Clinical trial results:
A Phase IIa, Multicentre, Randomised, Double-Blind, Parallel Group, Placebo Controlled Study to Evaluate Safety, Tolerability and Clinical Efficacy of MT-1303 in Subjects with Moderate to Severe Chronic Plaque Psoriasis

Due to the EudraCT – Results system being out of service between 31 July 2015 and 12 January 2016, these results have been published in compliance with revised timelines.

Summary

EudraCT number	2012-005750-27
Trial protocol	LV HU EE PL BG
Global end of trial date	21 November 2014

Results information

Result version number	v1 (current)
This version publication date	16 July 2016
First version publication date	16 July 2016

Trial information

Trial identification

Sponsor protocol code	MT-1303-E06

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01987843
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mitsubishi Tanabe Pharma Corporation
Sponsor organisation address	17-10, Nihonbashi-Koamicho, Chuo-ku, Tokyo, Japan, 103-8405
Public contact	General Information, Mitsubishi Tanabe Pharma Europe Ltd. (MTPE), regulatory@mt-pharma-eu.com
Scientific contact	General Information, Mitsubishi Tanabe Pharma Europe Ltd. (MTPE), regulatory@mt-pharma-eu.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	18 March 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 November 2014
Global end of trial reached?	Yes
Global end of trial date	21 November 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the safety and tolerability of 3 dose levels of MT1303 in subjects with moderate to severe chronic plaque psoriasis. It is also to evaluate the efficacy of 3 dose levels of MT-1303 in subjects with moderate to severe chronic plaque psoriasis compared to placebo after 16 weeks of treatment on Psoriasis Area and Severity Index (PASI).

Protection of trial subjects:

Subjects will be permanently withdrawn from study medication in the following circumstances:
• Confirmed absolute lymphocyte count values <200/µL, on 2 consecutive occasions
• Development of any clinically significant abnormalities on ECG, including but not limited to: Symptomatic bradycardia; New onset 2nd degree AV block, Mobitz Type II; New onset 3rd degree AV block; Confirmed QTcF interval prolongation >500msec and/or QTcF interval increase from baseline >60msec
• Development of any clinically significant liver dysfunction as follows:
  o ALT or AST > 8 × ULN, or
  o ALT or AST >5 × ULN and persists for more than 2 consecutive visits, or
  o ALT or AST >3 × ULN in conjunction with elevated total bilirubin >2 × ULN or
  o ALT or AST >3 × ULN with appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash and/or eosinophilia (>5%)
• Development of macular oedema during the study
• Initiation of treatment with a disease-modifying medication for a worsening of psoriasis
• Recurrence of the abnormality at re-challenge
• Interruption to study medication lasting more than 14 days.

In addition, a subject may voluntarily withdraw or be permanently withdrawn from the study at any time for reasons including, but not limited to, the following:
• The subject wishes to withdraw from further participation
• The subject is non-compliant with the protocol
• The treatment blind is broken for the subject for the reasons other than regulatory reporting
• Continuation in the study would be detrimental to the subject's safety in the opinion of the Investigator
• Pregnancy
• The Investigator or the Sponsor, for any reason, stops the study

Background therapy: -
Evidence for comparator: -

Actual start date of recruitment	02 October 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 46

Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	Germany: 33
Country: Number of subjects enrolled	Hungary: 9
Country: Number of subjects enrolled	Latvia: 21
Country: Number of subjects enrolled	Russian Federation: 18
Country: Number of subjects enrolled	Ukraine: 11
Worldwide total number of subjects	142
EEA total number of subjects	113

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)	142
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

142 subjects randomised across 40 sites in 8 countries (Bulgaria, Estonia, Germany, Hungary, Latvia, Poland, Russia, and Ukraine). FSFV (screen) 02 Oct 2013, LSI (screen) 22 Apr 2014. FSFV (randomised) 21 Oct 2013. LSI (randomised) 13 May 2014.
The study was conducted in university/public/private hospitals and specialised dermatology practices.

Pre-assignment

Screening details:

Up to 4 week screening period

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Assessor

Blinding implementation details:

Lymphotcyte count and WBC differential were not provided to any site/study personel except the Unblinded Independent Monitor to maintain the study medication blind. PK results were not provided by the PK lab until after database lock.
MT-1303/placebo capsules appeared the same and same number of capsules were given.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Once daily oral placebo capsules taken from Baseline Week 0 to End of Treatment

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule, containing placebo taken orally daily for 16 weeks.

Arm title	MT-1303 0.1mg

Arm description:

Once daily oral MT-1303 0.1mg capsules taken from Baseline Week 0 to End of Treatment

Arm type	Experimental
Investigational medicinal product name	MT-1303
Investigational medicinal product code	MT-1303
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule, containing MT-1303 0.1mg taken orally daily for 16 weeks.

Arm title	MT-1303 0.2mg

Arm description:

Once daily oral MT-1303 0.2mg capsules taken from Baseline Week 0 to End of Treatment

Arm type	Experimental

Investigational medicinal product name	MT-1303
Investigational medicinal product code	MT-1303
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule, containing MT-1303 0.2mg taken orally daily for 16 weeks.

Arm title	MT-1303 0.4mg

Arm description:

Once daily oral MT-1303 0.4mg capsules taken from Baseline Week 0 to End of Treatment

Arm type	Experimental
Investigational medicinal product name	MT-1303
Investigational medicinal product code	MT-1303
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

1 capsule, containing MT-1303 0.4mg taken orally daily for 16 weeks.

Number of subjects in period 1	Placebo	MT-1303 0.1mg	MT-1303 0.2mg
Started	35	36	35
Completed	30	30	25
Not completed	5	6	10
Consent withdrawn by subject	3	3	4
Adverse event, non-fatal	2	1	2
Other	-	1	2
Lost to follow-up	-	1	1
Lack of efficacy	-	-	1
Protocol deviation	-	-	-

Number of subjects in period 1	MT-1303 0.4mg
Started	36
Completed	32
Not completed	4
Consent withdrawn by subject	1
Adverse event, non-fatal	1
Other	1
Lost to follow-up	-
Lack of efficacy	-
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Once daily oral placebo capsules taken from Baseline Week 0 to End of Treatment	
Reporting group title	MT-1303 0.1mg
Reporting group description:	
Once daily oral MT-1303 0.1mg capsules taken from Baseline Week 0 to End of Treatment	
Reporting group title	MT-1303 0.2mg
Reporting group description:	
Once daily oral MT-1303 0.2mg capsules taken from Baseline Week 0 to End of Treatment	
Reporting group title	MT-1303 0.4mg
Reporting group description:	
Once daily oral MT-1303 0.4mg capsules taken from Baseline Week 0 to End of Treatment	

Reporting group values	Placebo	MT-1303 0.1mg	MT-1303 0.2mg
Number of subjects	35	36	35
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	35	36	35
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	38.7	42	39
standard deviation	± 9.8	± 11.2	± 11.2
Gender categorical Units: Subjects			
Female	9	11	6
Male	26	25	29
Baseline PASI Score			
Psoriasis severity index score taken at baseline			
Units: Not Applicable			
arithmetic mean	19.26	19.05	18.04
standard deviation	± 5.78	± 6.77	± 5.34

Reporting group values	MT-1303 0.4mg	Total	
Number of subjects	36	142	

Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	36	142	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	40.9		
standard deviation	± 9.6	-	
Gender categorical Units: Subjects			
Female	11	37	
Male	25	105	
Baseline PASI Score			
Psoriasis severity index score taken at baseline			
Units: Not Applicable			
arithmetic mean	19.41		
standard deviation	± 7.15	-	

Subject analysis sets

Subject analysis set title	ITT - placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description: The ITT pop will include all randomised subjects who received at least one dose of study medication and have at least one post-dose PASI score	
Subject analysis set title	ITT - 0.1mg
Subject analysis set type	Intention-to-treat
Subject analysis set description: The ITT pop will include all randomised subjects who received at least one dose of study medication and have at least one post-dose PASI score	
Subject analysis set title	ITT - 0.2mg
Subject analysis set type	Intention-to-treat
Subject analysis set description: The ITT pop will include all randomised subjects who received at least one dose of study medication and have at least one post-dose PASI score	
Subject analysis set title	ITT - 0.4mg
Subject analysis set type	Intention-to-treat
Subject analysis set description: The ITT pop will include all randomised subjects who received at least one dose of study medication and have at least one post-dose PASI score	

Reporting group values	ITT - placebo	ITT - 0.1mg	ITT - 0.2mg
Number of subjects	35	35	34
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	35	35	34
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	38.7	42.1	39.4
standard deviation	± 9.8	± 11.3	± 11.1
Gender categorical			
Units: Subjects			
Female	9	11	5
Male	26	24	29
Baseline PASI Score			
Psoriasis severity index score taken at baseline			
Units: Not Applicable			
arithmetic mean	19.26	18.95	18.01
standard deviation	± 5.78	± 6.84	± 5.42

Reporting group values	ITT - 0.4mg		
Number of subjects	35		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	35		
From 65-84 years	0		
85 years and over	0		
Age continuous			
Units: years			
arithmetic mean	41.1		
standard deviation	± 9.7		
Gender categorical			
Units: Subjects			
Female	10		
Male	25		

Baseline PASI Score			
Psoriasis severity index score taken at baseline			
Units: Not Applicable			
arithmetic mean	19.43		
standard deviation	± 7.26		

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Once daily oral placebo capsules taken from Baseline Week 0 to End of Treatment	
Reporting group title	MT-1303 0.1mg
Reporting group description:	
Once daily oral MT-1303 0.1mg capsules taken from Baseline Week 0 to End of Treatment	
Reporting group title	MT-1303 0.2mg
Reporting group description:	
Once daily oral MT-1303 0.2mg capsules taken from Baseline Week 0 to End of Treatment	
Reporting group title	MT-1303 0.4mg
Reporting group description:	
Once daily oral MT-1303 0.4mg capsules taken from Baseline Week 0 to End of Treatment	
Subject analysis set title	ITT - placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT pop will include all randomised subjects who received at least one dose of study medication and have at least one post-dose PASI score	
Subject analysis set title	ITT - 0.1mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT pop will include all randomised subjects who received at least one dose of study medication and have at least one post-dose PASI score	
Subject analysis set title	ITT - 0.2mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT pop will include all randomised subjects who received at least one dose of study medication and have at least one post-dose PASI score	
Subject analysis set title	ITT - 0.4mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT pop will include all randomised subjects who received at least one dose of study medication and have at least one post-dose PASI score	

Primary: The proportion of subjects that achieved PASI 75 (at least 75% reduction from baseline in PASI score) at Week 16 (LOCF)

End point title	The proportion of subjects that achieved PASI 75 (at least 75% reduction from baseline in PASI score) at Week 16 (LOCF)
End point description:	
The least squares mean are back transformed into estimates of the odds of achieving PASI 75	
End point type	Primary
End point timeframe:	
Week 16 LOCF	

End point values	ITT - placebo	ITT - 0.1mg	ITT - 0.2mg	ITT - 0.4mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	34	35
Units: Proportion of subjects				
least squares mean (confidence interval 95%)	0.06 (0.01 to 0.24)	0.09 (0.03 to 0.3)	0.27 (0.12 to 0.61)	0.28 (0.13 to 0.63)

Statistical analyses

Statistical analysis title	PASI 75 at week 16 LOCF 0.1 mg vs placebo
Statistical analysis description:	
Estimated odds and odds ratios were based on logistic regression model with treatment fixed effect and baseline PASI score as a covariate. Two sided 95% Cis and p-values were computed using Wald's test	
Comparison groups	ITT - placebo v ITT - 0.1mg
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.644
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.24
upper limit	9.97

Statistical analysis title	PASI 75 at week 16 LOCF 0.2 mg vs placebo
Statistical analysis description:	
Estimated odds and odds ratios were based on logistic regression model with treatment fixed effect and baseline PASI score as a covariate. Two sided 95% Cis and p-values were computed using Wald's test	
Comparison groups	ITT - placebo v ITT - 0.2mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.073
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	24.13

Statistical analysis title	PASI 75 at week 16 LOCF 0.4 mg vs placebo

Statistical analysis description:

Estimated odds and odds ratios were based on logistic regression model with treatment fixed effect and baseline PASI score as a covariate. Two sided 95% Cis and p-values were computed using Wald's test

Comparison groups	ITT - placebo v ITT - 0.4mg
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.058
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	25.05

Secondary: The proportion of subjects that achieved PASI 75 (at least 75% reduction from baseline in PASI score) at Weeks 4, 8 and 12

End point title	The proportion of subjects that achieved PASI 75 (at least 75% reduction from baseline in PASI score) at Weeks 4, 8 and 12

End point description:

The least square means are back transformed into estimates of the odds of achieving PASI 75

End point type	Secondary

End point timeframe:

Weeks 4

End point values	ITT - placebo	ITT - 0.1mg	ITT - 0.2mg	ITT - 0.4mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	34	33[1]	33	34[2]
Units: Proportion of subjects				
least squares mean (confidence interval 95%)	0 (0 to 0)	0 (0 to 999)	0.03 (0 to 0.25)	0 (0 to 999)

Notes:

[1] - '999' represents a non evaluable value (NE). The system does not allow to enter 'NE'.

[2] - '999' represents a non evaluable value (NE). The system does not allow to enter 'NE'.

Statistical analyses

Statistical analysis title	PASI 75 at week 4 0.1 mg vs placebo

Statistical analysis description:

Estimated odds and odds ratios were based on logistic regression model with treatment fixed effect and baseline PASI score as a covariate. Two sided 95% Cis and p-values were computed using Wald's test

Comparison groups	ITT - placebo v ITT - 0.1mg

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 999 [3]
Method	Regression, Logistic

Notes:

[3] - 999' represents a non evaluable value (NE). The system does not allow to enter 'NE'.

Statistical analysis title	PASI 75 at week 4 0.2 mg vs placebo

Statistical analysis description:

Estimated odds and odds ratios were based on logistic regression model with treatment fixed effect and baseline PASI score as a covariate. Two sided 95% Cis and p-values were computed using Wald's test

Comparison groups	ITT - placebo v ITT - 0.2mg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 999 [4]
Method	Regression, Logistic

Notes:

[4] - 999' represents a non evaluable value (NE). The system does not allow to enter 'NE'.

Statistical analysis title	PASI 75 at week 4 0.4 mg vs placebo

Statistical analysis description:

Estimated odds and odds ratios were based on logistic regression model with treatment fixed effect and baseline PASI score as a covariate. Two sided 95% Cis and p-values were computed using Wald's test

Comparison groups	ITT - placebo v ITT - 0.4mg
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 999 [5]
Method	Regression, Logistic

Notes:

[5] - 999' represents a non evaluable value (NE). The system does not allow to enter 'NE'.

Secondary: The proportion of subjects that achieved PASI 75 (at least 75% reduction from baseline in PASI score) at Weeks 4, 8 and 12

End point title	The proportion of subjects that achieved PASI 75 (at least 75% reduction from baseline in PASI score) at Weeks 4, 8 and 12

End point description:

The least squares mean are back transformed into estimates of the odds of achieving PASI 75

End point type	Secondary

End point timeframe:

Weeks 8

End point values	ITT - placebo	ITT - 0.1mg	ITT - 0.2mg	ITT - 0.4mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	33	31	27	33
Units: Proportion of subjects				
least squares mean (confidence interval 95%)	0.02 (0 to 0.19)	0.02 (0 to 0.22)	0.12 (0.03 to 0.41)	0.04 (0.01 to 0.22)

Statistical analyses

Statistical analysis title	PASI 75 at week 8 0.1 mg vs placebo
Statistical analysis description:	
Estimated odds and odds ratios were based on logistic regression model with treatment fixed effect and baseline PASI score as a covariate. Two sided 95% Cis and p-values were computed using Wald's test	
Comparison groups	ITT - placebo v ITT - 0.1mg
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.976
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.05
upper limit	17.91

Statistical analysis title	PASI 75 at week 8 0.2 mg vs placebo
Statistical analysis description:	
Estimated odds and odds ratios were based on logistic regression model with treatment fixed effect and baseline PASI score as a covariate. Two sided 95% Cis and p-values were computed using Wald's test	
Comparison groups	ITT - placebo v ITT - 0.2mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.198
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	4.77
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	51.56

Statistical analysis title	PASI 75 at week 8 0.4 mg vs placebo

Statistical analysis description:

Estimated odds and odds ratios were based on logistic regression model with treatment fixed effect and baseline PASI score as a covariate. Two sided 95% Cis and p-values were computed using Wald's test

Comparison groups	ITT - placebo v ITT - 0.4mg
Number of subjects included in analysis	66
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.659
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	21.72

Secondary: The proportion of subjects that achieved PASI 75 (at least 75% reduction from baseline in PASI score) at Weeks 4, 8 and 12

End point title	The proportion of subjects that achieved PASI 75 (at least 75% reduction from baseline in PASI score) at Weeks 4, 8 and 12

End point description:

The least squares mean are back transformed into estimates of the odds of achieving PASI 75

End point type	Secondary

End point timeframe:

Weeks 12

End point values	ITT - placebo	ITT - 0.1mg	ITT - 0.2mg	ITT - 0.4mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	30	30	26	33
Units: Proportion of subjects				
least squares mean (confidence interval 95%)	0.03 (0 to 0.24)	0.07 (0.02 to 0.31)	0.18 (0.06 to 0.53)	0.25 (0.11 to 0.6)

Statistical analyses

Statistical analysis title	PASI 75 at week 12 0.1 mg vs placebo

Statistical analysis description:

Estimated odds and odds ratios were based on logistic regression model with treatment fixed effect and baseline PASI score as a covariate. Two sided 95% Cis and p-values were computed using Wald's test

Comparison groups	ITT - placebo v ITT - 0.1mg

Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.522
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	2.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	26.34

Statistical analysis title	PASI 75 at week 12 0.2 mg vs placebo
Statistical analysis description:	
Estimated odds and odds ratios were based on logistic regression model with treatment fixed effect and baseline PASI score as a covariate. Two sided 95% Cis and p-values were computed using Wald's test	
Comparison groups	ITT - placebo v ITT - 0.2mg
Number of subjects included in analysis	56
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.141
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	5.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	52.85

Statistical analysis title	PASI 75 at week 12 0.4 mg vs placebo
Comparison groups	ITT - placebo v ITT - 0.4mg
Number of subjects included in analysis	63
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.065
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	7.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	67.01

Secondary: Mean percent change from baseline in PASI score at Weeks 4, 8, 12 and 16

End point title	Mean percent change from baseline in PASI score at Weeks 4, 8, 12 and 16

End point description:

End point type	Secondary

End point timeframe:

Week 4

End point values	ITT - placebo	ITT - 0.1mg	ITT - 0.2mg	ITT - 0.4mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	34	35
Units: %				
least squares mean (standard error)	-13.52 (± 4.04)	-12.51 (± 4.09)	-10.83 (± 4.1)	-16.17 (± 4.04)

Statistical analyses

Statistical analysis title	% change from baseline at wk 4 0.1mg vs placebo

Statistical analysis description:

P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.1mg
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.86
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.36
upper limit	12.39

Statistical analysis title	% change from baseline at wk 4 0.2mg vs placebo

Statistical analysis description:

P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.2mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.641
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	2.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.71
upper limit	14.09

Statistical analysis title	% change from baseline at wk 4 0.4mg vs placebo

Statistical analysis description:

P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.4mg
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.643
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-2.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.93
upper limit	8.64

Secondary: Mean percent change from baseline in PASI score at Weeks 4, 8, 12 and 16

End point title	Mean percent change from baseline in PASI score at Weeks 4, 8, 12 and 16

End point description:

End point type	Secondary

End point timeframe:

Week 8

End point values	ITT - placebo	ITT - 0.1mg	ITT - 0.2mg	ITT - 0.4mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	34	35
Units: %				
least squares mean (standard error)	-19.84 (± 4.71)	-25.42 (± 4.81)	-20.27 (± 4.95)	-29.94 (± 4.71)

Statistical analyses

Statistical analysis title	% change from baseline at wk 8 0.1mg vs placebo

Statistical analysis description:

P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.1mg
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.409
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-5.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	-18.89
upper limit	7.75

Statistical analysis title	% change from baseline at wk 8 0.2mg vs placebo

Statistical analysis description:

P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.2mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.951
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-0.42

Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.95
upper limit	13.11

Statistical analysis title	% change from baseline at wk 8 0.4mg vs placebo

Statistical analysis description:

P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.4mg
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.132
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-10.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-23.27
upper limit	3.08

Secondary: Mean percent change from baseline in PASI score at Weeks 4, 8, 12 and 16

End point title	Mean percent change from baseline in PASI score at Weeks 4, 8, 12 and 16

End point description:

End point type	Secondary

End point timeframe:

Week 12

End point values	ITT - placebo	ITT - 0.1mg	ITT - 0.2mg	ITT - 0.4mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	34	35
Units: %				
least squares mean (standard error)	-28.89 (± 5.22)	-33.16 (± 5.3)	-27.07 (± 5.54)	-45.32 (± 5.13)

Statistical analyses

Statistical analysis title	% change from baseline at wk 12 0.1mg vs placebo

Statistical analysis description:

"P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.1mg
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.567
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-4.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-19.02
upper limit	10.46

Statistical analysis title	% change from baseline at wk 12 0.2mg vs placebo

Statistical analysis description:

"P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.2mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.812
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	1.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	-13.27
upper limit	16.9

Statistical analysis title	% change from baseline at wk 12 0.4mg vs placebo

Statistical analysis description:

"P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.4mg
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-16.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-30.91
upper limit	-1.96

Secondary: Mean percent change from baseline in PASI score at Weeks 4, 8, 12 and 16

End point title	Mean percent change from baseline in PASI score at Weeks 4, 8, 12 and 16

End point description:

End point type	Secondary

End point timeframe:

Week 16

End point values	ITT - placebo	ITT - 0.1mg	ITT - 0.2mg	ITT - 0.4mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	35	35	34	35
Units: %				
least squares mean (standard error)	-34.07 (± 5.48)	-41.35 (± 5.54)	-33.55 (± 5.87)	-47.92 (± 5.36)

Statistical analyses

Statistical analysis title	% change from baseline at wk 16 0.1mg vs placebo

Statistical analysis description:

P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.1mg
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.353
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-7.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-22.73
upper limit	8.17

Statistical analysis title	% change from baseline at wk 16 0.2mg vs placebo

Statistical analysis description:

P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.2mg
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.949
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.39
upper limit	16.43

Statistical analysis title	% change from baseline at wk 16 0.4mg vs placebo

Statistical analysis description:

P-values are based on a mixed model for repeated measures with percentage change from baseline in PASI Score at each post-baseline scheduled visit as the response variable. The independent variables are treatment, visit, treatment-by-visit interaction as fixed effects and baseline PASI Score and baseline PASI score-by-visit interaction as the covariates. Covariance Structure: Unstructured.

Comparison groups	ITT - placebo v ITT - 0.4mg
Number of subjects included in analysis	70
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.073
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	-13.84

Confidence interval	
level	95 %
sides	2-sided
lower limit	-29.01
upper limit	1.32

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Start of double-blind treatment to end of 12 week follow-up period. Treatment-Emergent AEs were defined as those which started or worsened in severity after the first dose of double-blind study medication.

Adverse event reporting additional description:

During the study visits regular questioning of each subject by study staff. No leading questions were asked. Data recorded under "Non-Serious Adverse Events" also includes serious adverse events as that is how data was reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17

Reporting groups

Reporting group title	Placebo

Reporting group description:

Once daily oral placebo capsules taken from Baseline Week 0 to end of treatment

Reporting group title	MT-1303 0.1mg

Reporting group description:

Once daily oral MT-1303 0.1mg capsules taken from Baseline Week 0 to end of treatment

Reporting group title	MT-1303 0.2mg

Reporting group description:

Once daily oral MT-1303 0.2mg capsules taken from Baseline Week 0 to end of treatment

Reporting group title	MT-1303 0.4mg

Reporting group description:

Once daily oral MT-1303 0.4mg capsules taken from Baseline Week 0 to end of treatment

Serious adverse events	Placebo	MT-1303 0.1mg	MT-1303 0.2mg
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 35 (5.71%)	0 / 36 (0.00%)	0 / 35 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events			
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alanine aminotransferase increased			

subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increaased			
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
AV Block 2nd Degree			
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	MT-1303 0.4mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 36 (2.78%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Alanine aminotransferase increased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood bilirubin increased			

subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gamma-glutamyltransferase increaased			
subjects affected / exposed	1 / 36 (2.78%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
AV Block 2nd Degree			
subjects affected / exposed	0 / 36 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Placebo	MT-1303 0.1mg	MT-1303 0.2mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	17 / 35 (48.57%)	20 / 36 (55.56%)	25 / 35 (71.43%)
Investigations			
Blood creatine phosphokinase increased	Additional description: Number of occurrences were not reported		
subjects affected / exposed	2 / 35 (5.71%)	2 / 36 (5.56%)	5 / 35 (14.29%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased	Additional description: Number of occurrences were not reported		
subjects affected / exposed	1 / 35 (2.86%)	2 / 36 (5.56%)	2 / 35 (5.71%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased	Additional description: Number of occurrences were not reported		
subjects affected / exposed	2 / 35 (5.71%)	0 / 36 (0.00%)	3 / 35 (8.57%)
occurrences (all)	0	0	0
Alanine aminotransferase increased	Additional description: Number of occurrences were not reported		
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	0
Blood triglycerides increased	Additional description: Number of occurrences were not reported		

subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension	Additional description: Number of occurrences were not reported		
subjects affected / exposed	1 / 35 (2.86%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia	Additional description: Number of occurrences were not reported		
subjects affected / exposed	0 / 35 (0.00%)	3 / 36 (8.33%)	2 / 35 (5.71%)
occurrences (all)	0	0	0
Supraventricular tachycardia	Additional description: Number of occurrences were not reported		
subjects affected / exposed	1 / 35 (2.86%)	2 / 36 (5.56%)	1 / 35 (2.86%)
occurrences (all)	0	0	0
Ventricular tachycardia	Additional description: Number of occurrences were not reported		
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	0	0
Nervous system disorders			
Headache	Additional description: Number of occurrences were not reported		
subjects affected / exposed	2 / 35 (5.71%)	1 / 36 (2.78%)	4 / 35 (11.43%)
occurrences (all)	0	0	0
Dizziness	Additional description: Number of occurrences were not reported		
subjects affected / exposed	0 / 35 (0.00%)	0 / 36 (0.00%)	2 / 35 (5.71%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia	Additional description: Number of occurrences were not reported		
subjects affected / exposed	1 / 35 (2.86%)	0 / 36 (0.00%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea	Additional description: Number of occurrences were not reported		
subjects affected / exposed	1 / 35 (2.86%)	1 / 36 (2.78%)	2 / 35 (5.71%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Psoriasis	Additional description: Number of occurrences were not reported		
subjects affected / exposed	2 / 35 (5.71%)	4 / 36 (11.11%)	4 / 35 (11.43%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			

Arthralgia	Additional description: Number of occurrences were not reported		
subjects affected / exposed	0 / 35 (0.00%)	1 / 36 (2.78%)	1 / 35 (2.86%)
occurrences (all)	0	0	0
Infections and infestations			
Nasopharyngitis	Additional description: Number of occurrences were not reported		
subjects affected / exposed	5 / 35 (14.29%)	5 / 36 (13.89%)	8 / 35 (22.86%)
occurrences (all)	0	0	0
Rhinitis	Additional description: Number of occurrences were not reported		
subjects affected / exposed	2 / 35 (5.71%)	1 / 36 (2.78%)	0 / 35 (0.00%)
occurrences (all)	0	0	0
Oral viral infection	Additional description: Number of occurrences were not reported		
subjects affected / exposed	0 / 35 (0.00%)	2 / 36 (5.56%)	0 / 35 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	MT-1303 0.4mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	26 / 36 (72.22%)		
Investigations			
Blood creatine phosphokinase increased	Additional description: Number of occurrences were not reported		
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased	Additional description: Number of occurrences were not reported		
subjects affected / exposed	4 / 36 (11.11%)		
occurrences (all)	0		
Aspartate aminotransferase increased	Additional description: Number of occurrences were not reported		
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	0		
Alanine aminotransferase increased	Additional description: Number of occurrences were not reported		
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	0		
Blood triglycerides increased	Additional description: Number of occurrences were not reported		
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	0		
Vascular disorders			
Hypertension	Additional description: Number of occurrences were not reported		

subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	0		
Cardiac disorders			
Tachycardia	Additional description: Number of occurrences were not reported		
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Supraventricular tachycardia	Additional description: Number of occurrences were not reported		
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Ventricular tachycardia	Additional description: Number of occurrences were not reported		
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	0		
Nervous system disorders			
Headache	Additional description: Number of occurrences were not reported		
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	0		
Dizziness	Additional description: Number of occurrences were not reported		
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
General disorders and administration site conditions			
Pyrexia	Additional description: Number of occurrences were not reported		
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Rhinorrhoea	Additional description: Number of occurrences were not reported		
subjects affected / exposed	1 / 36 (2.78%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Psoriasis	Additional description: Number of occurrences were not reported		
subjects affected / exposed	3 / 36 (8.33%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia	Additional description: Number of occurrences were not reported		
subjects affected / exposed	2 / 36 (5.56%)		
occurrences (all)	0		
Infections and infestations			

Nasopharyngitis	Additional description: Number of occurrences were not reported		
subjects affected / exposed	5 / 36 (13.89%)		
occurrences (all)	0		
Rhinitis	Additional description: Number of occurrences were not reported		
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		
Oral viral infection	Additional description: Number of occurrences were not reported		
subjects affected / exposed	0 / 36 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 July 2014	Clarification of safety follow up period for withdrawn subjects

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported