Clinical trial results:
A Phase III open-label study to evaluate the safety, tolerability and efficacy of TMC435 plus PegIFN-2a (Pegasys®) and ribavirin (Copegus®) triple therapy in chronic hepatitis C genotype-1 infected subjects who are co-infected with Human Immunodeficiency Virus type 1 (HIV-1).

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

Summary

EudraCT number	2010-021337-31
Trial protocol	GB ES PT
Global end of trial date	28 August 2013

Results information

Result version number	v2 (current)
This version publication date	30 June 2016
First version publication date	31 July 2015
Version creation reason	• Correction of full data set Review of data

Trial information

Trial identification

Sponsor protocol code	TMC435-TiDP16-C212

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01479868
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Sciences Ireland
Sponsor organisation address	Eastgate Village, Eastgate, Little Island, Co. Cork, Ireland,
Public contact	Clinical Registry Group, Janssen Sciences Ireland, 353 21 4673500, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Sciences Ireland, 353 21 4673500, 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	28 August 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of TMC435 plus pegylated interferon alpha-2a (PegIFNα- 2a) and ribavirin (RBV) triple therapy in hepatitis C virus (HCV) genotype-1 infected participants, co-infected with human immunodeficiency virus- 1 (HIV-1).
To evaluate the proportion of participants with sustained virologic response (SVR) 12 weeks after the planned end of treatment (SVR12).

Protection of trial subjects:

Safety and tolerability were evaluated throughout the study by monitoring of adverse events (AEs), Performing laboratory tests, measurement of vital signs, electrocardiogram (ECG) and performing physical examinations throughout the study.

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	19 September 2011
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: 8
Country: Number of subjects enrolled	Germany: 17
Country: Number of subjects enrolled	Spain: 11
Country: Number of subjects enrolled	France: 8
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	Portugal: 12
Country: Number of subjects enrolled	United States: 41
Worldwide total number of subjects	106
EEA total number of subjects	57

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)	104
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 160 participants were screened, 107 were enrolled of whom 106 participants 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	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	TMC435 150mg 12Wks PR24/48

Arm description:

Participants On HAART (n=93) and Not on HAART (n=13) were given TMC435 150 mg once daily plus peginterferon alfa-2a (PegIFN alfa-2a) and ribavirin (RBV) for 12 Weeks (Wks) followed by PegIFN alfa-2a (P) and RBV (R) until Week 24/48 (PR24/48). Treatment was to be stopped at Week 24 for HCV treatment-naïve and prior HCV relapsers who met the response guided therapy criteria, and who did not have cirrhosis. All prior HCV non-responders (null and partial), Participants with cirrhosis, and HCV treatment-naïve and prior HCV relapsers who did not meet the response guided therapy criteria had a 48-week treatment period.

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

Dosage and administration details:

Participants were administered JNJ-38733214-AAA - capsule , hard 150 mg orally, once daily.

Investigational medicinal product name	Pegasys
Investigational medicinal product code	
Other name	PEGINTERFERON ALFA-2A
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Participants were administered PEGINTERFERON ALFA-2A (PegIFNα-2a) 180 microgram(s)/millilitre (µg/ml) once weekly as subcutaneous injection of 0.5 mL.

Investigational medicinal product name	Copegus
Investigational medicinal product code	
Other name	Ribavirin
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were administered Ribavirin 1000 or 1200 milligrams (mg) orally, twice a day.

Number of subjects in period 1	TMC435 150mg 12Wks PR24/48
Started	106
Completed	97
Not completed	9
Sponsor's decision	1
Adverse event, serious fatal	1
Consent withdrawn by subject	1
Participant non-compliant	1
Participant initiated new HCV therapy	1
Lost to follow-up	4

Baseline characteristics

Reporting groups	
Reporting group title	TMC435 150mg 12Wks PR24/48

Reporting group description:

Participants On HAART (n=93) and Not on HAART (n=13) were given TMC435 150 mg once daily plus peginterferon alfa-2a (PegIFN alfa-2a) and ribavirin (RBV) for 12 Weeks (Wks) followed by PegIFN alfa-2a (P) and RBV (R) until Week 24/48 (PR24/48). Treatment was to be stopped at Week 24 for HCV treatment-naïve and prior HCV relapsers who met the response guided therapy criteria, and who did not have cirrhosis. All prior HCV non-responders (null and partial), Participants with cirrhosis, and HCV treatment-naïve and prior HCV relapsers who did not meet the response guided therapy criteria had a 48-week treatment period.

Reporting group values	TMC435 150mg 12Wks PR24/48	Total	
Number of subjects	106	106	
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	104	104	
From 65 to 84 years	2	2	
85 years and over	0	0	
Title for AgeContinuous Units: years			
median	48		
full range (min-max)	27 to 67	-	
Title for Gender Units: subjects			
Female	16	16	
Male	90	90	

End points

End points reporting groups

Reporting group title	TMC435 150mg 12Wks PR24/48

Reporting group description:

Participants On HAART (n=93) and Not on HAART (n=13) were given TMC435 150 mg once daily plus peginterferon alfa-2a (PegIFN alfa-2a) and ribavirin (RBV) for 12 Weeks (Wks) followed by PegIFN alfa-2a (P) and RBV (R) until Week 24/48 (PR24/48). Treatment was to be stopped at Week 24 for HCV treatment-naïve and prior HCV relapsers who met the response guided therapy criteria, and who did not have cirrhosis. All prior HCV non-responders (null and partial), Participants with cirrhosis, and HCV treatment-naïve and prior HCV relapsers who did not meet the response guided therapy criteria had a 48-week treatment period.

Primary: Percentage of Participants With Sustained Virologic Response at Week 12 (SVR 12)

End point title	Percentage of Participants With Sustained Virologic Response at Week 12 (SVR 12)[1]

End point description:

The SVR 12 was defined as hepatitis C virus (HCV) ribonucleic acid (RNA) levels less than (<) 25 international unit per millilitre (IU/mL) undetectable at the planned end of treatment (EOT), and HCV RNA levels <25 IU/mL undetectable or HCV RNA levels <25 IU/mL detectable at 12 Weeks after end of treatment.

End point type	Primary

End point timeframe:

12 weeks after planned end of treatment (Week 24 or 48)

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: Descriptive statistics were done, no inferential statistical analyses were performed

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Percentage of Participants				
number (not applicable)	73.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Sustained Virologic Response at Week 24 (SVR 24)

End point title	Percentage of Participants With Sustained Virologic Response at Week 24 (SVR 24)

End point description:

The SVR 24 was defined as hepatitis C virus (HCV) ribonucleic acid (RNA) levels less than (<) 25 international unit per millilitre (IU/mL) undetectable at the planned end of treatment (EOT), and HCV RNA levels <25 IU/mL undetectable or HCV RNA levels <25 IU/mL detectable at 24 weeks after end of treatment.

End point type	Secondary

End point timeframe:

24 weeks after planned end of treatment (Week 24 or 48).

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Percentage of Participants				
number (not applicable)	72.6			

Statistical analyses

No statistical analyses for this end point

Secondary: On treatment data for percentage of Participants With Hepatitis C Virus Ribonucleic Acid (HCV-RNA) Less Than (<) 25 International Units (IU/mL) Undetectable or Detectable/Undetectable

End point title	On treatment data for percentage of Participants With Hepatitis C Virus Ribonucleic Acid (HCV-RNA) Less Than (<) 25 International Units (IU/mL) Undetectable or Detectable/Undetectable

End point description:

Percentage of participants with HCV RNA less than (<) 25 IU/mL undetectable (undet.) or detectable (det.)/undetectable at specific time points were observed. ITT population included all participants who had at least 1 dose of study drug. Here, "N" (number of participants analysed) is the number of participants analysed for this outcome measure, "n" is the number of participants analysed for this outcome measure at specific time points.

End point type	Secondary

End point timeframe:

Week 4, 12, 24, 36, and 48

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Percentage of Participants				
number (not applicable)				
Week 4: < 25 IU/mL HCV-RNA undet. (n=105)	65.7			
Week 4:< 25 IU/mL HCV-RNA det./undet. (n=105)	88.6			
Week 12:< 25 IU/mL HCV-RNA undet. (n=97)	94.8			
Week 12:< 25 IU/mL HCV-RNA det./undet. (n=97)	97.9			

Week 24:< 25 IU/mL HCV-RNA undet. (n=90)	90			
Week 24:< 25 IU/mL HCV-RNA det./undet. (n=90)	93.3			
Week 48:< 25 IU/mL HCV-RNA undet. (n=28)	100			
Week 48:< 25 IU/mL HCV-RNA det./undet. (n=28)	100			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With On-treatment Failure

End point title	Percentage of Participants With On-treatment Failure

End point description:

Participants were considered as an on-treatment failure if, at actual end of treatment (EOT), there was confirmed detectable HCV RNA levels.

End point type	Secondary

End point timeframe:

Actual EOT (Week 24 or Week 48 or Early Withdrawal)

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Percentage of Participants				
number (not applicable)	17			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Viral Breakthrough

End point title	Percentage of Participants With Viral Breakthrough

End point description:

Confirmed increase of more than 1 log10 IU per mL in HCV RNA level from the lowest level reached, or a confirmed HCV RNA level of more than 100 IU per mL in participants whose HCV RNA levels had previously been below the limit of quantification (less than 25 IU per mL detectable) or undetectable (less than 25 IU per mL undetectable), while on study therapy.

End point type	Secondary

End point timeframe:

Up to Actual EOT (Week 24 or Week 48 or Early Withdrawal)

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	105			
Units: Percentage of Participants				
number (not applicable)	11.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Viral Relapse

End point title	Percentage of Participants With Viral Relapse

End point description:

Participants were considered to have a viral relapse when, at actual end of treatment, HCV RNA levels were less than 25 IU per mL undetectable; and during the follow-up period, HCV RNA levels were more than or equal to 25 IU per mL. The incidence of viral relapse is only calculated for subjects with undetectable (or unconfirmed detectable) HCV RNA levels at actual end of treatment, and with at least one follow-up HCV RNA measurement.

End point type	Secondary

End point timeframe:

Actual EOT (Week 24 or Week 48 or Early Withdrawal) up to end of follow-up period

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	87			
Units: Percentage of Participants				
number (not applicable)	10.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Normalized Alanine Aminotransferase Levels

End point title	Percentage of Participants With Normalized Alanine Aminotransferase Levels

End point description:

Participants with normalized alanine aminotransferase levels observed whose alanine aminotransferase levels were out of normal range at Baseline.

End point type	Secondary
End point timeframe: Baseline up to Week 72	

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: Percentage of Participants				
number (not applicable)	81.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Human Immunodeficiency Virus (HIV) Participants With Virologic Failure

End point title	Percentage of Human Immunodeficiency Virus (HIV) Participants With Virologic Failure
End point description: Participants had confirmed HIV virologic failure if HIV viral load values were greater than or equal to 50 or 200 copies/mL among those who previously had less than 50 copies/mL for participants on HAART (n=93).	
End point type	Secondary
End point timeframe: Baseline to Week 72.	

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: Percentage of Participants				
number (not applicable)				
Greater than or equal to 50 copies/mL	5.4			
Greater than or equal to 200 copies/mL	2.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in Log10 Plasma Human Immunodeficiency

Virus (HIV) Viral Load

End point title	Mean Change From Baseline in Log10 Plasma Human Immunodeficiency Virus (HIV) Viral Load

End point description:

Participants who received potent anti-HIV treatment with a combination of more than 3 antiretroviral therapies to reduce HIV RNA viral load to undetectable levels were analyzed. Here "n" signifies participants evaluable for this measure at specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 2, 4, 8, 12, 16, 20, 24, 28, 36, 42, 48, 52, 60 and 72

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: copies per milliliter				
arithmetic mean (standard deviation)				
Baseline (n=93)	1.3726 (± 0.25796)			
Change at Week 2 (n=91)	-0.0724 (± 0.23857)			
Change at Week 4 (n=93)	-0.0704 (± 0.25817)			
Change at Week 8 (n=92)	-0.0442 (± 0.40974)			
Change at Week 12 (n=90)	-0.0655 (± 0.3051)			
Change at Week 16 (n=88)	-0.0829 (± 0.23986)			
Change at Week 20 (n=86)	-0.0847 (± 0.25111)			
Change at Week 24 (n=88)	-0.0689 (± 0.24785)			
Change at Week 28 (n=82)	-0.0564 (± 0.26319)			
Change at Week 36 (n=85)	0.0004 (± 0.24395)			
Change at Week 42 (n=35)	-0.0623 (± 0.29365)			
Change at Week 48 (n=79)	-0.0041 (± 0.36177)			
Change at Week 52 (n=36)	0.0011 (± 0.20767)			
Change at Week 60 (n=40)	-0.0184 (± 0.2094)			
Change at Week 72 (n=38)	-0.0265 (± 0.18323)			
Change at End of study (n=93)	0.0099 (± 0.33435)			

Statistical analyses

No statistical analyses for this end point

Secondary: Mean Change From Baseline in CD4+ Cell Count

End point title	Mean Change From Baseline in CD4+ Cell Count

End point description:

Participants who received potent anti-HIV treatment with a combination of more than 3 antiretroviral therapies to reduce HIV RNA viral load to undetectable levels were analyzed. Here, "n" is the number of participants analysed for this outcome measure at specific time points for participants on HAART (n=93).

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 2, 4, 8, 12, 16, 20, 24, 28, 36, 42, 48, 52, 60 and 72

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: cell counts per microliter				
arithmetic mean (standard deviation)				
Baseline (n=93)	640.3 (± 243.11)			
Change at Week 2 (n=89)	-95 (± 190.34)			
Change at Week 4 (n=91)	-171.5 (± 170.67)			
Change at Week 8 (n=92)	-244.2 (± 185.04)			
Change at Week 12 (n=91)	-271.7 (± 194.49)			
Change at Week 16 (n=88)	-275.5 (± 183.96)			
Change at Week 20 (n=84)	-283.5 (± 175.27)			
Change at Week 24 (n=89)	-288.8 (± 202.31)			
Change at Week 28 (n=82)	-252.3 (± 203.45)			
Change at Week 36 (n=83)	-198.7 (± 225.62)			
Change at Week 42 (n=33)	-336.8 (± 240.64)			
Change at Week 48 (n=77)	-166.6 (± 248.25)			
Change at Week 52 (n=35)	-202.7 (± 222.89)			
Change at Week 60 (n=40)	-90.6 (± 189.74)			
Change at Week 72 (n=38)	-62.9 (± 175.61)			
Change at End of Study (n=93)	-51.1 (± 178.2)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in CD4+ Cell Count in Percentage

End point title	Change From Baseline in CD4+ Cell Count in Percentage

End point description:

Participants who received potent anti-HIV treatment with a combination of more than 3 antiretroviral therapies to reduce HIV RNA viral load to undetectable levels were analysed. Here, "n" is the number of participants analysed for this outcome measure at specific time points for participants on HAART (n=93).

End point type	Secondary

End point timeframe:

Baseline (Day 1), Week 2, 4, 8, 12, 16, 20, 24, 28, 36, 42, 48, 52, 60 and 72

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: percentage of lymphocyte				
arithmetic mean (standard deviation)				
Baseline (n=93)	31.65 (± 8.39)			
Change at Week 2 (n=89)	0.42 (± 6.49)			
Change at Week 4 (n=91)	2.5 (± 5.943)			
Change at Week 8 (n=92)	3.85 (± 5.93)			
Change at Week 12 (n=91)	3.93 (± 6.264)			
Change at Week 16 (n=88)	5.47 (± 6.301)			
Change at Week 20 (n=84)	5.27 (± 6.961)			
Change at Week 24 (n=89)	5.5 (± 7.029)			
Change at Week 28 (n=82)	3.79 (± 6.759)			
Change at Week 36 (n=83)	2.75 (± 6.492)			
Change at Week 42 (n=33)	6.41 (± 6.213)			
Change at Week 48 (n=77)	2.09 (± 7.356)			
Change at Week 52 (n=35)	3.26 (± 6.838)			
Change at Week 60 (n=40)	0.25 (± 5.296)			
Change at Week 72 (n=38)	0.7 (± 4.406)			
Change at End of study (n=93)	0.13 (± 6.169)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants Reporting Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point title	Number of Participants Reporting Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point description:

An adverse event (AE) was any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent were events between administration of study drug and up to Day 126 that were absent before treatment or that worsened relative to pre-treatment state.

End point type	Secondary

End point timeframe:

Baseline up to End of Treatment (EOT: Week 24 or Week 48 or Early Withdrawal) +4 weeks.

End point values	TMC435 150mg 12Wks PR24/48			
Subject group type	Reporting group			
Number of subjects analysed	106			
Units: Participants				
number (not applicable)				
TEAEs	102			
TESAEs	6			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Baseline up to End of Treatment (EOT: Week 24 or Week 48 or Early Withdrawal) +4 weeks.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	TMC435 150mg 12Wks PR24/48

Reporting group description:

Participants On HAART (n=93) and Not on HAART (n=13) were given TMC435 150 mg once daily plus peginterferon alfa-2a (PegIFN alfa-2a) and ribavirin (RBV) for 12 Weeks (Wks) followed by PegIFN alfa-2a (P) and RBV (R) until Week 24/48 (PR24/48). Treatment was to be stopped at Week 24 for HCV treatment-naïve and prior HCV relapsers who met the response guided therapy criteria, and who did not have cirrhosis. All prior HCV non-responders (null and partial), subjects with cirrhosis, and HCV treatment-naïve and prior HCV relapsers who did not meet the response guided therapy criteria had a 48-week treatment period.

Serious adverse events	TMC435 150mg 12Wks PR24/48		
Total subjects affected by serious adverse events			
subjects affected / exposed	11 / 106 (10.38%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Investigations			
Aspartate aminotransferase increased			
alternative assessment type: Systematic			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Thoracic vertebral fracture			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Angina pectoris			

subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
General physical health deterioration			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Anal haemorrhage			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hyperbilirubinaemia			

subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Mental status changes			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychotic disorder			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Cervical spinal stenosis			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Catheter site infection			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Malnutrition			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	TMC435 150mg 12Wks PR24/48		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	103 / 106 (97.17%)		
Investigations			
Weight decreased			
subjects affected / exposed	13 / 106 (12.26%)		
occurrences (all)	13		
Neutrophil count decreased			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	8		
Nervous system disorders			
Headache			
subjects affected / exposed	35 / 106 (33.02%)		
occurrences (all)	48		
Dizziness			
subjects affected / exposed	13 / 106 (12.26%)		
occurrences (all)	13		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	48 / 106 (45.28%)		
occurrences (all)	57		
Influenza like illness			
subjects affected / exposed	25 / 106 (23.58%)		
occurrences (all)	37		
Asthenia			
subjects affected / exposed	24 / 106 (22.64%)		
occurrences (all)	29		
Pyrexia			
subjects affected / exposed	12 / 106 (11.32%)		
occurrences (all)	12		
Chills			
subjects affected / exposed	9 / 106 (8.49%)		
occurrences (all)	10		
Injection site erythema			
subjects affected / exposed	6 / 106 (5.66%)		
occurrences (all)	6		

Injection site reaction subjects affected / exposed occurrences (all) Pain subjects affected / exposed occurrences (all)	 8 / 106 (7.55%) 8 7 / 106 (6.60%) 9		
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Neutropenia subjects affected / exposed occurrences (all) Thrombocytopenia subjects affected / exposed occurrences (all)	 30 / 106 (28.30%) 47 33 / 106 (31.13%) 76 6 / 106 (5.66%) 14		
Gastrointestinal disorders Vomiting subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all)	 14 / 106 (13.21%) 17 31 / 106 (29.25%) 34 25 / 106 (23.58%) 33 12 / 106 (11.32%) 13		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Dyspnoea subjects affected / exposed occurrences (all)	 11 / 106 (10.38%) 13 10 / 106 (9.43%) 10		

Oropharyngeal pain subjects affected / exposed occurrences (all)	9 / 106 (8.49%) 9		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all) Eczema subjects affected / exposed occurrences (all) Dry skin subjects affected / exposed occurrences (all) Alopecia subjects affected / exposed occurrences (all) Rash subjects affected / exposed occurrences (all)	 19 / 106 (17.92%) 21 8 / 106 (7.55%) 8 16 / 106 (15.09%) 17 7 / 106 (6.60%) 8 7 / 106 (6.60%) 7		
Psychiatric disorders Depression subjects affected / exposed occurrences (all) Mood altered subjects affected / exposed occurrences (all) Insomnia subjects affected / exposed occurrences (all) Anxiety subjects affected / exposed occurrences (all) Sleep disorder subjects affected / exposed occurrences (all)	 19 / 106 (17.92%) 20 20 / 106 (18.87%) 26 27 / 106 (25.47%) 27 13 / 106 (12.26%) 14 6 / 106 (5.66%) 6		
Musculoskeletal and connective tissue disorders			

Myalgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Arthralgia subjects affected / exposed occurrences (all) Pain in extremity subjects affected / exposed occurrences (all)	17 / 106 (16.04%) 17 8 / 106 (7.55%) 8 15 / 106 (14.15%) 16 6 / 106 (5.66%) 6		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection subjects affected / exposed occurrences (all)	7 / 106 (6.60%) 8 7 / 106 (6.60%) 8		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	21 / 106 (19.81%) 21		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 January 2012	The amendment was created to implement the changes to the protocol based on the feedback from the Health Authorities, mainly on primary efficacy endpoint for ongoing and future TMC435 Phase III trials could be changed from SVR24 to SVR12. SVR24 became a secondary endpoint.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported