1. To evaluate the comparative bioavailability of the MK-1439 100 mg adult formulation tablets under fasting conditions to MK-1439 100 mg investigational oral pediatric uncoated and coated granule formulation under fasting conditions; 2. To evaluate the comparative bioavailability of the MK-1439 100 mg oral pediatric uncoated granule formulation under fasting conditions to MK-1439 100 mg investigational oral pediatric uncoated granule formulation when given with vanilla pudding and with applesauce; 3. To evaluate the comparative bioavailability of the MK-1439 100 mg investigational oral pediatric coated granule formulation under fasting conditions to MK-1439 100 mg investigational oral pediatric uncoated granule formulation when given with vanilla pudding and with applesauce.

Protection of trial subjects:

This study was conducted in conformance with Good Clinical Practice standards and applicable country and/or local statutes and regulations regarding ethical committee review, informed consent, and the protection of human subjects participating in biomedical research.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 May 2016
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 24
Worldwide total number of subjects	24
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This is an open-label, single-dose, partially randomized, five-period, seven treatment, six-sequence, crossover, comparative bioavailability study. Each participant was assigned to 1 of 6 treatment sequences.

Pre-assignment

Screening details:

Study was to enroll healthy, non-smoking, male and female subjects, from 18 to 55 years of age. Other inclusion and exclusion criteria applied.

Period 1

Period 1 title	Period 1
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence ABCWX

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MK-1439 Adult formulation (Treatment A)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose administered after an overnight fast of at least 10 hours

Arm title	Sequence ACBXW

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MK-1439 Adult formulation (Treatment A)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose administered after an overnight fast of at least 10 hours

Arm title	Sequence BACWX

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric uncoated oral granules formulation (Treatment B)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of uncoated granules administered after an overnight fast of at least 10 hours

Arm title	Sequence BCAZY
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric uncoated oral granules formulation (Treatment B)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of uncoated granules administered after an overnight fast of at least 10 hours

Arm title	Sequence CABYZ
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation (Treatment C)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of coated granules administered after an overnight fast of at least 10 hours

Arm title	Sequence CBAZY
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation (Treatment C)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of coated granules administered after an overnight fast of at least 10 hours

Number of subjects in period 1	Sequence ABCWX	Sequence ACBXW	Sequence BACWX
Started	4	4	4
Completed	4	4	4

Number of subjects in period 1	Sequence BCAZY	Sequence CABYZ	Sequence CBAZY
Started	4	4	4
Completed	4	4	4

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence ABCWX

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg pediatric uncoated oral granules formulation (Treatment B)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of uncoated granules administered after an overnight fast of at least 10 hours

Arm title	Sequence ACBXW

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation (Treatment C)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of coated granules administered after an overnight fast of at least 10 hours

Arm title	Sequence BACWX

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MK-1439 Adult formulation (Treatment A)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose administered after an overnight fast of at least 10 hours

Arm title	Sequence BCAZY

Arm description: -

Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation (Treatment C)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of coated granules administered after an overnight fast of at least 10 hours

Arm title	Sequence CABYZ
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 Adult formulation (Treatment A)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Single oral 100 mg dose administered after an overnight fast of at least 10 hours	

Arm title	Sequence CBAZY
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric uncoated oral granules formulation (Treatment B)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use
Dosage and administration details: Single oral 100 mg dose of uncoated granules administered after an overnight fast of at least 10 hours	

Number of subjects in period 2	Sequence ABCWX	Sequence ACBXW	Sequence BACWX
Started	4	4	4
Completed	4	4	4
Not completed	0	0	0
Suspected multiple study participation	-	-	-

Number of subjects in period 2	Sequence BCAZY	Sequence CABYZ	Sequence CBAZY
Started	4	4	4
Completed	4	4	3
Not completed	0	0	1
Suspected multiple study participation	-	-	1

Period 3

Period 3 title	Period 3
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes

Arm title	Sequence ABCWX
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation (Treatment C)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use
Dosage and administration details: Single oral 100 mg dose of coated granules administered after an overnight fast of at least 10 hours	

Arm title	Sequence ACBXW
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric uncoated oral granules formulation (Treatment B)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use
Dosage and administration details: Single oral 100 mg dose of uncoated granules administered after an overnight fast of at least 10 hours	

Arm title	Sequence BACWX
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation (Treatment C)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use
Dosage and administration details: Single oral 100 mg dose of coated granules administered after an overnight fast of at least 10 hours	

Arm title	Sequence BCAZY
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 Adult formulation (Treatment A)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use
Dosage and administration details: Single oral 100 mg dose administered after an overnight fast of at least 10 hours	

Arm title	Sequence CABYZ
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric uncoated oral granules formulation (Treatment B)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules

Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of uncoated granules administered after an overnight fast of at least 10 hours

Arm title	Sequence CBAZY
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 Adult formulation (Treatment A)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose administered after an overnight fast of at least 10 hours

Number of subjects in period 3	Sequence ABCWX	Sequence ACBXW	Sequence BACWX
Started	4	4	4
Completed	4	4	4

Number of subjects in period 3	Sequence BCAZY	Sequence CABYZ	Sequence CBAZY
Started	4	4	3
Completed	4	4	3

Period 4

Period 4 title	Period 4
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence ABCWX
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric uncoated oral granules formulation with vanilla pudding (Treatment W)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of uncoated granules administered with vanilla pudding after an overnight fast of at least 10 hours

Arm title	Sequence ACBXW
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric uncoated oral granules formulation with applesauce (Treatment X)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of uncoated granules administered with apple sauce after an overnight fast of at least 10 hours

Arm title	Sequence BACWX
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric uncoated oral granules formulation with vanilla pudding (Treatment W)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of uncoated granules administered with vanilla pudding after an overnight fast of at least 10 hours

Arm title	Sequence BCAZY
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation with applesauce (Treatment Z)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of coated granules administered with apple sauce after an overnight fast of at least 10 hours

Arm title	Sequence CABYZ
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation with vanilla pudding (Treatment Y)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of coated granules administered with vanilla pudding after an overnight fast of at least 10 hours

Arm title	Sequence CBAZY
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation with applesauce (Treatment Z)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of coated granules administered with apple sauce after an overnight fast of at least 10 hours

Number of subjects in period 4	Sequence ABCWX	Sequence ACBXW	Sequence BACWX
Started	4	4	4
Completed	4	4	4
Not completed	0	0	0
Adverse event, non-fatal	-	-	-

Number of subjects in period 4	Sequence BCAZY	Sequence CABYZ	Sequence CBAZY
Started	4	4	3
Completed	4	4	2
Not completed	0	0	1
Adverse event, non-fatal	-	-	1

Period 5

Period 5 title	Period 5
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Sequence ABCWX
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric uncoated oral granules formulation with applesauce (Treatment X)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of uncoated granules administered with apple sauce after an overnight fast of

at least 10 hours

Arm title	Sequence ACBXW
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric uncoated oral granules formulation with vanilla pudding (Treatment W)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of uncoated granules administered with vanilla pudding after an overnight fast of at least 10 hours

Arm title	Sequence BACWX
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric uncoated granules formulation with applesauce (Treatment X)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of uncoated granules administered with apple sauce after an overnight fast of at least 10 hours

Arm title	Sequence BCAZY
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation with vanilla pudding (Treatment Y)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of coated granules administered with vanilla pudding after an overnight fast of at least 10 hours

Arm title	Sequence CABYZ
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation with applesauce (Treatment Z)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of coated granules administered with apple sauce after an overnight fast of at least 10 hours

Arm title	Sequence CBAZY
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	MK-1439 100 mg (0.8 mg/granule) pediatric coated oral granules formulation with vanilla pudding (Treatment Y)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Single oral 100 mg dose of coated granules administered with vanilla pudding after an overnight fast of at least 10 hours

Number of subjects in period 5	Sequence ABCWX	Sequence ACBXW	Sequence BACWX
Started	4	4	4
Completed	4	4	4

Number of subjects in period 5	Sequence BCAZY	Sequence CABYZ	Sequence CBAZY
Started	4	4	2
Completed	4	4	2

Baseline characteristics

Reporting groups	
Reporting group title	Period 1
Reporting group description:	
All enrolled participants regardless of assigned sequence.	

Reporting group values	Period 1	Total	
Number of subjects	24	24	
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	41		
standard deviation	± 11	-	
Gender Categorical Units: Subjects			
Female	11	11	
Male	13	13	

End points

End points reporting groups

Reporting group title	Sequence ABCWX
Reporting group description: -	
Reporting group title	Sequence ACBXW
Reporting group description: -	
Reporting group title	Sequence BACWX
Reporting group description: -	
Reporting group title	Sequence BCAZY
Reporting group description: -	
Reporting group title	Sequence CABYZ
Reporting group description: -	
Reporting group title	Sequence CBAZY
Reporting group description: -	
Reporting group title	Sequence ABCWX
Reporting group description: -	
Reporting group title	Sequence ACBXW
Reporting group description: -	
Reporting group title	Sequence BACWX
Reporting group description: -	
Reporting group title	Sequence BCAZY
Reporting group description: -	
Reporting group title	Sequence CABYZ
Reporting group description: -	
Reporting group title	Sequence CBAZY
Reporting group description: -	
Reporting group title	Sequence ABCWX
Reporting group description: -	
Reporting group title	Sequence ACBXW
Reporting group description: -	
Reporting group title	Sequence BACWX
Reporting group description: -	
Reporting group title	Sequence BCAZY
Reporting group description: -	
Reporting group title	Sequence CABYZ
Reporting group description: -	
Reporting group title	Sequence CBAZY
Reporting group description: -	
Reporting group title	Sequence ABCWX
Reporting group description: -	
Reporting group title	Sequence ACBXW
Reporting group description: -	
Reporting group title	Sequence BACWX
Reporting group description: -	
Reporting group title	Sequence BCAZY
Reporting group description: -	
Reporting group title	Sequence CABYZ
Reporting group description: -	
Reporting group title	Sequence CBAZY

Reporting group description: -	
Reporting group title	Sequence ABCWX
Reporting group description: -	
Reporting group title	Sequence ACBXW
Reporting group description: -	
Reporting group title	Sequence BACWX
Reporting group description: -	
Reporting group title	Sequence BCAZY
Reporting group description: -	
Reporting group title	Sequence CABYZ
Reporting group description: -	
Reporting group title	Sequence CBAZY
Reporting group description: -	
Subject analysis set title	MK-1439 Adult Tablet (Treatment A)- Pooled
Subject analysis set type	Per protocol
Subject analysis set description:	
All participants that received single dose of 1 adult 100 mg tablet administered after an overnight fast of at least 10 hours regardless of assigned sequence.	
Subject analysis set title	Uncoated Granules (Treatment B) - Pooled
Subject analysis set type	Per protocol
Subject analysis set description:	
All participants that received a single dose of 100 mg pediatric uncoated oral granules administered after an overnight fast of at least 10 hours regardless of assigned sequence.	
Subject analysis set title	Coated Granules (Treatment C) - Pooled
Subject analysis set type	Per protocol
Subject analysis set description:	
All participants that received a single dose of 100 mg pediatric coated oral granules administered after an overnight fast of at least 10 hours regardless of assigned sequence.	
Subject analysis set title	Uncoated Granules with Vanilla Pudding (Treatment W) - Pooled
Subject analysis set type	Per protocol
Subject analysis set description:	
All participants that received 1 dose of 100 mg uncoated oral granules administered with vanilla pudding after an overnight fast of at least 10 hours regardless of assigned sequence	
Subject analysis set title	Uncoated Granules with Apple Sauce (Treatment X) - Pooled
Subject analysis set type	Per protocol
Subject analysis set description:	
All participants that received 1 dose of 100 mg uncoated oral granules administered with apple sauce after an overnight fast of at least 10 hours regardless of assigned sequence	
Subject analysis set title	Coated Granules with Vanilla Pudding (Treatment Y) - Pooled
Subject analysis set type	Per protocol
Subject analysis set description:	
All participants that received 1 dose of 100 mg coated oral granules administered with vanilla pudding after an overnight fast of at least 10 hours regardless of assigned sequence	
Subject analysis set title	Coated Granules with Apple Sauce (Treatment Z) - Pooled
Subject analysis set type	Per protocol
Subject analysis set description:	
All participants that received 1 dose of 100 mg coated oral granules administered with apple sauce after an overnight fast of at least 10 hours regardless of assigned sequence	

Primary: Area Under the Concentration Curve from 0 to infinity (AUCinf) of MK-1439 Following Single Oral Dose Administration of 100 mg Adult Tablet, 100 mg Pediatric Uncoated Granules and 100 mg Pediatric Coated Granules Under Fasted Conditions

End point title	Area Under the Concentration Curve from 0 to infinity (AUCinf) of MK-1439 Following Single Oral Dose Administration of 100 mg Adult Tablet, 100 mg Pediatric Uncoated Granules and 100 mg Pediatric Coated Granules Under Fasted Conditions

End point description:

Blood samples drawn prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration to determine the AUCinf

End point type	Primary

End point timeframe:

Prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration

End point values	MK-1439 Adult Tablet (Treatment A)- Pooled	Uncoated Granules (Treatment B) - Pooled	Coated Granules (Treatment C) - Pooled	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	23	24	24	
Units: hr·µM				
geometric mean (confidence interval 95%)	43.1 (37.7 to 49.3)	39.6 (34.3 to 45.7)	38.5 (33.9 to 43.7)	

Statistical analyses

Statistical analysis title	Uncoated Granules vs. Adult Tablet

Statistical analysis description:

Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values

Comparison groups	MK-1439 Adult Tablet (Treatment A)- Pooled v Uncoated Granules (Treatment B) - Pooled
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	Geometric Mean Ratio (GMR)
Point estimate	0.92
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.87
upper limit	0.97

Statistical analysis title	Coated Granules vs. Adult Tablet

Statistical analysis description:

Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on

natural log-transformed values

Comparison groups	MK-1439 Adult Tablet (Treatment A)- Pooled v Coated Granules (Treatment C) - Pooled
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	0.89
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.85
upper limit	0.94

Primary: Maximum Concentration (Cmax) of MK-1439 Following Single Oral Dose Administration of 100 mg Adult Tablet, 100 mg Pediatric Uncoated Granules and 100 mg Pediatric Coated Granules Under Fasted Conditions

End point title	Maximum Concentration (Cmax) of MK-1439 Following Single Oral Dose Administration of 100 mg Adult Tablet, 100 mg Pediatric Uncoated Granules and 100 mg Pediatric Coated Granules Under Fasted Conditions

End point description:

Blood samples drawn prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration to determine the AUCinf.

End point type	Primary

End point timeframe:

Prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration

End point values	MK-1439 Adult Tablet (Treatment A)- Pooled	Uncoated Granules (Treatment B) - Pooled	Coated Granules (Treatment C) - Pooled	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	23	24	24	
Units: nM				
geometric mean (confidence interval 95%)	2100 (1880 to 2340)	1950 (1780 to 2140)	1610 (1440 to 1790)	

Statistical analyses

Statistical analysis title	Uncoated Granules vs. Adult Tablet

Statistical analysis description:

Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values

Comparison groups	MK-1439 Adult Tablet (Treatment A)- Pooled v Uncoated Granules (Treatment B) - Pooled

Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	0.93
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.86
upper limit	1.01

Statistical analysis title	Coated Granules vs. Adult Tablet
Statistical analysis description:	
Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values	
Comparison groups	MK-1439 Adult Tablet (Treatment A)- Pooled v Coated Granules (Treatment C) - Pooled
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	0.77
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.7
upper limit	0.84

Primary: Concentration at 24 hours Post Dose (C24) of MK-1439 Following Single Oral Dose Administration of 100 mg Adult Tablet, 100 mg Pediatric Uncoated Granules and 100 mg Pediatric Coated Granules Under Fasted Conditions

End point title	Concentration at 24 hours Post Dose (C24) of MK-1439 Following Single Oral Dose Administration of 100 mg Adult Tablet, 100 mg Pediatric Uncoated Granules and 100 mg Pediatric Coated Granules Under Fasted Conditions
End point description:	
Blood sample taken at 24 hours post dose to determine the concentration of MK-1439	
End point type	Primary
End point timeframe:	
24 hours post dose	

End point values	MK-1439 Adult Tablet (Treatment A)- Pooled	Uncoated Granules (Treatment B) - Pooled	Coated Granules (Treatment C) - Pooled	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	23	24	24	
Units: nM				
geometric mean (confidence interval 95%)	650 (556 to 759)	622 (527 to 735)	615 (541 to 700)	

Statistical analyses

Statistical analysis title	Uncoated Granules vs. Adult Tablet
Statistical analysis description:	
Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values	
Comparison groups	MK-1439 Adult Tablet (Treatment A)- Pooled v Uncoated Granules (Treatment B) - Pooled
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	0.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.9
upper limit	1.02

Statistical analysis title	Coated Granules vs. Adult Tablet
Statistical analysis description:	
Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values	
Comparison groups	MK-1439 Adult Tablet (Treatment A)- Pooled v Coated Granules (Treatment C) - Pooled
Number of subjects included in analysis	47
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	0.95
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.89
upper limit	1.01

Primary: Area Under the Concentration Curve from 0 to infinity (AUCinf) of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Uncoated Granules Alone, with Vanilla Pudding or with Apple Sauce

End point title	Area Under the Concentration Curve from 0 to infinity (AUCinf) of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Uncoated Granules Alone, with Vanilla Pudding or with Apple Sauce

End point description:

Blood samples drawn prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration to determine the AUCinf

End point type	Primary

End point timeframe:

Prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration

End point values	Uncoated Granules (Treatment B) - Pooled	Uncoated Granules with Vanilla Pudding (Treatment W) - Pooled	Uncoated Granules with Apple Sauce (Treatment X) - Pooled	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	12	12	
Units: hr·µM				
geometric mean (confidence interval 95%)	39.6 (34.3 to 45.7)	43.7 (37.1 to 51.5)	51.2 (43.9 to 59.7)	

Statistical analyses

Statistical analysis title	Uncoated Granules With Pudding vs Without

Statistical analysis description:

Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values

Comparison groups	Uncoated Granules (Treatment B) - Pooled v Uncoated Granules with Vanilla Pudding (Treatment W) - Pooled
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	1.1
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.02
upper limit	1.19

Statistical analysis title	Uncoated Granules With Apple Sauce vs Without

Statistical analysis description:

Back-transformed least-squares mean difference and confidence interval from linear mixed-effects

model performed on natural log-transformed values

Comparison groups	Uncoated Granules (Treatment B) - Pooled v Uncoated Granules with Apple Sauce (Treatment X) - Pooled
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	1.29
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.2
upper limit	1.39

Primary: Maximum Concentration (Cmax) of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Uncoated Granules Alone, with Vanilla Pudding or with Apple Sauce

End point title	Maximum Concentration (Cmax) of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Uncoated Granules Alone, with Vanilla Pudding or with Apple Sauce

End point description:

Blood samples drawn prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration to determine the Cmax

End point type	Primary

End point timeframe:

Prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration

End point values	Uncoated Granules (Treatment B) - Pooled	Uncoated Granules with Vanilla Pudding (Treatment W) - Pooled	Uncoated Granules with Apple Sauce (Treatment X) - Pooled	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	12	12	
Units: nM				
geometric mean (confidence interval 95%)	1950 (1780 to 2140)	2030 (1750 to 2360)	3040 (2750 to 3370)	

Statistical analyses

Statistical analysis title	Uncoated Granules With Pudding vs Without

Statistical analysis description:

Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values

Comparison groups	Uncoated Granules (Treatment B) - Pooled v Uncoated Granules with Vanilla Pudding (Treatment W) - Pooled

Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	1.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.93
upper limit	1.17

Statistical analysis title	Uncoated Granules With Apple Sauce vs Without
Statistical analysis description:	
Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values	
Comparison groups	Uncoated Granules (Treatment B) - Pooled v Uncoated Granules with Apple Sauce (Treatment X) - Pooled
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	1.56
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.43
upper limit	1.7

Primary: Concentration at 24 hours Post Dose (C24) of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Uncoated Granules Alone, with Vanilla Pudding or with Apple Sauce

End point title	Concentration at 24 hours Post Dose (C24) of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Uncoated Granules Alone, with Vanilla Pudding or with Apple Sauce
End point description:	
Blood sample drawn at 24 hours post dose to determine the C24	
End point type	Primary
End point timeframe:	
24 hours post dose	

End point values	Uncoated Granules (Treatment B) - Pooled	Uncoated Granules with Vanilla Pudding (Treatment W) - Pooled	Uncoated Granules with Apple Sauce (Treatment X) - Pooled	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	12	12	
Units: nM				
geometric mean (confidence interval 95%)	622 (527 to 735)	645 (539 to 773)	743 (615 to 899)	

Statistical analyses

Statistical analysis title	Uncoated Granules With Pudding vs Without
Statistical analysis description:	
Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values	
Comparison groups	Uncoated Granules (Treatment B) - Pooled v Uncoated Granules with Vanilla Pudding (Treatment W) - Pooled
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	1.04
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.95
upper limit	1.13

Statistical analysis title	Uncoated Granules With Apple Sauce vs Without
Statistical analysis description:	
Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values	
Comparison groups	Uncoated Granules (Treatment B) - Pooled v Uncoated Granules with Apple Sauce (Treatment X) - Pooled
Number of subjects included in analysis	36
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	1.2
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.09
upper limit	1.31

Primary: Area Under the Concentration Curve from 0 to infinity (AUCinf) of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Coated Granules Alone, with Vanilla Pudding or with Apple Sauce

End point title	Area Under the Concentration Curve from 0 to infinity (AUCinf) of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Coated Granules Alone, with Vanilla Pudding or with Apple Sauce

End point description:

Blood samples drawn prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration to determine the AUCinf

End point type	Primary

End point timeframe:

Prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration

End point values	Coated Granules (Treatment C) - Pooled	Coated Granules with Vanilla Pudding (Treatment Y) - Pooled	Coated Granules with Apple Sauce (Treatment Z) - Pooled	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	10	11	
Units: hr·µM				
geometric mean (confidence interval 95%)	38.5 (33.9 to 43.7)	38.1 (32.3 to 44.9)	48.4 (42.5 to 55.1)	

Statistical analyses

Statistical analysis title	Coated Granules With Pudding vs Without

Statistical analysis description:

Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values

Comparison groups	Coated Granules (Treatment C) - Pooled v Coated Granules with Vanilla Pudding (Treatment Y) - Pooled
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	0.99
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.91
upper limit	1.07

Statistical analysis title	Uncoated Granules With Apple Sauce vs Without

Statistical analysis description:

Back-transformed least-squares mean difference and confidence interval from linear mixed-effects

model performed on natural log-transformed values

Comparison groups	Coated Granules (Treatment C) - Pooled v Coated Granules with Apple Sauce (Treatment Z) - Pooled
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	1.26
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.18
upper limit	1.34

Primary: Maximum Concentration (Cmax) of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Coated Granules Alone, with Vanilla Pudding or with Apple Sauce

End point title	Maximum Concentration (Cmax) of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Coated Granules Alone, with Vanilla Pudding or with Apple Sauce

End point description:

Blood samples drawn prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration to determine the Cmax

End point type	Primary

End point timeframe:

Prior to dosing (0-hour) and 0.5, 1, 1.5, 2, 2.5, 3, 4, 5, 6, 12, 24, 48, and 72 hours after drug administration

End point values	Coated Granules (Treatment C) - Pooled	Coated Granules with Vanilla Pudding (Treatment Y) - Pooled	Coated Granules with Apple Sauce (Treatment Z) - Pooled	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	10	11	
Units: nM				
geometric mean (confidence interval 95%)	1610 (1440 to 1790)	1460 (1230 to 1730)	2560 (2390 to 2760)	

Statistical analyses

Statistical analysis title	Coated Granules With Pudding vs Without

Statistical analysis description:

Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values

Comparison groups	Coated Granules (Treatment C) - Pooled v Coated Granules with Vanilla Pudding (Treatment Y) - Pooled

Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	0.9
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.79
upper limit	1.03

Statistical analysis title	Coated Granules With Apple Sauce vs Without
Statistical analysis description:	
Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values	
Comparison groups	Coated Granules (Treatment C) - Pooled v Coated Granules with Apple Sauce (Treatment Z) - Pooled
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	1.59
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.47
upper limit	1.73

Primary: Concentration at 24 hours Post Dose (C24)of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Coated Granules Alone, with Vanilla Pudding or with Apple Sauce

End point title	Concentration at 24 hours Post Dose (C24)of MK-1439 Following Single Oral Dose Administration of MK-1439 100 mg Pediatric Coated Granules Alone, with Vanilla Pudding or with Apple Sauce
End point description:	
Blood sample drawn at 24 hours after drug administration to determine the C24	
End point type	Primary
End point timeframe:	
24 hours post dose	

End point values	Coated Granules (Treatment C) - Pooled	Coated Granules with Vanilla Pudding (Treatment Y) - Pooled	Coated Granules with Apple Sauce (Treatment Z) - Pooled	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	24	10	11	
Units: nM				
geometric mean (confidence interval 95%)	615 (541 to 700)	588 (502 to 689)	745 (641 to 866)	

Statistical analyses

Statistical analysis title	Coated Granules With Pudding vs Without
Statistical analysis description:	
Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values	
Comparison groups	Coated Granules (Treatment C) - Pooled v Coated Granules with Vanilla Pudding (Treatment Y) - Pooled
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	0.96
Confidence interval	
level	90 %
sides	2-sided
lower limit	0.88
upper limit	1.04

Statistical analysis title	Coated Granules With Apple Sauce vs Without
Statistical analysis description:	
Back-transformed least-squares mean difference and confidence interval from linear mixed-effects model performed on natural log-transformed values	
Comparison groups	Coated Granules (Treatment C) - Pooled v Coated Granules with Apple Sauce (Treatment Z) - Pooled
Number of subjects included in analysis	35
Analysis specification	Pre-specified
Analysis type	other
Parameter estimate	GMR
Point estimate	1.21
Confidence interval	
level	90 %
sides	2-sided
lower limit	1.12
upper limit	1.3

Adverse events

Adverse events information	
Timeframe for reporting adverse events: up to 14 days post last dose	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Treatment A
Reporting group description: All participants that received single dose of 1 adult 100 mg tablet administered after an overnight fast of at least 10 hours regardless of assigned sequence.	
Reporting group title	Treatment B
Reporting group description: All participants that received a single dose of 125 pediatric uncoated oral granules administered after an overnight fast of at least 10 hours regardless of assigned sequence.	
Reporting group title	Treatment C
Reporting group description: All participants that received a single dose of 125 pediatric coated oral granules administered after an overnight fast of at least 10 hours regardless of assigned sequence.	
Reporting group title	Treatment W
Reporting group description: All participants that received 1 dose of 125 uncoated oral granules administered with vanilla pudding after an overnight fast of at least 10 hours regardless of assigned sequence	
Reporting group title	Treatment X
Reporting group description: All participants that received 1 dose of 125 uncoated oral granules administered with apple sauce after an overnight fast of at least 10 hours regardless of assigned sequence	
Reporting group title	Treatment Y
Reporting group description: All participants that received 1 dose of 125 coated oral granules administered with vanilla pudding after an overnight fast of at least 10 hours regardless of assigned sequence	
Reporting group title	Treatment Z
Reporting group description: All participants that received 1 dose of 125 coated oral granules administered with apple sauce after an overnight fast of at least 10 hours regardless of assigned sequence	

Serious adverse events	Treatment A	Treatment B	Treatment C
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Treatment W	Treatment X	Treatment Y
Total subjects affected by serious			

adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0

Serious adverse events	Treatment Z		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Treatment A	Treatment B	Treatment C
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)	7 / 24 (29.17%)	7 / 24 (29.17%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	1 / 24 (4.17%)
occurrences (all)	0	1	1
Somnolence			
subjects affected / exposed	0 / 23 (0.00%)	2 / 24 (8.33%)	2 / 24 (8.33%)
occurrences (all)	0	2	2
General disorders and administration site conditions			
Catheter site related reaction			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia oral			

subjects affected / exposed	0 / 23 (0.00%)	5 / 24 (20.83%)	4 / 24 (16.67%)
occurrences (all)	0	5	4
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Throat irritation			
subjects affected / exposed	0 / 23 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 23 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1

Non-serious adverse events	Treatment W	Treatment X	Treatment Y
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	5 / 12 (41.67%)	3 / 10 (30.00%)
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
General disorders and administration site conditions			
Catheter site related reaction			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			

Dry mouth			
subjects affected / exposed	0 / 12 (0.00%)	1 / 12 (8.33%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Hypoaesthesia oral			
subjects affected / exposed	0 / 12 (0.00%)	4 / 12 (33.33%)	0 / 10 (0.00%)
occurrences (all)	0	4	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Throat irritation			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Treatment Z		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 11 (0.00%)		
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Catheter site related reaction			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Fatigue			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Gastrointestinal disorders Dry mouth subjects affected / exposed occurrences (all) Hypoaesthesia oral subjects affected / exposed occurrences (all)	 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Rhinorrhoea subjects affected / exposed occurrences (all) Throat irritation subjects affected / exposed occurrences (all)	 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0		
Skin and subcutaneous tissue disorders Erythema subjects affected / exposed occurrences (all) Pruritus subjects affected / exposed occurrences (all)	 0 / 11 (0.00%) 0 0 / 11 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported