Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Dose-response Study of the Efficacy and Safety of MEDI7352 in Subjects with Painful Osteoarthritis of the Knee

Summary

EudraCT number	2020-003797-51
Trial protocol	DE DK
Global end of trial date	16 August 2023

Results information

Result version number	v2 (current)
This version publication date	11 December 2024
First version publication date	30 August 2024
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	D5680C00003

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04675034
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca
Sponsor organisation address	151 85, Sodertalje, Sweden,
Public contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 8772409479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca Clinical Study Information Center, +1 8772409479, information.center@astrazeneca.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	14 September 2023
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 August 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the efficacy of MEDI7352 compared with placebo on chronic pain in participants with painful osteoarthritis (OA) of the knee at Week 12.

Protection of trial subjects:

The conduct of this clinical study met all local and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and are consistent with International Conference on Harmonization guideline: Good Clinical Practice, and applicable regulatory requirements. Participants signed an informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 December 2020
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	Denmark: 3
Country: Number of subjects enrolled	Estonia: 14
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Poland: 129
Country: Number of subjects enrolled	Spain: 76
Country: Number of subjects enrolled	United Kingdom: 112
Worldwide total number of subjects	345
EEA total number of subjects	233

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)	185
From 65 to 84 years	160
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study was conducted at 50 sites in 6 countries (the United Kingdom, Denmark, Estonia, Germany, Poland, and Spain).

Pre-assignment

Screening details:

A total of 345 participants were randomized, of which 344 participants received at least one dose of study drug.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MEDI7352 Dose Level 1

Arm description:

Participants received 6 doses of subcutaneous (SC) MEDI7352 Dose Level 1 injection once every 2 weeks (Q2W) during a 12-week parallel-group treatment period.

Arm type	Experimental
Investigational medicinal product name	MEDI7352
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Six doses of SC MEDI7352 Dose Level 1 Q2W given during a 12-week parallel-group treatment period.

Arm title	MEDI7352 Dose Level 2

Arm description:

Participants received 6 doses of SC MEDI7352 Dose Level 2 injection Q2W during a 12-week parallel-group treatment period.

Arm type	Experimental
Investigational medicinal product name	MEDI7352
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Six doses of SC MEDI7352 Dose Level 2 Q2W given during a 12-week parallel-group treatment period.

Arm title	MEDI7352 Dose Level 3

Arm description:

Participants received 6 doses of SC MEDI7352 Dose Level 3 injection Q2W during a 12-week parallel-group treatment period.

Arm type	Experimental

Investigational medicinal product name	MEDI7352
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Six doses of SC MEDI7352 Dose Level 3 Q2W given during a 12-week parallel-group treatment period.

Arm title	MEDI7352 Dose Level 4

Arm description:

Participants received 6 doses of SC MEDI7352 Dose Level 4 injection Q2W during a 12-week parallel-group treatment period.

Arm type	Experimental
Investigational medicinal product name	MEDI7352
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Powder for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Six doses of SC MEDI7352 Dose Level 4 Q2W given during a 12-week parallel-group treatment period.

Arm title	Placebo

Arm description:

Participants received 6 doses of SC placebo injection matched to MEDI7352 Q2W during a 12-week parallel-group treatment period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Six doses of SC placebo injection matched to MEDI7352 Q2W given during a 12-week parallel-group treatment period.

Number of subjects in period 1	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3
Started	70	68	69
Treated	70	68	69
Completed	59	64	65
Not completed	11	4	4
Consent withdrawn by subject	9	3	4
Lost to follow-up	1	1	-
Protocol deviation	1	-	-

Number of subjects in period 1	MEDI7352 Dose Level 4	Placebo
Started	68	70
Treated	68	69

Completed	57	61
Not completed	11	9
Consent withdrawn by subject	8	6
Lost to follow-up	2	-
Protocol deviation	1	3

Baseline characteristics

Reporting groups	
Reporting group title	MEDI7352 Dose Level 1
Reporting group description:	
Participants received 6 doses of subcutaneous (SC) MEDI7352 Dose Level 1 injection once every 2 weeks (Q2W) during a 12-week parallel-group treatment period.	
Reporting group title	MEDI7352 Dose Level 2
Reporting group description:	
Participants received 6 doses of SC MEDI7352 Dose Level 2 injection Q2W during a 12-week parallel-group treatment period.	
Reporting group title	MEDI7352 Dose Level 3
Reporting group description:	
Participants received 6 doses of SC MEDI7352 Dose Level 3 injection Q2W during a 12-week parallel-group treatment period.	
Reporting group title	MEDI7352 Dose Level 4
Reporting group description:	
Participants received 6 doses of SC MEDI7352 Dose Level 4 injection Q2W during a 12-week parallel-group treatment period.	
Reporting group title	Placebo
Reporting group description:	
Participants received 6 doses of SC placebo injection matched to MEDI7352 Q2W during a 12-week parallel-group treatment period.	

Reporting group values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3
Number of subjects	70	68	69
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)	32	33	40
From 65-84 years	38	35	29
85 years and over	0	0	0
Age Continuous Units: Years			
arithmetic mean	65.8	63.3	63.8
standard deviation	± 7.90	± 7.73	± 6.91
Sex: Female, Male Units: Participants			
Female	43	51	48
Male	27	17	21
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	1	2

Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	69	66	67
More than one race	0	0	0
Unknown or Not Reported	1	1	0
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	1	2
Not Hispanic or Latino	69	67	67
Unknown or Not Reported	0	0	0

Reporting group values	MEDI7352 Dose Level 4	Placebo	Total
Number of subjects	68	70	345
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)	38	42	185
From 65-84 years	30	28	160
85 years and over	0	0	0
Age Continuous			
Units: Years			
arithmetic mean	63.3	62.5	
standard deviation	± 7.52	± 8.03	-
Sex: Female, Male			
Units: Participants			
Female	46	42	230
Male	22	28	115
Race (NIH/OMB)			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	3	3	9
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	0	0	0
White	65	67	334
More than one race	0	0	0
Unknown or Not Reported	0	0	2
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	1	0	5
Not Hispanic or Latino	67	70	340
Unknown or Not Reported	0	0	0

End points

End points reporting groups

Reporting group title	MEDI7352 Dose Level 1
Reporting group description:	
Participants received 6 doses of subcutaneous (SC) MEDI7352 Dose Level 1 injection once every 2 weeks (Q2W) during a 12-week parallel-group treatment period.	
Reporting group title	MEDI7352 Dose Level 2
Reporting group description:	
Participants received 6 doses of SC MEDI7352 Dose Level 2 injection Q2W during a 12-week parallel-group treatment period.	
Reporting group title	MEDI7352 Dose Level 3
Reporting group description:	
Participants received 6 doses of SC MEDI7352 Dose Level 3 injection Q2W during a 12-week parallel-group treatment period.	
Reporting group title	MEDI7352 Dose Level 4
Reporting group description:	
Participants received 6 doses of SC MEDI7352 Dose Level 4 injection Q2W during a 12-week parallel-group treatment period.	
Reporting group title	Placebo
Reporting group description:	
Participants received 6 doses of SC placebo injection matched to MEDI7352 Q2W during a 12-week parallel-group treatment period.	

Primary: Change From Baseline in Weekly Average of Daily Numerical Rating Scale (NRS) Pain Score to Week 12

End point title	Change From Baseline in Weekly Average of Daily Numerical Rating Scale (NRS) Pain Score to Week 12
End point description:	
Change from baseline in weekly average of daily NRS pain score to Week 12 is reported. The NRS is an 11-point Likert scale used to assess pain, where participants were asked to describe their average pain in the target knee by identifying a number from 0 = "no pain" to 10 = "most severe pain imaginable over the previous 24 hours". This was recorded on a daily basis at approximately the same time every morning via electronic patient recorded outcome (ePRO) diary. A two-step multiple imputation procedure was used to address missing post-baseline scores. Full analysis set (FAS) included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received.	
End point type	Primary
End point timeframe:	
Baseline (Day -7 to Day -1, inclusive) through Week 12	

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Units on a scale				
arithmetic mean (standard deviation)	-2.19 (± 2.243)	-3.00 (± 2.342)	-2.83 (± 2.522)	-2.81 (± 2.835)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: Units on a scale				
arithmetic mean (standard deviation)	-2.35 (± 2.364)			

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Least Square (LS) mean and treatment group difference with associated 95% confidence intervals (CIs) are modelled using ANCOVA on imputed data including treatment group, baseline score and Kellgren and Lawrence (KL) grade.

Comparison groups	MEDI7352 Dose Level 1 v Placebo
Number of subjects included in analysis	140
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.36
Method	ANCOVA
Parameter estimate	Combined estimate for LS mean
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.968
upper limit	0.67
Variability estimate	Standard error of the mean
Dispersion value	0.416

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Least Square mean and treatment group difference with associated 95% CIs are modelled using ANCOVA on imputed data including treatment group, baseline score and KL grade.

Comparison groups	MEDI7352 Dose Level 2 v Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.029
Method	ANCOVA
Parameter estimate	Combined estimate for LS mean
Point estimate	-0.8

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.619
upper limit	0.027
Variability estimate	Standard error of the mean
Dispersion value	0.418

Statistical analysis title	Statistical Analysis 3
Statistical analysis description:	
Least Square mean and treatment group difference with associated 95% CIs are modelled using ANCOVA on imputed data including treatment group, baseline score and KL grade.	
Comparison groups	MEDI7352 Dose Level 3 v Placebo
Number of subjects included in analysis	139
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.026
Method	ANCOVA
Parameter estimate	Combined estimate for LS mean
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.618
upper limit	0.009
Variability estimate	Standard error of the mean
Dispersion value	0.413

Statistical analysis title	Statistical Analysis 4
Statistical analysis description:	
Least Square mean and treatment group difference with associated 95% CIs are modelled using ANCOVA on imputed data including treatment group, baseline score and KL grade.	
Comparison groups	MEDI7352 Dose Level 4 v Placebo
Number of subjects included in analysis	138
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.083
Method	ANCOVA
Parameter estimate	Combined estimate for LS mean
Point estimate	-0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.423
upper limit	0.245
Variability estimate	Standard error of the mean
Dispersion value	0.424

Secondary: Change From Baseline in Western Ontario and McMaster Universities Arthritis Index (WOMAC) Pain Subscale to Week 12

End point title	Change From Baseline in Western Ontario and McMaster Universities Arthritis Index (WOMAC) Pain Subscale to Week 12

End point description:

The WOMAC multiscale index is used to assess pain, stiffness, and joint functionality in the past 48 hours in participants with OA of the knee or hip. The WOMAC pain subscale consists of 5 questions assessing the participant's pain due to osteoarthritis (OA) in the target knee. Each question was scored on a NRS scale from 0 to 10, and the WOMAC pain subscale score is calculated as the mean score from all 5 questions, where higher scores represent higher pain. A two-step multiple imputation procedure was used to address missing post-baseline scores. Change from baseline in WOMAC pain subscale to Week 12 is reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received.

End point type	Secondary

End point timeframe:

Week 0 (Day 1; baseline) through Week 12

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.88 (± 2.047)	-2.88 (± 2.407)	-2.62 (± 2.305)	-2.57 (± 2.992)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: Units on a scale				
arithmetic mean (standard deviation)	-2.62 (± 2.558)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WOMAC Physical Function Subscale to Week 12

End point title	Change From Baseline in WOMAC Physical Function Subscale to Week 12

End point description:

The WOMAC multiscale index is used to assess pain, stiffness, and joint functionality in the past 48 hours in participants with OA of the knee or hip. The WOMAC physical function (PF) subscale consists of 17 questions assessing the participant’s difficulty in performing activities of daily living due to OA in the target knee. Each question is scored on an NRS scale from 0 to 10, and the WOMAC PF subscale score is

calculated as the mean score from all 17 questions, where higher scores represent worse function. A two-step multiple imputation procedure was used to address missing post-baseline scores. Change from baseline in WOMAC physical function to Week 12 is reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received.

End point type	Secondary

End point timeframe:

Week 0 (Day 1; baseline) through Week 12

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.48 (± 2.233)	-2.56 (± 2.352)	-2.45 (± 1.909)	-2.22 (± 2.887)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: Units on a scale				
arithmetic mean (standard deviation)	-2.14 (± 2.338)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Patient's Global Assessment (PGA) of OA to Week 12

End point title	Change From Baseline in Patient's Global Assessment (PGA) of OA to Week 12

End point description:

The PGA of OA was a 5-point Likert scale used to assess symptoms and activity impairment due to OA of the knee. Participants were asked to identify a number from 1 = "very good (asymptomatic and no limitation to normal activities)" to 5 = "very poor (very severe symptoms which are intolerable and inability to carry out all normal activities)" based on the question "Considering all the ways that OA of the knee affects you, how are you feeling today?". A two-step multiple imputation procedure was used to address missing post-baseline scores. Change from baseline in PGA of OA to Week 12 is reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received.

End point type	Secondary

End point timeframe:

Week 0 (Day 1; baseline) through Week 12

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Units on a scale				
arithmetic mean (standard deviation)	-0.34 (± 0.933)	-0.72 (± 1.123)	-0.81 (± 1.032)	-0.69 (± 1.377)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	70			
Units: Units on a scale				
arithmetic mean (standard deviation)	-0.57 (± 1.003)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WOMAC Pain Subscale Over Time

End point title	Change From Baseline in WOMAC Pain Subscale Over Time

End point description:

The WOMAC multiscale index is used to assess pain, stiffness, and joint functionality in the past 48 hours in participants with OA of the knee or hip. The WOMAC pain subscale consists of 5 questions assessing the participant's pain due to OA in the target knee. Each question was scored on an NRS scale from 0 to 10, and the WOMAC pain subscale score is calculated as the mean score from all 5 questions, where higher scores represent higher pain. Change from baseline in WOMAC pain subscale to Weeks 2,4,6, 8, 10, and 18 is reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received. Number of participants analyzed (N) denotes the number of participants evaluated for this endpoint. Number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0; Day 1), Weeks 2 (Day 14), 4 (Day 28), 6 (Day 42), 8 (Day 56), 10 (Day 70), and 18 (Day 126)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	63	63	65
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=63,63,63,65,58)	-1.32 (± 1.501)	-1.79 (± 1.988)	-1.58 (± 1.571)	-1.88 (± 1.953)
Week 4(n=57,61,60,59,61)	-1.62 (± 1.635)	-2.33 (± 2.230)	-2.41 (± 1.939)	-2.60 (± 2.077)

Week 6(n=59,61,57,56,55)	-2.01 (± 1.541)	-2.76 (± 2.223)	-2.73 (± 1.852)	-3.07 (± 2.065)
Week 8(n=54,56,57,49,46)	-2.01 (± 1.840)	-2.96 (± 2.259)	-2.91 (± 1.954)	-3.33 (± 1.964)
Week 10(n=53,56,52,48,46)	-2.14 (± 1.886)	-3.22 (± 2.282)	-2.89 (± 2.052)	-3.54 (± 2.055)
Week 18(n=45,51,51,39,43)	-2.00 (± 2.090)	-3.02 (± 2.388)	-2.61 (± 2.107)	-3.50 (± 1.988)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=63,63,63,65,58)	-1.30 (± 1.968)			
Week 4(n=57,61,60,59,61)	-2.08 (± 2.000)			
Week 6(n=59,61,57,56,55)	-2.40 (± 2.114)			
Week 8(n=54,56,57,49,46)	-2.56 (± 2.431)			
Week 10(n=53,56,52,48,46)	-2.89 (± 2.283)			
Week 18(n=45,51,51,39,43)	-2.97 (± 2.219)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WOMAC PF Subscale Over Time

End point title	Change From Baseline in WOMAC PF Subscale Over Time

End point description:

The WOMAC multiscale index is used to assess pain, stiffness, and joint functionality in the past 48 hours in participants with OA of the knee or hip. The WOMAC PF subscale consists of 17 questions assessing the participant's difficulty in performing activities of daily living due to OA in the target knee. Each question is scored on an NRS scale from 0 to 10, and the WOMAC PF subscale score is calculated as the mean score from all 17 questions, where higher scores represent worse function. Change from baseline in WOMAC physical function to Weeks 2,4,6, 8, 10, and 18 is reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received. Number of participants analyzed (N) denotes the number of participants evaluated for this endpoint. Number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0; Day 1), Weeks 2 (Day 14), 4 (Day 28), 6 (Day 42), 8 (Day 56), 10 (Day 70), and 18 (Day 126)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	63	63	65
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=63,63,63,65,58)	-1.06 (± 1.621)	-1.64 (± 1.877)	-1.56 (± 1.417)	-1.80 (± 1.778)
Week 4(n=57,61,60,59,61)	-1.59 (± 1.812)	-2.07 (± 1.933)	-2.20 (± 1.701)	-2.39 (± 2.062)
Week 6(n=59,61,57,56,55)	-1.77 (± 1.670)	-2.43 (± 1.946)	-2.43 (± 1.436)	-2.71 (± 2.001)
Week 8(n=54,56,57,49,46)	-1.64 (± 1.856)	-2.82 (± 1.960)	-2.68 (± 1.792)	-3.06 (± 1.858)
Week 10(n=53,56,52,48,46)	-1.74 (± 1.994)	-2.85 (± 1.944)	-2.65 (± 1.671)	-3.30 (± 1.979)
Week 18(n=45,51,51,39,43)	-1.55 (± 2.267)	-2.71 (± 2.141)	-2.37 (± 1.722)	-3.17 (± 1.812)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=63,63,63,65,58)	-0.96 (± 1.728)			
Week 4(n=57,61,60,59,61)	-1.62 (± 1.708)			
Week 6(n=59,61,57,56,55)	-1.92 (± 1.945)			
Week 8(n=54,56,57,49,46)	-2.06 (± 2.114)			
Week 10(n=53,56,52,48,46)	-2.26 (± 2.063)			
Week 18(n=45,51,51,39,43)	-2.24 (± 1.810)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WOMAC Overall Score Over Time

End point title	Change From Baseline in WOMAC Overall Score Over Time

End point description:

The WOMAC overall score consisted of all 24 questions reported in the WOMAC questionnaire to assess: i) pain subscale, ii) PF subscale and iii) stiffness subscale. WOMAC overall score was calculated as the mean score from all 24 questions each scored on a Likert scale from 0 to 10 where higher scores represent worse outcome. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received. Number of participants analyzed (N) denotes the number of participants evaluated for this endpoint. Number analyzed (n) denotes those participants who were evaluable at the specified time point. Change from baseline in weekly average of WOMAC overall score to Weeks 2, 4, 6, 8, 10, 12, and 18 is reported.

End point type	Secondary

End point timeframe:

Baseline (Week 0; Day 1), Weeks 2 (Day 14), 4 (Day 28), 6 (Day 42), 8 (Day 56), 10 (Day 70), 12 (Day 84), and 18 (Day 126)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	63	64	65
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=64,63,64,65,58)	-1.11 (± 1.546)	-1.71 (± 1.836)	-1.58 (± 1.343)	-1.88 (± 1.735)
Week 4(n=58,61,60,59,61)	-1.66 (± 1.706)	-2.14 (± 1.958)	-2.25 (± 1.667)	-2.45 (± 2.000)
Week 6(n=59,62,57,57,56)	-1.85 (± 1.583)	-2.54 (± 1.968)	-2.52 (± 1.426)	-2.79 (± 1.951)
Week 8(n=54,56,58,49,46)	-1.75 (± 1.792)	-2.85 (± 1.995)	-2.69 (± 1.757)	-3.12 (± 1.822)
Week 10(n=53,56,52,48,46)	-1.86 (± 1.907)	-2.94 (± 1.995)	-2.72 (± 1.663)	-3.35 (± 1.954)
Week 12(n=47,54,52,41,42)	-1.82 (± 1.945)	-3.00 (± 2.087)	-2.76 (± 1.616)	-3.48 (± 2.121)
Week 18(n=45,51,51,39,43)	-1.68 (± 2.148)	-2.78 (± 2.153)	-2.46 (± 1.718)	-3.24 (± 1.784)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=64,63,64,65,58)	-1.04 (± 1.695)			
Week 4(n=58,61,60,59,61)	-1.74 (± 1.671)			
Week 6(n=59,62,57,57,56)	-1.98 (± 1.984)			
Week 8(n=54,56,58,49,46)	-2.19 (± 2.102)			
Week 10(n=53,56,52,48,46)	-2.43 (± 2.022)			
Week 12(n=47,54,52,41,42)	-2.56 (± 1.956)			
Week 18(n=45,51,51,39,43)	-2.42 (± 1.767)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in WOMAC Stiffness Scores Over Time

End point title	Change From Baseline in WOMAC Stiffness Scores Over Time

End point description:

The WOMAC stiffness function subscale consists of 2 questions assessing stiffness due to OA in the target knee. Stiffness is defined as a sensation of decreased ease of movement in the target knee. Each question is scored on an NRS scale from 0 to 10, and the WOMAC stiffness function subscale score is calculated as the mean score from the 2 questions, where higher scores represent higher stiffness. Change from baseline in WOMAC stiffness score to Weeks 2, 4, 6, 8, 10, 12, and 18 is reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received. Number of participants analyzed (N) denotes the number of participants evaluated for this endpoint. Number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0; Day 1), Weeks 2 (Day 14), 4 (Day 28), 6 (Day 42), 8 (Day 56), 10 (Day 70), 12 (Day 84), and 18 (Day 126)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	64	63	64	65
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=64,63,64,65,58)	-1.30 (± 1.887)	-2.06 (± 2.015)	-1.85 (± 1.927)	-2.13 (± 2.020)
Week 4(n=58,61,60,59,61)	-1.88 (± 1.938)	-2.26 (± 2.146)	-2.33 (± 2.127)	-2.55 (± 2.368)
Week 6(n=59,62,57,57,56)	-2.13 (± 1.837)	-2.79 (± 2.307)	-2.72 (± 1.871)	-2.97 (± 2.428)
Week 8(n=54,56,58,49,46)	-1.99 (± 2.125)	-2.85 (± 2.260)	-2.85 (± 2.103)	-3.07 (± 2.104)
Week 10(n=53,56,52,48,46)	-2.13 (± 2.060)	-2.99 (± 2.277)	-2.96 (± 1.977)	-3.29 (± 2.091)
Week 12(n=47,54,52,41,42)	-2.29 (± 2.034)	-3.06 (± 2.380)	-3.06 (± 2.040)	-3.43 (± 2.407)
Week 18(n=45,51,51,39,43)	-2.04 (± 2.192)	-2.76 (± 2.401)	-2.86 (± 1.988)	-3.17 (± 1.797)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=64,63,64,65,58)	-0.99 (± 1.805)			
Week 4(n=58,61,60,59,61)	-1.91 (± 2.009)			
Week 6(n=59,62,57,57,56)	-2.27 (± 2.314)			

Week 8(n=54,56,58,49,46)	-2.39 (± 2.633)			
Week 10(n=53,56,52,48,46)	-2.67 (± 2.329)			
Week 12(n=47,54,52,41,42)	-2.85 (± 2.372)			
Week 18(n=45,51,51,39,43)	-2.62 (± 2.152)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in PGA of OA Over Time

End point title	Change From Baseline in PGA of OA Over Time

End point description:

The PGA of OA was a 5-point Likert scale used to assess symptoms and activity impairment due to OA of the knee. Participants were asked to identify a number from 1 = "very good (asymptomatic and no limitation to normal activities)" to 5 = "very poor (very severe symptoms which are intolerable and inability to carry out all normal activities)" based on the question "Considering all the ways that OA of the knee affects you, how are you feeling today?". Change from baseline in PGA of OA to Weeks 2, 4, 8, 10, and 18 is reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received. Number of participants analyzed (N) denotes the number of participants who were evaluable for the specified endpoint. Number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline, Weeks 2 (Day 14), 4 (Day 28), 8 (Day 56), 10 (Day 70), and 18 (Day 126)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	62	60	65
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=62,62,60,65,57)	-0.35 (± 0.812)	-0.56 (± 0.917)	-0.67 (± 0.933)	-0.42 (± 1.059)
Week 4(n=56,60,57,59,60)	-0.48 (± 0.738)	-0.68 (± 1.066)	-0.86 (± 1.043)	-0.86 (± 1.106)
Week 8(n=53,55,54,49,45)	-0.57 (± 0.910)	-0.80 (± 1.026)	-1.02 (± 1.090)	-1.04 (± 1.098)
Week 10(n=52,55,49,48,45)	-0.42 (± 0.723)	-0.76 (± 0.922)	-1.02 (± 1.010)	-1.06 (± 1.295)
Week 18(n=44,50,48,39,43)	-0.39 (± 0.655)	-0.66 (± 1.022)	-0.83 (± 1.117)	-1.10 (± 1.294)

End point values	Placebo			

Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=62,62,60,65,57)	-0.37 (± 0.698)			
Week 4(n=56,60,57,59,60)	-0.48 (± 0.792)			
Week 8(n=53,55,54,49,45)	-0.51 (± 0.843)			
Week 10(n=52,55,49,48,45)	-0.67 (± 0.826)			
Week 18(n=44,50,48,39,43)	-0.56 (± 0.700)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Responder Participants Measured by Osteoarthritis Research Society International (OARSI) Responder Index Using Outcome Measures in Rheumatology-Osteoarthritis Research Society International (OMERACT-OARSI) Definition

End point title	Percentage of Responder Participants Measured by Osteoarthritis Research Society International (OARSI) Responder Index Using Outcome Measures in Rheumatology-Osteoarthritis Research Society International (OMERACT-OARSI) Definition

End point description:

OMERACT-OARSI responder index is calculated from WOMAC Pain subscale, WOMAC PF Subscale and PGA of OA. A participant is classified as responder if: 1. >=2-point absolute change from Baseline to Week X or >=50% improvement is reported in WOMAC pain or PF subscales; 2. At least 2 of following 3 conditions are true: >=1-point absolute change from Baseline to Week X or >=20% improvement is reported in WOMAC Pain subscale, >=1-point absolute change from Baseline to Week X or >=20% improvement is reported in WOMAC PF subscale or >=1-point absolute change from Baseline to Week X in PGA of OA. Percentage of responder participants are reported. FAS: all randomized participants analyzed according to intent-to-treat principle whereby randomized study treatment will be analyzed regardless of study treatment actually received. Number of participants analyzed (N): participants evaluated for this endpoint. Number analyzed (n): participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Weeks 2 (Day 14), 4 (Day 28), 8 (Day 56), 12 (Day 84), and 18 (Day 126)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	65	64	68	67
Units: Percentage of participants				
number (not applicable)				
Week 2(n=65,64,68,67,64)	47.7	62.5	61.8	59.7
Week 4(n=59,62,64,61,65)	59.3	67.7	73.4	65.6
Week 8(n=56,57,60,51,51)	58.9	80.7	80.0	86.3

Week 12(n=49,55,55,42,46)	59.2	80.0	80.0	85.7
Week 18(n=47,52,54,41,47)	55.3	78.8	72.2	80.5

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: Percentage of participants				
number (not applicable)				
Week 2(n=65,64,68,67,64)	40.6			
Week 4(n=59,62,64,61,65)	63.1			
Week 8(n=56,57,60,51,51)	68.6			
Week 12(n=49,55,55,42,46)	67.4			
Week 18(n=47,52,54,41,47)	70.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Improvement of >= 2 points in PGA of OA

End point title	Percentage of Participants With Improvement of >= 2 points in PGA of OA

End point description:

The PGA of OA was a 5-point Likert scale used to assess symptoms and activity impairment due to OA of the knee. Participants were asked to identify a number from 1 = "very good (asymptomatic and no limitation to normal activities)" to 5 = "very poor (very severe symptoms which are intolerable and inability to carry out all normal activities)" based on the question "Considering all the ways that OA of the knee affects you, how are you feeling today?". Percentage of participants with improvement of >= 2 points in PGA of OA at Weeks 2, 4, 8, 12, and 18 is reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received. Number of participants analyzed (N) denotes the number of participants evaluated for this endpoint. Number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Weeks 2 (Day 14), 4 (Day 28), 8 (Day 56), 12 (Day 84), and 18 (Day 126)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	62	62	60	65
Units: Percentage of participants				
number (not applicable)				
Week 2(n=62,62,60,65,57)	9.7	9.7	16.7	12.3
Week 4(n=56,60,57,59,60)	8.9	26.7	24.6	22.0
Week 8(n=53,55,54,49,45)	17.0	23.6	25.9	28.6
Week 12(n=46,53,49,40,41)	10.9	18.9	20.4	32.5

Week 18(n=44,50,48,39,43)	2.3	20.0	22.9	25.6

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	60			
Units: Percentage of participants				
number (not applicable)				
Week 2(n=62,62,60,65,57)	7.0			
Week 4(n=56,60,57,59,60)	6.7			
Week 8(n=53,55,54,49,45)	4.4			
Week 12(n=46,53,49,40,41)	7.3			
Week 18(n=44,50,48,39,43)	4.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Average of Daily NRS Pain Score Over Time

End point title	Change From Baseline in Weekly Average of Daily NRS Pain Score Over Time

End point description:

The NRS is an 11-point Likert scale used to assess pain, where participants were asked to describe their average pain in the target knee by identifying a number from 0 = "no pain" to 10 = "most severe pain imaginable over the previous 24 hours". This will be recorded on a daily basis at approximately the same time every morning via ePRO diary. Change from baseline in weekly average of daily NRS to Weeks 2, 4, 6, 8, 10, and 18 is reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received. Number of participants analyzed (N) denotes the number of participants evaluated for this endpoint. Number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day -7 to Day -1, inclusive), Weeks 2 (Day 14), 4 (Day 28), 6 (Day 42), 8 (Day 56), 10 (Day 70), and 18 (Day 126)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	64	65	66
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=66,64,65,66,65)	-1.62 (± 1.704)	-1.86 (± 1.949)	-1.97 (± 2.012)	-2.26 (± 2.129)
Week 4(n=61,64,64,65,64)	-1.88 (± 1.653)	-2.50 (± 2.163)	-2.68 (± 2.177)	-2.65 (± 2.333)
Week 6(n=62,63,61,57,58)	-2.17 (± 1.687)	-2.83 (± 2.248)	-3.00 (± 2.192)	-3.35 (± 2.498)

Week 8(n=55,59,61,52,52)	-2.27 (± 1.736)	-2.91 (± 2.084)	-3.09 (± 2.205)	-3.45 (± 2.365)
Week 10(n=55,55,56,51,46)	-2.38 (± 2.001)	-3.18 (± 1.930)	-3.24 (± 2.294)	-3.57 (± 2.274)
Week 18(n=42,48,52,38,44)	-2.08 (± 2.120)	-3.18 (± 2.237)	-2.90 (± 2.157)	-3.63 (± 2.383)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Week 2(n=66,64,65,66,65)	-1.10 (± 1.811)			
Week 4(n=61,64,64,65,64)	-1.66 (± 1.854)			
Week 6(n=62,63,61,57,58)	-1.97 (± 2.020)			
Week 8(n=55,59,61,52,52)	-2.18 (± 2.274)			
Week 10(n=55,55,56,51,46)	-2.28 (± 2.047)			
Week 18(n=42,48,52,38,44)	-2.45 (± 1.969)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With >= 30% and >= 50% Reductions in Weekly Average of Daily NRS Pain Score Over Time

End point title	Percentage of Participants With >= 30% and >= 50% Reductions in Weekly Average of Daily NRS Pain Score Over Time

End point description:

The NRS is an 11-point Likert scale used to assess pain, where participants were asked to describe their average pain in the target knee by identifying a number from 0 = "no pain" to 10 = "most severe pain imaginable over the previous 24 hours". This will be recorded on a daily basis at approximately the same time every morning via ePRO diary. Percentage of participants with >= 30% and >= 50% reductions in weekly average of daily NRS pain score are reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received. Number of participants analyzed (N) denotes the number of participants evaluated for this endpoint. Number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day -7 to Day -1, inclusive), Weeks 2 (Day 14), 4 (Day 28), 8 (Day 56), 12 (Day 84), and 18 (Day 126)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	64	65	66
Units: Percentage of participants				
number (not applicable)				
>=30%: Week 2(n=66,64,65,66,65)	34.8	34.4	41.5	43.9
>=30%: Week 4(n=61,64,64,65,64)	47.5	50.0	64.1	53.8
>=30%: Week 8(n=55,59,61,52,52)	56.4	67.8	67.2	61.5
>=30%: Week 12(n=50,55,55,44,46)	58.0	76.4	65.5	72.7
>=30%: Week 18(n=42,48,52,38,44)	42.9	72.9	67.3	65.8
>=50%: Week 2(n=66,64,65,66,65)	15.2	25.0	29.2	30.3
>=50%: Week 4(n=61,64,64,65,64)	24.6	32.8	40.6	36.9
>=50%: Week 8(n=55,59,61,52,52)	32.7	45.8	54.1	57.7
>=50%: Week 12(n=50,55,55,44,46)	44.0	54.5	49.1	54.5
>=50%: Week 18(n=42,48,52,38,44)	26.2	54.2	50.0	52.6

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	65			
Units: Percentage of participants				
number (not applicable)				
>=30%: Week 2(n=66,64,65,66,65)	21.5			
>=30%: Week 4(n=61,64,64,65,64)	29.7			
>=30%: Week 8(n=55,59,61,52,52)	42.3			
>=30%: Week 12(n=50,55,55,44,46)	47.8			
>=30%: Week 18(n=42,48,52,38,44)	54.5			
>=50%: Week 2(n=66,64,65,66,65)	13.8			
>=50%: Week 4(n=61,64,64,65,64)	15.6			
>=50%: Week 8(n=55,59,61,52,52)	26.9			
>=50%: Week 12(n=50,55,55,44,46)	26.1			
>=50%: Week 18(n=42,48,52,38,44)	29.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With >= 30% and >= 50% Reductions in WOMAC Pain Subscale Score Over Time

End point title	Percentage of Participants With >= 30% and >= 50% Reductions in WOMAC Pain Subscale Score Over Time

End point description:

The WOMAC multiscale index is used to assess pain, stiffness, and joint functionality in the past 48 hours in participants with OA of the knee or hip. The WOMAC pain subscale consists of 5 questions assessing the participant's pain due to OA in the target knee. Each question was scored on an NRS scale from 0 to 10, and the WOMAC pain subscale score is calculated as the mean score from all 5 questions, where higher scores represent higher pain. Percentage of participants with >= 30% and >= 50% reductions in WOMAC pain subscale score over time are reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will

be analyzed regardless of the study treatment actually received. Number of participants analyzed (N) denotes the number of participants evaluated for this endpoint. Number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0; Day 1), Weeks 2 (Day 14), 4 (Day 28), 8 (Day 56), 12 (Day 84), and 18 (Day 126)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	63	63	65
Units: Percentage of participants				
number (not applicable)				
>=30%: Week 2(n=63,63,63,65,58)	30.2	39.7	36.5	50.8
>=30%: Week 4(n=57,61,60,59,61)	40.4	54.1	61.7	61.0
>=30%: Week 8(n=54,56,57,49,46)	55.6	64.3	64.9	71.4
>=30%: Week 12(n=47,54,52,40,42)	59.6	68.5	67.3	75.0
>=30%: Week 18(n=45,51,51,39,43)	51.1	70.6	62.7	76.9
>=50%: Week 2(n=63,63,63,65,58)	14.3	23.8	17.5	33.8
>=50%: Week 4(n=57,61,60,59,61)	24.6	31.1	40.0	55.9
>=50%: Week 8(n=54,56,57,49,46)	35.2	46.4	49.1	57.1
>=50%: Week 12(n=47,54,52,40,42)	31.9	51.9	50.0	62.5
>=50%: Week 18(n=45,51,51,39,43)	33.3	51.0	43.1	59.0

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Percentage of participants				
number (not applicable)				
>=30%: Week 2(n=63,63,63,65,58)	24.1			
>=30%: Week 4(n=57,61,60,59,61)	47.5			
>=30%: Week 8(n=54,56,57,49,46)	56.5			
>=30%: Week 12(n=47,54,52,40,42)	66.7			
>=30%: Week 18(n=45,51,51,39,43)	69.8			
>=50%: Week 2(n=63,63,63,65,58)	10.3			
>=50%: Week 4(n=57,61,60,59,61)	26.2			
>=50%: Week 8(n=54,56,57,49,46)	34.8			
>=50%: Week 12(n=47,54,52,40,42)	42.9			
>=50%: Week 18(n=45,51,51,39,43)	41.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With >= 30% and >= 50% Reductions in WOMAC Physical Function Subscale Over Time

End point title	Percentage of Participants With >= 30% and >= 50% Reductions in WOMAC Physical Function Subscale Over Time

End point description:

The WOMAC PF subscale consists of 17 questions assessing the participant's difficulty in performing activities of daily living due to OA in the target knee. Each question is scored on an NRS scale from 0 to 10, and the WOMAC PF subscale score is calculated as the mean score from all 17 questions, where higher scores represent worse function. Percentage of participants with >= 30% and >= 50% reductions in WOMAC physical function subscale over time are reported. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received. Number of participants analyzed (N) denotes the number of participants evaluated for this endpoint. Number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline (Week 0; Day 1), Weeks 2 (Day 14), 4 (Day 28), 8 (Day 56), 12 (Day 84), and 18 (Day 126)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	63	63	63	65
Units: Percentage of participants				
number (not applicable)				
>=30%: Week 2(n=63,63,63,65,58)	30.2	42.9	39.7	47.7
>=30%: Week 4(n=57,61,60,59,61)	47.4	52.5	61.7	59.3
>=30%: Week 8(n=54,56,57,49,46)	50.0	64.3	63.2	69.4
>=30%: Week 12(n=47,54,52,40,42)	42.6	72.2	67.3	72.5
>=30%: Week 18(n=45,51,51,39,43)	42.2	72.5	64.7	74.4
>=50%: Week 2(n=63,63,63,65,58)	14.3	22.2	23.8	33.8
>=50%: Week 4(n=57,61,60,59,61)	28.1	31.1	41.7	54.2
>=50%: Week 8(n=54,56,57,49,46)	33.3	51.8	47.4	57.1
>=50%: Week 12(n=47,54,52,40,42)	34.0	46.3	50.0	62.5
>=50%: Week 18(n=45,51,51,39,43)	33.3	45.1	39.2	59.0

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	61			
Units: Percentage of participants				
number (not applicable)				
>=30%: Week 2(n=63,63,63,65,58)	22.4			
>=30%: Week 4(n=57,61,60,59,61)	37.7			
>=30%: Week 8(n=54,56,57,49,46)	47.8			
>=30%: Week 12(n=47,54,52,40,42)	54.8			
>=30%: Week 18(n=45,51,51,39,43)	60.5			
>=50%: Week 2(n=63,63,63,65,58)	12.1			
>=50%: Week 4(n=57,61,60,59,61)	19.7			
>=50%: Week 8(n=54,56,57,49,46)	26.1			
>=50%: Week 12(n=47,54,52,40,42)	35.7			

>=50%: Week 18(n=45,51,51,39,43)	34.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Serum Concentration of MEDI7352

End point title	Serum Concentration of MEDI7352[1]

End point description:

Serum concentration of MEDI7352 is reported. Pharmacokinetic (PK) analysis set included participants who received at least one dose of double-blind study treatment per the protocol for whom any post-baseline PK data are available and who did not violate or deviate from the protocol in ways that would significantly affect the PK analyses. The arbitrary numbers 99.999 and 99999 signified mean and standard deviation, respectively, not reported as the Geometric mean and geometric CV% were not calculated as samples were lost (unfrozen) during shipment. Number of participants analyzed (N) denotes those participants who were analyzed for this endpoint. Number analyzed (n) denotes those participants who had adequate serum samples.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Day 7; pre-dose on Days 14, 28, 42, 56, and 70; and on Days 74, 77, 84, 126, and 224

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Only those baseline period arms for which analysis was planned were reported in the end point.

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	67	68
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1(n=0,0,0,0)	99.999 (± 99999)	99.999 (± 99999)	99.999 (± 99999)	99.999 (± 99999)
Day 7(n=63,62,66,65)	326.863 (± 98.989)	681.322 (± 159.914)	2149.062 (± 109.2763)	3582.265 (± 364.200)
Day 14(n=65,63,67,67)	50.337 (± 538.604)	144.242 (± 475.607)	379.882 (± 488.933)	650.864 (± 624.642)
Day 28(n=57,58,62,56)	11.025 (± 853.538)	28.332 (± 2745.856)	43.644 (± 6705.491)	222.665 (± 3963.855)
Day 42(n=55,54,59,50)	5.895 (± 846.517)	12.375 (± 2578.767)	30.005 (± 11978.840)	116.951 (± 14993.947)
Day 56(n=0,53,58,51)	99.999 (± 99999)	6.625 (± 2133.678)	20.546 (± 13626.951)	85.779 (± 15987.305)
Day 70(n=0,0,55,44)	99.999 (± 99999)	99999 (± 99999)	17.124 (± 15147.088)	57.042 (± 18183.372)
Day 74(n=48,53,55,42)	10.943 (± 1833.135)	22.074 (± 4305.129)	116.544 (± 25316.322)	551.099 (± 18558.506)
Day 77(n=45,50,52,44)	5.011 (± 1322.708)	9.356 (± 3099.752)	47.108 (± 39692.068)	271.511 (± 36387.885)
Day 84(n=0,0,56,45)	99.999 (± 99999)	99.999 (± 99999)	10.482 (± 6086.596)	43.062 (± 13640.856)

Day 126(n=0,0,0,0)	99.999 (± 99999)	99.999 (± 99999)	99.999 (± 99999)	99.999 (± 99999)
Day 224(n=0,0,0,0)	99.999 (± 99999)	99.999 (± 99999)	99.999 (± 99999)	99.999 (± 99999)

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Positive Anti-Drug Antibodies (ADA) to MEDI7352

End point title	Number of Participants With Positive Anti-Drug Antibodies (ADA) to MEDI7352

End point description:

Number of participants with ADA to MEDI7352 are reported. Treatment-induced ADA positive: ADA negative at baseline (Bl) and positive at least 1 post-BL ADA assessment. Treatment-boosted ADA positive: ADA positive at BL, and BL titre is boosted by greater than variability of assay at >=1 post-BL timepoint. Persistent positive: ADA negative at BL and having at least 2 post-BL ADA positive results (>=16 weeks between first and last positive)/ADA positive at last post-BL test. Transiently positive: ADA negative at BL and at least 1 post-BL ADA positive measurement and not fulfilling conditions for persistently positive. ADA evaluable participants included all participants in safety analysis set who have non-missing BL and at least 1 non-missing post-BL ADA results. Number of participants analyzed (N): number of participants who were evaluable for specified endpoint. No. analyzed (n): participants who had adequate ADA sample.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Day 7; pre-dose on Days 14, 28, 42, 56, and 70; and on Days 74, 77, 84, 126, and 224

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	66	67
Units: Participants				
Treatment-induced ADA positive	52	49	42	52
Treatment-boosted ADA positive	6	9	8	2
Persistent positive ADA	43	39	33	42
Transiently positive ADA	9	10	9	10

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	67			
Units: Participants				
Treatment-induced ADA positive	6			
Treatment-boosted ADA positive	2			
Persistent positive ADA	4			
Transiently positive ADA	2			

Statistical analyses

No statistical analyses for this end point

Secondary: ADA Titre in Participants who were ADA Positive at Baseline and/or Post-baseline

End point title	ADA Titre in Participants who were ADA Positive at Baseline and/or Post-baseline

End point description:

The ADA titre in participants who were ADA positive at baseline and/or post-baseline is reported. ADA evaluable participants included all participants in safety analysis set who have non-missing baseline and at least 1 non-missing post-baseline ADA results. Number of participants analyzed (N): number of participants who were ADA positive at baseline and/or post-baseline. Number analyzed (n): participants who had adequate ADA sample.

End point type	Secondary

End point timeframe:

Baseline (Day 1), Day 7; pre-dose on Days 14, 28, 42, 56, and 70; and on Days 74, 77, 84, 126, and 224

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	61	59	52	54
Units: Ratio				
median (full range (min-max))	960.0 (30 to 122880)	960.0 (30 to 245760)	960.0 (30 to 15360)	720.0 (30 to 122880)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	19			
Units: Ratio				
median (full range (min-max))	240.0 (30 to 3840)			

Statistical analyses

No statistical analyses for this end point

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

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

End point description:

An adverse event (AE) is any untoward medical occurrence in a participant who received study drug without regard to possibility of causal relationship. A serious adverse event (SAE) is an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. The TEAEs are defined as events present at baseline that worsened in intensity after administration of study drug or events absent at baseline that emerged after administration of study drug. Safety analysis set included all participants who received at least 1 dose of any double-blind study drug and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 41 weeks (maximum observed duration)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Participants				
Any TEAEs	51	45	54	51
Any TESAEs	3	5	3	1

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Participants				
Any TEAEs	41			
Any TESAEs	2			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Findings in Physical Examination Reported as TEAEs

End point title	Number of Participants With Clinically Significant Findings in Physical Examination Reported as TEAEs

End point description:

Number of participants with clinically significant findings in physical examination reported as TEAE are reported. A physical examination included assessments of general appearance, skin, head and neck, examination of the oral cavity for any lesions, lymph nodes, thyroid, abdomen (bowel sounds, liver, and spleen palpation), back (including costovertebral angle tenderness), musculoskeletal/extremities, cardiovascular, and respiratory systems. Safety analysis set included all participants who received at least 1 dose of any double-blind study drug and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 41 weeks (maximum observed duration)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Participants	0	0	0	1

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Abnormal Findings in Neurological Examination

End point title	Number of Participants With Clinically Significant Abnormal Findings in Neurological Examination

End point description:

Number of participants with clinically significant abnormal findings in neurological examination is reported. The neurological examination included assessment of mental status, cranial nerves, motor examination (muscle strength and tone), upper and lower extremity deep tendon reflexes, plantar responses, sensory system examination, coordination, and gait. Safety analysis set included all participants who received at least 1 dose of any double-blind study drug and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Baseline (Day -45 to Day -1), Weeks 0 (Day 1), 2 (Day 14), 4 (Day 28), 6 (Day 42), 8 (Day 56), 10 (Day 70), 12 (Day 84), 18 (Day 126), 28 (Day 168), 32 (Day 224), and 36 (Day 252)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Participants				
Baseline	0	0	0	0
Week 0	0	0	0	0
Week 2	1	0	0	0
Week 4	0	0	0	0

Week 6	0	0	0	0
Week 8	0	0	0	0
Week 10	0	0	0	0
Week 12	0	0	0	1
Week 18	0	0	0	1
Week 28	0	0	0	1
Week 32	0	0	0	1
Week 36	0	0	0	2

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Participants				
Baseline	0			
Week 0	0			
Week 2	0			
Week 4	1			
Week 6	0			
Week 8	0			
Week 10	0			
Week 12	0			
Week 18	0			
Week 28	0			
Week 32	0			
Week 36	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Total Neuropathy Score-Nurse (TNSn) Over Time

End point title	Total Neuropathy Score-Nurse (TNSn) Over Time

End point description:

The TNSn, is a semiquantitative clinical assessment of peripheral nervous system function. The TNSn assessment is collected as scores of motor symptom, autonomic symptom, pin sensibility, sensory symptom, and vibration sensibility score. Each neuropathy item is scored on a 0 to 4 scale with total score ranging from 0 to 20. Higher total scores correlate with more severe neuropathy. Safety analysis set included all participants who received at least 1 dose of any double-blind study drug and were analyzed according to the treatment they actually received. Number of participants analyzed (N) denotes the number of participants evaluated for this endpoint. Number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Baseline (Day -45 to Day -1), Weeks 0 (Day 1), 2 (Day 14), 4 (Day 28), 6 (Day 42), 8 (Day 56), 10 (Day 70), 12 (Day 84), 28 (Day 196), and 32 (Day 224)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	66	69	68
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=51,55,59,56,61)	1.5 (± 2.40)	1.4 (± 1.94)	1.0 (± 1.56)	1.2 (± 1.69)
Week 0(n=70,66,69,68,67)	1.3 (± 1.92)	1.7 (± 2.26)	1.4 (± 2.03)	1.5 (± 2.29)
Week 2(n=66,65,69,67,65)	1.1 (± 1.84)	1.6 (± 2.42)	1.2 (± 1.97)	1.0 (± 1.70)
Week 4(n=61,64,64,64,65)	1.0 (± 1.66)	1.3 (± 1.98)	0.9 (± 1.54)	0.9 (± 1.61)
Week 6(n=61,62,62,60,61)	1.0 (± 1.55)	1.4 (± 2.23)	0.9 (± 1.73)	0.9 (± 1.48)
Week 8(n=56,57,62,52,52)	1.0 (± 1.65)	1.1 (± 1.86)	0.6 (± 0.91)	0.8 (± 1.62)
Week 10(n=56,56,55,51,50)	1.1 (± 1.85)	1.3 (± 2.06)	0.8 (± 1.53)	0.7 (± 1.20)
Week 12(n=48,58,59,52,49)	0.9 (± 1.35)	1.2 (± 1.88)	0.8 (± 1.37)	0.7 (± 1.23)
Week 28(n=6,9,8,10,9)	1.7 (± 2.25)	3.3 (± 2.69)	2.5 (± 2.83)	0.8 (± 0.92)
Week 32(n=41,49,51,43,48)	1.5 (± 1.98)	1.0 (± 1.50)	0.5 (± 0.88)	0.9 (± 1.64)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	67			
Units: Units on a scale				
arithmetic mean (standard deviation)				
Baseline(n=51,55,59,56,61)	1.5 (± 2.02)			
Week 0(n=70,66,69,68,67)	1.8 (± 2.26)			
Week 2(n=66,65,69,67,65)	1.5 (± 2.18)			
Week 4(n=61,64,64,64,65)	1.4 (± 2.16)			
Week 6(n=61,62,62,60,61)	1.5 (± 2.51)			
Week 8(n=56,57,62,52,52)	1.2 (± 1.84)			
Week 10(n=56,56,55,51,50)	1.1 (± 2.10)			
Week 12(n=48,58,59,52,49)	1.1 (± 2.00)			
Week 28(n=6,9,8,10,9)	2.9 (± 2.67)			
Week 32(n=41,49,51,43,48)	1.0 (± 1.98)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weight (kg) to Week 12

End point title	Change From Baseline in Weight (kg) to Week 12

End point description:

Change from baseline in weight (kg) to Week 12 is reported. Safety analysis set included all participants who received at least 1 dose of any double-blind study drug and were analyzed according to the treatment they actually received. Number of participants analyzed (N) denotes the number of participants evaluated at Week 12

End point type	Secondary

End point timeframe:

Baseline (Day -45 to -1) and Week 12

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	66	66	65	66
Units: kg				
arithmetic mean (standard deviation)	-0.25 (± 2.048)	0.10 (± 2.343)	0.34 (± 1.932)	-0.03 (± 1.864)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	64			
Units: kg				
arithmetic mean (standard deviation)	-0.34 (± 2.004)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Vital Signs Reported as TEAEs

End point title	Number of Participants With Abnormal Vital Signs Reported as TEAEs

End point description:

Number of participants with abnormal vital signs reported as TEAEs are reported. Abnormal vital signs are defined as any abnormal finding in the vital sign parameters (body temperature, supine and standing blood pressure, pulse rate, and respiratory rate). Safety analysis set included all participants who received at least 1 dose of any double-blind study drug and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 41 weeks (maximum observed duration)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Participants				
Bradycardia	0	0	0	0
Tachycardia	1	0	0	0
Tachycardia paroxysmal	1	0	0	0
Hypertension	0	2	3	0
Hypertensive crisis	1	0	0	0

Orthostatic hypotension	1	1	1	0
Pyrexia	0	0	0	0

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Participants				
Bradycardia	1			
Tachycardia	0			
Tachycardia paroxysmal	0			
Hypertension	0			
Hypertensive crisis	0			
Orthostatic hypotension	1			
Pyrexia	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Survey of Autonomic Symptoms (SAS) Total Impact Score

End point title	Change from Baseline in Survey of Autonomic Symptoms (SAS) Total Impact Score

End point description:

SAS is an instrument that measures autonomic symptoms used for assessing autonomic neuropathies. It evaluates presence and severity of symptoms. SAS consists of 11 questions in women and 12 in men, with Yes/No answer to symptoms occurring 6 months prior to study drug administration. "Yes" responses further rated from 1 to 5 (1=not at all; 5=a lot) by asking participant how much each symptom is bothering, thus contributing to a total symptom impact score. Questions assess following domains: orthostatic intolerance [10 points (pts)]; vasomotor [6 pts]; secretomotor [7 pts]; gastrointestinal [28 pts]; bladder [9 pts]; pupillomotor [15 pts]. Higher score indicates worse autonomic dysfunction. Safety analysis set: participants who received at least 1 dose of any double-blind study drug and were analyzed according to received treatment. No. of participants analyzed (N): participants that are evaluable for specified endpoint. No. analyzed (n): participants who had adequate SAS impact score.

End point type	Secondary

End point timeframe:

Baseline (Day 1; Week 0) and Day 252 (Week 36)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	40	42	44	38
Units: Units on a scale				
arithmetic mean (standard deviation)	-1.5 (± 4.78)	-1.1 (± 4.63)	-0.9 (± 4.13)	-1.6 (± 4.62)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	44			
Units: Units on a scale				
arithmetic mean (standard deviation)	-0.8 (± 3.50)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Clinically Significant Abnormal Electrocardiograms (ECGs)

End point title	Number of Participants With Clinically Significant Abnormal Electrocardiograms (ECGs)

End point description:

Number of participants with clinically significant abnormal ECGs are reported. Safety analysis set included all participants who received at least 1 dose of any double-blind study drug and were analyzed according to the treatment they actually received. Number of participants analyzed (N) denotes the number of participants who were evaluable for the specified outcome measure. Number analyzed (n) denotes those participants who were evaluable at the specified time point.

End point type	Secondary

End point timeframe:

Weeks 0 (Day 1), 2 (Day 14), 4 (Day 28), 8 (Day 56), 10 (Day 70), 12 (Day 84), 28 (Day 168), and 32 (Day 224)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Participants				
Week 0(n=70,68,69,68,69)	0	0	0	0
Week 2(n=66,64,68,68,66)	0	0	0	0
Week 4(n=62,63,63,60,64)	0	0	0	0
Week 8(n=55,57,60,52,49)	0	0	0	0
Week 10(n=54,55,56,48,50)	0	0	0	1
Week 12(n=66,66,67,65,65)	0	0	0	0
Week 28(n=8,10,11,10,9)	0	0	0	0
Week 32(n=48,50,54,45,49)	0	0	1	0

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	69			

Units: Participants				
Week 0(n=70,68,69,68,69)	0			
Week 2(n=66,64,68,68,66)	0			
Week 4(n=62,63,63,60,64)	0			
Week 8(n=55,57,60,52,49)	0			
Week 10(n=54,55,56,48,50)	0			
Week 12(n=66,66,67,65,65)	0			
Week 28(n=8,10,11,10,9)	0			
Week 32(n=48,50,54,45,49)	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal Clinical Laboratory Parameters Reported as TEAEs

End point title	Number of Participants With Abnormal Clinical Laboratory Parameters Reported as TEAEs

End point description:

Number of participants with abnormal clinical laboratory parameters reported as TEAEs are reported. Safety analysis set included all participants who received at least 1 dose of any double-blind study drug and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 41 weeks (maximum observed duration)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Participants				
COVID-19	16	5	10	12
Anaemia	0	1	1	0
Leukopenia	1	0	0	0
Lymphopenia	0	0	0	1
Neutropenia	0	0	0	1
Hypercholesterolaemia	1	0	1	1
Hyperkalaemia	0	2	0	0
Hypertriglyceridaemia	1	0	0	2
Hypokalaemia	0	0	1	0
Hyponatraemia	0	0	1	0
Type 2 diabetes mellitus	0	0	0	0
Vitamin D deficiency	0	1	0	0
Glycosuria	0	1	0	0
Leukocyturia	0	2	0	0
Proteinuria	0	0	2	0
Activated partial thromboplastin time prolonged	0	0	1	0

Alanine aminotransferase increased	0	0	0	0
Aspartate aminotransferase increased	0	0	0	0
Blood creatine phosphokinase increased	2	1	1	0
Blood folate decreased	1	0	0	0
Blood glucose increased	0	1	0	1
Blood uric acid increased	0	0	0	1
C-reactive protein increased	1	0	0	1
Coagulation factor increased	1	0	0	0
Gamma-glutamyltransferase increased	0	1	0	0
Glycosylated haemoglobin increased	1	0	0	0

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Participants				
COVID-19	8			
Anaemia	0			
Leukopenia	1			
Lymphopenia	1			
Neutropenia	1			
Hypercholesterolaemia	0			
Hyperkalaemia	0			
Hypertriglyceridaemia	1			
Hypokalaemia	1			
Hyponatraemia	0			
Type 2 diabetes mellitus	1			
Vitamin D deficiency	0			
Glycosuria	2			
Leukocyturia	1			
Proteinuria	2			
Activated partial thromboplastin time prolonged	0			
Alanine aminotransferase increased	1			
Aspartate aminotransferase increased	1			
Blood creatine phosphokinase increased	2			
Blood folate decreased	0			
Blood glucose increased	0			
Blood uric acid increased	0			
C-reactive protein increased	0			
Coagulation factor increased	0			
Gamma-glutamyltransferase increased	1			
Glycosylated haemoglobin increased	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in Weekly Average of Daily NRS Pain Score to Week 12 due to Baseline Biomarker C-reactive Protein

End point title	Change From Baseline in Weekly Average of Daily NRS Pain Score to Week 12 due to Baseline Biomarker C-reactive Protein

End point description:

Change from baseline in weekly average of daily NRS pain score to Week 12 due to baseline biomarker C-reactive protein is reported. The NRS is an 11-point Likert scale used to assess pain, where participants were asked to describe their average pain in the target knee by identifying a number from 0 = "no pain" to 10 = "most severe pain imaginable over the previous 24 hours". This was recorded on a daily basis at approximately the same time every morning via electronic patient recorded outcome (ePRO) diary. FAS included all randomized participants analyzed according to the intent-to-treat principle whereby randomized study treatment will be analyzed regardless of the study treatment actually received. Number of participants analyzed (N) denotes the number of participants evaluated at Week 12.

End point type	Secondary

End point timeframe:

Baseline (Day -7 to -1, inclusive) through Week 12

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	50	55	54	43
Units: Units on a scale				
arithmetic mean (standard deviation)	-2.55 (± 1.975)	-3.34 (± 2.004)	-3.30 (± 2.422)	-3.68 (± 2.313)

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: Units on a scale				
arithmetic mean (standard deviation)	-2.38 (± 1.971)			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Injection Site Reactions

End point title	Number of Participants With Injection Site Reactions

End point description:

Number of participants with injection site reactions are reported. Safety analysis set included all participants who received at least 1 dose of any double-blind study drug and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Day 1 through 41 weeks (maximum observed duration)

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Participants	2	3	0	4

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	69			
Units: Participants	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Participants With Abnormal X-ray and/or Magnetic Resonance Imaging (MRI) of Large Joints

End point title	Number of Participants With Abnormal X-ray and/or Magnetic Resonance Imaging (MRI) of Large Joints

End point description:

Number of participants with abnormal X-ray and/or MRI of large joints is reported. Safety analysis set included all participants who received at least 1 dose of any double-blind study drug and were analyzed according to the treatment they actually received.

End point type	Secondary

End point timeframe:

Baseline (Day -45 to -1) and Week 32

End point values	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3	MEDI7352 Dose Level 4
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	70	68	69	68
Units: Participants				
X-ray	1	0	0	1
MRI	0	1	0	0

End point values	Placebo			
Subject group type	Reporting group			
Number of subjects analysed	69			

Units: Participants				
X-ray	2			
MRI	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Day 1 through 41 weeks (maximum observed duration)

Adverse event reporting additional description:

Safety analysis set included all participants who received at least 1 dose of any double-blind study drug and were analyzed according to the treatment they actually received.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups

Reporting group title	MEDI7352 Dose Level 1

Reporting group description:

Participants received 6 doses of subcutaneous (SC) MEDl7352 Dose Level 1 injection once every 2 weeks (Q2W) during 12-week treatment period.

Reporting group title	MEDI7352 Dose Level 2

Reporting group description:

Participants received 6 doses of SC MEDl7352 Dose Level 2 injection Q2W during 12-week treatment period.

Reporting group title	MEDI7352 Dose Level 3

Reporting group description:

Participants received 6 doses of SC MEDl7352 Dose Level 3 injection Q2W during 12-week treatment period.

Reporting group title	MEDI7352 Dose Level 4

Reporting group description:

Participants received 6 doses of SC MEDl7352 Dose 4 Level injection Q2W during 12-week treatment period.

Reporting group title	Placebo

Reporting group description:

Participants received 6 doses of SC placebo injection matched to MEDl7352 Q2W during 12-week treatment period.

Serious adverse events	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 70 (4.29%)	5 / 68 (7.35%)	3 / 69 (4.35%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Liver function test abnormal			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			

Ovarian neoplasm			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (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 carcinoma			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Traumatic renal injury			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (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
Splenic rupture			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (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
Multiple injuries			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (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
Cardiac disorders			
Cardiovascular insufficiency			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (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
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Large intestine polyp			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (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
Dyspnoea			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (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
Respiratory failure			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (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
Skin and subcutaneous tissue disorders			
Henoch-schonlein purpura			

subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (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
Renal and urinary disorders			
Loss of bladder sensation			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (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
Nephrolithiasis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinoma			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (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
Musculoskeletal and connective tissue disorders			
Arthritis reactive			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (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

Serious adverse events	MEDI7352 Dose Level 4	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 68 (1.47%)	2 / 69 (2.90%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Investigations			
Liver function test abnormal			

subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Ovarian neoplasm			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal carcinoma			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Traumatic renal injury			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Splenic rupture			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiovascular insufficiency			

subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Large intestine polyp			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Henoch-schonlein purpura			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Loss of bladder sensation			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinoma			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthritis reactive			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences causally related to treatment / all	0 / 0	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
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: 0 %

Non-serious adverse events	MEDI7352 Dose Level 1	MEDI7352 Dose Level 2	MEDI7352 Dose Level 3
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 70 (72.86%)	45 / 68 (66.18%)	54 / 69 (78.26%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of liver			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Haemangioma of bone			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Acrochordon			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Lipoma			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Seborrhoeic keratosis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Tumour ulceration			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	1 / 69 (1.45%)
occurrences (all)	0	1	1
Hypertension			
subjects affected / exposed	0 / 70 (0.00%)	2 / 68 (2.94%)	3 / 69 (4.35%)
occurrences (all)	0	2	3
Hypertensive crisis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Orthostatic hypotension			
subjects affected / exposed	1 / 70 (1.43%)	1 / 68 (1.47%)	1 / 69 (1.45%)
occurrences (all)	1	1	1
Peripheral coldness			

subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Superficial vein prominence			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Feeling hot			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Asthenia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	1	0	1
Chest discomfort			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Chills			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 70 (2.86%)	1 / 68 (1.47%)	1 / 69 (1.45%)
occurrences (all)	2	1	1
Temperature regulation disorder			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Injection site bruising			
subjects affected / exposed	2 / 70 (2.86%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	2	1	0
Injection site erythema			
subjects affected / exposed	2 / 70 (2.86%)	6 / 68 (8.82%)	6 / 69 (8.70%)
occurrences (all)	2	8	7
Injection site induration			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Injection site pain			

subjects affected / exposed	0 / 70 (0.00%)	5 / 68 (7.35%)	4 / 69 (5.80%)
occurrences (all)	0	7	5
Injection site pruritus			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	2 / 69 (2.90%)
occurrences (all)	0	1	2
Injection site reaction			
subjects affected / exposed	2 / 70 (2.86%)	3 / 68 (4.41%)	0 / 69 (0.00%)
occurrences (all)	3	4	0
Injection site swelling			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Malaise			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Peripheral swelling			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Pyrexia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Thirst			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Drug hypersensitivity			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0

Seasonal allergy			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Type iv hypersensitivity reaction			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Bartholin's cyst			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Pelvic pain			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	1 / 70 (1.43%)	3 / 68 (4.41%)	1 / 69 (1.45%)
occurrences (all)	1	3	1
Cough			
subjects affected / exposed	5 / 70 (7.14%)	1 / 68 (1.47%)	1 / 69 (1.45%)
occurrences (all)	5	1	1
Dysphonia			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Epistaxis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Haemoptysis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Nasal congestion			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Aphonia			

subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Pleuritic pain			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Productive cough			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Pulmonary mass			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Rhinorrhoea			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Depressed mood			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Insomnia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Irritability			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Investigations			
Activated partial thromboplastin time prolonged			

subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Alanine aminotransferase increased			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Blood creatine phosphokinase increased			
subjects affected / exposed	2 / 70 (2.86%)	1 / 68 (1.47%)	1 / 69 (1.45%)
occurrences (all)	2	1	1
Blood folate decreased			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Blood glucose increased			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Blood pressure increased			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Blood uric acid increased			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
C-reactive protein increased			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Coagulation factor increased			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Liver function test increased			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Glycosylated haemoglobin increased			

subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Faecal calprotectin abnormal			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Drug screen positive			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Electrocardiogram qt prolonged			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Electrocardiogram t wave inversion			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Chillblains			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Cartilage injury			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Bone contusion			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Animal bite			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	1	0	1
Adverse event following immunisation			

subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Accidental exposure to product			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Back injury			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Post procedural contusion			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Musculoskeletal injury			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Muscle strain			
subjects affected / exposed	1 / 70 (1.43%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	1	1	0
Muscle injury			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Limb injury			
subjects affected / exposed	0 / 70 (0.00%)	2 / 68 (2.94%)	2 / 69 (2.90%)
occurrences (all)	0	2	2
Ligament sprain			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	2
Joint injury			
subjects affected / exposed	1 / 70 (1.43%)	1 / 68 (1.47%)	3 / 69 (4.35%)
occurrences (all)	1	2	3
Head injury			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Fracture			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Foot fracture			

subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Fall			
subjects affected / exposed	1 / 70 (1.43%)	1 / 68 (1.47%)	1 / 69 (1.45%)
occurrences (all)	1	1	2
Post-traumatic pain			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	1	0	1
Tooth fracture			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Skin injury			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Soft tissue injury			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	2
Congenital, familial and genetic disorders			
Accessory spleen			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Vascular malformation			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Mitral valve incompetence			

subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Palpitations			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Tachycardia paroxysmal			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Atrial fibrillation			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Bradycardia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Areflexia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Disturbance in attention			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Carpal tunnel syndrome			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Cervical radiculopathy			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Burning sensation			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Dizziness			
subjects affected / exposed	0 / 70 (0.00%)	2 / 68 (2.94%)	1 / 69 (1.45%)
occurrences (all)	0	2	1

Dizziness postural			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	2 / 70 (2.86%)	7 / 68 (10.29%)	9 / 69 (13.04%)
occurrences (all)	2	8	9
Hypoaesthesia			
subjects affected / exposed	1 / 70 (1.43%)	1 / 68 (1.47%)	4 / 69 (5.80%)
occurrences (all)	1	1	4
Migraine			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	3	0	0
Paraesthesia			
subjects affected / exposed	4 / 70 (5.71%)	3 / 68 (4.41%)	2 / 69 (2.90%)
occurrences (all)	5	4	3
Tremor			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	1	0	1
Presyncope			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Resting tremor			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Sciatica			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Sensory loss			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Polyneuropathy			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0

Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	1 / 69 (1.45%)
occurrences (all)	0	1	1
Leukopenia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Lymphadenopathy			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Lymphopenia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Neutropenia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Ear congestion			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Tympanic membrane perforation			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	2
Vertigo			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Vertigo positional			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Amaurosis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Conjunctival haemorrhage			

subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Glaucoma			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Lacrimation increased			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Photopsia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Vitreous floaters			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 70 (0.00%)	2 / 68 (2.94%)	0 / 69 (0.00%)
occurrences (all)	0	2	0
Abdominal mass			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Abdominal pain			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	2
Abdominal pain lower			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Hiatus hernia			
subjects affected / exposed	0 / 70 (0.00%)	2 / 68 (2.94%)	0 / 69 (0.00%)
occurrences (all)	0	2	0
Colitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	2 / 70 (2.86%)	2 / 68 (2.94%)	1 / 69 (1.45%)
occurrences (all)	2	2	1

Dental discomfort			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Diarrhoea			
subjects affected / exposed	3 / 70 (4.29%)	2 / 68 (2.94%)	2 / 69 (2.90%)
occurrences (all)	3	2	2
Diverticulum intestinal			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Duodenitis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Dyspepsia			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Food poisoning			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Gastric ulcer			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal inflammation			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Abdominal pain upper			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	2
Mesenteric panniculitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	1 / 70 (1.43%)	2 / 68 (2.94%)	1 / 69 (1.45%)
occurrences (all)	1	2	1

Noninfective gingivitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Oesophageal stenosis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Oesophagitis			
subjects affected / exposed	0 / 70 (0.00%)	2 / 68 (2.94%)	0 / 69 (0.00%)
occurrences (all)	0	2	0
Toothache			
subjects affected / exposed	1 / 70 (1.43%)	2 / 68 (2.94%)	2 / 69 (2.90%)
occurrences (all)	1	2	2
Vomiting			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Tongue discomfort			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Hypertransaminasaemia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Hepatic steatosis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Cholelithiasis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Cholestasis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Hepatic lesion			

subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Pustular psoriasis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Dermatitis contact			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Eczema			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Miliaria			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	1 / 70 (1.43%)	1 / 68 (1.47%)	4 / 69 (5.80%)
occurrences (all)	1	1	4
Psoriasis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Dermal cyst			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	3
Rosacea			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Skin lesion			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0

Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Glycosuria			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Leukocyturia			
subjects affected / exposed	0 / 70 (0.00%)	2 / 68 (2.94%)	0 / 69 (0.00%)
occurrences (all)	0	2	0
Micturition urgency			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Proteinuria			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	2
Renal cyst			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Urinary incontinence			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Urinary retention			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Urinary tract inflammation			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 70 (10.00%)	6 / 68 (8.82%)	5 / 69 (7.25%)
occurrences (all)	7	7	5

Musculoskeletal pain			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Muscle tightness			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Muscle spasms			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Limb discomfort			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Joint swelling			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Intervertebral disc degeneration			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Facet joint syndrome			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	2 / 69 (2.90%)
occurrences (all)	0	0	2
Back pain			
subjects affected / exposed	3 / 70 (4.29%)	1 / 68 (1.47%)	5 / 69 (7.25%)
occurrences (all)	3	3	5
Limb mass			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0

Myalgia			
subjects affected / exposed	1 / 70 (1.43%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	1	1	0
Neck pain			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	2
Osteoarthritis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	1 / 69 (1.45%)
occurrences (all)	0	1	2
Pain in extremity			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	2	0
Pain in jaw			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Plantar fasciitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Polymyalgia rheumatica			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Rapidly progressive osteoarthritis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Rotator cuff syndrome			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Soft tissue disorder			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Spinal osteoarthritis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Spinal pain			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0

Subchondral insufficiency fracture			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Tendon disorder			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Tendon pain			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Tendonitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Trigger finger			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Pharyngitis			
subjects affected / exposed	0 / 70 (0.00%)	2 / 68 (2.94%)	0 / 69 (0.00%)
occurrences (all)	0	2	0
Periodontitis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Oral herpes			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	6 / 70 (8.57%)	4 / 68 (5.88%)	6 / 69 (8.70%)
occurrences (all)	7	4	7
Lower respiratory tract infection			
subjects affected / exposed	2 / 70 (2.86%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	2	0	1
Sinusitis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	1	0	1
Rhinitis			

subjects affected / exposed	2 / 70 (2.86%)	1 / 68 (1.47%)	1 / 69 (1.45%)
occurrences (all)	3	1	1
Respiratory tract infection viral			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Skin infection			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Pulpitis dental			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 70 (2.86%)	3 / 68 (4.41%)	4 / 69 (5.80%)
occurrences (all)	2	3	4
Urinary tract infection			
subjects affected / exposed	2 / 70 (2.86%)	5 / 68 (7.35%)	2 / 69 (2.90%)
occurrences (all)	2	6	4
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Bronchitis			
subjects affected / exposed	2 / 70 (2.86%)	3 / 68 (4.41%)	0 / 69 (0.00%)
occurrences (all)	2	3	0
Cellulitis			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	1 / 69 (1.45%)
occurrences (all)	0	1	1
Acarodermatitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Conjunctivitis			

subjects affected / exposed	1 / 70 (1.43%)	1 / 68 (1.47%)	1 / 69 (1.45%)
occurrences (all)	1	1	1
Cystitis			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	3 / 69 (4.35%)
occurrences (all)	0	0	5
Ear infection			
subjects affected / exposed	0 / 70 (0.00%)	2 / 68 (2.94%)	0 / 69 (0.00%)
occurrences (all)	0	2	0
Ear infection fungal			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Erysipelas			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	2	0	0
Influenza			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Furuncle			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Epstein-barr virus infection			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0

Covid-19			
subjects affected / exposed	16 / 70 (22.86%)	5 / 68 (7.35%)	10 / 69 (14.49%)
occurrences (all)	16	5	10
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Hypokalaemia			
subjects affected / exposed	0 / 70 (0.00%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	0	0	1
Hypertriglyceridaemia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	0 / 69 (0.00%)
occurrences (all)	2	0	0
Hyperkalaemia			
subjects affected / exposed	0 / 70 (0.00%)	2 / 68 (2.94%)	0 / 69 (0.00%)
occurrences (all)	0	2	0
Hypercholesterolaemia			
subjects affected / exposed	1 / 70 (1.43%)	0 / 68 (0.00%)	1 / 69 (1.45%)
occurrences (all)	2	0	1
Vitamin d deficiency			
subjects affected / exposed	0 / 70 (0.00%)	1 / 68 (1.47%)	0 / 69 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	MEDI7352 Dose Level 4	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	51 / 68 (75.00%)	40 / 69 (57.97%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Haemangioma of liver			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Haemangioma of bone			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	

Acrochordon			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Lipoma			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Seborrhoeic keratosis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Tumour ulceration			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Vascular disorders			
Hot flush			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Hypertension			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Hypertensive crisis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Orthostatic hypotension			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Peripheral coldness			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Superficial vein prominence			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
General disorders and administration site conditions			
Feeling hot			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Asthenia			

subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Chest discomfort			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Chills			
subjects affected / exposed	2 / 68 (2.94%)	1 / 69 (1.45%)	
occurrences (all)	2	1	
Fatigue			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Temperature regulation disorder			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Injection site bruising			
subjects affected / exposed	0 / 68 (0.00%)	3 / 69 (4.35%)	
occurrences (all)	0	3	
Injection site erythema			
subjects affected / exposed	9 / 68 (13.24%)	2 / 69 (2.90%)	
occurrences (all)	10	2	
Injection site induration			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Injection site pain			
subjects affected / exposed	1 / 68 (1.47%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
Injection site pruritus			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Injection site reaction			
subjects affected / exposed	4 / 68 (5.88%)	0 / 69 (0.00%)	
occurrences (all)	7	0	
Injection site swelling			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Malaise			

subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Peripheral swelling			
subjects affected / exposed	2 / 68 (2.94%)	2 / 69 (2.90%)	
occurrences (all)	2	2	
Pyrexia			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Influenza like illness			
subjects affected / exposed	0 / 68 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
Thirst			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Drug hypersensitivity			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Seasonal allergy			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Type iv hypersensitivity reaction			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Reproductive system and breast disorders			
Bartholin's cyst			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Benign prostatic hyperplasia			

subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Pelvic pain			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	2 / 68 (2.94%)	0 / 69 (0.00%)	
occurrences (all)	2	0	
Cough			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Dysphonia			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Haemoptysis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Nasal congestion			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Aphonia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Pleuritic pain			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Productive cough			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Pulmonary mass			

subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Rhinorrhoea			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Insomnia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Irritability			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Investigations			
Activated partial thromboplastin time prolonged			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	2	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Blood creatine phosphokinase increased			

subjects affected / exposed	0 / 68 (0.00%)	2 / 69 (2.90%)		
occurrences (all)	0	2		
Blood folate decreased				
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)		
occurrences (all)	0	0		
Blood glucose increased				
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)		
occurrences (all)	1	0		
Blood pressure increased				
subjects affected / exposed	2 / 68 (2.94%)	0 / 69 (0.00%)		
occurrences (all)	3	0		
Blood uric acid increased				
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)		
occurrences (all)	1	0		
C-reactive protein increased				
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)		
occurrences (all)	1	0		
Coagulation factor increased				
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)		
occurrences (all)	0	0		
Liver function test increased				
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)		
occurrences (all)	0	0		
Glycosylated haemoglobin increased				
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)		
occurrences (all)	0	0		
Gamma-glutamyltransferase increased				
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)		
occurrences (all)	0	1		
Faecal calprotectin abnormal				
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)		
occurrences (all)	0	0		
Drug screen positive				
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)		
occurrences (all)	1	0		

Electrocardiogram qt prolonged			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Electrocardiogram t wave inversion			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Chillblains			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Cartilage injury			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Bone contusion			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Arthropod bite			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Animal bite			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Adverse event following immunisation			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Accidental exposure to product			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Back injury			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Post procedural contusion			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal injury			

subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Muscle strain			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Muscle injury			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Limb injury			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Ligament sprain			
subjects affected / exposed	1 / 68 (1.47%)	1 / 69 (1.45%)	
occurrences (all)	1	1	
Joint injury			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Head injury			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Fracture			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Foot fracture			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Fall			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Post-traumatic pain			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Contusion			
subjects affected / exposed	2 / 68 (2.94%)	1 / 69 (1.45%)	
occurrences (all)	2	2	
Tooth fracture			

subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Procedural pain			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Skin injury			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Soft tissue injury			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Congenital, familial and genetic disorders			
Accessory spleen			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Vascular malformation			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Cardiac disorders			
Extrasystoles			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Mitral valve incompetence			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Palpitations			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Tachycardia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Tachycardia paroxysmal			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Atrial fibrillation			

subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Bradycardia			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Nervous system disorders			
Areflexia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Disturbance in attention			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Carpal tunnel syndrome			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Cervical radiculopathy			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Burning sensation			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Dizziness			
subjects affected / exposed	1 / 68 (1.47%)	3 / 69 (4.35%)	
occurrences (all)	1	4	
Dizziness postural			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Headache			
subjects affected / exposed	9 / 68 (13.24%)	3 / 69 (4.35%)	
occurrences (all)	11	3	
Hypoaesthesia			
subjects affected / exposed	2 / 68 (2.94%)	0 / 69 (0.00%)	
occurrences (all)	4	0	
Migraine			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	

Paraesthesia			
subjects affected / exposed	4 / 68 (5.88%)	1 / 69 (1.45%)	
occurrences (all)	5	1	
Tremor			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Presyncope			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Resting tremor			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Sciatica			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Sensory loss			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Polyneuropathy			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Leukopenia			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Lymphadenopathy			
subjects affected / exposed	1 / 68 (1.47%)	1 / 69 (1.45%)	
occurrences (all)	1	1	
Lymphopenia			

subjects affected / exposed	1 / 68 (1.47%)	1 / 69 (1.45%)	
occurrences (all)	1	1	
Neutropenia			
subjects affected / exposed	1 / 68 (1.47%)	1 / 69 (1.45%)	
occurrences (all)	1	1	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Ear congestion			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Tympanic membrane perforation			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Vertigo			
subjects affected / exposed	3 / 68 (4.41%)	0 / 69 (0.00%)	
occurrences (all)	3	0	
Vertigo positional			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Eye disorders			
Amaurosis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Conjunctival haemorrhage			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Glaucoma			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Lacrimation increased			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Photopsia			

subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Vitreous floaters			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Abdominal mass			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Abdominal pain			
subjects affected / exposed	0 / 68 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
Abdominal pain lower			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Hiatus hernia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Colitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	1 / 68 (1.47%)	1 / 69 (1.45%)	
occurrences (all)	1	1	
Dental discomfort			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Diarrhoea			
subjects affected / exposed	2 / 68 (2.94%)	0 / 69 (0.00%)	
occurrences (all)	3	0	
Diverticulum intestinal			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	

Duodenitis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Dyspepsia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Food poisoning			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Gastric ulcer			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Gastritis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Abdominal pain upper			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Mesenteric panniculitis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Nausea			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Noninfective gingivitis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Oesophageal stenosis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Oesophagitis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	

Toothache			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Vomiting			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Tongue discomfort			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatomegaly			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Hypertransaminasaemia			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Hepatic steatosis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Cholelithiasis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Cholestasis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Hepatic lesion			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Pustular psoriasis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Dermatitis contact			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Eczema			

subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Erythema			
subjects affected / exposed	2 / 68 (2.94%)	0 / 69 (0.00%)	
occurrences (all)	2	0	
Miliaria			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Pruritus			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Psoriasis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Dermal cyst			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Rosacea			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Skin lesion			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Glycosuria			
subjects affected / exposed	0 / 68 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
Leukocyturia			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	

Micturition urgency			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Proteinuria			
subjects affected / exposed	0 / 68 (0.00%)	2 / 69 (2.90%)	
occurrences (all)	0	2	
Renal cyst			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Urinary incontinence			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Urinary retention			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Urinary tract inflammation			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Endocrine disorders			
Goitre			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 68 (4.41%)	4 / 69 (5.80%)	
occurrences (all)	6	4	
Musculoskeletal pain			
subjects affected / exposed	2 / 68 (2.94%)	0 / 69 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal chest pain			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Muscular weakness			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Muscle tightness			

subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Muscle spasms			
subjects affected / exposed	3 / 68 (4.41%)	2 / 69 (2.90%)	
occurrences (all)	5	2	
Musculoskeletal stiffness			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Limb discomfort			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Joint swelling			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	2	
Intervertebral disc degeneration			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Facet joint syndrome			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Back pain			
subjects affected / exposed	7 / 68 (10.29%)	3 / 69 (4.35%)	
occurrences (all)	9	3	
Limb mass			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Myalgia			
subjects affected / exposed	3 / 68 (4.41%)	0 / 69 (0.00%)	
occurrences (all)	3	0	
Neck pain			
subjects affected / exposed	2 / 68 (2.94%)	2 / 69 (2.90%)	
occurrences (all)	2	2	
Osteoarthritis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Pain in extremity			

subjects affected / exposed	1 / 68 (1.47%)	3 / 69 (4.35%)	
occurrences (all)	1	3	
Pain in jaw			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Plantar fasciitis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Polymyalgia rheumatica			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Rapidly progressive osteoarthritis			
subjects affected / exposed	1 / 68 (1.47%)	2 / 69 (2.90%)	
occurrences (all)	1	2	
Rotator cuff syndrome			
subjects affected / exposed	2 / 68 (2.94%)	1 / 69 (1.45%)	
occurrences (all)	2	1	
Soft tissue disorder			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Spinal pain			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Subchondral insufficiency fracture			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Tendon disorder			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	2	
Tendon pain			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Tendonitis			

subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Trigger finger			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Infections and infestations			
Pharyngitis			
subjects affected / exposed	2 / 68 (2.94%)	1 / 69 (1.45%)	
occurrences (all)	2	1	
Periodontitis			
subjects affected / exposed	2 / 68 (2.94%)	0 / 69 (0.00%)	
occurrences (all)	2	0	
Oral herpes			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Nasopharyngitis			
subjects affected / exposed	5 / 68 (7.35%)	9 / 69 (13.04%)	
occurrences (all)	5	11	
Lower respiratory tract infection			
subjects affected / exposed	0 / 68 (0.00%)	3 / 69 (4.35%)	
occurrences (all)	0	3	
Sinusitis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Rhinitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Respiratory tract infection viral			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Respiratory tract infection			
subjects affected / exposed	3 / 68 (4.41%)	0 / 69 (0.00%)	
occurrences (all)	3	0	
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	

Skin infection			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Pulpitis dental			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	3 / 68 (4.41%)	2 / 69 (2.90%)	
occurrences (all)	3	2	
Urinary tract infection			
subjects affected / exposed	4 / 68 (5.88%)	1 / 69 (1.45%)	
occurrences (all)	6	1	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Bronchitis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Cellulitis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Acarodermatitis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Conjunctivitis			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	2	
Cystitis			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Ear infection			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Ear infection fungal			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	

Erysipelas			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Fungal skin infection			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Gastroenteritis			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Gastroenteritis viral			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Influenza			
subjects affected / exposed	1 / 68 (1.47%)	1 / 69 (1.45%)	
occurrences (all)	1	1	
Furuncle			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Epstein-barr virus infection			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Covid-19			
subjects affected / exposed	12 / 68 (17.65%)	8 / 69 (11.59%)	
occurrences (all)	12	8	
Metabolism and nutrition disorders			
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Hyponatraemia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Hypokalaemia			

subjects affected / exposed	0 / 68 (0.00%)	1 / 69 (1.45%)	
occurrences (all)	0	1	
Hypertriglyceridaemia			
subjects affected / exposed	2 / 68 (2.94%)	1 / 69 (1.45%)	
occurrences (all)	2	1	
Hyperkalaemia			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	
Hypercholesterolaemia			
subjects affected / exposed	1 / 68 (1.47%)	0 / 69 (0.00%)	
occurrences (all)	1	0	
Vitamin d deficiency			
subjects affected / exposed	0 / 68 (0.00%)	0 / 69 (0.00%)	
occurrences (all)	0	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 March 2021	Added that on study Visit 4 (Day 14) and Visit 5 (Day 28), study participants will remain under observation for at least 2 hours after investigational product (IP) administration. Modified inclusion requirement that participants have history of inadequate pain relief from paracetamol, nonsteroidal anti-inflammatory drug (NSAID)/cyclooxygenase-2 (COX-2) inhibitors, and opioid analgesics to allow for inclusion of participants who refuse to take opioids or for whom opioids are unavailable. Added coronavirus disease 2019 (COVID-19) vaccine exclusion criterion and as prohibited concomitant medication. Changed exclusion criterion limiting blood loss within 2 months prior to screening from 50 mL to 500 mL. Reduced exclusion period prior to screening for corticosteroid or intra-articular hyaluronic acid injection on a target knee joint to 12 weeks, and for intra-articular hyaluronic acid injection on a non-target joint to 6 weeks. Removed 45-day limit on rescreening attempt. Extended validity of screening X-ray and magnetic resonance imaging (MRI) results from 45 to 90 days. Modified liver stopping criteria to include: alanine aminotransferase (ALT) or aspartate aminotransferase (AST) > 5 × upper limit of normal (ULN) for more than 2 weeks and ALT or AST >= 3 × ULN and coexisting normalized ratio (internal normalized ratio [INR]) > 1.5 Updated guidance for evaluation of abnormal liver function tests. Removed systemic infections from AESIs and replaced with infections that meet the serious adverse event (SAE) or severe adverse event (AE) criteria.
14 October 2021	Increased duration of follow up period from 20 to 24 weeks, updated number and timing of follow up visits to reflect this. Added exploratory objective for urine C-telopeptide of crosslinked collagen type II (CTX-II). Inclusion and exclusion criteria were updated to expand the eligible participant population. Increased permitted low dose aspirin from 100 mg/day to 325 mg/day. Added limited (no more than 10 days per 8-week period) concomitant use of prescription or over the counter (OTC) NSAIDs for conditions not related to osteoarthritis (OA) to the list of permitted concomitant therapies. Removed stopping criterion "Renal toxicity, defined as serum creatinine ≥ 1.5 × ULN". Added recommendation that participants had at least 3 weeks between last IP dose and joint replacement surgery. Added a minimum follow up period of 4 months for participants who underwent joint replacement surgery. Added serious or severe hypersensitivity reactions as adverse events of special interest (AESIs).
28 June 2022	Increased approximate number of participants to be recruited from 300 to 350, and for recruitment to continue until either statistical information equivalent to 255 participants completing the treatment period or 350 participants randomized was reached (previously when 255 participants completed treatment period). Changed the following COVID-19 requirements: i) Removed requirement for participants to have no signs of an acute viral respiratory illness at baseline and prior to all subsequent dosing visits. ii) Changed exclusion criteria to allow participants who have asymptomatic COVID-19 or have fully recovered from mild or moderate COVID-19 one month prior to randomization to be eligible for the study. iii) Changed requirement for participants diagnosed with COVID-19 to permanently discontinue IP to only require interruption of IP if other discontinuation criteria were not met.

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.

Concomitant medication and therapies data do not necessarily evaluate the safety and are therefore not considered as outcome measures in this study.

Notes: