Clinical trial results:
A Phase 1, open-label, randomized, 3-way crossover study in 3 panels of healthy, adult subjects to assess the relative bioavailability of TMC207 following single-dose administration of two pediatric formulations using a 100-mg tablet formulation as the reference, with and without food.

Due to a system error, the data reported in v1 is not correct and has been removed from public view.

Summary

EudraCT number	2012-005492-13
Trial protocol	NL
Global end of trial date	26 August 2013

Results information

Result version number	v2 (current)
This version publication date	15 July 2016
First version publication date	06 August 2015
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	TMC207TBC1002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01803373
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen-Cilag International NV
Sponsor organisation address	Archimedesweg 29, Leiden, Netherlands, 233CM
Public contact	Clinical Registry Group, Janssen-Cilag International NV, +31 71524166, clinicaltrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen-Cilag International NV, +31 71524166, clinicaltrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	Yes
EMA paediatric investigation plan number(s)	EMEA-000912-PIP01-10
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 August 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective is to assess the relative bioavailability of TMC207 after single-dose administration of 100 mg of TMC207 as water dispersible tablets or granules using a 100-mg tablet formulation as the reference, with and without food.

Protection of trial subjects:

The safety assessments include clinical laboratory results (Haematology, Serum chemistry, Urinalysis) physical examination, electrocardiogram (ECG), vital signs, alcohol breath test and adverse events were monitored throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	16 April 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 36
Worldwide total number of subjects	36
EEA total number of subjects	36

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)	36

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 86 participants were Screened, among those 36 participants were randomized and received at least 1 dose of study drug.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Panel 1

Arm description:

Participants administered with treatment F001, G003 and G004 in six sequences with standard breakfast.

Arm type	Experimental
Investigational medicinal product name	Bedaquiline fumarate
Investigational medicinal product code	F001
Other name	TMC207
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants administered with Bedaquiline (TMC207) 100 mg as 1x100 mg tablet orally with approximately 240 mL of water once daily.

Investigational medicinal product name	Bedaquiline fumarate
Investigational medicinal product code	G003
Other name	TMC207
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Participants administered with Bedaquiline (TMC207) 100 mg as 5 X 20 mg Water dispersible tablets as oral suspension once daily.

Investigational medicinal product name	Bedaquiline fumarate
Investigational medicinal product code	G004
Other name	TMC207
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Participants administered with Bedaquiline (TMC207) 100 mg as 5 g of granules containing 20mg/g as oral solution once daily.

Arm title	Panel 3

Arm description:

Participants administered with treatment F001, G003 and G004 in six sequences after 10 hours overnight fast.

Arm type	Experimental

Investigational medicinal product name	Bedaquiline fumarate
Investigational medicinal product code	F001
Other name	TMC207
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants administered with Bedaquiline (TMC207) 100 mg as 1x100 mg tablet orally with approximately 240 mL of water once daily.

Investigational medicinal product name	Bedaquiline fumarate
Investigational medicinal product code	G003
Other name	TMC207
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Participants administered with Bedaquiline (TMC207) 100 mg as 5 X 20 mg Water dispersible tablets as oral suspension once daily.

Investigational medicinal product name	Bedaquiline fumarate
Investigational medicinal product code	G004
Other name	TMC207
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Participants administered with Bedaquiline (TMC207) 100 mg as 5 g of granules containing 20mg/g as oral solution once daily.

Arm title	Panel 2

Arm description:

Participants were administered with treatment F001, G003 and G004 in six sequences with standard regular fat yog-hurt.

Arm type	Experimental
Investigational medicinal product name	Bedaquiline fumarate
Investigational medicinal product code	F001
Other name	TMC207
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants administered with Bedaquiline (TMC207) 100 mg as 1x100 mg tablet orally with approximately 240 mL of water once daily.

Investigational medicinal product name	Bedaquiline fumarate
Investigational medicinal product code	G003
Other name	TMC207
Pharmaceutical forms	Dispersible tablet
Routes of administration	Oral use

Dosage and administration details:

Participants administered with Bedaquiline (TMC207) 100 mg as 5 X 20 mg Water dispersible tablets as oral suspension once daily.

Investigational medicinal product name	Bedaquiline fumarate
Investigational medicinal product code	G004
Other name	TMC207
Pharmaceutical forms	Granules
Routes of administration	Oral use

Dosage and administration details:

Participants administered with Bedaquiline (TMC207) 100 mg as 5 g of granules containing 20mg/g as oral solution once daily.

Number of subjects in period 1	Panel 1	Panel 3	Panel 2
Started	12	12	12
Completed	11	9	12
Not completed	1	3	0
Consent withdrawn by subject	1	1	-
Lost to follow-up	-	2	-

Baseline characteristics

Reporting groups	
Reporting group title	Panel 1
Reporting group description:	
Participants administered with treatment F001, G003 and G004 in six sequences with standard breakfast.	
Reporting group title	Panel 3
Reporting group description:	
Participants administered with treatment F001, G003 and G004 in six sequences after 10 hours overnight fast.	
Reporting group title	Panel 2
Reporting group description:	
Participants were administered with treatment F001, G003 and G004 in six sequences with standard regular fat yog-hurt.	

Reporting group values	Panel 1	Panel 3	Panel 2
Number of subjects	12	12	12
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	12	12	12
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous			
Units: years			
arithmetic mean	36.8	32.8	32.5
standard deviation	± 10.24	± 12.4	± 13.63
Title for Gender			
Units: subjects			
Female	0	1	0
Male	12	11	12

Reporting group values	Total		
Number of subjects	36		
Title for AgeCategorical			
Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	36		
From 65 to 84 years	0		
85 years and over	0		
Title for AgeContinuous			
Units: years			
arithmetic mean			
standard deviation	-		

Title for Gender Units: subjects			
Female	1		
Male	35		

End points

End points reporting groups

Reporting group title	Panel 1
Reporting group description:	
Participants administered with treatment F001, G003 and G004 in six sequences with standard breakfast.	
Reporting group title	Panel 3
Reporting group description:	
Participants administered with treatment F001, G003 and G004 in six sequences after 10 hours overnight fast.	
Reporting group title	Panel 2
Reporting group description:	
Participants were administered with treatment F001, G003 and G004 in six sequences with standard regular fat yog-hurt.	
Subject analysis set title	Panel 1: Standard Breakfast-Tablet (F001)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered with Tablet (FOO1) in panel 1 with standardized breakfast.	
Subject analysis set title	Panel 1: Standard Breakfast-Water Dispersible Tablets (G003)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered with Water Dispersible Tablets (G003) in panel 1 with standardized breakfast.	
Subject analysis set title	Panel 1: Standard Breakfast-Granules (G004)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered with Water Dispersible Granules (G004) in panel 1 with standardized breakfast.	
Subject analysis set title	Panel 2: Yoghurt-Tablet (F001)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered with tablet (F001) in panel 2 with Standardized Regular-Fat Yoghurt.	
Subject analysis set title	Panel 2: Yoghurt-Water Dispersible Tablets (G003)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered with water Dispersible Tablets (G003) in panel 2 with Standardized Regular-Fat Yoghurt.	
Subject analysis set title	Panel 2: Yoghurt-Granules (G004)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered with granules (G004) in panel 2 with Standardized Regular-Fat Yoghurt.	
Subject analysis set title	Panel 3: Fasted-Tablet (F001)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered with tablet (F001) in panel 3 with fasted condition.	
Subject analysis set title	Panel 3: Fasted-Water Dispersible Tablets (G003)
Subject analysis set type	Per protocol
Subject analysis set description:	
Participants were administered with Water Dispersible Tablets (G003) in panel 3 with fasted conditions.	
Subject analysis set title	Panel 3: Fasted-Granules (G004)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants were administered with granules (G004) in panel 3 with fasted conditions.

Subject analysis set title	Tablet 100 milligram (mg)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants were administerd with 100 mg tablet orally once in a day.

Subject analysis set title	Water Dispersible Tablets 100 milligram (mg)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants were administerd with 5x20 mg water dispersible tablet orally once in a day.

Subject analysis set title	Granules 5 x 20 milligram (mg)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Participants were administerd with 5x20 mg water dispersible tablet orally once in a day.

Primary: Maximum Observed Plasma Concentration (Cmax) of Bedaquiline

End point title	Maximum Observed Plasma Concentration (Cmax) of Bedaquiline

End point description:

The Cmax is the maximum amount of plasma analyte concentration observed in blood sample.

End point type	Primary

End point timeframe:

Predose, 1, 2, 3, 4, 5, 6, 8, 9, 12, 24, 48 and 72 hours postdose

End point values	Panel 1: Standard Breakfast-Tablet (F001)	Panel 1: Standard Breakfast-Water Dispersible Tablets (G003)	Panel 1: Standard Breakfast-Granules (G004)	Panel 2: Yoghurt-Tablet (F001)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	11	12	12
Units: nanogram per millilitre (ng/mL)				
arithmetic mean (standard deviation)	939 (± 311)	1005 (± 380)	910 (± 339)	605 (± 175)

End point values	Panel 2: Yoghurt-Water Dispersible Tablets (G003)	Panel 2: Yoghurt-Granules (G004)	Panel 3: Fasted-Tablet (F001)	Panel 3: Fasted-Water Dispersible Tablets (G003)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	10	10
Units: nanogram per millilitre (ng/mL)				
arithmetic mean (standard deviation)	679 (± 211)	743 (± 279)	367 (± 168)	371 (± 142)

End point values	Panel 3: Fasted-Granules			

	(G004)			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: nanogram per millilitre (ng/mL)				
arithmetic mean (standard deviation)	398 (± 148)			

Statistical analyses

Statistical analysis title	Panel 1: F001 vs. G003
Comparison groups	Panel 1: Standard Breakfast-Tablet (F001) v Panel 1: Standard Breakfast-Water Dispersible Tablets (G003)
Number of subjects included in analysis	23
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	Cmax LSmeans Ratio
Point estimate	105.42
Confidence interval	
level	90 %
sides	2-sided
lower limit	97.07
upper limit	114.49

Statistical analysis title	Panel 1: F001 vs. G004
Comparison groups	Panel 1: Standard Breakfast-Tablet (F001) v Panel 1: Standard Breakfast-Granules (G004)
Number of subjects included in analysis	24
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	Cmax LSmeans Ratio
Point estimate	95.72
Confidence interval	
level	90 %
sides	2-sided
lower limit	88.39
upper limit	103.65

Statistical analysis title	Panel 2: F001 vs. G003
Comparison groups	Panel 2: Yoghurt-Tablet (F001) v Panel 2: Yoghurt-Water Dispersible Tablets (G003)

Number of subjects included in analysis	24
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	Cmax LSmeans Ratio
Point estimate	111.93
Confidence interval	
level	90 %
sides	2-sided
lower limit	100.23
upper limit	124.99

Statistical analysis title	Panel 2: F001 vs. G004
Comparison groups	Panel 2: Yoghurt-Granules (G004) v Panel 2: Yoghurt-Tablet (F001)
Number of subjects included in analysis	24
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	Cmax LSmeans Ratio
Point estimate	119.74
Confidence interval	
level	90 %
sides	2-sided
lower limit	107.22
upper limit	133.71

Statistical analysis title	Panel 3: F001 vs. G003
Comparison groups	Panel 3: Fasted-Tablet (F001) v Panel 3: Fasted-Water Dispersible Tablets (G003)
Number of subjects included in analysis	20
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	Cmax LSmeans Ratio
Point estimate	103.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	84.01
upper limit	127.52

Statistical analysis title	Panel 3: F001 vs. G004
Comparison groups	Panel 3: Fasted-Tablet (F001) v Panel 3: Fasted-Granules (G004)

Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	Cmax LSmeans Ratio
Point estimate	107.48
Confidence interval	
level	90 %
sides	2-sided
lower limit	87.17
upper limit	132.52

Primary: Area Under the Plasma Concentration Time Curve From Time of Administration up to 72 Hours Post Dosing (AUC[0-72]) of Bedaquiline

End point title	Area Under the Plasma Concentration Time Curve From Time of Administration up to 72 Hours Post Dosing (AUC[0-72]) of Bedaquiline

End point description:

AUC (0-72)is defined as Area Under Curve from time of administration of to 72 hours post dosing, and it is calculated by linear trapezoidal summation.

End point type	Primary

End point timeframe:

Predose, 1, 2, 3, 4, 5, 6, 8, 9, 12, 24, 48 and 72 hours postdose

End point values	Panel 1: Standard Breakfast-Tablet (F001)	Panel 1: Standard Breakfast-Water Dispersible Tablets (G003)	Panel 1: Standard Breakfast-Granules (G004)	Panel 2: Yoghurt-Tablet (F001)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	11	12	12
Units: AUC nanogram.hours/millilitre (ng.h/mL)				
arithmetic mean (standard deviation)	13133 (± 4343)	13316 (± 5188)	12865 (± 4276)	9535 (± 1580)

End point values	Panel 2: Yoghurt-Water Dispersible Tablets (G003)	Panel 2: Yoghurt-Granules (G004)	Panel 3: Fasted-Tablet (F001)	Panel 3: Fasted-Water Dispersible Tablets (G003)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	10	10
Units: AUC nanogram.hours/millilitre (ng.h/mL)				
arithmetic mean (standard deviation)	10854 (± 2355)	11431 (± 3211)	7308 (± 3665)	7249 (± 2459)

End point values	Panel 3: Fasted-Granules (G004)			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: AUC nanogram.hours/millilitre (ng.h/mL)				
arithmetic mean (standard deviation)	7394 (± 2154)			

Statistical analyses

Statistical analysis title	Panel 1: F001 vs. G003
Comparison groups	Panel 1: Standard Breakfast-Tablet (F001) v Panel 1: Standard Breakfast-Water Dispersible Tablets (G003)
Number of subjects included in analysis	23
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	AUC72h, ng.h/mL LSmeans Ratio
Point estimate	97.94
Confidence interval	
level	90 %
sides	2-sided
lower limit	91.8
upper limit	104.5

Statistical analysis title	Panel 1: F001 vs. G004
Comparison groups	Panel 1: Standard Breakfast-Tablet (F001) v Panel 1: Standard Breakfast-Granules (G004)
Number of subjects included in analysis	24
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	AUC72h, ng.h/mL LSmeans Ratio
Point estimate	97.8
Confidence interval	
level	90 %
sides	2-sided
lower limit	91.87
upper limit	104.1

Statistical analysis title	Panel 2: F001 vs. G003
Comparison groups	Panel 2: Yoghurt-Tablet (F001) v Panel 2: Yoghurt-Water Dispersible Tablets (G003)

Number of subjects included in analysis	24
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	AUC72h, ng.h/mL LSmeans Ratio
Point estimate	113.01
Confidence interval	
level	90 %
sides	2-sided
lower limit	105.43
upper limit	121.14

Statistical analysis title	Panel 2: F001 vs. G004
Comparison groups	Panel 2: Yoghurt-Tablet (F001) v Panel 2: Yoghurt-Granules (G004)
Number of subjects included in analysis	24
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	AUC72h, ng.h/mL LSmeans Ratio
Point estimate	117.61
Confidence interval	
level	90 %
sides	2-sided
lower limit	109.72
upper limit	126.07

Statistical analysis title	Panel 3: F001 vs. G003
Comparison groups	Panel 3: Fasted-Tablet (F001) v Panel 3: Fasted-Water Dispersible Tablets (G003)
Number of subjects included in analysis	20
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	AUC72h, ng.h/mL LSmeans Ratio
Point estimate	104.66
Confidence interval	
level	90 %
sides	2-sided
lower limit	86.94
upper limit	125.99

Statistical analysis title	Panel 3: F001 vs. G004
Comparison groups	Panel 3: Fasted-Tablet (F001) v Panel 3: Fasted-Granules (G004)

Number of subjects included in analysis	22
Analysis specification	Post-hoc
Analysis type	equivalence
Parameter estimate	AUC72h, ng.h/mL LSmeans Ratio
Point estimate	106.61
Confidence interval	
level	90 %
sides	2-sided
lower limit	88.51
upper limit	128.4

Secondary: Maximum Observed Plasma Concentration (Cmax) of Metabolite M2

End point title	Maximum Observed Plasma Concentration (Cmax) of Metabolite M2

End point description:

The Cmax is the maximum amount of plasma analyte concentration observed in blood sample.

End point type	Secondary

End point timeframe:

Predose, 1, 2, 3, 4, 5, 6, 8, 9, 12, 24, 48 and 72 hours postdose

End point values	Panel 1: Standard Breakfast-Tablet (F001)	Panel 1: Standard Breakfast-Water Dispersible Tablets (G003)	Panel 1: Standard Breakfast-Granules (G004)	Panel 2: Yoghurt-Tablet (F001)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	11	12	12
Units: nanogram per millilitre (ng/mL)				
arithmetic mean (standard deviation)	17.4 (± 4.31)	15 (± 4.52)	16.8 (± 5.38)	15.6 (± 4)

End point values	Panel 2: Yoghurt-Water Dispersible Tablets (G003)	Panel 2: Yoghurt-Granules (G004)	Panel 3: Fasted-Tablet (F001)	Panel 3: Fasted-Water Dispersible Tablets (G003)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	10	10
Units: nanogram per millilitre (ng/mL)				
arithmetic mean (standard deviation)	16.7 (± 4.09)	16.3 (± 2.9)	13.6 (± 7.47)	12.6 (± 3.61)

End point values	Panel 3: Fasted-Granules (G004)			

Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: nanogram per millilitre (ng/mL)				
arithmetic mean (standard deviation)	13.7 (± 3.95)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration Time Curve From Time of Administration up to 72 Hours Post Dosing (AUC[0-72]) of Metabolite M2

End point title	Area Under the Plasma Concentration Time Curve From Time of Administration up to 72 Hours Post Dosing (AUC[0-72]) of Metabolite M2

End point description:

AUC (0-72)is defined as Area Under Curve from time of administration of to 72 hours post dosing, and it is calculated by linear trapezoidal summation.

End point type	Secondary

End point timeframe:

Predose, 1, 2, 3, 4, 5, 6, 8, 9, 12, 24, 48 and 72 hours postdose

End point values	Panel 1: Standard Breakfast-Tablet (F001)	Panel 1: Standard Breakfast-Water Dispersible Tablets (G003)	Panel 1: Standard Breakfast-Granules (G004)	Panel 2: Yoghurt-Tablet (F001)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	11	12	12
Units: AUC nanogram.hours/millilitre (ng.h/mL)				
arithmetic mean (standard deviation)	889 (± 248)	851 (± 262)	901 (± 294)	830 (± 240)

End point values	Panel 2: Yoghurt-Water Dispersible Tablets (G003)	Panel 2: Yoghurt-Granules (G004)	Panel 3: Fasted-Tablet (F001)	Panel 3: Fasted-Water Dispersible Tablets (G003)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	12	12	10	10
Units: AUC nanogram.hours/millilitre (ng.h/mL)				
arithmetic mean (standard deviation)	900 (± 237)	876 (± 199)	679 (± 297)	662 (± 171)

End point values	Panel 3: Fasted-Granules			

	(G004)			
Subject group type	Subject analysis set			
Number of subjects analysed	12			
Units: AUC nanogram.hours/millilitre (ng.h/mL)				
arithmetic mean (standard deviation)	716 (± 193)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Up to 72 hours	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16

Reporting groups	
Reporting group title	F001
Reporting group description:	
Participants were administered with F001 100 mg oral tablet orally once a day.	
Reporting group title	G003
Reporting group description:	
Participants were administered with G003 20 mg water dispersible tablet orally once in a day.	
Reporting group title	G004
Reporting group description:	
Participants were administered with G004 5 mg (20 mg/g) oral granules once in a day	

Serious adverse events	F001	G003	G004
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 34 (0.00%)	0 / 33 (0.00%)	0 / 36 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			

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

Non-serious adverse events	F001	G003	G004
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 34 (17.65%)	3 / 33 (9.09%)	6 / 36 (16.67%)
Nervous system disorders			
Headache			
alternative assessment type: Systematic			
subjects affected / exposed	5 / 34 (14.71%)	2 / 33 (6.06%)	4 / 36 (11.11%)
occurrences (all)	5	2	4
Infections and infestations			
Nasopharyngitis			
alternative assessment type: Systematic			

subjects affected / exposed occurrences (all)	1 / 34 (2.94%) 1	1 / 33 (3.03%) 1	2 / 36 (5.56%) 2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 March 2013	The contraception inclusion criteria was adjusted to reflect 6 months of precautions (instead of 3 months) for men, inclusion criteria for women were adjusted to only include women that are >2 years postmenopausal, surgically sterile women were no longer allowed to enter the study, and some minor editorial changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported