



Clinical trial results:

An Open-label, Multicenter, Phase 1/2 Study of JNJ-40346527, an FMS Inhibitor, in Subjects with Relapsed or Refractory Hodgkin Lymphoma

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

Summary

EudraCT number	2011-005795-42
Trial protocol	DE
Global end of trial date	13 August 2013

Results information

Result version number	v2 (current)
This version publication date	15 July 2016
First version publication date	03 August 2015
Version creation reason	<ul style="list-style-type: none">• Correction of full data setReview of data

Trial information

Trial identification

Sponsor protocol code	40346527HKL1001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01572519
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Research & Development, LLC
Sponsor organisation address	Archimedesweg 29-2333CM, Leiden, Netherlands, B235-0
Public contact	Clinical Registry Group, Janssen Research & Development, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Research & Development, LLC, 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	13 August 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	13 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To determine the safety, pharmacokinetics, and preliminary efficacy information of JNJ-40346527 in participants with relapsed or refractory Hodgkin lymphoma.
To establish the recommended Phase 2 dose for JNJ-40346527.

Protection of trial subjects:

Safety was evaluated based on the variables like adverse events, Clinical laboratory tests (hematology, serum chemistry, and urinalysis), Vital sign measurements, Physical examinations, Electrocardiograms (ECGs) and Eastern Cooperative Oncology Group (ECOG) performance status.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	06 July 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	Germany: 10
Country: Number of subjects enrolled	France: 11
Worldwide total number of subjects	21
EEA total number of subjects	21

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)	18
From 65 to 84 years	3
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 21 participants were enrolled and treated with JNJ 40346527.

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

Are arms mutually exclusive?	Yes
Arm title	150 mg once daily (QD)

Arm description:

Participants received JNJ-40346527, 150 milligram (mg) capsules once daily.

Arm type	Experimental
Investigational medicinal product name	JNJ-40346527
Investigational medicinal product code	JNJ-40346527-AAC
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

JNJ-40346527 Capsules 150 mg once daily

Arm title	300 mg QD
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Arm description:

Participants received JNJ-40346527, 300 mg capsules once daily.

Arm type	Experimental
Investigational medicinal product name	JNJ-40346527
Investigational medicinal product code	JNJ-40346527-AAC
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

JNJ-40346527 Capsules 300 mg once daily

Arm title	450 mg QD
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Arm description:

Participants received JNJ-40346527, 450 mg capsules once daily.

Arm type	Experimental
Investigational medicinal product name	JNJ-40346527
Investigational medicinal product code	JNJ-40346527-AAC
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

JNJ-40346527 Capsules 450 mg once daily

Arm title	600 mg QD
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Arm description:

Participants received JNJ-40346527, 600 mg capsules once daily.

Arm type	Experimental
Investigational medicinal product name	JNJ-40346527
Investigational medicinal product code	JNJ-40346527-AAC
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

JNJ-40346527 Capsules 600 mg once daily

Arm title	150 mg twice daily (BID)
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Arm description:

Participants received JNJ-40346527, 150 mg capsules twice daily.

Arm type	Experimental
Investigational medicinal product name	JNJ-40346527
Investigational medicinal product code	JNJ-40346527-AAC
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

JNJ-40346527 Capsules 150 mg twice daily

Number of subjects in period 1	150 mg once daily (QD)	300 mg QD	450 mg QD
Started	3	5	3
Completed	0	0	0
Not completed	3	5	3
Physician decision	1	-	-
Adverse event, non-fatal	-	-	-
Other	1	-	-
Lack of efficacy	1	5	3

Number of subjects in period 1	600 mg QD	150 mg twice daily (BID)
Started	3	7
Completed	0	0
Not completed	3	7
Physician decision	-	-
Adverse event, non-fatal	-	1
Other	-	-
Lack of efficacy	3	6

Baseline characteristics

Reporting groups

Reporting group title	150 mg once daily (QD)
Reporting group description:	
Participants received JNJ-40346527, 150 milligram (mg) capsules once daily.	
Reporting group title	300 mg QD
Reporting group description:	
Participants received JNJ-40346527, 300 mg capsules once daily.	
Reporting group title	450 mg QD
Reporting group description:	
Participants received JNJ-40346527, 450 mg capsules once daily.	
Reporting group title	600 mg QD
Reporting group description:	
Participants received JNJ-40346527, 600 mg capsules once daily.	
Reporting group title	150 mg twice daily (BID)
Reporting group description:	
Participants received JNJ-40346527, 150 mg capsules twice daily.	

Reporting group values	150 mg once daily (QD)	300 mg QD	450 mg QD
Number of subjects	3	5	3
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2	5	2
From 65 to 84 years	1	0	1
85 years and over	0	0	0
Title for AgeContinuous Units: Years			
arithmetic mean	48	33.4	49
standard deviation	± 24.88	± 9.99	± 18.52
Title for Gender Units: subjects			
Female	0	1	2
Male	3	4	1

Reporting group values	600 mg QD	150 mg twice daily (BID)	Total
Number of subjects	3	7	21
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	3	6	18
From 65 to 84 years	0	1	3
85 years and over	0	0	0

Title for AgeContinuous Units: Years arithmetic mean standard deviation	29.3 ± 10.5	38.6 ± 18.57	-
Title for Gender Units: subjects			
Female	2	5	10
Male	1	2	11

End points

End points reporting groups

Reporting group title	150 mg once daily (QD)
Reporting group description: Participants received JNJ-40346527, 150 milligram (mg) capsules once daily.	
Reporting group title	300 mg QD
Reporting group description: Participants received JNJ-40346527, 300 mg capsules once daily.	
Reporting group title	450 mg QD
Reporting group description: Participants received JNJ-40346527, 450 mg capsules once daily.	
Reporting group title	600 mg QD
Reporting group description: Participants received JNJ-40346527, 600 mg capsules once daily.	
Reporting group title	150 mg twice daily (BID)
Reporting group description: Participants received JNJ-40346527, 150 mg capsules twice daily.	
Subject analysis set title	JNJ-40346527
Subject analysis set type	Per protocol
Subject analysis set description: Participants who received at least one dose of study medication.	
Subject analysis set title	Evaluable Participant Population (EPP)
Subject analysis set type	Full analysis
Subject analysis set description: Evaluable Participant Population includes Participants who received at least 1 dose of the study treatment, and had baseline and at least one post- treatment tumor assessment.	
Subject analysis set title	Safety Analysis Set (SAS)
Subject analysis set type	Safety analysis
Subject analysis set description: Participants who received at least one dose of study medication.	

Primary: Recommended Phase 2 dose (RP2D) for JNJ-40346527

End point title	Recommended Phase 2 dose (RP2D) for JNJ-40346527 ^[1]
End point description: RP2D will be determined based on pharmacodynamics, biomarker response or clinical response, as well as the incidence rate and nature of the toxicities observed.	

End point type	Primary
End point timeframe: Up to 24 hours after last dose administration	

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	JNJ-40346527			
Subject group type	Subject analysis set			
Number of subjects analysed	21 ^[2]			
Units: milligram (mg)				
number (not applicable)	150			

Notes:

[2] - EPP

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants with Overall Response Rate

End point title	Number of Participants with Overall Response Rate ^[3]
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End point description:

Overall response rate is defined as the number of participants who achieve complete response or partial response, during or after study treatment. Here 'N' signifies number of subjects who were analysed for this outcome measure.

End point type	Primary
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End point timeframe:

Up to 6 months after the last subject is enrolled

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	150 mg once daily (QD)	300 mg QD	450 mg QD	600 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3 ^[4]	5 ^[5]	3 ^[6]	3 ^[7]
Units: Participants				
number (not applicable)				
Complete Response (CR)	1	0	0	0
Partial Response (PR)	0	0	0	0

Notes:

[4] - EPP

[5] - EPP

[6] - EPP

[7] - EPP

End point values	150 mg twice daily (BID)			
Subject group type	Reporting group			
Number of subjects analysed	6 ^[8]			
Units: Participants				
number (not applicable)				
Complete Response (CR)	0			
Partial Response (PR)	0			

Notes:

[8] - EPP

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Treatment-Emergent Adverse Events

End point title	Number of Participants With Treatment-Emergent Adverse Events
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End point description:

A treatment-emergent adverse event (TEAE) was defined as an event that occurred up to 30 days after the last dose of study medication treatment period during which it emerged (i.e. started or worsened in severity, relation, or other attribute), and even if the event continued to be present.

End point type	Secondary
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End point timeframe:

Up to 30 days after the last dose of study medication

End point values	JNJ-40346527			
Subject group type	Subject analysis set			
Number of subjects analysed	21 ^[9]			
Units: participants				
number (not applicable)	19			

Notes:

[9] - SAS

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (C_{max}) of JNJ-40346527

End point title	Maximum Plasma Concentration (C _{max}) of JNJ-40346527
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End point description:

C_{max} refers to the highest measured drug concentration which is obtained by collecting a series of blood samples and measuring the concentrations of drug in each sample. Here 'n' signifies number of subjects who were analysed for this outcome measure.

End point type	Secondary
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End point timeframe:

Day 1 and Day 21

End point values	150 mg once daily (QD)	300 mg QD	450 mg QD	600 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3 ^[10]	5 ^[11]	3 ^[12]	3 ^[13]
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1 (n= 3, 5, 3, 3, 7)	278 (± 71.4)	552 (± 198)	552 (± 655)	358 (± 244)

Day 21 (n= 2, 3, 3, 3, 6)	304 (± 321)	598 (± 156)	1157 (± 409)	843 (± 394)
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Notes:

[10] - EPP

[11] - EPP

[12] - EPP

[13] - EPP

End point values	150 mg twice daily (BID)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[14]			
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)				
Day 1 (n= 3, 5, 3, 3, 7)	313 (± 86.9)			
Day 21 (n= 2, 3, 3, 3, 6)	483 (± 182)			

Notes:

[14] - EPP

Statistical analyses

No statistical analyses for this end point

Secondary: Minimum Plasma Concentration (Cmin) of JNJ-40346527

End point title	Minimum Plasma Concentration (Cmin) of JNJ-40346527
End point description:	
Cmin refers to the lowest measured drug concentration which is obtained by collecting a series of blood samples and measuring the concentrations of drug in each sample. Here 'N' signifies number of subjects who were analysed for this outcome measure.	
End point type	Secondary
End point timeframe:	
Day 21	

End point values	150 mg once daily (QD)	300 mg QD	450 mg QD	600 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[15]	3 ^[16]	3 ^[17]	3 ^[18]
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	100 (± 101)	160 (± 63.2)	277 (± 89)	129 (± 45.4)

Notes:

[15] - EPP

[16] - EPP

[17] - EPP

[18] - EPP

End point values	150 mg twice daily (BID)			
Subject group type	Reporting group			
Number of subjects analysed	6 ^[19]			
Units: nanogram per milliliter (ng/mL)				
arithmetic mean (standard deviation)	196 (± 41)			

Notes:

[19] - EPP

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Reach the Maximum Plasma Concentration (Tmax) of JNJ-40346527

End point title	Time to Reach the Maximum Plasma Concentration (Tmax) of JNJ-40346527
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End point description:

The Tmax is defined as actual sampling time to reach maximum observed analyte concentration. Here 'n' signifies number of subjects who were analysed for this outcome measure

End point type	Secondary
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End point timeframe:

Day 1 and Day 21

End point values	150 mg once daily (QD)	300 mg QD	450 mg QD	600 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3 ^[20]	5 ^[21]	3 ^[22]	3 ^[23]
Units: hours				
median (full range (min-max))				
Day 1 (n= 3, 5, 3, 3, 7)	4.1 (1 to 4.5)	3 (2 to 4)	2.1 (2.1 to 2.1)	3 (2 to 4)
Day 21 (n= 2, 3, 3, 3, 6)	1 (1 to 3.1)	4.1 (4 to 5.9)	3 (2 to 4.5)	3.9 (3 to 4)

Notes:

[20] - EPP

[21] - EPP

[22] - EPP

[23] - EPP

End point values	150 mg twice daily (BID)			
Subject group type	Reporting group			
Number of subjects analysed	7 ^[24]			
Units: hours				
median (full range (min-max))				
Day 1 (n= 3, 5, 3, 3, 7)	1 (1 to 6)			
Day 21 (n= 2, 3, 3, 3, 6)	2.5 (1.9 to 8)			

Notes:

[24] - EPP

Statistical analyses

No statistical analyses for this end point

Secondary: Area Under the Plasma Concentration-Time Curve From 0 to 24 Hours (AUC[0-24]) Post Dose of JNJ-40346527

End point title	Area Under the Plasma Concentration-Time Curve From 0 to 24 Hours (AUC[0-24]) Post Dose of JNJ-40346527
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End point description:

The AUC (0-24) calculated by trapezoidal summation [time t is the time 24 hours after dose administration). Here 'n' signifies number of subjects who were analysed for this outcome measure. The value '99999' indicates that the data were not reported at specific time points.

End point type	Secondary
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End point timeframe:

Day 1 and Day 21

End point values	150 mg once daily (QD)	300 mg QD	450 mg QD	600 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3 ^[25]	5 ^[26]	3 ^[27]	3 ^[28]
Units: nanogram * hour per milliliter (ng*h/mL)				
arithmetic mean (standard deviation)				
Day 1 (n= 3, 5, 3, 3, 7)	1931 (± 404)	3935 (± 2001)	2536 (± 4135)	2657 (± 1255)
Day 21 (n= 2, 3, 3, 3, 6)	3417 (± 3436)	7588 (± 2248)	12804 (± 4875)	6961 (± 2656)

Notes:

[25] - EPP

[26] - EPP

[27] - EPP

[28] - EPP

End point values	150 mg twice daily (BID)			
Subject group type	Reporting group			
Number of subjects analysed	6 ^[29]			
Units: nanogram * hour per milliliter (ng*h/mL)				
arithmetic mean (standard deviation)				
Day 1 (n= 3, 5, 3, 3, 7)	99999 (± 99999)			
Day 21 (n= 2, 3, 3, 3, 6)	7471 (± 2349)			

Notes:

[29] - EPP

Statistical analyses

No statistical analyses for this end point

Secondary: Total drug Clearance of JNJ-40346527 (CL/F)

End point title	Total drug Clearance of JNJ-40346527 (CL/F)
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End point description:

The CL is a quantitative measure of the rate at which a drug substance is removed from the body. Here 'N' signifies number of subjects who were analysed for this outcome measure.

End point type	Secondary
End point timeframe:	
Day 21	

End point values	150 mg once daily (QD)	300 mg QD	450 mg QD	600 mg QD
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2 ^[30]	3 ^[31]	3 ^[32]	3 ^[33]
Units: Litre per hour				
arithmetic mean (standard deviation)	43.7 (± 43.9)	42.4 (± 14.5)	39.4 (± 17)	97.7 (± 45.6)

Notes:

[30] - EPP

[31] - EPP

[32] - EPP

[33] - EPP

End point values	150 mg twice daily (BID)			
Subject group type	Reporting group			
Number of subjects analysed	6 ^[34]			
Units: Litre per hour				
arithmetic mean (standard deviation)	49.3 (± 16.8)			

Notes:

[34] - EPP

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 30 days after the last dose of study medication

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	16
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Reporting groups

Reporting group title	300 mg QD
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Reporting group description:

Participants received JNJ-40346527, 300 mg capsules once daily.

Reporting group title	150 mg once daily (QD)
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Reporting group description:

Participants received JNJ-40346527, 150 milligram (mg) capsules once daily.

Reporting group title	600 mg QD
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Reporting group description:

Participants received JNJ-40346527, 600 mg capsules once daily.

Reporting group title	150 mg twice daily (BID)
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Reporting group description:

Participants received JNJ-40346527, 150 mg capsules twice daily.

Reporting group title	450 mg QD
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Reporting group description:

Participants received JNJ-40346527, 450 mg capsules once daily.

Serious adverse events	300 mg QD	150 mg once daily (QD)	600 mg QD
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 5 (40.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	1	0	0
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Acute Phase Reaction			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Gastrointestinal disorders			
Obstruction Gastric			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (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

Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 3 (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
Lung Disorder			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

Serious adverse events	150 mg twice daily (BID)	450 mg QD	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 7 (14.29%)	1 / 3 (33.33%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
General disorders and administration site conditions			
Acute Phase Reaction			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Obstruction Gastric			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Disorder			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	300 mg QD	150 mg once daily (QD)	600 mg QD
Total subjects affected by non-serious adverse events subjects affected / exposed	4 / 5 (80.00%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Fatigue			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oedema Peripheral			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	4 / 5 (80.00%)	3 / 3 (100.00%)	1 / 3 (33.33%)
occurrences (all)	5	6	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Laryngeal Inflammation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Oropharyngeal Pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Pleural Effusion subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Investigations Blood Creatine Phosphokinase Increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 6	0 / 3 (0.00%) 0
Eosinophil Count Increased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Weight Decreased subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Injury, poisoning and procedural complications Ankle Fracture subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Procedural Pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Cardiac disorders Tachycardia			

subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 3	2 / 3 (66.67%) 5	1 / 3 (33.33%) 1
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Lymph Node Pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Lymphopenia subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	2 / 3 (66.67%) 2
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Eye disorders Eczema Eyelids subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Gastrointestinal disorders Abdominal Pain Upper subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1
Constipation subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1
Diarrhoea subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Dyspepsia subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0

Nausea subjects affected / exposed occurrences (all)	3 / 5 (60.00%) 3	1 / 3 (33.33%) 1	1 / 3 (33.33%) 1
Oral Pain subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Stomatitis subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 2
Tongue Ulceration subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	2 / 5 (40.00%) 3	1 / 3 (33.33%) 1	2 / 3 (66.67%) 4
Hepatobiliary disorders Hepatic Function Abnormal subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 2	0 / 3 (0.00%) 0
Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all)	1 / 5 (20.00%) 1	0 / 3 (0.00%) 0	0 / 3 (0.00%) 0
Pruritus subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Night Sweats subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	0 / 3 (0.00%) 0	1 / 3 (33.33%) 1
Rash subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Renal and urinary disorders Renal Failure subjects affected / exposed occurrences (all)	0 / 5 (0.00%) 0	1 / 3 (33.33%) 1	0 / 3 (0.00%) 0
Musculoskeletal and connective tissue			

disorders			
Arthralgia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Back Pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal Pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Torticollis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Fungal Skin Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Herpes Virus Infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	1 / 3 (33.33%)
occurrences (all)	0	1	1
Oral Candidiasis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oral Herpes			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Otitis Media			

subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Scrotal Infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Urinary Tract Infection			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Dehydration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Enzyme Abnormality			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperamylasaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hyperglycaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyperlipasaemia			
subjects affected / exposed	0 / 5 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Hypokalaemia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 5 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	150 mg twice daily (BID)	450 mg QD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 7 (85.71%)	2 / 3 (66.67%)	
Vascular disorders			
Haematoma			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Chills			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Fatigue			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Oedema Peripheral			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Pyrexia			
subjects affected / exposed	2 / 7 (28.57%)	1 / 3 (33.33%)	
occurrences (all)	3	1	
Respiratory, thoracic and mediastinal disorders			
Cough			

subjects affected / exposed	2 / 7 (28.57%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Dyspnoea			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Laryngeal Inflammation			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Oropharyngeal Pain			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Pleural Effusion			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	3 / 7 (42.86%)	1 / 3 (33.33%)	
occurrences (all)	3	1	
Investigations			
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	1 / 7 (14.29%)	1 / 3 (33.33%)	
occurrences (all)	1	1	
Eosinophil Count Increased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Weight Decreased			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
Ankle Fracture			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Procedural Pain			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1	
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0	
Nervous system disorders Headache subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 2	0 / 3 (0.00%) 0	
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all) Lymph Node Pain subjects affected / exposed occurrences (all) Lymphopenia subjects affected / exposed occurrences (all)	2 / 7 (28.57%) 5 0 / 7 (0.00%) 0 1 / 7 (14.29%) 1	1 / 3 (33.33%) 2 0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	
Ear and labyrinth disorders Vertigo subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0	
Eye disorders Eczema Eyelids subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0	
Gastrointestinal disorders Abdominal Pain Upper subjects affected / exposed occurrences (all) Constipation subjects affected / exposed occurrences (all) Diarrhoea	1 / 7 (14.29%) 3 2 / 7 (28.57%) 2	0 / 3 (0.00%) 0 0 / 3 (0.00%) 0	

subjects affected / exposed	2 / 7 (28.57%)	0 / 3 (0.00%)	
occurrences (all)	4	0	
Dyspepsia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	2 / 7 (28.57%)	0 / 3 (0.00%)	
occurrences (all)	3	0	
Oral Pain			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Stomatitis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Tongue Ulceration			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	2	0	
Hepatobiliary disorders			
Hepatic Function Abnormal			
subjects affected / exposed	0 / 7 (0.00%)	1 / 3 (33.33%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Night Sweats			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Rash			

subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0	
Renal and urinary disorders Renal Failure subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0	
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0	
Back Pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	1 / 3 (33.33%) 1	
Musculoskeletal Pain subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0	
Torticollis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0	
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0	
Fungal Skin Infection subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0	
Furuncle subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	0 / 3 (0.00%) 0	
Herpes Virus Infection subjects affected / exposed occurrences (all)	0 / 7 (0.00%) 0	0 / 3 (0.00%) 0	
Nasopharyngitis subjects affected / exposed occurrences (all)	1 / 7 (14.29%) 1	1 / 3 (33.33%) 1	
Oral Candidiasis			

subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Oral Herpes			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Otitis Media			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Scrotal Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Urinary Tract Infection			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Dehydration			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Enzyme Abnormality			
subjects affected / exposed	1 / 7 (14.29%)	1 / 3 (33.33%)	
occurrences (all)	1	2	
Hyperamylasaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hyperglycaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Hyperkalaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	

Hyperlipasaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypoalbuminaemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Hypokalaemia			
subjects affected / exposed	0 / 7 (0.00%)	0 / 3 (0.00%)	
occurrences (all)	0	0	
Hypophosphataemia			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	0	
Type 2 Diabetes Mellitus			
subjects affected / exposed	1 / 7 (14.29%)	0 / 3 (0.00%)	
occurrences (all)	1	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