Clinical trial results:
A Phase 2 Single-Center, Proof-of-Concept Safety and Efficacy Study of Orally Administered OLT1177 Capsules with Successive, Result-Dependent Dose Adaptation in Subjects with an Acute Gout Flare

Summary

EudraCT number	2016-000943-14
Trial protocol	NL
Global end of trial date	04 February 2019

Results information

Result version number	v1 (current)
This version publication date	25 June 2022
First version publication date	25 June 2022

Trial information

Trial identification

Sponsor protocol code	OLT1177-05

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Olatec Therapeutics LLC
Sponsor organisation address	800 Fifth Avenue, Fl 25, New York, United States,
Public contact	Clinical Trials Inquiries, Olatec Therapeutics LLC, +1 833-652-8321, inquiries@olatec.com
Scientific contact	Clinical Trials Inquiries, Olatec Therapeutics LLC, +1 833-652-8321, inquiries@olatec.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	27 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 February 2019
Global end of trial reached?	Yes
Global end of trial date	04 February 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the safety and tolerability of OLT1177 Capsule after oral administration in subjects with an acute gout flare

Protection of trial subjects:

The OLT1177-05 Study Protocol and associated documents, including the Investigator Brochure, Informed Consent Form and any informational documentation given to study subjects, were reviewed by an appropriately constituted Institutional Review Board (IRB), or Ethics Committee (EC). Proposed changes to the conduct of the study were documented in Protocol Amendments and submitted to and reviewed and approved by the EC before implementation. If at any time during the study a subject was unable to tolerate his/her pain and wished to receive standard medical intervention for their gout flare, the subject was withdrawn from the study, considered a Treatment Failure and treated with either methylprednisolone 500 mg IV, prednisolone (30 mg PO QD), or colchicine (0.5 mg PO TID). Subjects were also given Rescue Medication (paracetamol, 1 g/dose or up to 4 g/day) at the Baseline Visit to use if needed following the first 12 hours post-initial dose of Investigational Product. Additionally, a Data Monitoring Committee (DMC) was convened to review all relevant safety and efficacy data for all subjects in a cohort to determine if an increase or decrease in total daily exposure was warranted for the subsequent cohort.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 May 2017
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	Netherlands: 34
Worldwide total number of subjects	34
EEA total number of subjects	34

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	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	21
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were recruited for the study directly from the Investigator’s clinic as well as by referral from general practitioners in the Netherlands and by local and internet advertisements. The first subject was enrolled in May 2017 and the last subject completed the final study visit in February 2019.

Pre-assignment

Screening details:

Subjects had to meet all inclusion and no exclusion criteria to be eligible for enrollment. Presence of monosodium urate in synovial fluid of the target joint at Baseline with confirmed gout flare starting within 96 hours of Baseline Visit were required for enrollment. Both first-time gout and recurrent gout patients were included in the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Cohort 1

Arm description:

500 mg BID for 8 days (1000 mg total/day)

Arm type	Experimental
Investigational medicinal product name	OLT1177 Capsule
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

500 mg twice daily (BID) for 8 days

Arm title	Cohort 2

Arm description:

500 mg QID for 8 days (2000 mg total/day)

Arm type	Experimental
Investigational medicinal product name	OLT1177 Capsule
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

500 mg four times daily (QID) for 8 days

Arm title	Cohort 3

Arm description:

200 mg (am) and 100 mg (pm) BID for 8 days (300 mg total/day)

Arm type	Experimental

Investigational medicinal product name	OLT1177 Capsule
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

200 mg (am) and 100 mg (pm) for 8 days

Arm title	Cohort 4

Arm description:

100 mg QD for 8 days (100 mg total/day)

Arm type	Experimental
Investigational medicinal product name	OLT1177 Capsule
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100 mg once daily (QD) for 8 days

Number of subjects in period 1	Cohort 1	Cohort 2	Cohort 3
Started	10	8	8
Completed	6	8	8
Not completed	4	0	0
Adverse event, non-fatal	2	-	-
Worsening condition as determined by Investigator	2	-	-

Number of subjects in period 1	Cohort 4
Started	8
Completed	8
Not completed	0
Adverse event, non-fatal	-
Worsening condition as determined by Investigator	-

Baseline characteristics

Reporting groups	
Reporting group title	Cohort 1
Reporting group description:	
500 mg BID for 8 days (1000 mg total/day)	
Reporting group title	Cohort 2
Reporting group description:	
500 mg QID for 8 days (2000 mg total/day)	
Reporting group title	Cohort 3
Reporting group description:	
200 mg (am) and 100 mg (pm) BID for 8 days (300 mg total/day)	
Reporting group title	Cohort 4
Reporting group description:	
100 mg QD for 8 days (100 mg total/day)	

Reporting group values	Cohort 1	Cohort 2	Cohort 3
Number of subjects	10	8	8
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)	5	7	5
From 65-84 years	5	1	3
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	63.4	50.9	61.8
standard deviation	± 10.77	± 11.83	± 11.39
Gender categorical Units: Subjects			
Female	0	1	0
Male	10	7	8
Target Joint			
The acutely inflamed and tender joint			
Units: Subjects			
Ankle	3	0	4
Knee	1	1	0
Forefoot/Toe	6	7	4
Target Joint - Side			
The acutely inflamed and tender joint, side affected. MTP1 = first metatarsophalangeal joint TMT1 = first tarsometatarsal joint			
Units: Subjects			

Knee - Left	1	0	0
Knee - Right	0	1	0
MTP1 - Left	2	2	1
MTP1- Right	4	5	2
TMT1 - Right	0	0	1
Ankle - Left	1	0	4
Ankle - Right	2	0	0
Duration from Gout Flare to Treatment			
Time in hours from gout flare to treatment with OLT1177 Capsules			
Units: hours			
arithmetic mean	54.5	45.0	32.9
standard deviation	± 25.88	± 29.24	± 14.76
Body Mass Index			
Units: kilogram(s)/square metre			
arithmetic mean	28.99	29.14	27.98
standard deviation	± 3.409	± 4.031	± 3.275

Reporting group values	Cohort 4	Total	
Number of subjects	8	34	
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)	4	21	
From 65-84 years	4	13	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	62.9		
standard deviation	± 8.61	-	
Gender categorical			
Units: Subjects			
Female	0	1	
Male	8	33	
Target Joint			
The acutely inflamed and tender joint			
Units: Subjects			
Ankle	3	10	
Knee	0	2	
Forefoot/Toe	5	22	
Target Joint - Side			
The acutely inflamed and tender joint, side affected. MTP1 = first metatarsophalangeal joint TMT1 = first tarsometatarsal joint			
Units: Subjects			
Knee - Left	0	1	
Knee - Right	0	1	

MTP1 - Left	3	8	
MTP1- Right	2	13	
TMT1 - Right	0	1	
Ankle - Left	1	6	
Ankle - Right	2	4	
Duration from Gout Flare to Treatment			
Time in hours from gout flare to treatment with OLT1177 Capsules			
Units: hours			
arithmetic mean	63.1		
standard deviation	± 16.85	-	
Body Mass Index			
Units: kilogram(s)/square metre			
arithmetic mean	28.53		
standard deviation	± 2.004	-	

Subject analysis sets

Subject analysis set title	Cohort 1 - Per-Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol (PP) set consists of all subjects who took 80% or more of the total expected doses of investigational product and had no major protocol violations as determined by the Medical Monitor. Four subjects in Cohort 1 were excluded from the PP due to major protocol deviations.

Subject analysis set title	Cohort 2 - Per-Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol (PP) set consists of all subjects who took 80% or more of the total expected doses of investigational product and had no major protocol violations as determined by the Medical Monitor.

Subject analysis set title	Cohort 3 - Per-Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol (PP) set consists of all subjects who took 80% or more of the total expected doses of investigational product and had no major protocol violations as determined by the Medical Monitor. One subject in Cohort 3 was excluded from the PP set due to a major protocol deviation.

Subject analysis set title	Cohort 4 - Per-Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol (PP) set consists of all subjects who took 80% or more of the total expected doses of investigational product and had no major protocol violations as determined by the Medical Monitor.

Subject analysis set title	Overall - Per-Protocol
Subject analysis set type	Per protocol

Subject analysis set description:

The Per-Protocol (PP) set consists of all subjects who took 80% or more of the total expected doses of investigational product and had no major protocol violations as determined by the Medical Monitor. Overall, five subjects were excluded from the PP set due to major protocol deviations.

Reporting group values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol
Number of subjects	6	8	7
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)	2	7	4
From 65-84 years	4	1	3
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	66.7	50.9	62.1
standard deviation	± 11.62	± 11.83	± 12.24
Gender categorical			
Units: Subjects			
Female	0	1	0
Male	6	7	7
Target Joint			
The acutely inflamed and tender joint			
Units: Subjects			
Ankle	1	0	3
Knee	1	1	0
Forefoot/Toe	4	7	4
Target Joint - Side			
The acutely inflamed and tender joint, side affected. MTP1 = first metatarsophalangeal joint TMT1 = first tarsometatarsal joint			
Units: Subjects			
Knee - Left	1	0	0
Knee - Right	0	1	0
MTP1 - Left	1	2	1
MTP1- Right	3	5	2
TMT1 - Right	0	0	1
Ankle - Left	1	0	3
Ankle - Right	0	0	0
Duration from Gout Flare to Treatment			
Time in hours from gout flare to treatment with OLT1177 Capsules			
Units: hours			
arithmetic mean	58.3	45.0	33.3
standard deviation	± 20.68	± 29.24	± 15.89
Body Mass Index			
Units: kilogram(s)/square metre			
arithmetic mean	28.73	29.14	28.05
standard deviation	± 3.303	± 4.031	± 3.530

Reporting group values	Cohort 4 - Per-Protocol	Overall - Per-Protocol	
Number of subjects	8	29	
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)	4	17	
From 65-84 years	4	12	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	62.9	60.2	
standard deviation	± 8.61	± 12.10	
Gender categorical			
Units: Subjects			
Female	0	1	
Male	8	28	
Target Joint			
The acutely inflamed and tender joint			
Units: Subjects			
Ankle	3	7	
Knee	0	2	
Forefoot/Toe	5	20	
Target Joint - Side			
The acutely inflamed and tender joint, side affected. MTP1 = first metatarsophalangeal joint TMT1 = first tarsometatarsal joint			
Units: Subjects			
Knee - Left	0	1	
Knee - Right	0	1	
MTP1 - Left	3	7	
MTP1- Right	2	12	
TMT1 - Right	0	1	
Ankle - Left	1	5	
Ankle - Right	2	2	
Duration from Gout Flare to Treatment			
Time in hours from gout flare to treatment with OLT1177 Capsules			
Units: hours			
arithmetic mean	63.1	49.9	
standard deviation	± 16.85	± 23.58	
Body Mass Index			
Units: kilogram(s)/square metre			
arithmetic mean	28.53	28.62	
standard deviation	± 2.004	± 3.138	

End points

End points reporting groups

Reporting group title	Cohort 1
Reporting group description: 500 mg BID for 8 days (1000 mg total/day)	
Reporting group title	Cohort 2
Reporting group description: 500 mg QID for 8 days (2000 mg total/day)	
Reporting group title	Cohort 3
Reporting group description: 200 mg (am) and 100 mg (pm) BID for 8 days (300 mg total/day)	
Reporting group title	Cohort 4
Reporting group description: 100 mg QD for 8 days (100 mg total/day)	
Subject analysis set title	Cohort 1 - Per-Protocol
Subject analysis set type	Per protocol
Subject analysis set description: The Per-Protocol (PP) set consists of all subjects who took 80% or more of the total expected doses of investigational product and had no major protocol violations as determined by the Medical Monitor. Four subjects in Cohort 1 were excluded from the PP due to major protocol deviations.	
Subject analysis set title	Cohort 2 - Per-Protocol
Subject analysis set type	Per protocol
Subject analysis set description: The Per-Protocol (PP) set consists of all subjects who took 80% or more of the total expected doses of investigational product and had no major protocol violations as determined by the Medical Monitor.	
Subject analysis set title	Cohort 3 - Per-Protocol
Subject analysis set type	Per protocol
Subject analysis set description: The Per-Protocol (PP) set consists of all subjects who took 80% or more of the total expected doses of investigational product and had no major protocol violations as determined by the Medical Monitor. One subject in Cohort 3 was excluded from the PP set due to a major protocol deviation.	
Subject analysis set title	Cohort 4 - Per-Protocol
Subject analysis set type	Per protocol
Subject analysis set description: The Per-Protocol (PP) set consists of all subjects who took 80% or more of the total expected doses of investigational product and had no major protocol violations as determined by the Medical Monitor.	
Subject analysis set title	Overall - Per-Protocol
Subject analysis set type	Per protocol
Subject analysis set description: The Per-Protocol (PP) set consists of all subjects who took 80% or more of the total expected doses of investigational product and had no major protocol violations as determined by the Medical Monitor. Overall, five subjects were excluded from the PP set due to major protocol deviations.	

Primary: Change in Pain Intensity Score from Baseline to Day 3 and from Baseline to Day 7

End point title	Change in Pain Intensity Score from Baseline to Day 3 and from Baseline to Day 7[1]
End point description: Target joint pain was measured using a 100-mm Visual Analog Scale (VAS).	
End point type	Primary
End point timeframe: Baseline, Day 3, and Day 7	

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: Statistical inference tests were not conducted. The purpose of the study was to assess, on an unblinded basis, a small number of subjects exposed for safety, tolerability, and clinical and inflammatory biomarker activity of oral OLT1177 Capsules in the treatment of acute gout flare. As such, the study was not powered to achieve significance.

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed				
Units: millimetre(s)				
arithmetic mean (standard deviation)				
Baseline (Pre-dose)	82.2 (± 14.82)	68.9 (± 9.52)	70.6 (± 5.88)	64.1 (± 9.61)
Day 3 (pm)	40.2 (± 42.14)	29.4 (± 27.31)	22.4 (± 24.07)	29.8 (± 19.96)
Day 3 (pm) - Change from Baseline	-42.0 (± 32.63)	-39.5 (± 27.37)	-48.1 (± 24.17)	-34.4 (± 22.72)
Day 7	28.8 (± 33.91)	11.1 (± 10.96)	11.3 (± 11.69)	9.7 (± 11.67)
Day 7 - Change from Baseline	-53.3 (± 24.25)	-57.8 (± 13.42)	-59.3 (± 12.16)	-51.3 (± 19.20)

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed				
Units: millimetre(s)				
arithmetic mean (standard deviation)				
Baseline (Pre-dose)	70.7 (± 11.57)			
Day 3 (pm)	30.0 (± 27.64)			
Day 3 (pm) - Change from Baseline	-40.7 (± 25.64)			
Day 7	14.8 (± 19.24)			
Day 7 - Change from Baseline	-55.7 (± 16.65)			

Statistical analyses

No statistical analyses for this end point

Secondary: Subject-reported Global Evaluation of Treatment on Day 7

End point title	Subject-reported Global Evaluation of Treatment on Day 7

End point description:

The Global Evaluation of Treatment was used to measure overall perceived quality of the investigational product in treating the subject's symptoms and was completed at the Day 7 visit. A 5-point Likert scale, with numerical values assigned as follows, was used: 0 = poor, 1 = reasonable, 2 = good, 3 = very good and 4 = excellent.

End point type	Secondary

End point timeframe:

Day 7

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	8	7	8
Units: Subjects				
Poor	0	2	0	3
Fair	1	1	2	1
Good	1	2	1	1
Very Good	2	0	4	1
Excellent	1	3	0	2
Not Done	1	0	0	0

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: Subjects				
Poor	5			
Fair	5			
Good	5			
Very Good	7			
Excellent	6			
Not Done	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Subject-reported Pain Intensity Score

End point title	Subject-reported Pain Intensity Score

End point description:

Subjects reported pain in target joint from Baseline to Day 14 using a 100 mm Visual Analog Scale (VAS).

End point type	Secondary

End point timeframe:

Baseline (pre-dose) to Day 14

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	8	7	8
Units: millimetre(s)				
arithmetic mean (standard deviation)				
Baseline (pre-dose)	82.2 (± 14.82)	68.9 (± 9.52)	70.6 (± 5.88)	64.1 (± 9.61)
2 hours (post-dose)	59.3 (± 30.22)	61.8 (± 17.81)	58.6 (± 30.12)	65.1 (± 14.55)
2 hours (post-dose) - Change from Baseline	-22.8 (± 26.39)	-7.1 (± 18.56)	-12.0 (± 29.73)	1.0 (± 14.54)
4 hours (post-dose)	62.2 (± 28.85)	58.3 (± 20.67)	55.9 (± 30.57)	60.5 (± 8.96)
4 hours (post-dose) - Change from Baseline	-20.0 (± 22.45)	-10.6 (± 22.21)	-14.7 (± 30.14)	-3.6 (± 9.96)
6 hours (post-dose)	62.8 (± 28.96)	49.8 (± 24.74)	55.4 (± 31.42)	61.3 (± 14.87)
6 hours (post-dose) - Change from Baseline	-19.3 (± 21.90)	-19.1 (± 24.71)	-15.1 (± 31.65)	-2.9 (± 16.65)
12 hours (post-dose)	70.3 (± 31.51)	54.5 (± 25.57)	45.3 (± 33.80)	65.1 (± 18.00)
12 hours (post-dose) - Change from Baseline	-11.8 (± 22.89)	-14.4 (± 22.80)	-25.3 (± 33.64)	1.0 (± 19.49)
Day 1 (am)	60.0 (± 34.18)	43.5 (± 26.86)	43.0 (± 33.66)	61.1 (± 18.99)
Day 1 (am) - Change from Baseline	-22.2 (± 23.94)	-25.4 (± 23.18)	-27.6 (± 32.95)	-3.0 (± 20.59)
Day 1 (pm)	55.5 (± 36.06)	54.1 (± 30.92)	42.3 (± 29.32)	51.5 (± 18.45)
Day 1 (pm) - Change from Baseline	-26.7 (± 25.63)	-14.8 (± 27.90)	-28.3 (± 29.51)	-12.6 (± 21.93)
Day 2 (am)	47.2 (± 38.57)	44.1 (± 26.80)	32.0 (± 25.42)	39.8 (± 20.62)
Day 2 (am) - Change from Baseline	-35.0 (± 28.40)	-24.8 (± 27.67)	-38.6 (± 24.99)	-24.4 (± 20.65)
Day 2 (pm)	43.7 (± 42.58)	38.1 (± 26.27)	27.3 (± 26.35)	38.9 (± 27.45)
Day 2 (pm) - Change from Baseline	-38.5 (± 32.29)	-30.8 (± 27.09)	-43.3 (± 25.75)	-26.0 (± 29.02)
Day 3 (am)	42.8 (± 40.69)	31.4 (± 24.85)	25.4 (± 27.50)	33.3 (± 23.7)
Day 3 (am) - Change from Baseline	-39.3 (± 31.25)	-37.5 (± 26.12)	-45.1 (± 27.56)	-31.6 (± 26.89)
Day 3 (pm)	40.2 (± 42.14)	29.4 (± 27.31)	22.4 (± 24.07)	29.8 (± 19.96)
Day 3 (pm) - Change from Baseline	-42.0 (± 32.63)	-39.5 (± 27.37)	-48.1 (± 24.17)	-34.4 (± 22.72)
Day 4 (am)	38.5 (± 43.45)	27.8 (± 23.90)	19.1 (± 22.52)	25.1 (± 20.97)
Day 4 (am) - Change from Baseline	-43.7 (± 34.13)	-41.1 (± 26.88)	-51.4 (± 23.39)	-39.0 (± 22.77)
Day 4 (pm)	37.0 (± 44.01)	29.9 (± 26.10)	17.7 (± 19.62)	21.9 (± 20.93)
Day 4 (pm) - Change from Baseline	-45.2 (± 34.94)	-39.0 (± 31.80)	-52.9 (± 20.53)	-42.3 (± 23.61)
Day 5 (am)	40.0 (± 44.37)	30.7 (± 24.83)	17.9 (± 19.16)	25.0 (± 29.80)
Day 5 (am) - Change from Baseline	-42.2 (± 33.61)	-36.6 (± 23.20)	-52.7 (± 19.96)	-39.1 (± 34.39)
Day 5 (pm)	37.5 (± 42.18)	21.6 (± 18.51)	10.7 (± 12.45)	23.3 (± 28.67)
Day 5 (pm) - Change from Baseline	-44.7 (± 32.38)	-47.3 (± 24.45)	-60.3 (± 12.85)	-40.9 (± 32.83)
Day 6 (am)	35.2 (± 40.95)	17.0 (± 12.49)	18.3 (± 19.99)	24.5 (± 28.86)
Day 6 (am) - Change from Baseline	-47.0 (± 31.00)	-51.9 (± 17.35)	-52.7 (± 19.70)	-39.6 (± 33.34)
Day 6 (pm)	36.5 (± 44.28)	18.1 (± 15.31)	17.1 (± 17.11)	17.8 (± 25.34)
Day 6 (pm) - Change from Baseline	-45.7 (± 34.78)	-50.8 (± 18.85)	-53.4 (± 17.66)	-43.2 (± 30.45)
Day 7 (am)	36.3 (± 37.88)	13.3 (± 11.39)	15.7 (± 17.90)	13.7 (± 19.00)
Day 7 (am) - Change from Baseline	-45.8 (± 27.01)	-55.6 (± 16.54)	-54.9 (± 18.07)	-47.3 (± 25.11)

Day 7 (pm)	17.8 (± 22.90)	9.7 (± 11.03)	11.4 (± 12.01)	11.4 (± 12.16)
Day 7 (pm) - Change from Baseline	-60.8 (± 17.81)	-58.9 (± 14.10)	-59.4 (± 13.46)	-50.0 (± 21.15)
Day 8 (am)	13.0 (± 14.72)	8.4 (± 11.13)	9.6 (± 7.92)	10.2 (± 13.29)
Day 8 (am) - Change from Baseline	-65.8 (± 5.74)	-60.1 (± 15.44)	-61.2 (± 10.47)	-50.8 (± 20.67)
Day 14	6.2 (± 8.38)	11.9 (± 11.62)	2.4 (± 3.41)	13.9 (± 27.12)
Day 14 - Change from Baseline	-76.0 (± 11.05)	-57.0 (± 16.80)	-68.1 (± 6.57)	-50.3 (± 23.91)

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: millimetre(s)				
arithmetic mean (standard deviation)				
Baseline (pre-dose)	70.7 (± 11.57)			
2 hours (post-dose)	61.4 (± 22.28)			
2 hours (post-dose) - Change from Baseline	-9.3 (± 22.92)			
4 hours (post-dose)	59.1 (± 21.94)			
4 hours (post-dose) - Change from Baseline	-11.6 (± 21.65)			
6 hours (post-dose)	57.0 (± 24.45)			
6 hours (post-dose) - Change from Baseline	-13.7 (± 23.90)			
12 hours (post-dose)	58.5 (± 27.52)			
12 hours (post-dose) - Change from Baseline	-12.2 (± 25.59)			
Day 1 (am)	51.7 (± 28.29)			
Day 1 (am) - Change from Baseline	-19.1 (± 26.09)			
Day 1 (pm)	50.8 (± 27.69)			
Day 1 (pm) - Change from Baseline	-19.9 (± 25.86)			
Day 2 (am)	40.6 (± 26.86)			
Day 2 (am) - Change from Baseline	-30.1 (± 24.83)			
Day 2 (pm)	36.8 (± 29.53)			
Day 2 (pm) - Change from Baseline	-34.4 (± 27.65)			
Day 3 (am)	32.8 (± 28.23)			
Day 3 (am) - Change from Baseline	-38.3 (± 26.67)			
Day 3 (pm)	30.0 (± 27.64)			
Day 3 (pm) - Change from Baseline	-40.7 (± 25.64)			
Day 4 (am)	27.2 (± 27.27)			
Day 4 (am) - Change from Baseline	-43.6 (± 25.66)			
Day 4 (pm)	26.2 (± 27.58)			
Day 4 (pm) - Change from Baseline	-44.5 (± 26.98)			
Day 5 (am)	27.9 (± 29.61)			

Day 5 (am) - Change from Baseline	-42.5 (± 27.63)			
Day 5 (pm)	23.1 (± 27.23)			
Day 5 (pm) - Change from Baseline	-47.7 (± 26.66)			
Day 6 (am)	23.3 (± 26.26)			
Day 6 (am) - Change from Baseline	-47.5 (± 25.42)			
Day 6 (pm)	21.9 (± 26.36)			
Day 6 (pm) - Change from Baseline	-48.6 (± 24.39)			
Day 7 (am)	19.1 (± 23.31)			
Day 7 (am) - Change from Baseline	-51.4 (± 20.74)			
Day 7 (pm)	12.3 (± 14.14)			
Day 7 (pm) - Change from Baseline	-57.4 (± 15.95)			
Day 8 (am)	10.0 (± 11.09)			
Day 8 (am) - Change from Baseline	-58.9 (± 14.99)			
Day 14	9.0 (± 15.95)			
Day 14 - Change from Baseline	-61.8 (± 18.51)			

Statistical analyses

No statistical analyses for this end point

Secondary: Subject-reported General Disability Score

End point title	Subject-reported General Disability Score

End point description:

Subjects recorded their level of general disability on a 100 mm Visual Analog Scale (VAS) in response to the question "How limited do you feel right now, this [insert time of day,] in your daily activities as a result of this gout attack?". The scale went from 0 (I can do everything I was able to do before this gout attack started) to 100 (I cannot do anything).

End point type	Secondary

End point timeframe:

Baseline (pre-dose) to Day 14

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	8	7	8
Units: millimetre(s)				
arithmetic mean (standard deviation)				
Baseline (pre-dose)	60.7 (± 24.47)	68.3 (± 16.20)	63.6 (± 27.81)	62.8 (± 18.11)
2 hours (post-dose)	63.7 (± 31.30)	62.6 (± 20.62)	55.9 (± 30.97)	69.6 (± 12.37)
2 hours (post-dose) - Change from Baseline	3.0 (± 14.72)	-5.6 (± 10.84)	-7.7 (± 16.15)	6.9 (± 12.94)
4 hours (post-dose)	63.8 (± 27.76)	56.6 (± 18.81)	52.4 (± 34.07)	63.4 (± 7.91)

4 hours (post-dose) - Change from Baseline	3.2 (± 13.50)	-11.6 (± 10.95)	-11.1 (± 22.33)	0.6 (± 10.56)
6 hours (post-dose)	65.0 (± 27.52)	47.4 (± 22.48)	59.0 (± 30.19)	62.4 (± 19.33)
6 hours (post-dose) - Change from Baseline	4.3 (± 17.53)	-20.9 (± 14.73)	-4.6 (± 21.78)	-0.4 (± 9.84)
12 hours (post-dose)	69.2 (± 29.82)	50.5 (± 22.39)	49.9 (± 37.34)	64.6 (± 23.95)
12 hours (post-dose) - Change from Baseline	8.5 (± 21.89)	-17.8 (± 17.79)	-13.7 (± 24.49)	1.9 (± 13.45)
Day 1 (am)	59.2 (± 36.34)	40.1 (± 23.74)	45.9 (± 34.55)	59.6 (± 23.93)
Day 1 (am) - Change from Baseline	-1.5 (± 28.91)	-28.1 (± 21.06)	-17.7 (± 22.23)	-3.1 (± 17.64)
Day 1 (pm)	55.0 (± 36.71)	49.4 (± 29.79)	45.7 (± 34.45)	53.8 (± 21.93)
Day 1 (pm) - Change from Baseline	-5.7 (± 31.40)	-18.9 (± 27.48)	-17.9 (± 24.99)	-9.0 (± 13.94)
Day 2 (am)	48.3 (± 39.64)	43.1 (± 26.37)	38.1 (± 31.49)	44.1 (± 21.37)
Day 2 (am) - Change from Baseline	-12.3 (± 33.89)	-25.1 (± 27.94)	-25.4 (± 22.17)	-18.6 (± 15.12)
Day 2 (pm)	42.8 (± 42.96)	39.4 (± 28.67)	37.6 (± 32.16)	44.4 (± 27.32)
Day 2 (pm) - Change from Baseline	-17.8 (± 35.91)	-28.9 (± 28.26)	-26.0 (± 25.59)	-19.3 (± 22.57)
Day 3 (am)	42.2 (± 41.22)	31.6 (± 27.70)	33.6 (± 34.69)	35.3 (± 23.48)
Day 3 (am) - Change from Baseline	-18.5 (± 34.72)	-36.6 (± 26.03)	-30.0 (± 29.50)	-28.4 (± 19.80)
Day 3 (pm)	38.8 (± 42.32)	30.5 (± 26.50)	31.9 (± 33.70)	31.0 (± 23.07)
Day 3 (pm) - Change from Baseline	-21.8 (± 35.56)	-37.8 (± 21.94)	-31.7 (± 28.14)	-31.8 (± 17.51)
Day 4 (am)	36.8 (± 39.95)	31.0 (± 26.42)	27.7 (± 31.20)	27.8 (± 23.03)
Day 4 (am) - Change from Baseline	-23.8 (± 32.93)	-37.3 (± 24.45)	-35.9 (± 27.03)	-35.0 (± 17.06)
Day 4 (pm)	38.0 (± 43.92)	30.5 (± 30.13)	24.4 (± 26.22)	24.8 (± 22.34)
Day 4 (pm) - Change from Baseline	-22.7 (± 36.98)	-37.8 (± 29.79)	-39.1 (± 23.19)	-38.0 (± 17.22)
Day 5 (am)	39.7 (± 44.52)	28.7 (± 25.84)	23.9 (± 26.18)	27.1 (± 31.59)
Day 5 (am) - Change from Baseline	-21.0 (± 38.68)	-42.6 (± 25.05)	-39.7 (± 22.70)	-35.6 (± 24.78)
Day 5 (pm)	36.5 (± 43.13)	24.3 (± 28.60)	18.8 (± 24.05)	26.0 (± 30.66)
Day 5 (pm) - Change from Baseline	-24.2 (± 36.95)	-44.0 (± 26.37)	-43.2 (± 24.35)	-36.8 (± 23.40)
Day 6 (am)	34.2 (± 42.78)	19.8 (± 27.69)	22.7 (± 23.46)	26.8 (± 30.87)
Day 6 (am) - Change from Baseline	-26.5 (± 36.26)	-48.5 (± 24.73)	-39.3 (± 22.11)	-36.0 (± 23.91)
Day 6 (pm)	34.8 (± 44.48)	21.5 (± 28.09)	22.9 (± 21.11)	21.2 (± 26.17)
Day 6 (pm) - Change from Baseline	-25.8 (± 37.35)	-46.8 (± 23.16)	-40.7 (± 19.76)	-44.5 (± 21.79)
Day 7 (am)	36.3 (± 37.59)	19.8 (± 27.03)	20.7 (± 22.68)	16.0 (± 20.57)
Day 7 (am) - Change from Baseline	-24.3 (± 31.00)	-48.5 (± 22.42)	-42.9 (± 23.50)	-49.7 (± 18.05)
Day 7 (pm)	20.6 (± 27.96)	14.4 (± 22.44)	14.2 (± 14.02)	13.8 (± 15.82)
Day 7 (pm) - Change from Baseline	-34.6 (± 29.38)	-53.0 (± 17.04)	-54.4 (± 14.99)	-53.8 (± 15.71)
Day 8 (am)	12.8 (± 15.00)	14.1 (± 20.71)	12.0 (± 9.59)	13.3 (± 18.46)
Day 8 (am) - Change from Baseline	-40.0 (± 26.26)	-53.3 (± 17.48)	-56.6 (± 13.59)	-52.3 (± 16.05)
Day 14	11.2 (± 19.68)	14.0 (± 15.25)	2.9 (± 3.13)	14.1 (± 26.61)
Day 14 - Change from Baseline	-49.5 (± 19.99)	-54.3 (± 14.83)	-60.7 (± 26.04)	-48.6 (± 36.53)

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: millimetre(s)				
arithmetic mean (standard deviation)				
Baseline (pre-dose)	64.0 (± 20.70)			
2 hours (post-dose)	63.1 (± 23.46)			
2 hours (post-dose) - Change from Baseline	-0.9 (± 14.30)			
4 hours (post-dose)	59.0 (± 22.66)			
4 hours (post-dose) - Change from Baseline	-5.1 (± 15.57)			
6 hours (post-dose)	58.0 (± 24.47)			
6 hours (post-dose) - Change from Baseline	-6.1 (± 18.18)			
12 hours (post-dose)	58.1 (± 28.25)			
12 hours (post-dose) - Change from Baseline	-5.9 (± 21.34)			
Day 1 (am)	50.8 (± 29.18)			
Day 1 (am) - Change from Baseline	-13.2 (± 23.89)			
Day 1 (pm)	50.9 (± 29.16)			
Day 1 (pm) - Change from Baseline	-13.2 (± 24.07)			
Day 2 (am)	43.3 (± 28.17)			
Day 2 (am) - Change from Baseline	-20.8 (± 24.29)			
Day 2 (pm)	40.9 (± 30.95)			
Day 2 (pm) - Change from Baseline	-23.4 (± 26.95)			
Day 3 (am)	35.3 (± 30.31)			
Day 3 (am) - Change from Baseline	-29.0 (± 26.86)			
Day 3 (pm)	32.7 (± 29.70)			
Day 3 (pm) - Change from Baseline	-31.3 (± 24.97)			
Day 4 (am)	30.5 (± 28.52)			
Day 4 (am) - Change from Baseline	-33.5 (± 24.46)			
Day 4 (pm)	29.0 (± 29.53)			
Day 4 (pm) - Change from Baseline	-35.0 (± 26.40)			
Day 5 (am)	29.4 (± 30.98)			
Day 5 (am) - Change from Baseline	-35.3 (± 27.47)			
Day 5 (pm)	26.2 (± 30.73)			
Day 5 (pm) - Change from Baseline	-37.5 (± 27.28)			
Day 6 (am)	25.5 (± 30.26)			
Day 6 (am) - Change from Baseline	-38.3 (± 26.54)			
Day 6 (pm)	24.7 (± 29.29)			

Day 6 (pm) - Change from Baseline	-40.0 (± 25.68)			
Day 7 (am)	22.9 (± 26.93)			
Day 7 (am) - Change from Baseline	-41.9 (± 24.68)			
Day 7 (pm)	15.6 (± 19.64)			
Day 7 (pm) - Change from Baseline	-49.3 (± 20.11)			
Day 8 (am)	13.2 (± 15.94)			
Day 8 (am) - Change from Baseline	-51.4 (± 17.75)			
Day 14	10.8 (± 18.12)			
Day 14 - Change from Baseline	-53.3 (± 25.07)			

Statistical analyses

No statistical analyses for this end point

Secondary: Subject-reported Walking Disability Score

End point title	Subject-reported Walking Disability Score

End point description:

Subjects were instructed to record their level of walking disability on a 100-mm Visual Analog Scale (VAS) in response to the question "How are you walking now, this [insert time of day]?" The scale went from 0 ("I am not experiencing any deterioration in walking") to 100 ("I can absolutely not walk").

End point type	Secondary

End point timeframe:

Baseline (pre-dose) to Day 14

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	8	7	8
Units: millimetre(s)				
arithmetic mean (standard deviation)				
Baseline (pre-dose)	79.5 (± 31.37)	73.0 (± 20.11)	70.3 (± 14.68)	71.9 (± 18.45)
2 hours (post-dose)	74.5 (± 31.57)	66.5 (± 21.53)	56.1 (± 27.53)	65.1 (± 21.31)
2-hours (post-dose) - Change from Baseline	-5.0 (± 7.40)	-6.5 (± 8.28)	-14.1 (± 18.59)	-6.8 (± 9.54)
4 hours (post-dose)	66.5 (± 36.36)	58.5 (± 21.20)	59.4 (± 28.58)	62.6 (± 19.78)
4 hours (post-dose) - Change from Baseline	-13.0 (± 20.92)	-14.5 (± 15.40)	-10.9 (± 19.63)	-9.3 (± 9.68)
6 hours (post-dose)	67.5 (± 36.45)	48.3 (± 23.90)	56.1 (± 29.95)	62.6 (± 20.78)
6 hours (post-dose) - Change from Baseline	-12.0 (± 20.81)	-24.8 (± 18.19)	-14.1 (± 21.33)	-9.3 (± 10.50)
12 hours (post-dose)	75.3 (± 33.10)	51.6 (± 25.64)	51.9 (± 34.98)	65.4 (± 23.74)
12 hours (post-dose) - Change from Baseline	-4.2 (± 12.50)	-21.4 (± 17.67)	-18.4 (± 30.65)	-6.5 (± 12.35)
Day 1 (am)	71.0 (± 35.66)	42.6 (± 25.07)	46.9 (± 33.01)	58.3 (± 23.21)

Day 1 (am) - Change from Baseline	-8.5 (± 11.73)	-30.4 (± 21.53)	-23.4 (± 26.37)	-13.6 (± 10.11)
Day 1 (pm)	66.3 (± 33.33)	48.8 (± 31.23)	46.4 (± 37.14)	53.1 (± 21.68)
Day 1 (pm) - Change from Baseline	-13.2 (± 9.75)	-24.3 (± 26.00)	-23.9 (± 27.66)	-18.8 (± 7.98)
Day 2 (am)	57.7 (± 37.16)	48.0 (± 29.36)	41.7 (± 34.22)	47.5 (± 23.66)
Day 2 (am) - Change from Baseline	-21.8 (± 20.72)	-25.0 (± 25.96)	-28.6 (± 25.62)	-24.4 (± 10.01)
Day 2 (pm)	47.8 (± 39.80)	43.1 (± 29.99)	39.9 (± 32.74)	46.9 (± 30.31)
Day 2 (pm) - Change from Baseline	-31.7 (± 28.73)	-29.9 (± 25.81)	-30.4 (± 24.07)	-26.7 (± 17.34)
Day 3 (am)	47.0 (± 40.48)	35.5 (± 27.66)	35.3 (± 37.19)	35.1 (± 23.36)
Day 3 (am) - Change from Baseline	-32.5 (± 30.83)	-37.5 (± 26.67)	-35.0 (± 26.78)	-38.4 (± 12.82)
Day 3 (pm)	42.3 (± 43.05)	35.9 (± 31.74)	32.1 (± 35.00)	37.4 (± 22.88)
Day 3 (pm) - Change from Baseline	-37.2 (± 35.11)	-37.1 (± 26.63)	-38.1 (± 25.28)	-34.5 (± 16.54)
Day 4 (am)	39.5 (± 42.95)	37.6 (± 32.05)	28.7 (± 31.10)	30.8 (± 24.92)
Day 4 (am) - Change from Baseline	-40.0 (± 37.12)	-35.4 (± 30.93)	-41.6 (± 20.46)	-41.1 (± 14.68)
Day 4 (pm)	38.7 (± 43.79)	37.4 (± 31.65)	27.9 (± 31.48)	26.4 (± 23.03)
Day 4 (pm) - Change from Baseline	-40.8 (± 37.95)	-35.6 (± 32.56)	-42.4 (± 20.48)	-45.5 (± 14.70)
Day 5 (am)	39.2 (± 44.01)	35.7 (± 27.17)	26.9 (± 28.73)	29.4 (± 33.23)
Day 5 (am) - Change from Baseline	-40.3 (± 39.02)	-38.4 (± 28.32)	-43.4 (± 18.44)	-42.5 (± 24.84)
Day 5 (pm)	38.0 (± 43.31)	31.1 (± 31.51)	18.7 (± 24.13)	26.6 (± 31.37)
Day 5 (pm) - Change from Baseline	-41.5 (± 37.85)	-41.9 (± 31.11)	-50.3 (± 13.95)	-45.3 (± 24.16)
Day 6 (am)	34.3 (± 40.50)	29.3 (± 31.62)	24.3 (± 25.22)	27.4 (± 33.21)
Day 6 (am) - Change from Baseline	-45.2 (± 36.21)	-43.8 (± 31.62)	-44.7 (± 24.64)	-44.5 (± 25.55)
Day 6 (pm)	34.7 (± 42.91)	26.3 (± 31.83)	22.1 (± 19.93)	22.5 (± 29.53)
Day 6 (pm) - Change from Baseline	-44.8 (± 37.93)	-46.8 (± 28.09)	-48.1 (± 17.43)	-46.7 (± 20.71)
Day 7 (am)	36.8 (± 36.80)	24.1 (± 28.38)	23.9 (± 23.29)	16.8 (± 20.61)
Day 7 (am) - Change from Baseline	-42.7 (± 33.11)	-48.9 (± 25.97)	-46.4 (± 24.64)	-52.3 (± 14.80)
Day 7 (pm)	20.4 (± 27.90)	16.1 (± 23.74)	15.0 (± 12.88)	13.4 (± 14.52)
Day 7 (pm) - Change from Baseline	-55.0 (± 31.87)	-54.6 (± 23.33)	-50.6 (± 12.03)	-57.6 (± 16.20)
Day 8 (am)	13.0 (± 14.72)	14.1 (± 19.60)	12.0 (± 9.92)	14.0 (± 19.04)
Day 8 (am) - Change from Baseline	-60.3 (± 35.06)	-56.6 (± 22.84)	-53.6 (± 10.41)	-55.2 (± 15.68)
Day 14	10.0 (± 19.02)	18.3 (± 22.34)	7.4 (± 15.34)	16.1 (± 26.77)
Day 14 - Change from Baseline	-69.5 (± 29.51)	-54.8 (± 21.04)	-62.9 (± 11.13)	-55.8 (± 27.37)

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: millimetre(s)				
arithmetic mean (standard deviation)				
Baseline (pre-dose)	73.4 (± 20.48)			

2 hours (post-dose)	65.3 (± 24.68)			
2-hours (post-dose) - Change from Baseline	-8.1 (± 11.67)			
4 hours (post-dose)	61.5 (± 25.11)			
4 hours (post-dose) - Change from Baseline	-11.9 (± 15.75)			
6 hours (post-dose)	58.1 (± 27.09)			
6 hours (post-dose) - Change from Baseline	-15.3 (± 17.99)			
12 hours (post-dose)	60.4 (± 29.29)			
12 hours (post-dose) - Change from Baseline	-13.0 (± 20.04)			
Day 1 (am)	53.8 (± 29.48)			
Day 1 (am) - Change from Baseline	-19.6 (± 19.71)			
Day 1 (pm)	53.0 (± 30.15)			
Day 1 (pm) - Change from Baseline	-20.3 (± 19.62)			
Day 2 (am)	48.3 (± 29.71)			
Day 2 (am) - Change from Baseline	-25.0 (± 20.40)			
Day 2 (pm)	44.3 (± 31.29)			
Day 2 (pm) - Change from Baseline	-29.6 (± 22.90)			
Day 3 (am)	37.8 (± 30.89)			
Day 3 (am) - Change from Baseline	-36.0 (± 23.69)			
Day 3 (pm)	36.7 (± 31.44)			
Day 3 (pm) - Change from Baseline	-36.7 (± 24.59)			
Day 4 (am)	34.0 (± 31.13)			
Day 4 (am) - Change from Baseline	-39.4 (± 25.21)			
Day 4 (pm)	32.3 (± 31.13)			
Day 4 (pm) - Change from Baseline	-41.1 (± 26.09)			
Day 5 (am)	32.4 (± 31.88)			
Day 5 (am) - Change from Baseline	-41.3 (± 26.45)			
Day 5 (pm)	28.6 (± 31.82)			
Day 5 (pm) - Change from Baseline	-44.6 (± 26.75)			
Day 6 (am)	28.8 (± 31.28)			
Day 6 (am) - Change from Baseline	-44.5 (± 28.00)			
Day 6 (pm)	26.2 (± 30.17)			
Day 6 (pm) - Change from Baseline	-46.7 (± 25.36)			
Day 7 (am)	25.3 (± 27.06)			
Day 7 (am) - Change from Baseline	-47.6 (± 24.22)			
Day 7 (pm)	16.2 (± 19.68)			
Day 7 (pm) - Change from Baseline	-54.5 (± 20.80)			
Day 8 (am)	13.4 (± 15.70)			
Day 8 (am) - Change from Baseline	-56.2 (± 20.22)			
Day 14	13.3 (± 20.96)			

Day 14 - Change from Baseline	-60.0 (± 22.68)			

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-assessed Index Joint Score - Joint Tenderness

End point title	Investigator-assessed Index Joint Score - Joint Tenderness

End point description:

investigator assessment of index joint tenderness from 0 to 3 with the following categories: 0 = no pain, 1 = mild pain , 2 = moderate pain, 3 = severe pain.

End point type	Secondary

End point timeframe:

Day 0 (pre-dose and post-dose), Day 3, Day 7

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6[2]	8	7	8
Units: Subjects				
Day 0 (pre-dose) - No Pain	0	0	0	0
Day 0 (pre-dose) - Mild Pain	1	1	0	0
Day 0 (pre-dose) - Moderate Pain	0	2	3	3
Day 0 (pre-dose) - Severe Pain	5	5	4	5
Day 0 (post-dose) - No Pain	0	0	1	0
Day 0 (post-dose) - Mild Pain	2	3	1	1
Day 0 (post-dose) - Moderate Pain	2	3	3	5
Day 0 (post-dose) - Severe Pain	2	2	2	2
Day 3 - No Pain	1	2	1	1
Day 3 - Mild Pain	2	3	3	2
Day 3 - Moderate Pain	1	3	2	3
Day 3 - Severe Pain	1	0	1	2
Day 7 - No Pain	3	5	2	6
Day 7 - Mild Pain	1	3	4	0
Day 7 - Moderate Pain	2	0	1	1
Day 7 - Severe Pain	0	0	0	1

Notes:

[2] - At Day 3, only 5 subjects were analyzed.

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29[3]			
Units: Subjects				
Day 0 (pre-dose) - No Pain	0			

Day 0 (pre-dose) - Mild Pain	2			
Day 0 (pre-dose) - Moderate Pain	8			
Day 0 (pre-dose) - Severe Pain	19			
Day 0 (post-dose) - No Pain	1			
Day 0 (post-dose) - Mild Pain	7			
Day 0 (post-dose) - Moderate Pain	13			
Day 0 (post-dose) - Severe Pain	8			
Day 3 - No Pain	5			
Day 3 - Mild Pain	10			
Day 3 - Moderate Pain	9			
Day 3 - Severe Pain	4			
Day 7 - No Pain	16			
Day 7 - Mild Pain	8			
Day 7 - Moderate Pain	4			
Day 7 - Severe Pain	1			

Notes:

[3] - At Day 3, only 28 subjects were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-assessed Index Joint Score - Joint Swelling

End point title	Investigator-assessed Index Joint Score - Joint Swelling

End point description:

Investigator assessment of index joint swelling, with numerical values assigned as follows: 0 = no swelling; 1 = mild swelling; 2 = moderate swelling; 3 = severe swelling (or bulging beyond joint margins).

End point type	Secondary

End point timeframe:

Day 0 (pre-dose and post-dose), Day 3, Day 7

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6[4]	8	7	8
Units: Subjects				
Day 0 (pre-dose) - No Swelling	0	0	0	0
Day 0 (pre-dose) - Mild Swelling	0	1	1	1
Day 0 (pre-dose) - Moderate Swelling	4	3	4	4
Day 0 (pre-dose) - Severe Swelling	2	4	2	3
Day 0 (post-dose) - No Swelling	1	0	0	0
Day 0 (post-dose) - Mild Swelling	1	3	3	2
Day 0 (post-dose) - Moderate Swelling	2	4	2	4
Day 0 (post-dose) - Severe Swelling	2	1	2	2
Day 3 - No Swelling	1	3	1	1
Day 3 - Mild Swelling	2	2	4	2
Day 3 - Moderate Swelling	2	3	2	2
Day 3 - Severe Swelling	0	0	0	3

Day 7 - No Swelling	4	3	3	5
Day 7 - Mild Swelling	1	5	4	2
Day 7 - Moderate Swelling	1	0	0	1
Day 7 - Severe Swelling	0	0	0	0

Notes:

[4] - At Day 3, only 5 subjects were analyzed.

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29[5]			
Units: Subjects				
Day 0 (pre-dose) - No Swelling	0			
Day 0 (pre-dose) - Mild Swelling	3			
Day 0 (pre-dose) - Moderate Swelling	15			
Day 0 (pre-dose) - Severe Swelling	11			
Day 0 (post-dose) - No Swelling	1			
Day 0 (post-dose) - Mild Swelling	9			
Day 0 (post-dose) - Moderate Swelling	12			
Day 0 (post-dose) - Severe Swelling	7			
Day 3 - No Swelling	6			
Day 3 - Mild Swelling	10			
Day 3 - Moderate Swelling	9			
Day 3 - Severe Swelling	3			
Day 7 - No Swelling	15			
Day 7 - Mild Swelling	12			
Day 7 - Moderate Swelling	2			
Day 7 - Severe Swelling	0			

Notes:

[5] - At Day 3, only 28 subjects were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-assessed Index Joint Score - Erythema

End point title	Investigator-assessed Index Joint Score - Erythema

End point description:

Investigator assessment of index joint erythema, with values assigned as follows: present, absent, and non-assessable.

End point type	Secondary

End point timeframe:

Day 0 (pre-dose and post-dose), Day 3, Day 7

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6[6]	8	7	8
Units: Subjects				
Day 0 (pre-dose) - Absent	1	2	1	0
Day 0 (pre-dose) - Present	5	6	6	8
Day 0 (pre-dose) - Non-assessable	0	0	0	0
Day 0 (post-dose) - Absent	2	1	2	0
Day 0 (post-dose) - Present	4	7	5	8
Day 0 (post-dose) - Non-assessable	0	0	0	0
Day 3 - Absent	3	2	4	1
Day 3 - Present	2	6	3	7
Day 3 - Non-assessable	0	0	0	0
Day 7 - Absent	4	3	5	4
Day 7 - Present	2	5	2	4
Day 7 - Non-assessable	0	0	0	0

Notes:

[6] - At Day 3, only 5 subjects were analyzed.

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29[7]			
Units: Subjects				
Day 0 (pre-dose) - Absent	4			
Day 0 (pre-dose) - Present	25			
Day 0 (pre-dose) - Non-assessable	0			
Day 0 (post-dose) - Absent	5			
Day 0 (post-dose) - Present	24			
Day 0 (post-dose) - Non-assessable	0			
Day 3 - Absent	10			
Day 3 - Present	18			
Day 3 - Non-assessable	0			
Day 7 - Absent	16			
Day 7 - Present	13			
Day 7 - Non-assessable	0			

Notes:

[7] - At Day 3, only 28 subjects were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-assessed Index Joint Score - Warmth

End point title	Investigator-assessed Index Joint Score - Warmth

End point description:

Investigator assessment of index joint warmth, with values assigned as follows: present, absent, and non-assessable.

End point type	Secondary

End point timeframe:

Day 0 (pre-dose and post-dose), Day 3, Day 7

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6[8]	8	7	8
Units: Subjects				
Day 0 (pre-dose) - Absent	0	0	0	0
Day 0 (pre-dose) - Present	6	8	7	8
Day 0 (pre-dose) - Non-assessable	0	0	0	0
Day 0 (post-dose) - Absent	1	0	1	0
Day 0 (post-dose) - Present	5	8	6	8
Day 0 (post-dose) - Non-assessable	0	0	0	0
Day 3 - Absent	4	4	4	1
Day 3 - Present	1	4	3	7
Day 3 - Non-assessable	0	0	0	0
Day 7 - Absent	4	5	3	5
Day 7 - Present	2	3	4	3
Day 7 - Non-assessable	0	0	0	0

Notes:

[8] - At Day 3, only 5 subjects were analyzed.

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29[9]			
Units: Subjects				
Day 0 (pre-dose) - Absent	0			
Day 0 (pre-dose) - Present	29			
Day 0 (pre-dose) - Non-assessable	0			
Day 0 (post-dose) - Absent	2			
Day 0 (post-dose) - Present	27			
Day 0 (post-dose) - Non-assessable	0			
Day 3 - Absent	13			
Day 3 - Present	15			
Day 3 - Non-assessable	0			
Day 7 - Absent	17			
Day 7 - Present	12			
Day 7 - Non-assessable	0			

Notes:

[9] - At Day 3, only 28 subjects were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Investigator-assessed Global Rating of Disease

End point title	Investigator-assessed Global Rating of Disease

End point description:

Global Rating of Disease was one general question the Investigator was asked to answer about the overall perceived status of the subject's symptoms. The Investigator responded to the following question: "Considering all of the patient's signs and symptoms, how well are they doing?" The Global Rating of Disease was assessed on a 5-point Likert scale, with numerical values to assigned as follows: (0 = poor, 1 = fair, 2 = good, 3 = very good and 4 = excellent).

End point type	Secondary

End point timeframe:

Day 0 (pre-dose and post-dose), Day 3, Day 7

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6[10]	8	7	8
Units: Subjects				
Day 0 (pre-dose) - Poor	1	3	3	2
Day 0 (pre-dose) - Fair	4	4	1	6
Day 0 (pre-dose) - Good	1	1	3	0
Day 0 (pre-dose) - Very Good	0	0	0	0
Day 0 (pre-dose) - Excellent	0	0	0	0
Day 0 (post-dose) - Poor	1	2	3	1
Day 0 (post-dose) - Fair	3	4	0	5
Day 0 (post-dose) - Good	1	2	4	2
Day 0 (post-dose) - Very Good	1	0	0	0
Day 0 (post-dose) - Excellent	0	0	0	0
Day 3 - Poor	0	0	0	2
Day 3 - Fair	2	3	2	4
Day 3 - Good	2	2	3	2
Day 3 - Very Good	0	1	1	0
Day 3 - Excellent	1	2	1	0
Day 7 - Poor	0	0	0	0
Day 7 - Fair	2	0	1	2
Day 7 - Good	1	3	3	1
Day 7 - Very Good	1	1	0	2
Day 7 - Excellent	2	4	3	3

Notes:

[10] - At Day 3, only 5 subjects were analyzed

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29[11]			
Units: Subjects				
Day 0 (pre-dose) - Poor	9			
Day 0 (pre-dose) - Fair	15			
Day 0 (pre-dose) - Good	5			
Day 0 (pre-dose) - Very Good	0			
Day 0 (pre-dose) - Excellent	0			
Day 0 (post-dose) - Poor	7			

Day 0 (post-dose) - Fair	12			
Day 0 (post-dose) - Good	9			
Day 0 (post-dose) - Very Good	1			
Day 0 (post-dose) - Excellent	0			
Day 3 - Poor	2			
Day 3 - Fair	11			
Day 3 - Good	9			
Day 3 - Very Good	2			
Day 3 - Excellent	4			
Day 7 - Poor	0			
Day 7 - Fair	5			
Day 7 - Good	8			
Day 7 - Very Good	4			
Day 7 - Excellent	12			

Notes:

[11] - At Day 3, only 28 subjects were analyzed

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Levels of C-reactive Protein

End point title	Blood Levels of C-reactive Protein

End point description:

Blood levels of the inflammatory biomarker C-reactive protein (CRP) were analyzed for changes from Baseline.

End point type	Secondary

End point timeframe:

Baseline, Day 3, Day 7, Day 14

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6[12]	8	7	8
Units: milligram(s)/litre				
arithmetic mean (standard deviation)				
Baseline	22.78 (± 31.204)	11.06 (± 8.565)	19.60 (± 16.271)	30.53 (± 63.836)
Day 3	39.54 (± 58.100)	9.18 (± 7.052)	41.01 (± 49.548)	39.94 (± 57.478)
Day 3 - Change from Baseline	15.60 (± 24.172)	-1.89 (± 9.985)	21.41 (± 40.099)	9.41 (± 26.785)
Day 7	6.10 (± 3.863)	4.93 (± 3.848)	9.90 (± 11.422)	32.56 (± 52.535)
Day 7 - Change from Baseline	-16.68 (± 28.922)	-6.14 (± 8.632)	-9.70 (± 11.128)	2.04 (± 34.898)
Day 14	1.33 (± 0.596)	4.43 (± 1.695)	6.56 (± 8.831)	2.96 (± 2.331)
Day 14 - Change from Baseline	-21.45 (± 31.246)	-6.64 (± 9.234)	-13.04 (± 20.021)	-27.56 (± 62.144)

Notes:

[12] - At Day 3, only 5 subjects were analyzed.

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29[13]			
Units: milligram(s)/litre				
arithmetic mean (standard deviation)				
Baseline	20.92 (± 36.373)			
Day 3	31.35 (± 46.035)			
Day 3 - Change from Baseline	10.29 (± 27.151)			
Day 7	13.99 (± 29.391)			
Day 7 - Change from Baseline	-6.92 (± 23.334)			
Day 14	3.90 (± 4.728)			
Day 14 - Change from Baseline	-17.02 (± 36.301)			

Notes:

[13] - At Day 3, only 28 subjects were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Blood Levels of Serum Amyloid A Protein

End point title	Blood Levels of Serum Amyloid A Protein

End point description:

Blood levels of inflammatory biomarker serum amyloid A protein (SAA) were analyzed for changes from Baseline.

End point type	Secondary

End point timeframe:

Baseline, Day 3, Day 7, Day 14

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6[14]	8	7	8
Units: milligram(s)/litre				
arithmetic mean (standard deviation)				
Baseline	96.20 (± 192.716)	15.25 (± 14.116)	49.26 (± 63.862)	228.51 (± 614.857)
Day 3	275.38 (± 502.153)	15.35 (± 17.418)	259.11 (± 397.833)	293.15 (± 508.943)
Day 3 - Change from Baseline	164.12 (± 291.205)	0.10 (± 16.980)	209.86 (± 337.459)	64.64 (± 359.248)
Day 7	9.88 (± 7.323)	7.01 (± 7.360)	6.84 (± 6.183)	216.19 (± 381.395)

Day 7 - Change from Baseline	-86.32 (± 187.345)	-8.24 (± 8.619)	-42.41 (± 59.364)	-12.33 (± 362.927)
Day 14	2.68 (± 1.778)	5.91 (± 2.892)	10.83 (± 19.053)	6.78 (± 7.631)
Day 14 - Change from Baseline	-93.52 (± 192.751)	-9.34 (± 14.410)	-38.43 (± 69.613)	-221.74 (± 615.038)

Notes:

[14] - At Day 3, only 5 subjects were analyzed.

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29[15]			
Units: milligram(s)/litre				
arithmetic mean (standard deviation)				
Baseline	99.04 (± 330.885)			
Day 3	202.10 (± 392.922)			
Day 3 - Change from Baseline	100.27 (± 280.396)			
Day 7	65.27 (± 213.037)			
Day 7 - Change from Baseline	-33.77 (± 202.233)			
Day 14	6.67 (± 10.144)			
Day 14 - Change from Baseline	-92.37 (± 331.318)			

Notes:

[15] - At Day 3, only 28 subjects were analyzed.

Statistical analyses

No statistical analyses for this end point

Other pre-specified: Treatment Failures

End point title	Treatment Failures

End point description:

Subjects unable to tolerate his/her pain who wished to receive standard medical intervention for an acute gout flare could withdraw from the study. These subjects were considered a Treatment Failure and were treated with either prednisolone (30 mg QD) or colchicine (0.5 mg TID). No subjects were considered a treatment failure.

End point type	Other pre-specified

End point timeframe:

Baseline through Day 35

End point values	Cohort 1 - Per-Protocol	Cohort 2 - Per-Protocol	Cohort 3 - Per-Protocol	Cohort 4 - Per-Protocol
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	6	8	7	8
Units: Subjects				
Treatment Failures	0	0	0	0

End point values	Overall - Per-Protocol			
Subject group type	Subject analysis set			
Number of subjects analysed	29			
Units: Subjects				
Treatment Failures	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Adverse events were reported from time of informed consent form signature through Day 14. Serious adverse events were reported from time of informed consent signature through Day 35.	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups	
Reporting group title	Cohort 1
Reporting group description: 500 mg BID for 8 days	
Reporting group title	Cohort 2
Reporting group description: 500 mg QID for 8 days	
Reporting group title	Cohort 3
Reporting group description: BID (am and pm dosing) for 8 days	
Reporting group title	Cohort 4
Reporting group description: 100 mg QD for 8 days	
Reporting group title	All Subjects
Reporting group description: Includes all subjects in the Safety Population (n=34).	

Serious adverse events	Cohort 1	Cohort 2	Cohort 3
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 10 (20.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Post procedural myocardial infarction			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 8 (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
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 8 (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

Serious adverse events	Cohort 4	All Subjects	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 8 (0.00%)	2 / 34 (5.88%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Post procedural myocardial infarction			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Gout			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 2 %

Non-serious adverse events	Cohort 1	Cohort 2	Cohort 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	8 / 10 (80.00%)	7 / 8 (87.50%)	4 / 8 (50.00%)
Investigations			
C-reactive protein increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Serum amyloid A protein increased			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Weight decreased			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	0	0	0
Post procedural myocardial infarction			

subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Dysgeusia			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Headache			
subjects affected / exposed	2 / 10 (20.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	3 / 10 (30.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	3	0	0
Flatulence			
subjects affected / exposed	2 / 10 (20.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	2	1	0
Gastrointestinal sounds abnormal			
subjects affected / exposed	0 / 10 (0.00%)	2 / 8 (25.00%)	0 / 8 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Skin and subcutaneous tissue disorders			

Hyperhidrosis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Influenza			
subjects affected / exposed	0 / 10 (0.00%)	0 / 8 (0.00%)	1 / 8 (12.50%)
occurrences (all)	0	0	1
Myringitis			
subjects affected / exposed	0 / 10 (0.00%)	1 / 8 (12.50%)	0 / 8 (0.00%)
occurrences (all)	0	1	0
Nasopharyngitis			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0
Gout			
subjects affected / exposed	4 / 10 (40.00%)	2 / 8 (25.00%)	3 / 8 (37.50%)
occurrences (all)	4	2	3
Hyponatraemia			
subjects affected / exposed	1 / 10 (10.00%)	0 / 8 (0.00%)	0 / 8 (0.00%)
occurrences (all)	1	0	0

Non-serious adverse events	Cohort 4	All Subjects	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 8 (75.00%)	25 / 34 (73.53%)	
Investigations			
C-reactive protein increased			

subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Serum amyloid A protein increased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Weight decreased			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Joint injury			
subjects affected / exposed	1 / 8 (12.50%)	1 / 34 (2.94%)	
occurrences (all)	1	1	
Post procedural myocardial infarction			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Dysgeusia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	0 / 8 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	3	
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Diarrhoea			
subjects affected / exposed	0 / 8 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	3	
Flatulence			
subjects affected / exposed	0 / 8 (0.00%)	3 / 34 (8.82%)	
occurrences (all)	0	3	
Gastrointestinal sounds abnormal			

subjects affected / exposed	0 / 8 (0.00%)	2 / 34 (5.88%)	
occurrences (all)	0	2	
Nausea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Rhinorrhoea			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Influenza			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Myringitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	5 / 8 (62.50%)	14 / 34 (41.18%)	
occurrences (all)	6	15	
Hyponatraemia			
subjects affected / exposed	0 / 8 (0.00%)	1 / 34 (2.94%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 September 2017	Key revisions included change of prohibited use of paracetamol before Baseline Visit to within 4 hours (from within 12 hours of Baseline Visit).
11 April 2018	Key revisions included added exclusion criteria for known diagnosis of chronic kidney disease or known history of renal impairment, change of Cohort 2 dose administration to 500 mg QID (from 1000 mg BID), change of urate-lowering therapy (a prohibited concomitant medication/therapy) stable dosing condition to 1 month (from 3 months), allowance of usage of medical data from synovial fluid collection/analysis from within 24 hours prior to Baseline Visit as part of standard medical diagnosis to be used and reported in study case report forms, addition of discretionary replacement of any subject who did not complete dosing through the Day 7 Visit, removal of requirement that at least three subjects per cohort be enrolled with a gout flare that began within 36 hours of the Baseline Visit, and addition of optional, suggested subject contact for dosing compliance.
10 October 2018	Key revisions included addition of Cohort 4 with 8 patients dosing at 100 mg per day thereby changing total enrollment to approximately 32 eligible subjects (from approximately 24 eligible subjects), and removal of decision tree for determination of dose schedules and replacement with a table to reflect actual trial dosages.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

This proof-of-concept trial was conducted in a small number subjects, therefore no statistical analyses between groups were conducted.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33005902