Clinical trial results:
A Phase I, open-label, randomized, 3-panel, 3-way crossover trial in healthy adult subjects to assess the relative bioavailability of TMC435 following administration of 2 liquid formulations or 2 different capsule concept formulations compared to the Phase III 150 mg capsule, and to assess the effect of food on the bioavailability of TMC435 following administration of the liquid formulations

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

Summary

EudraCT number	2011-005808-14
Trial protocol	GB
Global end of trial date	29 May 2012

Results information

Result version number	v2 (current)
This version publication date	16 July 2016
First version publication date	02 August 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	TMC435HPC1002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01571570
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Sciences Ireland
Sponsor organisation address	East gate Village, East gate, Little Island, Co. Cork, Ireland,
Public contact	Janssen Sciences Ireland, Clinical Registry Group, 353 214673500, ClinicalTrialsEU@its.jnj.com
Scientific contact	Janssen Sciences Ireland, Clinical Registry Group, 353 214673500, ClinicalTrialsEU@its.jnj.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 May 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 May 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of this study was to compare the rate and extent of absorption of a single 150 milligrams (mg) dose of 2 different liquid formulations of TMC435 to that of a single dose of the Phase III 150 mg capsule, after a high-fat breakfast in healthy adult subjects, to compare the rate and extent of absorption of a single 150 mg dose of 2 different liquid formulations of TMC435 in the fed (high-fat) and fasted state in healthy adult subjects and to compare the rate and extent of absorption of a single 150 mg dose of 2 different capsule concept formulations of TMC435 to that of a single dose of the Phase III 150 mg capsule, after a high-fat breakfast in healthy adult participants.

Protection of trial subjects:

The safety assessments included adverse events (AEs), electrocardiogram (ECG), clinical laboratory tests, physical examination and vital sign were monitored throughout the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 March 2012
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	United Kingdom: 72
Worldwide total number of subjects	72
EEA total number of subjects	72

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)	72
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 160 participants were screened, of this 72 participants were enrolled 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	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Panel 1

Arm description:

Participants were administered with single oral dose of 150 mg (milligrams) TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g (grams) fat, 928 kcal (kilocalories) / Single oral dose of 150 mg TMC435 oral suspension (20 mg/mL (milligram per millilitre), fasted / Single oral dose of 150 mg TMC435 oral suspension (20 mg/mL), fed high-fat breakfast consisted of 56 g fat, 928 kcal.

Arm type	Experimental
Investigational medicinal product name	Simeprevir
Investigational medicinal product code	TMC435
Other name	JNJ-38733214-AAA - capsule, hard (G007) - 150mg
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Participants were administered with one Simeprevir 150 mg (milligram) capsule orally under fed condition.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	TMC435
Other name	JNJ-38733214-AAA - oral suspension (G026) - 20mg/ml
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Participants were administered with Simeprevir 150 mg (milligram) oral suspension (20 mg/mL (milligram per millilitre))under fasted condition.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	TMC435
Other name	JNJ-38733214-AAA - oral suspension (G026) - 20mg/ml
Pharmaceutical forms	Oral suspension
Routes of administration	Oral use

Dosage and administration details:

Participants were administered with Simeprevir 150 mg (milligram) oral suspension (20 mg/mL (milligram per millilitre))under fed condition.

Arm title	Panel 3

Arm description:

Participants were administered with Single oral dose of 150 mg (milligrams) TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g (grams) fat, 928 kcal (kilocalories) / Single oral dose of 150 mg TMC435 concept capsule K, fed high-fat breakfast consisted of 56 g fat, 928 kcal / Single oral dose of 150 mg TMC435 concept capsule L, fed high-fat breakfast consisted of 56 g fat, 928 kcal

Arm type	Experimental
Investigational medicinal product name	Simeprevir
Investigational medicinal product code	TMC435
Other name	JNJ-38733214-AAA - capsule, hard (G007) - 150mg
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Participants were administered with one Simeprevir 150 mg (milligram) capsule orally under fed condition.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	TMC435
Other name	JNJ-38733214-AAA - capsule, hard (G019 concept K) - 150mg
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Participants were administered with one Simeprevir 150 mg (milligram) capsule (concept formulation K)orally under fed condition.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	TMC435
Other name	JNJ-38733214-AAA - capsule, hard (G019 concept L) - 150mg
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Participants were administered with one Simeprevir 150 mg (milligram) capsule (G019 concept formulation L) orally under fed condition.

Arm title	Panel 2

Arm description:

Participants were administered with single oral dose of 150 mg (milligrams) TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g (grams) fat, 928 kcal (kilocalories) / Single oral dose of 150 mg TMC435 oral solution (10 mg/mL) (milligram per millilitre)), fasted / Single oral dose of 150 mg TMC435 oral solution (10 mg/mL), fed high-fat breakfast consisted of 56 g fat, 928 kcal.

Arm type	Experimental
Investigational medicinal product name	Simeprevir
Investigational medicinal product code	TMC435
Other name	JNJ-38733214-AAA - capsule, hard (G007) - 150mg
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Participants were administered with one Simeprevir 150 mg (milligram) capsule orally under fed condition.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	TMC435
Other name	JNJ-38733214-AAA - oral solution (G025) - 10mg/ml
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants were administered with Simeprevir 150 mg (milligram) oral solution (10 mg/mL (milligram per millilitre))under fed condition.

Investigational medicinal product name	Simeprevir
Investigational medicinal product code	TMC435
Other name	JNJ-38733214-AAA - oral solution (G025) - 10mg/ml
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants were administered with Simeprevir 150 mg (milligram) oral solution (10 mg/mL (milligram per millilitre))under fasted condition.

Number of subjects in period 1	Panel 1	Panel 3	Panel 2
Started	24	24	24
Completed	24	24	24

Baseline characteristics

Reporting groups	
Reporting group title	Panel 1
Reporting group description:	
Participants were administered with single oral dose of 150 mg (milligrams) TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g (grams) fat, 928 kcal (kilocalories) / Single oral dose of 150 mg TMC435 oral suspension (20 mg/mL (milligram per millilitre), fasted / Single oral dose of 150 mg TMC435 oral suspension (20 mg/mL), fed high-fat breakfast consisted of 56 g fat, 928 kcal.	
Reporting group title	Panel 3
Reporting group description:	
Participants were administered with Single oral dose of 150 mg (milligrams) TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g (grams) fat, 928 kcal (kilocalories) / Single oral dose of 150 mg TMC435 concept capsule K, fed high-fat breakfast consisted of 56 g fat, 928 kcal / Single oral dose of 150 mg TMC435 concept capsule L, fed high-fat breakfast consisted of 56 g fat, 928 kcal	
Reporting group title	Panel 2
Reporting group description:	
Participants were administered with single oral dose of 150 mg (milligrams) TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g (grams) fat, 928 kcal (kilocalories) / Single oral dose of 150 mg TMC435 oral solution (10 mg/mL) (milligram per millilitre)), fasted / Single oral dose of 150 mg TMC435 oral solution (10 mg/mL), fed high-fat breakfast consisted of 56 g fat, 928 kcal.	

Reporting group values	Panel 1	Panel 3	Panel 2
Number of subjects	24	24	24
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	24	24	24
From 65 to 84 years	0	0	0
85 years and over	0	0	0
Title for AgeContinuous Units: years			
arithmetic mean	34.3	34.7	29.9
standard deviation	± 10.94	± 9.09	± 6.95
Title for Gender Units: subjects			
Female	9	9	11
Male	15	15	13

Reporting group values	Total		
Number of subjects	72		
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	72		
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	29		
Male	43		

End points

End points reporting groups

Reporting group title	Panel 1

Reporting group description:

Participants were administered with single oral dose of 150 mg (milligrams) TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g (grams) fat, 928 kcal (kilocalories) / Single oral dose of 150 mg TMC435 oral suspension (20 mg/mL (milligram per millilitre), fasted / Single oral dose of 150 mg TMC435 oral suspension (20 mg/mL), fed high-fat breakfast consisted of 56 g fat, 928 kcal.

Reporting group title	Panel 3

Reporting group description:

Participants were administered with Single oral dose of 150 mg (milligrams) TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g (grams) fat, 928 kcal (kilocalories) / Single oral dose of 150 mg TMC435 concept capsule K, fed high-fat breakfast consisted of 56 g fat, 928 kcal / Single oral dose of 150 mg TMC435 concept capsule L, fed high-fat breakfast consisted of 56 g fat, 928 kcal

Reporting group title	Panel 2

Reporting group description:

Participants were administered with single oral dose of 150 mg (milligrams) TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g (grams) fat, 928 kcal (kilocalories) / Single oral dose of 150 mg TMC435 oral solution (10 mg/mL) (milligram per millilitre)), fasted / Single oral dose of 150 mg TMC435 oral solution (10 mg/mL), fed high-fat breakfast consisted of 56 g fat, 928 kcal.

Subject analysis set title	PANEL 1: 150 mg Capsule Fed (Reference)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants were administered with one Simeprevir 150 mg (milligram) capsule orally under fed condition (Reference).

Subject analysis set title	PANEL 1: Oral Suspension (20 mg/mL) Fed (Test 2)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants were administered with Simeprevir 150 mg (milligram) oral suspension 20 mg/mL (milligram per millilitre) under fed condition (Test 2).

Subject analysis set title	PANEL 2: 150 mg Capsule Fed (Reference 1)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants were administered with simeprevir 150 mg(milligrams) capsule orally under Fed conditions (Reference 1).

Subject analysis set title	PANEL 1: Oral Suspension (20 mg/mL) Fasted (Test 1)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants were administered with Simeprevir 150 mg (milligram) oral suspension 20 mg/mL (milligram per millilitre) under fasted condition (Test 1).

Subject analysis set title	PANEL 2:Oral Solution (10 mg/mL) Fed (Test)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants were administered with Simeprevir Oral Solution (10 mg/mL milligram per millilitre) under Fed condition (Test).

Subject analysis set title	PANEL 3: 150 mg Capsule Fed (Reference)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants were administered with one Simeprevir 150 mg (milligram) capsule orally under fed condition (Reference).

Subject analysis set title	PANEL 3: 150 mg Capsule Concept K Fed (Test 1)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants were administered with concept K 150 mg(milligrams) capsule orally under Fed conditions (Test 1).

Subject analysis set title	PANEL 2: Oral Solution (10 mg/mL) Fasted (Reference 2)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants were administered with Simeprevir Oral Solution (10 mg/mL milligram per millilitre) under Fasted condition (Reference 2).

Subject analysis set title	PANEL 3: 150 mg Capsule Concept L Fed (Test 2)
Subject analysis set type	Per protocol

Subject analysis set description:

Participants were administered with concept L 150 mg(milligrams) capsule orally under Fed conditions (Test 2).

Primary: Maximum serum concentration (Cmax) after administration of a single dose of TMC435, Oral Suspension and Oral Solution

End point title	Maximum serum concentration (Cmax) after administration of a single dose of TMC435, Oral Suspension and Oral Solution

End point description:

The Cmax is defined as maximum observed serum concentrations of TMC435. The value '99999' indicates that the data were not reported at specific time points.

End point type	Primary

End point timeframe:

4 days

End point values	PANEL 1: 150 mg Capsule Fed (Reference)	PANEL 1: Oral Suspension (20 mg/mL) Fed (Test 2)	PANEL 2: 150 mg Capsule Fed (Reference 1)	PANEL 1: Oral Suspension (20 mg/mL) Fasted (Test 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: Nanogram per millilitre(ng/mL)				
arithmetic mean (standard deviation)	962 (± 331)	9.3 (± 6.67)	954 (± 375)	99999 (± 99999)

End point values	PANEL 2:Oral Solution (10 mg/mL) Fed (Test)	PANEL 3: 150 mg Capsule Fed (Reference)	PANEL 3: 150 mg Capsule Concept K Fed (Test 1)	PANEL 2: Oral Solution (10 mg/mL) Fasted (Reference 2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: Nanogram per millilitre(ng/mL)				
arithmetic mean (standard deviation)	1000 (± 440)	949 (± 330)	910 (± 256)	1250 (± 537)

End point values	PANEL 3: 150 mg Capsule Concept L Fed (Test 2)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Nanogram per millilitre(ng/mL)				
arithmetic mean (standard deviation)	941 (± 379)			

Statistical analyses

Statistical analysis title	Test vs Reference 1
Statistical analysis description:	
EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.	
Comparison groups	PANEL 2:Oral Solution (10 mg/mL) Fed (Test) v PANEL 2: 150 mg Capsule Fed (Reference 1)
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	103.69
Confidence interval	
level	90 %
sides	2-sided
lower limit	87.89
upper limit	122.34

Statistical analysis title	Test vs Reference 2
Statistical analysis description:	
EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.	
Comparison groups	PANEL 2: Oral Solution (10 mg/mL) Fasted (Reference 2) v PANEL 2:Oral Solution (10 mg/mL) Fed (Test)
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	80.62
Confidence interval	
level	90 %
sides	2-sided
lower limit	68.33
upper limit	95.12

Statistical analysis title	Test 1 vs Reference

Statistical analysis description:

EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.

Comparison groups	PANEL 3: 150 mg Capsule Concept K Fed (Test 1) v PANEL 3: 150 mg Capsule Fed (Reference)
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	97.37
Confidence interval	
level	90 %
sides	2-sided
lower limit	86.02
upper limit	110.21

Statistical analysis title	Test 2 vs Reference

Statistical analysis description:

EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.

Comparison groups	PANEL 3: 150 mg Capsule Concept L Fed (Test 2) v PANEL 3: 150 mg Capsule Fed (Reference)
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	97.5
Confidence interval	
level	90 %
sides	2-sided
lower limit	86.14
upper limit	110.35

Primary: The time taken to reach the maximum concentration (Tmax) after administration of a single Dose of TMC435, Oral Suspension and Oral Solution

End point title	The time taken to reach the maximum concentration (Tmax) after administration of a single Dose of TMC435, Oral Suspension and Oral Solution[1]

End point description:

The Tmax is defined as the time taken to reach the maximum concentration of TMC435 (Fed and Fasted Conditions).

End point type	Primary

End point timeframe:

4 days

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 analysis were performed for this endpoint.

End point values	PANEL 1: 150 mg Capsule Fed (Reference)	PANEL 1: Oral Suspension (20 mg/mL) Fed (Test 2)	PANEL 2: 150 mg Capsule Fed (Reference 1)	PANEL 1: Oral Suspension (20 mg/mL) Fasted (Test 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: hours (h)				
median (full range (min-max))	7.99 (1.98 to 24.05)	12 (3.98 to 24.02)	8.01 (3.97 to 12.03)	6 (3 to 8.02)

End point values	PANEL 2:Oral Solution (10 mg/mL) Fed (Test)	PANEL 3: 150 mg Capsule Fed (Reference)	PANEL 3: 150 mg Capsule Concept K Fed (Test 1)	PANEL 2: Oral Solution (10 mg/mL) Fasted (Reference 2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: hours (h)				
median (full range (min-max))	11.97 (4 to 24.05)	6 (1.98 to 12.08)	6.02 (1.98 to 12)	4 (2 to 6.03)

End point values	PANEL 3: 150 mg Capsule Concept L Fed (Test 2)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: hours (h)				
median (full range (min-max))	6.03 (1.98 to 12.02)			

Statistical analyses

No statistical analyses for this end point

Primary: Area under the plasma concentration-time curve from time 0 to time of the last quantifiable concentration (AUC last) after administration of a single Dose of TMC435, Oral Suspension and Oral Solution

End point title	Area under the plasma concentration-time curve from time 0 to time of the last quantifiable concentration (AUC last) after administration of a single Dose of TMC435, Oral Suspension and Oral Solution

End point description:

The AUC last is defined as Area under the plasma concentration-time curve from time 0 to time of the last quantifiable concentration (AUC last) of TMC435 (Fed and Fasted Conditions). The value '99999' indicates that the data were not reported at specific time points.

End point type	Primary

End point timeframe:

4 Days

End point values	PANEL 1: 150 mg Capsule Fed (Reference)	PANEL 1: Oral Suspension (20 mg/mL) Fed (Test 2)	PANEL 2: 150 mg Capsule Fed (Reference 1)	PANEL 1: Oral Suspension (20 mg/mL) Fasted (Test 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: Nanogram*hour/millilitre(ng*h/mL)				
arithmetic mean (standard deviation)	14503 (± 6308)	129 (± 123)	14939 (± 5517)	99999 (± 99999)

End point values	PANEL 2:Oral Solution (10 mg/mL) Fed (Test)	PANEL 3: 150 mg Capsule Fed (Reference)	PANEL 3: 150 mg Capsule Concept K Fed (Test 1)	PANEL 2: Oral Solution (10 mg/mL) Fasted (Reference 2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: Nanogram*hour/millilitre(ng*h/mL)				
arithmetic mean (standard deviation)	16483 (± 5163)	13477 (± 4332)	12908 (± 3933)	15223 (± 6971)

End point values	PANEL 3: 150 mg Capsule Concept L Fed (Test 2)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Nanogram*hour/millilitre(ng*h/mL)				
arithmetic mean (standard deviation)	12750 (± 5069)			

Statistical analyses

Statistical analysis title	Test vs Reference 1

Statistical analysis description:

EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.

Comparison groups	PANEL 2:Oral Solution (10 mg/mL) Fed (Test) v PANEL 2: 150 mg Capsule Fed (Reference 1)

Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	112.27
Confidence interval	
level	90 %
sides	2-sided
lower limit	99.04
upper limit	127.26

Statistical analysis title	Test vs Reference 2
Statistical analysis description:	
EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.	
Comparison groups	PANEL 2:Oral Solution (10 mg/mL) Fed (Test) v PANEL 2: Oral Solution (10 mg/mL) Fasted (Reference 2)
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	112.24
Confidence interval	
level	90 %
sides	2-sided
lower limit	99.02
upper limit	127.23

Statistical analysis title	Test 1 vs Reference
Statistical analysis description:	
EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.	
Comparison groups	PANEL 3: 150 mg Capsule Fed (Reference) v PANEL 3: 150 mg Capsule Concept K Fed (Test 1)
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	96.49
Confidence interval	
level	90 %
sides	2-sided
lower limit	88.45
upper limit	105.26

Statistical analysis title	Test 2 vs Reference

Statistical analysis description:

EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.

Comparison groups	PANEL 3: 150 mg Capsule Concept L Fed (Test 2) v PANEL 3: 150 mg Capsule Fed (Reference)
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	93.79
Confidence interval	
level	90 %
sides	2-sided
lower limit	85.98
upper limit	102.32

Primary: Area under the plasma concentration (AUC Infinite) after administration of a single Dose of TMC435, Oral Suspension and Oral Solution

End point title	Area under the plasma concentration (AUC Infinite) after administration of a single Dose of TMC435, Oral Suspension and Oral Solution

End point description:

The AUC (0-infinity) is the area under the serum TMC435 concentration-time curve from time 0 to infinite time, calculated as the sum of AUC (0-last) and C (last)/lambda (z), in which AUC (0-last) is area under the serum TMC435 concentration-time curve from time zero to time of the last quantifiable concentration of TMC435 (Fed and Fasted Conditions). The value '99999' indicates that the data were not reported at specific time points.

End point type	Primary

End point timeframe:

4 Days

End point values	PANEL 1: 150 mg Capsule Fed (Reference)	PANEL 1: Oral Suspension (20 mg/mL) Fed (Test 2)	PANEL 2: 150 mg Capsule Fed (Reference 1)	PANEL 1: Oral Suspension (20 mg/mL) Fasted (Test 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: Nanogram/millilitre*hour(ng/mL*h)				
arithmetic mean (standard deviation)	13831 (± 5237)	99999 (± 99999)	15377 (± 5533)	99999 (± 99999)

End point values	PANEL 2:Oral Solution (10 mg/mL) Fed (Test)	PANEL 3: 150 mg Capsule Fed (Reference)	PANEL 3: 150 mg Capsule Concept K Fed (Test 1)	PANEL 2: Oral Solution (10 mg/mL) Fasted (Reference 2)

Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: Nanogram/millilitre*hour(ng/mL*h)				
arithmetic mean (standard deviation)	16408 (± 5240)	13588 (± 4401)	13007 (± 3991)	15321 (± 7027)

End point values	PANEL 3: 150 mg Capsule Concept L Fed (Test 2)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: Nanogram/millilitre*hour(ng/mL*h)				
arithmetic mean (standard deviation)	12852 (± 5131)			

Statistical analyses

Statistical analysis title	Test vs Reference 1
Statistical analysis description:	
EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.	
Comparison groups	PANEL 2:Oral Solution (10 mg/mL) Fed (Test) v PANEL 2: 150 mg Capsule Fed (Reference 1)
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	111.38
Confidence interval	
level	90 %
sides	2-sided
lower limit	97.65
upper limit	127.03

Statistical analysis title	Test vs Reference 2
Statistical analysis description:	
EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.	
Comparison groups	PANEL 2:Oral Solution (10 mg/mL) Fed (Test) v PANEL 2: Oral Solution (10 mg/mL) Fasted (Reference 2)

Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	112.22
Confidence interval	
level	90 %
sides	2-sided
lower limit	98.57
upper limit	127.76

Statistical analysis title	Test 1 vs Reference
Statistical analysis description:	
EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.	
Comparison groups	PANEL 3: 150 mg Capsule Concept K Fed (Test 1) v PANEL 3: 150 mg Capsule Fed (Reference)
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	96.43
Confidence interval	
level	90 %
sides	2-sided
lower limit	88.44
upper limit	105.14

Statistical analysis title	Test 2 vs Reference
Statistical analysis description:	
EudraCT database performs auto-addition of number of subjects analyzed while reporting statistical analysis of two treatment groups. The number of subjects included in analysis were '24" instead of '48'.	
Comparison groups	PANEL 3: 150 mg Capsule Concept L Fed (Test 2) v PANEL 3: 150 mg Capsule Fed (Reference)
Number of subjects included in analysis	48
Analysis specification	Post-hoc
Analysis type	non-inferiority
Parameter estimate	LSmean Ratio
Point estimate	93.76
Confidence interval	
level	90 %
sides	2-sided
lower limit	85.98
upper limit	102.23

Primary: Rate constant (z) after administration of a single Dose of TMC435, Oral Suspension and Oral Solution

End point title	Rate constant (z) after administration of a single Dose of TMC435, Oral Suspension and Oral Solution[2]

End point description:

The z is defined as first-order rate constant associated with the terminal portion of the curve, determined by linear regression of the terminal points of the semi logarithmic drug concentration-time Curve of TMC435 (Fed and Fasted Conditions).The value '99999' indicates that the data were not reported at specific time points.

End point type	Primary

End point timeframe:

4 Days

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 analysis were performed for this endpoint.

End point values	PANEL 1: 150 mg Capsule Fed (Reference)	PANEL 1: Oral Suspension (20 mg/mL) Fed (Test 2)	PANEL 2: 150 mg Capsule Fed (Reference 1)	PANEL 1: Oral Suspension (20 mg/mL) Fasted (Test 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: 1 per hour (1/h)				
arithmetic mean (standard deviation)	0.0793 (± 0.0118)	99999 (± 99999)	0.076 (± 0.0134)	99999 (± 99999)

End point values	PANEL 2:Oral Solution (10 mg/mL) Fed (Test)	PANEL 3: 150 mg Capsule Fed (Reference)	PANEL 3: 150 mg Capsule Concept K Fed (Test 1)	PANEL 2: Oral Solution (10 mg/mL) Fasted (Reference 2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: 1 per hour (1/h)				
arithmetic mean (standard deviation)	0.0806 (± 0.0118)	0.0799 (± 0.0105)	0.0801 (± 0.0116)	0.0807 (± 0.0163)

End point values	PANEL 3: 150 mg Capsule Concept L Fed (Test 2)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: 1 per hour (1/h)				
arithmetic mean (standard deviation)	0.0798 (± 0.0126)			

Statistical analyses

No statistical analyses for this end point

Primary: Terminal elimination half-life (T1/2 term) after administration of a single Dose of TMC435, Oral Suspension and Oral Solution

End point title	Terminal elimination half-life (T1/2 term) after administration of a single Dose of TMC435, Oral Suspension and Oral Solution[3]

End point description:

The T1/2 term is defined as the time required to divide the plasma concentration by two after reaching pseudo-equilibrium, and not the time required to eliminate half the administered dose. of TMC435 (Fed and Fasted Conditions). The value '99999' indicates that the data were not reported at specific time points.

End point type	Primary

End point timeframe:

4 Days

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 analysis were performed for this endpoint.

End point values	PANEL 1: 150 mg Capsule Fed (Reference)	PANEL 1: Oral Suspension (20 mg/mL) Fed (Test 2)	PANEL 2: 150 mg Capsule Fed (Reference 1)	PANEL 1: Oral Suspension (20 mg/mL) Fasted (Test 1)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: hours (h)				
arithmetic mean (standard deviation)	8.9 (± 1.5)	99999 (± 99999)	9.4 (± 1.7)	99999 (± 99999)

End point values	PANEL 2:Oral Solution (10 mg/mL) Fed (Test)	PANEL 3: 150 mg Capsule Fed (Reference)	PANEL 3: 150 mg Capsule Concept K Fed (Test 1)	PANEL 2: Oral Solution (10 mg/mL) Fasted (Reference 2)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	24	24	24	24
Units: hours (h)				
arithmetic mean (standard deviation)	8.8 (± 1.1)	8.8 (± 1.4)	8.8 (± 1.4)	8.9 (± 1.6)

End point values	PANEL 3: 150 mg Capsule Concept L Fed (Test 2)			
Subject group type	Subject analysis set			
Number of subjects analysed	24			
Units: hours (h)				
arithmetic mean (standard deviation)	8.9 (± 1.5)			

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Taste

End point title	Overall Taste

End point description:

Participants had to select appropriate choice Bad, Almost acceptable, Acceptable and Good for the overall taste.

End point type	Secondary

End point timeframe:

Day 1 of Panel 1 and Panel 2

End point values	PANEL 1: Oral Suspension (20 mg/mL) Fasted (Test 1)	PANEL 2: Oral Solution (10 mg/mL) Fasted (Reference 2)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	24	24		
Units: Participants				
arithmetic mean (standard deviation)				
Overall taste	2.1 (± 0.65)	1.4 (± 0.77)		
Visual analog scale	0.7 (± 0.95)	-0.6 (± 0.83)		
Sweetness	1.9 (± 0.8)	0.5 (± 0.72)		
Bitterness	0.5 (± 0.83)	1.1 (± 1.18)		
Flavor	1.8 (± 0.59)	1.3 (± 0.92)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Screening to Follow up (5 and 7 days after last intake of TMC435)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	15.0

Reporting groups	
Reporting group title	Panel 1-150 mg Capsule Fed
Reporting group description: Single oral dose of 150 mg TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g fat, 928 kcal	
Reporting group title	Panel 2-150 mg Capsule Fed
Reporting group description: Single oral dose of 150 mg TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g fat, 928 kcal	
Reporting group title	Panel 1-Oral Suspension (20 mg/mL) Fed
Reporting group description: Single oral dose of 150 mg TMC435 oral suspension (20 mg/mL), fed high-fat breakfast consisted of 56 g fat, 928 kcal	
Reporting group title	Panel 1-Oral Suspension (20 mg/mL) Fasted
Reporting group description: Single oral dose of 150 mg TMC435 oral suspension (20 mg/mL), fasted	
Reporting group title	Panel 3-150 mg Capsule Concept K Fed
Reporting group description: Single oral dose of 150 mg TMC435 concept capsule K, fed high-fat breakfast consisted of 56 g fat, 928 kcal	
Reporting group title	Panel 3-150 mg Capsule Fed
Reporting group description: Single oral dose of 150 mg TMC435 Phase III capsule, fed high-fat breakfast consisted of 56 g fat, 928 kcal	
Reporting group title	Panel 2-Oral Solution (10 mg/mL) Fed
Reporting group description: Single oral dose of 150 mg TMC435 oral solution (10 mg/mL), fed high-fat breakfast consisted of 56 g fat, 928 kcal	
Reporting group title	Panel 3-150 mg Capsule Concept L Fed
Reporting group description: Single oral dose of 150 mg TMC435 concept capsule L, fed high-fat breakfast consisted of 56 g fat, 928 kcal	
Reporting group title	Panel 2-Oral Solution (10 mg/mL) Fasted
Reporting group description: Single oral dose of 150 mg TMC435 oral solution (10 mg/mL), fasted	

Serious adverse events	Panel 1-150 mg Capsule Fed	Panel 2-150 mg Capsule Fed	Panel 1-Oral Suspension (20 mg/mL) Fed
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (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			

Serious adverse events	Panel 1-Oral Suspension (20 mg/mL) Fasted	Panel 3-150 mg Capsule Concept K Fed	Panel 3-150 mg Capsule Fed
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (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			

Serious adverse events	Panel 2-Oral Solution (10 mg/mL) Fed	Panel 3-150 mg Capsule Concept L Fed	Panel 2-Oral Solution (10 mg/mL) Fasted
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 24 (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			

Frequency threshold for reporting non-serious adverse events: 4 %

Non-serious adverse events	Panel 1-150 mg Capsule Fed	Panel 2-150 mg Capsule Fed	Panel 1-Oral Suspension (20 mg/mL) Fed
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 24 (12.50%)	2 / 24 (8.33%)	0 / 24 (0.00%)
Cardiac disorders			
Palpitations			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 24 (8.33%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	2	0	0
Lethargy			

subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	3	1	0
Flatulence			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal Dreams			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Sleep Disorder			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Panel 1-Oral Suspension (20 mg/mL) Fasted	Panel 3-150 mg Capsule Concept K Fed	Panel 3-150 mg Capsule Fed
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 24 (8.33%)	1 / 24 (4.17%)	1 / 24 (4.17%)
Cardiac disorders			
Palpitations			
alternative assessment type: Systematic			

subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Lethargy			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	1 / 24 (4.17%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Nausea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Abnormal Dreams			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0

Sleep Disorder			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Panel 2-Oral Solution (10 mg/mL) Fed	Panel 3-150 mg Capsule Concept L Fed	Panel 2-Oral Solution (10 mg/mL) Fasted
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 24 (16.67%)	1 / 24 (4.17%)	0 / 24 (0.00%)
Cardiac disorders			
Palpitations			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 24 (0.00%)	1 / 24 (4.17%)	0 / 24 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Lethargy			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal Distension			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Diarrhoea			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Flatulence			
subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Nausea			

subjects affected / exposed	1 / 24 (4.17%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Abnormal Dreams			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	0
Sleep Disorder			
subjects affected / exposed	0 / 24 (0.00%)	0 / 24 (0.00%)	0 / 24 (0.00%)
occurrences (all)	0	0	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